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ANA LÚCIA RIBEIRO SALOMON

EVOLUÇÃO CLÍNICO-NUTRICIONAL DE PACIENTES PORTADORES DE DISFUNÇÕES NEUROLÓGICAS E CÂNCERES DE CABEÇA E PESCOÇO E GASTROINTESTINAIS EM TERAPIA DE NUTRIÇÃO ENTERAL DOMICILIAR NO DISTRITO FEDERAL

BRASÍLIA – DF, 2014

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Tese apresentada ao Curso de Pós-Graduação em Ciências da Saúde, Faculdade de Ciências da Saúde, Universidade de Brasília como requisito parcial à obtenção do título de Doutor em Ciências da Saúde.

Orientadora: Prof[a.] Dr[a.] Maria Rita C. Garbi Novaes

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I. Título.

FOLHA DE APROVAÇÃO

Ana Lúcia Ribeiro Salomon

Evolução clínico-nutricional de pacientes portadores de disfunções neurológicas e cânceres de cabeça e pescoço e gastrointestinais em terapia de nutrição enteral domiciliar no Distrito Federal.

Tese apresentada ao Curso de Pós-Graduação em Ciências da Saúde da Faculdade de Ciências da Saúde da Universidade de Brasília para obtenção do título de Doutor.
Linha de pesquisa: Fisiopatologia Médica

Aprovada em: ____ de _____ de _____.

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A todos os pacientes em terapia de nutrição enteral domiciliar
e aos profissionais que se responsabilizam por seu cuidado
Dedico

MINHA GRATIDÃO

A Deus, pelo dom da vida, pela força, coragem e sustento durante esses anos;

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"Jamais alguém concordará em rastejar,
se sentir um impulso para voar alto."
(Helen Keller)

SUMÁRIO

RESUMO

Salomon ALR. **Evolução clínico-nutricional de pacientes portadores de disfunções neurológicas e cânceres de cabeça e pescoço e gastrointestinais em terapia de nutrição enteral domiciliar no Distrito Federal.** 2014. 160 folhas. Tese [Doutorado] – Programa de Pós-Graduação em Ciências da Saúde, Universidade de Brasília. Orientadora: Profa Dra Maria Rita Carvalho Garbi Novaes.

Estudos internacionais têm mostrado que as principais doenças que requerem uma via alternativa de alimentação são as doenças neurológicas e o câncer. Como segunda via mais fisiológica de alimentação apresenta-se a nutrição enteral que, contudo, não é isenta de riscos. Há muitas controvérsias quanto ao uso desta via de alimentação aos pacientes com disfunções neurológicas, incluindo estágios avançados de demências. O presente estudo teve por objetivos avaliar os desfechos sobrevida, evolução nutricional e clínica e ocorrência de complicações, relacionados ao uso da terapia nutricional, seja via oral (por meio do uso de suplementação), via nasal (nasogástrica ou nasoentérica) e via estomias (gastrostomia ou jejunostomia), para pacientes portadores de disfunções neurológicas e cânceres gastrointestinal ou de cabeça e pescoço, bem como avaliar a associação do nível socioeconômico dos pacientes aos desfechos mencionados. Foram conduzidas inicialmente revisões sistemáticas sobre o tema em literatura científica publicada no período de 2009 a 2013. Em paralelo, foi conduzido um estudo descritivo e documental, demonstrando a aplicação de instrumentos de planificação funcional para a garantia da adequação de estruturas físicas para a manipulação de fórmulas enterais, no sentido de controle de qualidade dos insumos fornecidos aos pacientes. Posteriormente foi realizado um estudo prospectivo, observacional, com grupos de comparação para se avaliarem os desfechos em nutrição enteral domiciliar de sobrevida e evolução clínico-nutricional dos pacientes. Os grupos de comparação foram divididos por status socioeconômico e por estratos de via de alimentação. O estudo foi conduzido de Janeiro de 2010 a Junho de 2013 na Secretaria de Estado de Saúde do Distrito Federal, sendo devidamente aprovado pelo comitê de ética desta. O total de pacientes acompanhados no presente estudo correspondeu a 247, sendo 165 portadores de disfunções neurológicas e 82 de cânceres gastrointestinais ou de cabeça e pescoço. Para o grupo de pacientes portadores de disfunções neurológicas o status socioeconômico foi positivamente associado com a sobrevida, enquanto para os portadores de neoplasias, um status inferior foi associado à maior perda ponderal. Considerando as vias de acesso para alimentação, nos pacientes com disfunção neurológica, as vias enterais foram positivamente associadas ao ganho de peso, manutenção do estado clínico e dos parâmetros laboratoriais, melhora das úlceras de pressão e sobrevida. Para os portadores de cânceres, não houve diferença entre as vias de alimentação quanto aos desfechos clínicos, sendo que em relação à sobrevida os melhores resultados foram encontrados para as vias oral e nasal. Um adequado acompanhamento por uma equipe multidisciplinar especializada é fundamental para a garantia do sucesso da terapia nutricional e está relacionado à redução dos riscos inerentes a esta terapia, melhorando a sobrevida dos pacientes e seus desfechos clínicos. O tempo de implantação da terapia nutricional é decisivo quando se tratam de pacientes com risco nutricional. Nestes casos é de suma importância que a terapia nutricional seja antecipada, no sentido de se garantir melhor tolerância aos tratamentos convencionais. O estado nutricional é um fator decisivo para o sucesso terapêutico e para melhora de sobrevida, cicatrização de úlceras de pressão e redução das taxas de complicação.

Palavras-chave: serviços de assistência domiciliar, nutrição enteral, demência, doença de Alzheimer, câncer, desfechos.

ABSTRACT

Salomon ALR. **Clinical and nutritional evolution of patients with neurological impairments and head and neck and gastrointestinal cancers in home enteral nutrition therapy in the Federal District, Brazil.** 2014. 160 pages. PhD [Thesis] - Health Sciences Post-Graduation Program, Universidade de Brasilia. Advisor: Prof. Dr. Maria Rita Carvalho Garbi Novaes.

International studies have shown that main diseases that require an alternative route of feeding are neurological impairments and cancer. Enteral nutrition presents as the second more physiological route of feeding, though it is not absent of risks. There are a lot controversies concerning the use of enteral nutrition for patients with neurological impairments, including advanced stages of dementia. The present study aimed to assess outcomes such as survival, clinical and nutritional evolution and the occurrence of complications, related to the use of nutritional therapy, whether by oral route (oral supplements), nasal route (nasogastric or nasoenteric) or ostomies (gastrostomy or jejunostomy), for patients with neurological impairments and gastrointestinal or head and neck cancers, as well as to evaluate the association of patients' socioeconomic status to the mentioned outcomes. At the beginning of this research, systematic reviews were conducted on the theme, in the scientific literature published between 2009 and 2013. In parallel, a descriptive and documental study was done in order to demonstrate the application of functional planning tools to grant the adequacy of physical structures destined to the manipulation of enteral formulas, so that there was a quality control on products delivered to patients. After this, a prospective and observational study with comparison groups was made to assess the outcomes of survival and clinical-nutritional evolution of patients treated with home enteral nutrition. Comparison groups were constituted of socioeconomic strata and feeding routes strata. The study was conducted from January 2010 to June 2013 at the Public Health Department of the Federal District of Brazil, and was approved by ethics committee. The total amount of followed-up patients was of 247, of which 165 presented neurological impairments and 82 gastrointestinal or head and neck cancers. For the group of patients with neurological impairments, socioeconomic level was positively associated to survival, while for cancer patients an inferior level was associated to higher weight loss. Considering feeding routs, for neurologic impaired patients enteral routes were positively associated to weight gain, clinical status and laboratory parameters maintenance, pressure sores improvement and survival. For cancer patients there was no difference among feeding routes in relation to clinical outcomes and as for survival, better results were related to oral and nasal routes. An adequate follow-up by a specialized multidisciplinary team is fundamental to warrant the success of nutritional therapy and is related to lowering of risks inherent to this therapy, improving patients' survival and clinical outcomes. Timing of nutritional therapy is decisive when it comes to patients with nutritional risk. In these cases it is very important that an early therapy is initiated, in order to grant better tolerance to conventional treatments. Nutritional status is a decisive factor for therapeutic success and improved survival, pressure sores healing and reduction of complications rates.

Keywords: home care services, enteral nutrition, dementia, Alzheimer's disease, cancer, outcomes.

1 INTRODUÇÃO

1 INTRODUÇÃO

A Terapia de Nutrição Enteral (TNE) é um conjunto de procedimentos terapêuticos cujo objetivo é manter ou recuperar o estado nutricional do paciente de forma artificial, por meio de sondas ou estomias, através do fornecimento de nutrientes em quantidade e qualidade adequadas a fim de suprir suas necessidades, levando em consideração o tratamento específico de sua doença. É indicada quando a ingestão oral é insuficiente para manter o estado nutricional. É o tratamento de escolha de pessoas que possuem o trato gastrointestinal funcionante de forma parcial ou total (ASPEN, 2002; WAITZBERG, 2004; SALOMON ZABAN & NOVAES, 2009a).

A Terapia de Nutrição Enteral Domiciliar (TNED) é aplicada a pacientes que não têm indicação de permanecerem hospitalizados exclusivamente para manutenção da TNE, face aos riscos de complicação impostos pelo ambiente hospitalar (HEBUTERNE, 2003; SALOMON ZABAN & NOVAES, 2010). A TNED visa à melhoria da qualidade de vida dos pacientes, à humanização de seu tratamento e à redução dos custos aos serviços de saúde (PACCAGNELLA et al, 2007; VILLAR et al, 2008; ELIA & STRATTON, 2008).

Estudos internacionais demonstraram que as principais doenças que levam à indicação da TNED são as doenças neurológicas e o câncer (PLANAS et al, 2006; PIRONI et al, 2007; PACCAGNELLA et al, 2008), dados estes consonantes com o perfil de usuários desta terapia no Distrito Federal (SALOMON ZABAN & NOVAES, 2009a) e aos dados nacionais. Embora não existam dados precisos sobre a prevalência e incidência de doenças neurológicas no Brasil, é sabido que a maior causa de óbitos no país corresponde a Doenças do Aparelho Circulatório (DAC), dentre as quais figuram como mais prevalentes as Doenças Cérebro Vasculares (DCV). Figuram como segunda maior causa de morte as neoplasias malignas (tumores) (ISHITANI et al., 2006; MINISTÉRIO DA SAÚDE, 2009). Dados mundiais revelam que mais de 25 milhões de pessoas ao redor do mundo sofrem de doenças demenciais, sendo a Doença de Alzheimer a mais prevalente (40-60%). A prevalência desta doença aumenta exponencialmente com o avançar da idade de 1% na faixa de 60-65 anos para 30-35% em maiores de 80 anos (CACABELOS, 2008).

A desnutrição é frequentemente observada em pacientes portadores de doenças neurológicas, como decorrência da disfagia e hiporexia associadas a estas condições. Um estudo nacional com pacientes idosos, dentre os quais havia uma frequência média

de 56% de doenças neurológicas, verificou a ocorrência de desnutrição em 70% dos pacientes (SALOMON ZABAN & NOVAES, 2009b), com seus riscos associados.

Em pacientes com demências, há evidências de que as dificuldades concernentes à alimentação e deglutição que levam à perda de peso nesta população, são inerentes à fase avançada da doença e correspondem à disfunção de maior risco à sobrevida, acomentendo cerca de 50% dos pacientes em 8 anos após o diagnóstico (PRIEFER, 1997; PALACEK, 2010).

O Instituto Nacional de Câncer – INCA estimou em 270 mil a incidência de novos casos de neoplasias malignas no Brasil para os anos de 2010 e 2011. Os tumores mais prevalentes corresponderam ao de próstata, mama feminina, traquéia, brônquios e pulmão, cólon e reto e estômago (MINISTÉRIO DA SAÚDE, 2009).

A desnutrição é prevalente em mais da metade dos pacientes oncológicos (AZEVEDO et al. 2006), sendo a perda ponderal freqüentemente o primeiro sintoma que atinge esses pacientes em 30 a mais de 80% dos casos. Essa perda é grave em cerca de 15 a 30% dos pacientes, a depender do tipo de tumor (ARENDS et al, 2006). Além de a baixa ingestão de nutrientes corroborar para o déficit nutricional desses pacientes, fatores como a idade, o tempo de internação, o tipo histológico e localização do tumor, e os tratamentos instituídos relacionam-se à perda de peso e ingestão alimentar insuficiente (MARTINS et al., 2009).

A desnutrição é a responsável direta por maiores índices de morbimortalidade (comprometimento da cicatrização de feridas; aumento da taxa de infecção hospitalar; aumento do tempo de permanência hospitalar e índices de reinternações), favorecendo ainda a instalação de quadros resultantes da depleção protéico-muscular, como úlceras de decúbito e comprometimento da capacidade funcional dos pacientes (ARNAUD-BATTANDIER et al, 2004; BAXTER et al, 2005; FUJINO, 2007).

O objetivo geral do trabalho foi avaliar a evolução clínica e nutricional dos pacientes portadores de doenças neurológicas e cânceres de cabeça e pescoço e do trato gastrointestinal, de acordo com seu estrato socioeconômico e de acordo com a via de terapia nutricional implementada, correlacionando tal evolução com os parâmetros bioquímicos e hematológicos apresentados pelos usuários da Terapia de Nutrição Enteral Domiciliar no Distrito Federal.

Os objetivos específicos deste trabalho foram:

- Propor a planificação funcional de um laboratório de nutrição enteral de um hospital público de referência em terapia de nutrição enteral no Distrito Federal.

- Descrever o perfil demográfico, clínico e nutricional de usuários do Programa de Nutrição Enteral Domiciliar da Secretaria de Estado de Saúde do Distrito Federal (PNED/SES/DF).

- Avaliar a evolução clínica dos usuários do PNED/SES/DF, por meio dos parâmetros de sobrevida, evolução de parâmetros clínico-nutricionais como úlceras de decúbito, ocorrência de complicações (redução do uso de fórmulas e comorbidades) e necessidade de reinternação hospitalar.

- Avaliar a evolução do estado nutricional dos pacientes, por meio da evolução ponderal, correlacionando esses dados com sua evolução clínica.

- Avaliar parâmetros laboratoriais hematológicos e bioquímicos de pacientes em nutrição enteral domiciliar, correlacionando-os à evolução clínico-nutricional dos pacientes.

- Analisar a interferência dos fatores socioeconômicos sobre a recuperação nutricional dos pacientes.

- Analisar a interferência da via de acesso disponibilizada para a terapia nutricional sobre a evolução clínico-nutricional dos pacientes.

A coleta de dados deste trabalho foi conduzida no período de Janeiro de 2010 a Junho de 2013, sendo incluídos pacientes admitidos no Programa até Março de 2012 e acompanhados até Junho de 2013, sendo que os resultados dos estudos foram apresentados na forma de artigos científicos.

Em um primeiro momento foram elaborados dois artigos de revisão. O artigo ***Outcomes of enteral nutrition for patients with advanced dementia - a systematic review*** foi redigido em conformidade aos requisites estabelecidos pela proposta *meta-analysis of Observational Studies in Epidemiology (MOOSE)* (STROUP, 2000). Este artigo foi aceito para publicação no periódico ***The Journal of Nutrition, Health and Aging***, periódico científico classificado pelo Programa da CAPES - Qualis Medicina II como A2, com um Fator de Impacto de 2.394 no ano de 2013 e Fator de Impacto de 5 anos de 2.826, segundo o *Journal Citation Reports® (JCR).*

O artigo **O*utcomes of enteral nutrition for patients with head and neck and gastrointestinal cancers - a systematic review*** também foi redigido de acordo com os requisites estabelecidos pela proposta MOOSE (STROUP, 2000) e foi submetido para publicação no periódico ***Nutrition and Cancer***, periódico científico classificado pelo

Programa da CAPES - Qualis Medicina II como A2, com um Fator de Impacto de 2.695 no ano de 2013 e Fator de Impacto de 5 anos de 2.888, segundo o JCR.

Em conformidade com a Agência Nacional de Vigilância Sanitária (ANVISA), o Brasil é um dos países que compõem a Aliança Mundial para a Segurança do Paciente, estabelecida pela Organização Mundial da Saúde (OMS) em 2004. O principal propósito desta, é a instituição de medidas que aumentem a segurança do paciente e a qualidade dos serviços de saúde (ANVISA, 2014). Nesse sentido, antes da admissão dos pacientes no PNED/SES/DF é fundamental a adaptação intra-hospitalar à via de alimentação disponibilizada nesta unidade, bem como à fórmula industrializada que será continuada em domicílio pelo programa.

Com o intuito de garantia da segurança microbiológica da terapia de nutrição enteral, a ANVISA estabelece na Resolução RDC nº 63 (ANVISA, 2000) o Regulamento Técnico para fixar os requisitos mínimos exigidos para esta terapia. Desta forma, são garantidas as condições corretas de manipulação das fórmulas enterais nas unidades hospitalares, as quais servem de base para o treinamento dos cuidadores quanto às precauções necessárias para a diluição, envase e administração das dietas industrializadas em domicílio com segurança aos pacientes.

Neste sentido, no quarto capítulo se apresenta a planificação funcional de uma unidade hospitalar do Distrito Federal, em adequação ao regulamento da ANVISA, por meio de um estudo descritivo baseado nas ferramentas propostas por Udobro para os serviços de saúde (UDOBRO, 2005). O artigo ***Planificación funcional de una unidad de nutrición enteral de un hospital de Brasil, para la atención en el domicilio del paciente*** foi publicado no periódico ***Nutrición Hospitalaria 2013, vol. 28, n. 6, páginas 2027 a 2032***, periódico científico classificado pelo Programa da CAPES - Qualis Medicina II como B2, com um Fator de Impacto de 1.305 no ano de 2013 e Fator de Impacto de 5 anos de 1.307, segundo o JCR.

Inicialmente a pergunta principal desta pesquisa era esclarecer a influência do status socioeconômico sobre a evolução clínico-nutricional dos pacientes, com a hipótese de que pacientes e/ou cuidadores com melhor grau de instrução apresentarim uma maior probabilidade de compreenderem com mais clareza as instruções nutricionais, com melhor adesão ao tratamento, o que favoreceria a recuperação nutricional. Os resultados desta pergunta culminaram no artigo ***Does socioeconomic status influence survival for patients with neurological impairment and cancer in home enteral nutrition? A Brazilian study***. Este artigo foi submetido ao periódico

Health Economics, periódico científico classificado pelo Programa da CAPES - Qualis Medicina II como B1, com um Fator de Impacto de 2.232 no ano de 2013 e Fator de Impacto de 5 anos de 2.786, segundo o JCR.

Dada à escassez de estudos que abordem a interferência do status socioeconômico sobre os desfechos em terapia de nutrição enteral domiciliar, com o intuito de proporcionar a comparação dos resultados desta pesquisa a outros achados científicos, optou-se pela análise da evolução clínico-nutricional por via de acesso disponibilizada para a terapia nutricional, a saber vias oral (suplementação oral), nasal (nasogástrica ou nasoentérica) e ostomia (gastrostomia ou jejunostomia). Desta análise foram produzidos dois artigos científicos, mencionados a seguir:

- ***Does route of feeding influence clinical and nutritional outcomes for patients with neurological impairment? A Brazilian study***, submetido ao periódico ***Current Alzheimer Research***, periódico científico classificado pelo Programa da CAPES - Qualis Medicina I como A1, com um Fator de Impacto de 3.676 no ano de 2013 e Fator de Impacto de 5 anos de 4.203, segundo o JCR.

- ***How home enteral nutrition influences survival, nutritional and clinical outcomes for patients with gastrointestinal, head and neck cancers? A Brazilian study***, submetido ao periódico ***World Journal of Gastroenterology***, periódico científico classificado pelo Programa da CAPES - Qualis Medicina II como A2, com um Fator de Impacto de 2.547 no ano de 2013 e Fator de Impacto de 5 anos de 2.594, segundo o JCR.

2 ARTIGO DE REVISÃO

Outcomes of enteral nutrition for patients with advanced dementia - a systematic review - Salomon ALR, Novaes MRCG – J Nutr Health Aging

2 ARTIGO DE REVISÃO

OUTCOMES OF ENTERAL NUTRITION FOR PATIENTS WITH ADVANCED DEMENTIA - A SYSTEMATIC REVIEW

Abstract

The present article aims to evaluate the outcomes of enteral nutrition for people with advanced dementia. A systematic review was conducted by searching The Cochrane Library, MEDLINE, EMBASE, PROQUEST and LILACS for articles that were published from 2008 to 2013. Prospective and retrospective studies involving a control group were searched. Data were independently extracted and assessed by one reviewer and checked by a second. Searched outcomes included survival, clinical and nutritional parameters and complications. In total, nine controlled studies were identified from several parts of the world: Israel, Italy, Japan, the United States and Brazil. Most of the studies did not report any outcome of harm with enteral nutrition use in dementia patients compared with patients without dementia. A study with a higher follow-up period demonstrated improvements in albumin, weight and chronic inflammation parameters. It is not possible to affirm that tube feeding is harmful for dementia patients. Thus, an adequate follow-up by a multidisciplinary team may lower complications associated with this therapy and thus improve survival.

Keywords: home care services, enteral nutrition, dementia, Alzheimer's disease, outcomes.

Introduction

According to World Health Organization (WHO), dementia is classified by the International Code of Diseases version 10 (ICD-10) with the codes from F00 to F03. Dementia can be defined as a syndrome because it is a brain disease that is usually of a chronic or progressive nature in which there is disturbance of multiple higher cortical functions including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. Consciousness is not clouded. The impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation. This syndrome occurs in Alzheimer's disease, cerebrovascular disease, and other conditions that primarily or secondarily affect the brain (1).

The prevalence of dementia among Brazilian elders (people over 60 years old) who live in the community reached 7.1%, and Alzheimer's disease (AD) is responsible for 55% of these cases (1). Dementia represents an important cause of death in the United States of America, and cerebrovascular diseases are the leading cause of death in Brazil (2).

Cerebrovascular accident-associated dysphagia reached frequencies of 91% when evaluated by fluoroscopy and imposes the need for an alternative feeding and hydration route for patients when the degree of dysphagia is advanced (severe), which often leads to an enteral nutrition indication. However, very little evidence is available to demonstrate the clinical benefits from enteral tube feeding for advanced dementia patients (3, 4).

A small scale study was conducted to assess self-feeding dependency and self-feeding behaviour in individuals with early stage of AD. Though the majority of studies well document eating impairment in the late stage of AD (50% of patients lose the ability to feed themselves 8 years after diagnosis), this one documented a significant difference in self-feeding dependence in mild AD, as subjects demonstrated significantly prolonged swallow durations for the oral transit duration for solid consistency and pharyngeal response duration for liquids, as well as total swallowing duration for liquids, which may increase the risk for aspiration pneumonia (5). Dysphagia is an important cause of weight loss in nursing home residents with neurodegenerative diseases with a prevalence ranging between 40-60% (6).

That is a widely held belief that enteral feeding is harmful for patients with advanced dementia (4, 7-10). Criticisms of artificial nutrition are based on a failure to

show a favourable outcome or to lengthen survival (11). However, there are also several studies that stand against this belief affirming that there is not evidence that favours the decision of withholding artificial nutrition from these patients (11, 12).

The objective of this study was to evaluate the outcomes of enteral nutrition for people with advanced dementia.

Methods

The present study consists of a systematic scientific literature review. The Cochrane Library, MEDLINE, EMBASE, PROQUEST and LILACS were searched in the year of 2012 and 2014 for articles that had been published from 2008 to 2013. Citations were assessed. Titles and abstracts were analysed for Medical SubHeadings (MeSH) terms. Whenever it was not possible to accept or reject, the full citation text was obtained for further evaluation. The following search terms were used: ("home care services"[MeSH Terms] OR ("home"[All Fields] AND "care"[All Fields] AND "services"[All Fields]) OR "home care services"[All Fields]) AND "enteral nutrition" [MeSH Terms] OR ("enteral"[All Fields] AND "nutrition"[All Fields]) OR "enteral nutrition"[All Fields] AND ("dementia"[MeSH Terms] OR "dementia"[All Fields] OR "Alzheimer disease"[MeSH Terms] OR "Alzheimer"[All Fields] AND "disease"[All Fields]) OR "Alzheimer disease"[All Fields] AND "humans" [MeSH Terms] AND "aged"[MeSH Terms] AND "outcomes"[All Fields].

In order to complement the search of articles, the references of the obtained articles were also evaluated for relevant articles. This resulted of three more relevant studies (12-14), which were used for the purpose of the present article, despite of the fact that two of them had a retrospective nature.

Randomised Controlled Trials (RCT), controlled clinical trials, controlled before and after studies that evaluated enteral feeding via nasogastric tube (NGT) or percutaneous endoscopic gastrostomy (PEG) effectiveness were included, and prospective observational studies were also included. However, no controlled clinical trials or RCTs were identified. The authors claim that this was main reason for ethical concerns because it is not ethical to allow a group of patients to starve for the purposes of having a control group (4, 9, 14). Hence, controlled observational studies were used for the purposes of this paper.

The study population included elders (aged 60 and over) of both genders that had a primary diagnosis of degenerative dementia that was made according to validated

diagnostic criteria such as DSM-IV(15) or ICD-10(1). Where data were limited, studies that involved one group of dementia patients were also considered. Specific studies involving Home Enteral Nutrition (HEN) outcomes in demented patients are rare, but the retrieved article reference list was also searched focusing on more recent publications. The study selection criteria involved screening the citations by one of the review authors (ALRS). Following screening, the full texts of eligible citations were assessed for inclusion by the two review authors. Whenever the abstract met the inclusion criteria and the full text was not retrieved, the whole article was ordered to the Federal University Library. If this strategy was not successful, the main author was contacted via e-mail. If any differences of opinion existed, they were resolved by consensus between the authors. For the observational studies, methodological quality was evaluated using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies (16).

A data extraction form was used, which included the following information for each study: number of patients, number in each comparison group (whenever controlled), enteral route (whether tube feeding was used exclusively or if the oral route was also considered), follow-up time, survival outcome, pressure sore presence/development, incidence of aspiration pneumonia, length of hospital stay, hospital readmission frequency, oral rehabilitation, and nutritional indicators (weight, Body Mass Index (BMI), albumin concentration, haemoglobin levels, pre-albumin concentration, transferrin concentration, and lymphocyte count).

If study data were of sufficient quality and were sufficiently similar (in terms of patient population, diagnostic criteria, intervention, outcome measurement, length of follow-up and analysis type), they were combined in a meta-analysis to provide a pooled effect estimate.

The searched articles were published in Portuguese and English.

Methodological Issues

Despite the methodological frailty of observational studies, it is worth noting again that RCT are not suitable for this type of research for ethical reasons. The limitations of this study design can be compensated by its methodological quality as assessed by the Newcastle-Ottawa Scale. This scale focus on 3 pillars to assess: 1) patient selection (including representativeness of the exposed cohort, non-exposed cohort selection, exposure ascertainment and demonstration that the outcome of interest

was not present at start of study), 2) cohorts comparability on the basis of design or analysis, and 3) outcome (including outcome assessment, whether follow-up was long enough for outcome and cohort follow-up adequacy) (16). A total of 9 stars could be attributed to the studies; if they counted for more than 6 stars, they were considered to be good quality (17). Table 1 presents the methodological quality assessment of the considered articles; one may conclude that 78% (7 in 9) of the publications presented a satisfactory evaluation.

Conclusions that were withdrawn from study analysis are demonstrated in Table 2.

Results

In total, 29 articles were found related to the searched terms. However, not all were suitable for inclusion in this systematic review.

In total, 12 studies were found in MEDLINE when the terms "home care services", "enteral nutrition" and "outcomes" were searched, focusing the past 5 years of publications. Reasons for article exclusions are presented in Table 3.

When the MeSH term "dementia" was added, 5 studies relating this disease to enteral nutrition were found. Reasons for article exclusion are summarised in Table 4.

A new search in 2014, with the MeSH terms "enteral nutrition" and "dementia" lead to eight articles, from which two were duplicates (2, 9). Reasons for article exclusion are summarised in Table 4.

After applying the exclusion criteria, a total of 9 articles were considered for this study purpose, including one poster (18). Of these, 8 papers were published in the past five years, while 1 was published in 2006 (the citation was obtained from the Cochrane review reference list (4)).

As observed in Table 2, the outcome evaluation and intervention strategy differences among studies did not allow them to be combined in a meta-analysis to provide a pooled effect estimate.

According to a previous systematic review on the theme that was published by the Cochrane Library that involved studies published until April 2008, there was insufficient evidence for enteral feeding effectiveness in older people with advanced dementia on survival, quality of life, nutrition, pressure ulcers, function, and behavioural or psychiatric dementia symptoms. The main studies used for the purposes of this review were conducted in the US (4).

The present study focused on publications from 2008 to 2013; new questions arose concerning the benefit of enteral feeding for people with advanced dementia. There were very wide settings for these publications including two studies that were conducted in Israel (14, 19), three in Japan (13, 20, 21), one in Italy (18), two in the US (9, 12) and one in Brazil (2).

Participants and settings

Though it was established that dementia diagnosis should be made based on DSM-IV or ICD-10 criteria, not all of the studies were clear about what criteria was applied. Despite this, they were included because of research scarcity on the theme.

The study of Jaul et al (14) included 88 patients who had been diagnosed using the Cognitive Performance Scale with advanced cognitive impairment, and their mean age was 79 ± 9 years. The study was conducted in Jerusalem, Israel, and the study groups included the oral route versus enteral nutrition. The outcomes that were assessed by the authors were nutritional status according to weight, body mass index, albumin and haemoglobin levels, and the number of pressure ulcers.

Arinzon and co-workers' study (19) included 167 patients who had been diagnosed with advanced vascular and degenerative types of dementia, and diagnostic criteria was not mentioned. Mean participant age was of 80.17 years. The research was conducted in Netanya, Israel and the groups included the oral route versus enteral nutrition. The variables that the authors assessed included demographic data, indications for enteral nutrition, data on tube insertion, type of tube, weight subsequent to enteral nutrition, cognitive / functional status, pressure sores status, complete routine clinical and laboratory data and anthropometric measurements.

The study by Higaki and co-workers (13) included 311 patients from whom 143 presented the diagnosis of dementia, defined according to the Diagnostic and Statistical Manual of Mental Disorders, version III-R., and their mean age was 83.69 yrs ± 7.52. The research was conducted retrospectively in Japan and the study groups included patients with and without dementia that received a PEG. The authors assessed survival among groups as well as risk factors for mortality including previous subtotal gastrectomy, serum albumin and haemoglobin, age, comorbidities, gender, as well as short term complications of PEG (gastric bleeding and focal abcess) and long term ones (reflux, tube-related problems, focal abcess, gastric bleeding, diarrhoea, aspiration,

Methicillin-Resistant *Sthaphylococcus Aureus* (MRSA) enteritis, peritonitis and vomiting).

The Japanese study conducted by Kumagai et al (20) involved 261 patients with a mean age of 79.1 years for the PEG group and of 71.4 years for the NGT group, and the study was conducted from June 2002 to December 2010 in Tokyo, Japan. Dementia diagnosis was made according to ICD-10 criteria, and the comparison involved the enteral nutrition administration route (PEG versus NGT). Outcomes were evaluated at the beginning of the study and after 6 months of Enteral Nutrition (EN). As outcomes the authors evaluated survival rate, albumin level and incidence of aspiration.

The third Japanese study (21) evaluated retrospectively 80 patients in home artificial nutrition (parenteral and enteral nutrition) compared to oral intake. Mean age of participants varied from 76.9 ± 8.7 to 78.7 ± 7.7, among groups, without statistical difference. The factors considered for analysis were age, survival period after commencement of home care, swallowing function, serum albumin concentrations, levels of activity of daily living and behavioural, cognitive and communication functions. Authors don't leave clear how the diagnosis of dementia was made.

The study conducted by Venturini et al(18) was described in a poster. For this reason, data on how the diagnoses were made, follow-up time and mean participant age were not clear. The comparison groups included 82 dementia versus 89 non-dementia patients, and the study took place in Ancona, Italy. The authors assessed nutritional status, complications and hospitalisation related to HEN.

The work of Teno et al(9) was a propensity-matched cohort that comprehended 4421 patients and was conducted in the United States (US) of America and involved US nursing homes. The criteria applied for defining dementia was the Cognitive Performance Scale (score of 6), focusing on patients with advanced cognitive impairment. Mean participant age varied from 82.5 to 82.7 (± 7.5 to 7.6) for the control group (without feeding tube) and from 82.9 to 83 (± 7.1 to 7.5) for the intervention group (with feeding tube). The authors examined two outcomes: first, whether residents without a pressure ulcer developed a stage 2 or higher pressure ulcer, and second whether nursing homes residents with a pressure ulcer experienced improvement of the pressure ulcer by their first post-hospitalization.

The second American study (12) evaluated 190 patients who had undergone PEG over a 2-years period. It had a retrospective design and didn't make clear the time of patients follow-up. Its goal was to assess earlier mortality after PEG. 45 patients with

dementia were compared to 145 patients without dementia, though the authors don't mention on which basis the diagnosis of this disease was made. Median age of participants was 64 yrs. Data that reviewed included age, major co-morbid illnesses, serum albumin at the time of PEG, presence or absence of dementia or significant cognitive impairment due to neurologic injury, complications related to PEG or enteral feeding, date of PEG placement and date of death.

Martins et al' study (2) was conducted in Belo Horizonte, Brazil, with 79 patients that compared dementia patients (n=39) with patients who had other neurological diagnoses (n=40). Though the authors did not clarify what criteria were used for dementia diagnosis, they affirmed that the dementia group included Alzheimer's disease, dementia with Lewy bodies, vascular and senile dementias, Creutzfeldt-Jakob and Parkinson's with cognitive impairment. The mean participant age was 82.9 ± 10.4 years. The variables that were evaluated by authors included nutritional assessment through anthropometric measures, albumin, clinical signs of malnutrition, degree of self-dependence (Katz index), presence, development and evolution of pressure sores, complications related to nutritional therapy (pneumonia, tube loss, diarrhoea, constipation, vomits, ostomy leakage, tube obstruction, gastroesophageal reflux, myiasis), enteral nutrition route of access, type of formulas, hospital readmissions and death (survival analysis).

Regnard and co-workers' study questions the recognition of refeeding syndrome, gastric stasis and late use of enteral nutrition in the gastrostomy-dementia literature(11). In deed in the present study no mention of these problems was made.

Survival

Several studies (2, 12-14, 19-21) dealt with mortality and survival issues. The first Israeli study (14) identified that the mortality hazard ratio for the oral route group was almost 3 times higher than the EN group. After controlling for co-morbidities, this ratio was not significant. The second Israeli study (19) did not find any impact of EN to prolong life compared with the oral route. The authors applied Mantel-Cox log-rank test for equality of survival distributions between the groups and found there was no statistical significance ($p>0.05$).

The first Japanese study (13) compared patients with and without dementia who underwent a PEG and found that survival was not significantly different among groups ($p=0.62$). As method this study applied Kaplan-Meier and log-rank test. The second

study conducted in Japan (20) compared PEG to NGT enteral nutrition administration routes. This study found that the PEG group demonstrated a significantly higher survival rate by 27 months using the Cutler-Ederer method (p=0.019) than the NGT group. Shintani' study also took place in Japan and assessed survival (in days) according to the use of artificial nutrition (parenteral or enteral nutrition). The author found that survival periods of the patients in the PEG and Home Parenteral Nutrition (HPN) groups were twice that of the self-feeding oral-intake group ($p<0.05$).

The study of Gaines and co-workers (12) assessed earlier mortality after PEG, in patients with and without dementia. What is relevant to mention about this study is that though the analysis of Kaplan-Meier and log-rank test, the authors showed that patients with dementia or significant cognitive impairment do not have a significantly shorter survival after PEG than patients with intact cognitive function (p=0.85).

The Brazilian study (2) demonstrated a median survival time from EN beginning at 364 days (95% CI 243-455) and determined no significant differences in mortality rates among dementia patients and those with other neurological diagnoses. At the commencement of the study reasons for EN indication were dysphagia in 86.1% of the patients and oral feeding refusal in 13.1%. During the course of the study the authors claim that 13.9% (n=11) of patients resumed oral route, but no mention was made concerning the group of diseases to which these patients belonged or how mortality was calculated since there was a change of intervention – the lack of information on important aspects of patients' follow-up is among the reasons that led to an evaluation of this article as of a weak methodological quality (Table 1). It is most likely that patients who refused oral nutrition at the beginning of the study and the ones who presented mild to moderate degrees of dysphagia were the ones who resumed oral route.

Nutritional and Clinical Status

Four studies (2, 14, 19, 20) dealt with nutritional and clinical status outcomes. The first Israeli study (14) involving 88 patients and a follow-up time of 17 months failed to demonstrate any improvements on these parameters when comparing the oral route to enteral feeding. However, the second Israeli study (19), which dealt with a higher number of patients (167) and a follow-up of 21 months, demonstrated a significant improvement in albumin levels for the EN group, while the OR group experienced a reduction of this indicator. The OR group displayed a slight reduction in BMI, while the EN group had a reduction of almost 1 kg/m^2. However, the EN group

started the study with a significantly lower body weight compared with the OR group, and more patients in the first group experienced a 5% or more increase in initial body weight than OR group patients. The authors still relate an improvement in chronic inflammation parameters with EN.

The Japanese study (20) evaluated only albumin levels, and no differences were determined between the PEG and NGT groups after a 6 month follow-up (n=261). The authors claim that PEG feeding was effective in albumin preservation. Data on enteral formula types administered were not clear. The Brazilian study (2) that involved 79 patients and a follow-up of 11 months, which compared dementia versus other neurological diseases failed to demonstrate improved nutritional status or albumin levels. However, a lower survival rate was determined after 3 and 6 months of follow-up for patients with poor nutritional status at the beginning of the study (p=0.013 and 0.027, log rank). The authors also determined a lower survival rate among patients who at any time during the study presented with albumin levels lower than 3.5 g/dL (p=0.026, log rank) who had to be readmitted to the hospital (p=0.039, log rank) and who presented with a pressure sore after 6 months (p=0.001, log rank), whereas patients who had a healed pressure sore had better survival chances (p=0.007, log rank).

Enteral Feeding Complications

In total, 5 studies included an analysis of EN complications such as aspiration pneumonia (AP), tube displacement, number of hospital readmissions and pressure ulcers (PU) (2, 9, 13, 18, 20).

Aspiration Pneumonia (AP)

The Japanese study (20) revealed that AP incidence in PEG patients was 9.4%, whereas it was 52.9% in NGT patients. Inversely, patients in the PEG group that presented with AP before feeding had 51.6% recurrence.

The Italian study (18) had 171 patients, compared dementia versus non-dementia, and found no differences in AP frequency between groups. The Brazilian study (2) also compared dementia patients with patients who had other neurological diseases and found an overall AP incidence of 55.9% (the study did not clearly indicate the incidence for each study group). Increased attention to upright positioning of patients receiving enteral feeding decreases the incidence of these infections (22).

Tube displacement and number of hospital readmissions

Only one study assessed these complications(18) by comparing dementia versus non-dementia patients and found no differences in complication frequencies between groups. These data suggest that correctly performed nutritional therapy may not impose a higher risk of complications for dementia patients.

The study of Higaki et al (13) also mentioned that as a long-term complication of PEG tube-related problems were assessed. However, the authors didn't find any significant differences on these complications incidence among patients with or without dementia. This was also true for the other evaluated complications as reflux, focal abscess, gastric bleeding, diarrhoea, aspiration, MRSA enteritis, peritonitis and vomiting.

Pressure Ulcers (PU)

Among the analysed studies, three involved PU assessment (2, 9, 19). The Israeli study (19) involved 167 patients with dementia, which compared the oral route to enteral nutrition and found no differences on pressure sore development. Conversely, the American propensity-matched cohort (9) had 4421 patients; 1585 had PEG and 2836 did not. This study demonstrated that PEG was related to an increased risk of PU development and aggravation. General analysis demonstrated a lower possibility of PU healing for the PEG group with a HR = 0.7 (95% CI 0.55-0.89). However, when performing a sensitivity analysis stratifying for PU stage, no significance was determined– stage 2: HR = 0.66 (95% CI 0.45-0.97); stage 3: HR = 0.57 (95% CI 0.26-1.25); stage 4: HR = 1.00 (95% CI 0.55-1.86).

The authors describe that 74% of patients had 1 or more risk factors for developing a PU such as weight loss, AP, concern for inadequate fluid intake and/or concern for ability to swallow. The presence of one or more of these factors increased the risk of PU development– HR = 2.60 (95% CI 2.14-3.17), but not for a pressure ulcer improving while a PEG tube was in place – HR = 0.78 (95% CI 0.60-1.02) (9).

The authors cogitated that PEG may augment PU risk by enhancing the physical and pharmacological restraints that result in immobility, which is a risk factor. They suggest that another possibility is high osmolarity of formulas that may induce diarrhoea, which is another risk factor. The limitations of this study, according to the authors themselves, are that they relied on hospital documentation of PU. However, the hospitals receive increased reimbursements for PU, which might have caused over

documentation and the omission of confounders during subject matching (9). There was no information regarding the protein or antioxidant content, or the nutritional composition of the formulas the patients received because malnutrition is a risk factor for developing PUs.

In the Brazilian study (2), 41.2% of 43 patients who presented with a PU at the beginning of the study had healed their ulcer. Conversely, 20% of patients developed a new ulcer. The main limitation of the study was that the data were obtained from patients' charts without review by the authors.

Authors' considerations

Jaul et al. affirm that because tube feeding does not add to patient pain or discomfort, it should not be contraindicated when it complies with the values and wishes of patients and their families (14).

Higaki et al (13) state that there is no evidence to support a poorer prognosis after PEG in elderly people with dementia compared with the cognitively preserved elderly, emphasizing that survival after PEG was not significantly affected by the presence of dementia. For these reasons, caution should be taken in denying PEG based only in the presence of dementia. This is supported by the findings of Gaines and co-workers (12) who report that patients with dementia or significant cognitive impairment do not have a significantly shorter survival after PEG than patients with intact cognitive function.

Kumagai et al. (20) claim that nursing education for caregivers and staff as well as maintenance of the care environment in the area are necessary before introducing high-quality medical care.

Martins et al. (2) considered that there may be a subgroup of patients with dementia that do not benefit from enteral nutrition. They suggest that subsequent studies should focus on determining the characteristics of this subgroup to avoid complex and expensive therapies and adequately orient families to avoid unrealistic expectations and unnecessary suffering.

Discussion

When it comes to analyzing artificial nutrition impact on outcomes of patients with dementia, studies dealt mainly with survival, nutritional status improvement and enteral feeding complications, as aspiration pneumonia, tube displacement and number

of hospital readmissions and pressure ulcers. As previously discussed the absence of analysis of gastric stasis, late use of enteral feeding and refeeding syndrome may impose some bias to the results found until the present days.

Authors that criticize artificial nutrition for patients with advanced dementia usually state that this therapy brings no benefits on lengthening survival(11). However, both Kumagai et al' study(20) and the Brazilian one (2) bring a new insight on enteral feeding and PEG for the dementia patients showing that it can prolong life (20) or at least equal the length of survival of patients with dementia to the one presented by patients without dementia(2). This is reinforced by data of Israeli studies on patients' survival which suggest that enteral feeding was not harmful to patients either because the results were similar to those obtained with the oral route (14, 19). Advanced dementia is a life-limiting illness, which imposes some doubts related to the ability of EN on prolongation of life. This is particularly important when considering the findings of a similar survival among patients with and without dementia who receive enteral nutrition, as a positive aspect favouring artificial nutrition.

Only one study evaluated the influence of co-morbidities on survival and showed that previous subtotal gastrectomy and chronic heart failure are risk factors for earlier mortality after PEG (13). Increasing age was also associated with increased mortality (12, 13)

When it comes to nutritional status improvement, studies results are controversial. While some demonstrate a significant improvement of albumin and body weight (19), others fail to demonstrate any improvements on these parameters (14, 20). However, what is really important to emphasize is that, as found in the Brazilian study (2), a lower survival rate was determined for patients with poor nutritional status. This raises a question concerning the timing of enteral feeding introduction, as highlighted by Regnard and co-workers (11), since recovering nutritional status, specially of the elderly population, is harder than preventing malnutrition, usually demanding the use of non-nutritional strategies, as physical training and pharmacological approaches. The late use of enteral feeding would raise some bias on the efficacy of the therapy itself in recovering nutritional status, once nutritional strategies alone, when malnutrition is already installed, may not be enough to achieving this result. Reinforcing the importance of an adequate nutritional status on survival of patients with dementia, the studies of Higaki et al (13), Gaines et al (12) and Shintani (21) showed that hypoalbuminemia is a predictor of poor survival after PEG.

Interestingly, the study of Kimyagarov and co-workers (6) showed that compared with orally-fed dysphagic patients with dementia, PEG-fed patients received an additional mean energy intake of 30.5% kcal per day and mean protein intake of 26%. Despite the fact that there were no improvements on body composition parameters between groups, when analyzed at 3 and 6 months after PEG insertion, this procedure was successful in converting a negative nitrogen balance into steady state equilibrium. The authors themselves state that it is possible that longer time periods of nutritional interventions are needed in order to affect body composition.

Concerning the complications related to enteral feeding, while Kumagai et al (20) demonstrated lower rates of aspiration pneumonia with PEG compared to NGT, Venturini et al (18) and Higaki et al (13) didn't find any differences between patients with and without dementia. This was also true for tube displacement and hospital readmission. More important than the method of administration, is the attention given to upright positioning of patients receiving enteral nutrition, which decreases the risk of these infections (2, 22). Since this aspect was not evaluated on the articles in order to establish its correlation to AP incidence rather than enteral feeding itself, this may be considered a bias, harming the conclusion that artificial nutrition is associated with a higher incidence of AP. Besides, since gastric stasis was not assessed by any of the studies, specially by the ones that evaluated AP, it may also impose a bias to the final analysis on the association between EN and AP, since it is an independent risk factor for AP development, for which the management demands more than nutritional strategies.

In relation to PU assessment, studies results are also controversial. Arinzon et al (19) found no differences on PU rates between oral route and enteral nutrition, in a follow up period of 21 months. Martins et al (2) found that among the patients who started the study with an PU, 41.2% had it healed, while 20% of patients who didn't have an PU at the beginning of the study developed one, although there were no data on correlation of nutritional status and PU prevalence or incidence. Conversely, Teno et al (9) stated that PEG was related to an increased risk of PU development and aggravation. The period of analysis comprehended 1 yr. The authors themselves affirm that among the risk factors for PU development were weight loss, concern for inadequate fluid intake or for ability to swallow. Once again one may question the timing of EN introduction, since a prophylactic therapy would prevent malnutrition as well as inadequate fluid and nutrients intake, which would lower the risk of PU development and increase the probability of its healing.

The present study has some limitations that need to be taken into account. First, most of the studies included have a small sample size which requires caution while interpreting the results. Besides, the lack of proper diagnostic criteria documented by the selected studies raises the question as to whether the diagnosis or stage of dementia was accurately made. The lack of some analysis that should be included in patients' follow-up contributes to the frailty of the studies included in the present review, as well as of the review itself, such as the absence of analysis of gastric stasis – which may contribute to aspiration pneumonia occurrence -, the lack of information on patients' position while receiving enteral nutrition – since a wrong positioning increases the risk for aspiration pneumonia -, on late use of enteral nutrition – that may confound results concerning the real potential benefit of enteral nutrition for patients with dementia – and of refeeding syndrome occurrence – which may increase mortality and complications related to enteral nutrition therapy. However, data on these problems are missing in the gastrostomy-dementia literature, as reinforced by Regnard and co-workers (11).

Final Considerations

Because of the lack of uniformity of the selected studies on the searched theme and the quality of methods applied to each of them, it was not possible to combine the results to draw conclusions. However, the results presented suggest another perspective on enteral nutrition therapy for patients with advanced dementia: it is not yet possible to conclude that this therapy is harmful for this patient population, in lessening survival or increasing complications such as aspiration pneumonia, tube-related problems or pressure ulcers.

Compared to the oral route, enteral nutrition did not improve mortality. Rather, this outcome was more associated with the presence of co-morbidities such as peripheral vascular disease, diabetes and chronic heart failure than the feeding route itself. The route of diet administration demonstrated no differences in nutritional and clinical outcomes either, which may be due to the short follow-up period because the study with a longer period demonstrated improvement of albumin levels and weight gain. It is also important to emphasise that malnutrition is a poor predictor of survival and is also related to lower albumin levels, higher pressure sore incidence, and a higher difficulty of ulcer healing.

One complication that is associated with the enteral route is aspiration pneumonia, which can be prevented by measures of managing gastroesophageal reflux.

Though percutaneous endoscopic gastrostomy is highly associated with pressure ulcers, adequate patient care by a multidisciplinary team, such as changing the patients' position on their bed and following adequate nutrition, can prevent or minimise these occurrences. Adequate follow-up by this team can prevent complications and improve survival.

The need for other studies evaluating enteral feeding for patients with advanced dementia still persists. Future studies should include a representative patient sample with better control and intervention group matching, longer follow-up periods and more precise dementia diagnoses, as well as analysis on gastric stasis and patients' position while receiving enteral nutrition - and their relation to aspiration pneumonia -, on early use of enteral nutrition in order to prevent malnutrition, and on incidence of refeeding syndrome associated to complications related to enteral feeding. Only after controlling all potential confounders one may affirm that enteral nutrition is or not harmful to patients with advanced dementia.

Since dementia is a life-limiting illness it is possible that survival is not the best approach to assess enteral nutrition efficacy for these patients.

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Table 1. Methodological quality of the prospective studies included in the systematic review as assessed by the Newcastle-Ottawa Scale for Cohort Studies (n=9)

Reference	Methodological Quality
IMAJ 2006;8:870-874	Good
J Am Med Dir Assoc 2008;9:657-662	Good
Am J Gastroenterol 2008;113:1011-1016	Good
JPEN J Parenter Enteral Nutr 2009;33(1):62-66	Good
Clin Nutr Suppl 2012;7(1):57	Weak
Psychiatry Clin Neurosci 2012;66:418-422	Good
Arch Intern Med 2012;172(9):697-701	Good
Rev Assoc Med Bras 2012;58(6):691-697	Weak
J Clin Neurosci 2013;20:220-23	Good

Table 2. Home enteral nutrition outcomes in patients with dementia – data extracted from analysed articles (n=9)

Reference Nº	Patients	Follow up	Comparison Group	Outcomes
(14)	88 patients	17 months	OR = 26 EN = 62	No clinical or nutritional differences found among the groups. HR for mortality (OR versus NGT) = 2.86 (95% CI 1.50-5.45)
(19)	167 patients	21 months (before and after analysis)	OR = 110 EN = 57	Albumin OR: 3.75±4.43→ 3.63±2.82* Albumin EN: 3.39±3.50 → 3.74±2.81* BMI OR: 23.9±3.43 → 23.23±2.77* BMI EN: 22.9±3.14 → 21.98±1.67* Mortality rates: OR = 27,3%, EN = 42,1% (p>0.05) Improvement of chronic inflammation parameters with EN, but no impact on functional status, pressure sore development, or prolongation of life.
(13)	311 patients	3 years retrospectively	Dementia = 143 Without dementia=168	Survival was not significantly different among the groups (median survival: 356 days) Predictors of poor survival after PEG: Previous subtotal gastrectomy: HR = 2.619 (95% CI 1.367-5.019) Serum albumin < 2,8 g/dL: HR = 2.081 (95% CI 1.490-2.905) Age > 80 yr: HR = 1.721 (95% CI 1.234-2.399) Chronic heart failure: HR = 1.541 (95% CI 1.096-2.168)

				Male gender: HR = 1.407 (95% CI 1.037-1.909)
(20)	261 patients	6 months (before and after analysis)	PEG = 155 NGT = 106	Survival rate of the PEG group (65.6±5.6%) was significantly higher by 27 months than the NGT group (44.4±9.8%)* No differences in albumin levels before and after analysis.
(21)	80 patients	5 years retrospectively	Dementia = 30 Cerebrovascular disease = 50 Of these: OR = 23 HPN = 21 PEG = 36	Median Survival: OR = 399 ± 257 days HPN = 725 ± 616 days PEG = 736 ± 765 days
(18)	171 patients	Not clear	Dementia=82 Non-dementia=89	No differences found among the groups for tube displacement frequencies, aspiration pneumonia and the number of hospital readmissions.
(9)	4421 patients	1 year	PEG = 1585 Non PEG = 2836	PEG was related to an increased risk of developing a pressure ulcer: HR = 2.27 (95% CI 1.95-2.65) PEG was related to a higher risk of developing a pressure ulcer stage 4: HR = 3.21 (95% CI 2.14-4.89)
(12)	190 patients	2 years retrospectively	Dementia=45 (or significant cognitive impairement)	Median survival after PEG did not differ among groups. Factors associated with a 30-day mortality after PEG: Increasing Age: HR = 1.08 (95% CI 1.04-1.12)

			Without dementia=145	Decreasing serum albumin: HR = 0.43 (95% CI 0.22-0.84) Acute illness increase mortality after PEG Hospitalized patients who receive a PEG are significantly more likely to die in the next 30-days than similar patients who receive a PEG after discharge.
(2)	79 patients	11 months	Dementia = 39 Other neurological diagnoses = 40 (all in EN)	43% of patients presented with a pressure ulcer at the beginning of the study. Of these, 41.2% healed, and 20% developed a new ulcer. 13.9% resumed the oral route. Mortality in 3 months = 15.2% Mortality in 6 months = 22.8% Mortality in 11 months = 43% No improvements in nutritional status or albumin levels were observed.

OR: Oral Route, EN: Enteral Nutrition, HPN: Home Parenteral Nutrition, HR: Hazard Ratio, CI: Confidence Interval, BMI: Body Mass Index, PEG = Percutaneous Endoscopic Gastrostomy, NGT = Nasogastric Tube

* $p<0.05$

Table 3. Exclusion criteria for the systematic review of articles without the MeSH Term “dementia” (n=10)

Reference	Reason for exclusion
Nutr Clin Pract. 2009;24(2):196-205	Review article focusing on the need for expertise in nutrition support and geriatrics for professionals who interact with the elderly.
Pediatrics. 2010 Nov;126(5):e1056-63 Pediatr Cardiol. 2012 Dec;33(8):1315-22	Original articles with focus on paediatric patients.
Nutrition. 2008;24(10):998-1012 Arch Dis Child. 2009;94(12):938-43 JPEN J Parenter Enteral Nutr. 2012; 36(4):399-406 JPEN J Parenter Enteral Nutr. 2012; 36(4):407-14 JPEN J Parenter Enteral Nutr. 2012; 36(4):463-9 JPEN J Parenter Enteral Nutr. 2012; 36(5):603-10	Original articles with focus on Home Parenteral Nutrition.
Nutr Clin Pract. 2010 Jun;25(3):296-300	Original article with several patient types that did not focus on the elderly with dementia.

Table 4. Exclusion criteria for the systematic review of articles including the MeSH Term "dementia" (n=10)

Reference	Reason for exclusion
Neurology 2008; 71(23):1856-61	Original article. Oral supplement intervention rather than tube feeding.
J Nutr Health Aging 2013;17(9):752-55	
J Psychosoc Nurs 2010; 48(5):15-18	Review article focusing on care costs.
Arch Intern Med 2010;170(1):83-8	Original article with a focus on nursing homes culture on the use of feeding tubes.
J Am Geriatr Soc 2010;58(3):580-4	Original article with a focus on a proposal to bring clarity to decision-making regarding difficulty with eating.
J Palliat Med 2011; 14(9):1017-21	Original article with a focus on educational intervention rather than EN outcomes.
J Clin Nurs 2011;20(5-6):802-10	Original article on a survey of the reasons patients do not chose PEG/PEJ as a route for long-term feeding.
J Pain Symptom Manage 2011;42(3):366-78	Original article on evaluation of speech language pathologists
Am J Phys Med Rehabil 2012;91(2):141-7	Original article with a focus on the level of care rather than outcomes.
Amyotroph Lateral Scler. 2012;13(3):318-25	Original article with searched outcomes other than this article's purposes (predictors of feeding tubes and tracheostomy).

PEG – Percutaneous Endoscopic Gastrostomy; PEJ - Percutaneous Endoscopic Jejunostomy

3 ARTIGO DE REVISÃO

Outcomes of enteral nutrition for patients with head and neck; and gastrointestinal cancers - a systematic review – Salomon ALR, Novaes MRCG. Submetido ao periódico ***Nutrition and Cancer***

3 ARTIGO DE REVISÃO

OUTCOMES OF ENTERAL NUTRITION FOR PATIENTS WITH HEAD AND NECK; AND GASTROINTESTINAL CANCERS - A SYSTEMATIC REVIEW

Abstract

The aim of this study was to conduct a systematic review of the impact of enteral nutrition intervention on the outcomes in adult and elderly oncology outpatients receiving either radiotherapy or chemoradiotherapy for cancers of the Gastrointestinal or Head and Neck areas (or submitted to surgical resection of the affected area). A systematic review of scientific literature was conducted through searching The Cochrane Library, MEDLINE, EMBASE, PROQUEST, LILACS, Brazilian Health Virtual Library – BVS, Web of Science, CINAHL and Health and the Wellness Resouce Center for articles published in the period from 2009 to 2013. Randomized controlled trials and observational studies involving a control group were searched. Data were independently extracted and assessed by one reviewer and confirmed by a second reviewer. Outcomes were searched in relation to enteral feeding route. Four prospective and three retrospective studies were identified, involving participants from several parts of the world. Poor nutritional status has been linked with lower treatment tolerance and complications. Percutaneous endoscopic gastrostomy tubes should be considered the procedure of choice for long term enteral feeding for head and neck cancer patients, and it should be inserted prophylacticaly, followed by regular monitoring in order to prevent complications and maintain patients' nutritional status.

Key words: home care services, enteral nutrition, cancer, outcomes, systematic review.

Introduction

Head and neck cancer (HNC) is comprised of a variety of malignant tumors that can develop in the upper respiratory and digestive tracts. Further, HNC include cancers of the lip, oral cavity, tongue, salivary glands, pharynx, larynx, nasal cavity, ear and skull base (1). HNC is common in several regions of the world (2). The primary risk factors for HNC include tobacco use, alcohol consumption, human papillomavirus (HPV) infection and Epstein-Barr virus (EBV) infection, as a chronic exposure of the upper aerodigestive tract to these and other factors. Overall, HNC accounts for more than 550,000 cases annually worldwide, affecting significantly more males than females. The incidence rate in male exceeds 20 per 100,000 in regions of France, Hong Kong, the Indian subcontinent, central and eastern Europe, Spain, Italy, Brazil and among African Americans in the United States (US). In the US, HNC accounts for three percent of malignancies, with an estimate incidence of 53,000 per year and 11,500 deaths from the disease (2).

Gastrointestinal Cancer (GIC) is a term to describe cancers that affect the digestive system. GIC includes cancers of the esophagus, gallbladder, liver, pancreas, stomach and bowel (the bowel includes the small intestine, large intestine or colon and rectum) (3). Colorectal Cancer (CRC), the most common forms of GIC , is the third and most commonly diagnosed cancer in males and females, respectively. CRC is influenced by both environmental and genetic factors. Gastric Cancer (GC), is currently the fourth most common malignancy in the world (4,5). The incidence of GC has declined rapidly over the recent few years partly due to the recognition of certain risk factors such as H. pylori, dietary factors, environmental risks, as well as to the popularization of refrigerators.

About one million new cases of GC were estimated to have occurred in 2008 (988,000 cases, 7.8% of the total). More than 70% of cases (713,000) occur in developing countries (467,000 in men and 246,000 in women), and half of the total world cases occur in Eastern Asia (mainly in China). GC is the second leading cause of cancer deaths in both sexes worldwide (736,000 deaths, 9.7% of the total). The highest mortality rates are estimated in Eastern Asia (28.1 per 100,000 in men and 13.0 per 100,000 in women), the lowest rates are estimated in Northern America (2.8 per 100,000 in men and 1.5 per 100,000 in women). High mortality rates are also present in both sexes in Central and Eastern Europe, and in Central and South America (6).

CRC rates are also substantially higher in males (663,000 cases, 10% of the total) than in females (571,000 cases, 9.4% of the total), with over 1.2 million new cases and 608,700 deaths estimated to have occurred in 2008 (8% of all cancer deaths). Almost 60% of the cases occur in developed regions. The incidence rates vary 10-fold in both sexes worldwide, with the highest rates estimated in Australia/New Zealand and Western Europe, the lowest rates estimated in Africa (except Southern Africa) and South-Central Asia, and intermediate rates estimated in Latin America. CRC incidences rates are substantially higher in men than in women (overall sex ratio of 1.4:1) (4-6).

At present, concurrent chemoradiotherapy seems to be the most appropriate approach in order to preserve organ functions in patients with advanced HNC. Chemoradiotherapy is often associated with acute and late toxicity effects including mucositis that hinders oral feeding and sometimes requires a break in the treatment. Further, chemoradiotherapy side effects can also result in symptoms of an additional 10% of weight loss, associated with dysphagia, odynophagia, loss of sense of taste, xerostomia, nausea, vomiting and hyporexia (7).

Malnutrition occurs frequently in patients with cancers of the gastrointestinal (GI) or head and neck (HN) area due to factors other than cancer itself, such as limitations on oral intake, poor dietary habits, smoking and alcohol intake, resulting in negative outcomes (1,8). Side effects from antineoplasic therapy also play an important role in malnutrition development (1). Between 35 and 60% of HNC patients are malnourished and optimal nutritional support is vital for their post-treatment recovery (9). Malnutrition increases the risk of infections and treatment toxicity. Moreover, malnutrition decreases response to treatment, quality of life (QoL) and life expectancy which are directly linked to free fat mass loss (1,8,10,11).

Risk of malnutrition increases with the use of multi-modality treatments (Induction Chemotherapy and Chemoradiation) and 75-85% of patients present with significant weight loss during treatment. And a higher proportion of patients require enteral feeding (66-71% for combined modality treatment versus 12% for radiotherapy) (12,13). The use of enteral nutrition, and prophylactic gastrostomy tubes has been proposed as a way of improving nutritional outcomes for these patients (10) and it has also been touted to be essential to meet the nutritional needs of HNC patients (11). Surgical patients usually require enteral nutrition to bypass the oral cavity and pharynx in order to allow healing of the surgical site and the recovery of a safe swallow mechanism (9).

The aim of the present study was to systematically review the impact of enteral nutrition intervention on the outcomes in adult and elderly oncology outpatients receiving either radiotherapy or chemoradiotherapy to the GI or HN areas (or submitted to surgical resection of the affected area).

Material and Methods

The present study conducted a systematic review of the scientific literature. The Cochrane Library, MEDLINE, EMBASE, PROQUEST, LILACS, *Biblioteca Virtual de Saúde* – BVS (Brazilian Health Virtual Library), Web of Science, CINAHL and Health and Wellness Resouce Center were searched in 2013 for articles published in the period from 2009 to 2013. Citation reference checking was undertaken. Titles and abstracts were analyzed for Medical SubHeadings (MeSH) terms. Whenever it was not possible to conclude whether a citation should, the full text of the citation was obtained for further evaluation.

The strategy of search for each data basis follows:

1. PubMed / MEDLINE: advanced search for "enteral nutrition" [MeSH Terms] OR ("enteral"[All Fiels] AND "nutrition"[All Fields]) OR "enteral nutrition"[All Fields] AND ("cancer"[MeSH Terms] OR "cancer"[All Fields] AND "humans" [MeSH Terms] AND "adults"[MeSH Terms] AND "aged"[MeSH Terms] AND "outcomes"[All Fields] AND "last 5 years" [MeSH Terms] AND "clinical trials" [MeSH Terms]. As a result, 18 articles were identified.

2. EMBASE: advanced search for "enteral nutrition" AND "outcomes". Filters: "head and neck cancer AND digestive system cancer" AND "controlled studies OR clinical trials" AND "article" AND "2009 up to 2013". As a result, eight articles were identified, of which 2 were excluded because they were duplicates; thus, six articles remained.

3. PROQUEST Hospital Collection: Search for MeSH terms "enteral nutrition" AND "cancer" AND "outcomes"[All fields] AND "Comparative studies". Filters: humans AND (aged OR treatment outcome OR adult OR aged, 80 & over OR follow-up studies OR prospective studies OR risk factors OR enteral nutrition OR gastrointestinal neoplasms OR head & neck cancer OR quality of life OR survival rate OR comparative studies OR gastrostomy OR survival analysis OR weight loss) NOT (retrospective studies AND postoperative complications AND parenteral nutrition AND postoperative care AND predictive value of tests AND young adult AND adolescent

AND anastomotic leak AND combined modality therapy AND health care AND hyperglycemia AND hypoglycemia AND incidence AND administration, oral AND anastomosis, surgical AND blood glucose AND clinical protocols AND constriction, pathologic AND costs & cost analysis AND diabetes AND digestive system surgical procedures AND drainage AND glucose AND health risk assessment AND hospitals AND hospital mortality AND hypoglycemic agents AND inflammation AND insulin AND intensive care units AND laparoscopy AND nervous system diseases AND pain, postoperative AND pancreaticoduodenectomy AND pancreatic fistula AND pancreatic neoplasms AND patient compliance AND postoperative period AND prevalence AND reconstructive surgical procedures AND reference values AND taiwan AND tomography, x-ray computed AND manometry AND maryland AND tramadol) AND publishing date from 2009 up to 2013. As a result, five articles were identified.

4. LILACS: Search for MeSH terms “enteral nutrition” AND “cancer” AND “outcomes”[All fields]. As a result, two articles were identified, from which one was a duplicate; thus, one article remained for further analysis.

5. BVS**:** Search for MeSH terms “enteral nutrition” AND “cancer” AND “outcomes”[All fields]. Filters: “controlled clinical essay” OR “cohort studies” AND “prognostic OR therapy” AND “2009 up to 2013” AND “articles”. As a result, five articles were identified, from which one was a duplicate; thus, an amount of four articles remained.

6. Web of Science: Search for MeSH term “enteral nutrition” on title, AND for MeSH term “cancer” on title AND for “outcomes”[All fields] on topic. Filters: publications from 2009 up to 2013 AND “articles”. As a result, eight articles were identified, from which five were duplicates. An amount of three articles remained.

With the intent to find an article which could not be retrieved by the previous search, a complementary one was conducted on CINAHL and Health and Wellness Resource Center (Dot.Lib), applying the following terms “nasogastric” AND “percutaneous endoscopic gastrostomy” AND “tubes”. On CINAHL, 6 articles were identified that were published in the period from 2009 to 2013, which included one duplicate that was excluded. An amount of five articles remained. On the second search, one article was retrieved and was used for this review purposes. Though this complementary search was conducted, two recent articles were not able to be accessed, despite of contact with authors through e-mail communication, which led to their purchase (1,9).

Randomized Controlled Trials (RCT), controlled clinical trials, controlled before and after studies that evaluated the effectiveness of enteral feeding via a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy (PEG) were included. In addition, comparative observational studies were included. However, only a few controlled clinical trials were identified. The only RCT dealing with PEG and NGT identified, which was included on Cochrane's systematic review (11), was disregarded for the purpose of the present study, since its authors developed a prospective study latter (14), in which the sample from the first trial was also included. The other two controlled studies dealt with overall nutritional intervention, not aiming the comparison between PEG and NGT (7,8). Hence, controlled observational studies were used for the purposes of this article.

The study population included adults and elderly patients (aged 20 and over), of either genders, with a primary diagnosis of head and neck cancer (HNC) or a gastrointestinal one (GIC) undergoing treatment such as radiotherapy, or chemoradiotherapy, or chemotherapy, or surgery.

The selection criteria for studies comprehended the screening of citations by one of the review authors (ALRS). Following screening, the full text of eligible citations were assessed for inclusion by the two review authors. Whenever the abstract met the inclusion criteria and the full text was not retrieved, the whole article was ordered to the Library of the Federal University. If this strategy was not successful as well, a contact with the corresponding author was performed through e-mail communication. If any differences of opinion existed, they were resolved by consensus between the author reviewers. For the observational prospective studies, methodological quality was evaluated using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies, for retrospective ones, the Newcastle-Ottawa Quality Assessment Scale for Case Control Studies and for prospective randomized controlled trials, an adapted method of assessment was applied (15,16).

A data extraction form was used which included the following information for each study: the number of patients, the number in each comparison group (whenever controlled), enteral route (if via tube feeding exclusively or if oral route was also considered), follow-up time, study design and outcomes [such as weight changes, or survival, or length of hospital stay, or frequencies of hospital readmission, or oral rehabilitation, or complications related to method of feeding, or delays or gap in treatment, as well as mean duration of enteral nutrition, nutritional parameters

(circumferences, skin folds, Body Mass Index), biochemical ones (hemoglobin and albumin) and patient's satisfaction].

It was planned that if data from the studies were not of sufficient quality and sufficiently similar (in terms of patient population, diagnostic criteria, intervention, outcome measure, length of follow up and type of analysis), they would be combined in a meta-analysis to provide a pooled effect estimate.

No articles published in languages other than Portuguese, English, Spanish or French were identified. These four languages are currently spoken by the authors.

Results

The systematic review of the literature identified 43 articles. However not all were suitable for inclusion in this review. Reasons for exclusion of articles are presented in Table 1.

A total of seven articles were considered for the purpose of this study , including one RCT whose participants were included in a more recent publication of the same authors. One paper was retrieved from one of the references, leaving an amount of eight articles considered for the present review. Six papers were published in the past five years (while one was published in 2004 an RCT obtained from the reference list of Paccagnella *et al*, and other in 2008 RCT included in the Cochrane review).

Participants and settings

Though it was established that reviewed studies would include both HNC and GIC, only one article that included GIC was identified (8).

Of the studies included in the present review, three (42.8%) were conducted in Australia (8,10,14), two (28.6%) in the United Kingdom (9,12), one (14.3%) in Italy (7) and one (14.3%) in India (1).

Methodological Issues

Despite the methodological frailty of observational studies, the limitations of this study design can be compensated by its methodological quality, as assessed by Newcastle-Ottawa Scale. This scale includes two types of observational studies: case control and cohort studies (15).

In the present review, retrospective studies (7,9,10,12) were assessed on basis of the scale for case control studies, which evaluates 3 categories: 1) Selection (including

adequacy of case definition, representativeness of the cases, selection and definition of controls), 2) Comparability of cases and controls, 3) Exposure (including ascertainment of exposure, same method of ascertainment for cases and controls and non-response rate). For the prospective study (14), the scale designed for cohort research was applied. This scale focus on 3 pillars in order to assess: 1) selection of patients (including representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and demonstration that outcome of interest was not present at the start of the study), 2) comparability of cohorts on the basis of design or analysis, and 3) outcome (including assessment of outcome, if follow-up was long enough for outcome to occur and adequacy of follow-up of cohorts) (15). A total of 10 (case-control scale) or 9 (cohort scale) stars could be attributed to the studies – if they counted for more than 6 stars they were considered of a good quality (17).

For prospective randomized controlled trials (1,8), an adapted method of assessment was applied (16). The following were considered for evaluation: same initial prognostic groups, randomization of patients, blinding of randomization, blinding of study (and if not, if groups were homogeneous in terms of co-treatments and assessment of outcomes), completion of follow-up, occurrence of early interruptions, conduct of intra-group analysis, results presented in effect and impact measures, similarity of studied patients and real patients, feasibility of intervention, approach of outcomes that are important for patients, and efficacy of treatment.

Table 2 presents the result of assessment of the methodological quality of the considered articles, where it is possible to conclude that 85% (6 in 7) of the publications presented a satisfactory evaluation.

Considering the differences of studies designs, the heterogeneity of comparison groups in some studies, as well as measured outcomes, and the lack of information that would allow a meta-analysis to be performed, is was not possible to combine the results to provide a pooled effect estimate. Conclusions drawn from studies analysis are summarized in Tables 3, 4 and 5.

Discussion

According to a previous systematic review, published in the Cochrane Library and including studies published up to February 2012, there was insufficient evidence to determine the optimal method of enteral feeding for patients with head and neck cancer

receiving radiotherapy and/or chemoradiotherapy (11). The only study used for the Cochrane's review purposes was published in 2008 (18).

In the present study, focusing on publications from 2009 to 2013, some important aspects on nutritional intervention have to be taken to account.

Nutritional Intervention

One study conducted in Italy and another study from Australia (7,8) dealt with nutritional intensive intervention (Intervention Group = IG), including oral supplements and/or enteral nutrition, in comparison to conventional nutritional care (Control Group = CG).

The Italian study (7) was retrospective in which patient treatment included concurrent chemoradiotherapy (CCRT) in both sides of the neck. Outcomes were measured at time 0 (V0 = prior to CCRT), time 1 (V1 = 4 weeks from the beginning of CCRT), time 2 (V2 = completion of CCRT), time 3 (V3 = 1 month after completion), time 4 (V4 = 3 months after CCRT) and time 5 (V5 = 6 months after completion). Intervention led to a significant decrease in weight loss, fewer breaks in treatment, and a linear correlation between weight loss and radiation treatment delayed for toxicity. The control group had significantly more unplanned hospital admissions (Table 3). The authors concluded that providing intensive nutritional support with regular monitoring resulted in reduced weight loss. The limitations of this study comprised the small sample size (n=66) and the fact that it was not a controlled study. Also, there was no data provided on a tumor control or overall survival.

The Australian study (8) was the only study including GIC patients, in addition to HNC patients. It was a prospective randomized controlled trial involving 88% of HNC patients and 12% of abdominal or rectal cancer patients, receiving radiotherapy. The intervention resulted in patients being able to maintain body weight over 12 weeks and to show smaller deterioration in nutritional status scores, as evaluated by Patient-Generated Subjective Global Assessment (PG-SGA). Intervention Group (IG) also showed a faster recovery in global Quality of Life (QoL) and physical function (Table 5). The authors concluded that early and intensive nutritional intervention provided beneficial outcomes in terms of minimizing weight loss, deterioration in nutritional status, global QoL and physical function in outpatients. The limitations of this study consisted of the absence of a true control group, since CG still received an intervention for ethical reasons, less intensive than IG, and also a lack of long term follow-up to

study morbidity and mortality. The authors were not clear regarding how many patients received oral supplements, information that was requested through e-mail contact, but left with no answer.

The findings of these two studies are consistent with other studies that claim that nutritional support is essential for HNC patients in order to improve their outcomes (9-11).

Method of Enteral Feeding

a. Prospective Studies

Three studies dealt with this theme prospectively (1,14,18). The results of the last study were included in a second manuscript. The first was a prospective randomized controlled study conducted in India, the second was a prospective study that took place in Australia and the third was a randomized study carried out by the same authors of the second study in Australia. These studies compared the use of Percutaneous Endoscopic Gastrostomy (PEG) versus NasoGastric (NG) tubes.

The Indian study (1), a prospective randomized controlled trial, intended to provide follow-up for patients at weeks 1 and 6 of treatment (radiotherapy, chemo-radiotherapy or CCRT) and at 6 months of the study initiation. However all results were from a 6-weeks analysis, since at 6 months there were no patients remaining in the NG group – 10 from 44 patients resumed oral route, whereas the other patients converted to a PEG feeding. PEG showed a better performance in terms of hemoglobin, body weight and mid arm circumference, and was advantageous in patients' satisfaction (scores of pain, difficulty in learning to use the tube, inconvenience, uncomfortable feeds, altered body image, effect on family life and interference with social activities). The NG group had significantly more complications (local site infection and tube dislodgement) (Table 4). The authors conclude that low PEG-related site infections may be due to the fact that PEG insertion was under the care of senior physicians and that PEG is a better choice for long term enteral feeding in advanced HNC patients. Study limitations included the difference from groups in terms of treatment modality (NG patients received more CCRT a therapy associated with more serious complications), and initial body weight (PEG patients had lower weight at the beginning of treatment). Calorie intake was not assessed and the association of CCRT with site infection (that has been reported in other studies) was not assessed.

The Australian (14), a prospective study, followed patients for 6 weeks after treatment (chemoradiation) and 6 months post-treatment. 32 patients were in PEG group while 73 were in the NG group. At 6 weeks post-treatment PEG patients presented with weight gain, while patients in the NG group lost weight ($p<0.001$). At 6 months the weight loss from the tube insertion was greater in the NG group ($p=0.04$). And, at 6 weeks the self-assessed general physical condition and overall QoL scores were similar between groups; however, at 6 months NG was seen as more inconvenient ($p<0.001$), had more uncomfortable feeds ($p=0.02$) and had a greater impact on body image ($p=0.03$). The impact on family life was worse for NG ($p=0.04$) and it interfered more with social activities ($p=0.006$) compared to PEG. However, the costs associated with the procedures were almost ten times higher for PEG, while inpatient cost for PEG patients were three times higher than for NGT. Infections rates were higher for PEG group (Table 4). Authors concluded that PEG tube should be selective, not routine for HNC patients who can be predicted to have long term need for nutritional support.

b. Retrospective studies

Three studies compared PEG to NG tube retrospectively (9,10,12). Of these, one was conducted in Australia and two in the United Kingdom (UK).

The Australian study (10) compared prophylactic PEG (n=7) to reactive intensive nutrition (Control Group – CG – n=64, of whom 44% with NGT). Patients were treated with Radiotherapy (RT) and evaluated at the beginning and the final week of RT. Median absolute and mean percentage weight loss showed no significantly difference. After adjusting for risk factors (inability to take adequate nutrition orally and/or ≥5% weight loss), with linear regression, the PEG group had 5.2% (95% CI 1.0-9.3%) less weight loss than the CG ($p=0.016$). There were no statistical differences in the Odds Ratio for hospital admission for nutritional reasons and for treatment interruptions (Table 5). Authors concluded that there are problems related to a reactive tube placement that are largely overcome when they are placed prophylactically. The use of prophylactic tubes can reduce weight loss in patients undergoing radical RT for HNC. The limitations on this study included the number of patients in PEG group, which led to statistical uncertainty, the lack of evaluation of other outcomes (i.e. survival). And the PEG group had more risk factors for weight loss and nearly half of the CG ended up requiring NGT insertion.

The first article published in the UK (12) compared three different groups according to treatment modality: one group receiving induction-chemotherapy (n=24), one group on CCRT (n=76) and one group on RT (n=96). Oral supplements (OS) were compared to the Enteral Nutrition intra group (Prophylactic PEG – PPEG – and PEG inserted during treatment – PEG). PPEG lost the least amount of weight during treatment period, while PEG lost the most weight. The method of enteral nutrition was not statistically significant for outcomes (Table 5). The authors concluded that all the patients receiving CCRT should be considered for enteral nutrition and that no definitive answer could be given for the optimal method of enteral feeding. The limitations of the study include the fact that groups were heterogeneous because the different methods of treatment induce varying degrees of toxicity.

The latest UK study (9) compared NGT, PEG placed in the pre-operatory (PEG1) and PEG placed intra-surgery (PEG2) in reference to complications. No major complications were seen in the PEG1 group, while in PEG2 group, 2% of patients developed complications (one colonic injury secondary to insertion and one intra-abdominal leak from the PEG) and 16% developed minor complications (abdominal pain). For the NGT group 8% developed aspiration pneumonia and its main complication was tube dislodgement. Approximately 11% of patients continued to use PEG until the end of data collection and they were more likely to have had an adjuvant treatment or to have a more advanced disease. And 25% of patients on PEG died (Table 5). The authors developed a scoring system to help defining the best method of enteral feeding – Key to Appropriate Replacement Enteral Nutrition (KAREN) – which requires further validation from additional studies. They concluded that the lower number of PEG-related complications in comparison to other studies may be related to the fact that insertion of a PEG is completed only by a senior member of the surgical team and only after the airway has been secured. Limitations of this study include the fact that the study was conducted at a tertiary referral center, which led to a greater use of PEG (n=120 versus 24 NGT).

The studies that compared median duration of PEG versus one of NGT found that the former one was longer, ranging from 2.5 times greater than NGT (14) to 16 times (9). As a reason for that, Corry *et al* state that prolonged use of PEG may contribute to disuse atrophy associated to dysphagia, leading to a greater dependence on the tube (14).

Due to the lack of uniformity of the selected studies and the quality of methods applied on each of them, it was not possible to combine the results in order to draw a conclusion. However in face of the presented results some conclusions may be drawn that may be confirmed by additional studies.

Enteral nutrition, either in a form of oral supplements or of nasogastric or gastrostomy tubes, for head and neck and gastrointestinal cancers patients is essential to maintain nutritional status in order to improve tolerance for curative or palliative treatments (such as radiotherapy, chemotherapy, concurrent chemo-radiation therapy or surgery) and to improve patients' quality of life and physical status.

Though studies do not provide a clear message on the best route of enteral feeding, it can be inferred that early intervention is better than a corrective one, since this involves a greater difficulty related to patient's recovery and also a higher prevalence of adverse effects of treatment related to malnutrition. Further studies should not only assess the differences on outcomes related to the methods of feeding, but also to the timing of the beginning of enteral feeding.

Analyzed studies showed a tendency favoring PEG in maintaining better nutritional status (measured by body weight and subjective scores) and patients' satisfaction (probably related to the lack of visibility of the tube, than nasogastric tubes). Studies that affirm that no definitive answer can be given on the optimum method of enteral feeding usually relate to PEG-associated complications and its costs. However, other studies state that PEG complication rates decline with increasing experience of the PEG surgeon and consequently, and associated costs also decline.

PEG should be considered a better choice for long term enteral feeding for head and neck cancer patients, and it should be inserted prophylactically, followed by regular monitoring in order to prevent complications and maintain patients' nutritional status.

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Table 1. Reasons for exclusion of articles for the purpose of the Systematic Review, according to the searched databases (n=35)

Reference	Reason for exclusion
1. J Dig Dis 2012;13(8):401-406 2. Eur J Gynaecol Oncol 2009;30(4):418-421	Original articles which focused on immune-enhanced enteral nutrition. (PubMed)
3. Eur J Clin Nutr 2012;66(7):850-855 4. Nutr Cancer 2010;62(8):1105-1112	Original articles with focus on pre and perioperative immunonutrition. (PubMed)
5. Surgery 2012;152(5):832-842	Original article, with focus on synbiotics in perioperative phase. (PubMed)
6. J Korean Med Sci 2012;27(3):261-267 7. Asia Pac J Clin Nutr 2011;20(2):154-160 8. Dysphagia 2009;24(4):378-386	Original articles comparing (early) enteral nutrition with parenteral nutrition. (PubMed)
9. Clinics 2011;66(12):2001-2005	Original article with focus on oral feeding. (PubMed)
10. Clin Nutr 2011;30(5)560-566	Post-operative trial of early enteral nutrition. (PubMed)
11. Head Neck Oncol 2001;3:24	Original article focusing on techniques of insertion of nasogastric feeding tubes. (PubMed)
12. Dig Endosc 2011;23(2)135-139	Original article comparing materials of feeding tubes. (PubMed)
13. Am J Clin Nutr 2010;92(5):1151-1156	Original article focusing on perioperative arginine-supplemented nutrition. (PubMed)
14. J Invest Surg 2010;23(6):309-313	Original article focusing on diets enriched with MCT and protein for enteral nutrition. (PubMed)
15. Head Neck Surgery 2013;148:64-68	Retrospective study with focus on feeding tube and tracheotomy dependence. (PubMed)

16. Supportive Care in Cancer 2012;20(9):2111-2120	Prospective study which considers as intervention a dietitian-led clinic.(EMBASE)
17. World J of Surgical Oncology 2012;10:136	Meta-analysis with immunonutrition and focus on hospital costs. (EMBASE)
18. Supportive Care in Cancer 2011;19(8):1175-1182	Cross-sectional study designed to develop and validate a quality-of-life questionnaire. (EMBASE)
19. Nutrition in Clinical Practice 2009;24(5):635-641	Original study which includes enteral nutrition as an intervention for all kinds of diseases, from which head and neck cancers as well as abdominal ones counted only for 3.9% of diseases. (EMBASE)
20. The New England Journal of Medicine 2011; 365(19):1781-1789	Original article that deals with severe alcoholic hepatitis.(PROQUEST)
21. Bone Marrow Transplantation 2011;46(5):733-739	Original article with focus on safety of antifungal prophylaxis. (PROQUEST)
22. J of Gastrointestinal Surgery 2011;15(5):843-852	Original articles that deal with surgical techniques. (PROQUEST)
23. Surgical Endoscopy 2011;25(8):2492-2497	
24. Surgical and Radiologic Anatomy 2012;34(1):21-29	Original article on anatomy and physiology. (PROQUEST)
25. Rev Nutr 2010;23(5):715-730	Randomized clinical trial in children and adolescents with oral supplementation. (LILACS)
26. Langenbecks Arch Surg 2012;397(5):737-744	Retrospective study comparing parenteral versus enteral nutrition. (BVS)
27. Int J Radiat Oncol Biol Phys 2012;83(1):e87-92	Original article with focus on radiation therapy. (BVS)
28. Arch Surg 2009;144(10):950-956	Original article focusing on pancreatic surgery. (BVS)
29. British Journal of Surgery	Randomized Clinical Trial which

2012;99(3):346-355	considers as intervention an omega-3 enriched enteral nutrition. (Web of Science)
30. European Surgical Research 2012;48(2):79-84	Randomized Clinical Trial comparing parenteral versus enteral nutrition. (Web of Science)
31. European Review for Medical and Pharmacological Sciences 2010;14(11):941-945	Randomized Clinical Trial comparing different doses of arginine. (Web of Science)
32. Journal of Clinical Nursing 2011;20(5/6):802-810	Cross-sectional article on reasons patients refuse to use PEG or PEJ. (CINAHL)
33. Nursing Standard 2012;26(39):41-46	An overview of enteral nutrition methods of enteral feeding. (CINAHL)
34. Journal of Clinical Nursing 2010;19(19/20):2897-906	Qualitative study on nursing directors' experiences with PEG. (CINAHL)
35. Journal of Human Nutrition & Dietetics 2010;23(4):408-415	Retrospective case note review focusing on motor neurone disease. (CINAHL)

Table 2. Methodological quality of the prospective studies included in the Systematic Review, assessed by the Newcastle-Ottawa Scale for Case-Control and Cohort Studies and by a Brazilian Guideline of Medicine Based on Evidence (n=7)

Reference	**Methodological Quality**
Journal of Medical Imaging and Radiation Oncology 2009;53:494-499	Moderate
British Journal of Oral and Maxillofacial Surgery 2012;50:601-605	Good
Journal of Human Nutrition and Dietetics 2010;23:277-284	Good
Support Care Cancer 2010;18:837-845	Good
Head Neck 2009;31:867-876	Good
British Journal of Cancer, 2004;91(3):447-452	Good
Journal of Pain and Palliative Care Pharmacotherapy 2012;26:226-232	Good

Table 3. Nutritional intervention outcomes in patients with head and neck cancer (n=2)

Reference	Patients	Follow up	Study Design	Outcomes
British Journal of Cancer 2004; 91(3):447-452	60 patients Nutrition Intervention (NI): 29 Usual care (UC): 31 88% HNC 12% GIC	12 weeks	Prospective randomized controlled trial	Weight changes after 12 weeks = NI: -0.4 kg* UC: - 4.7 kg* No differences in free fat mass between groups. NI group showed smaller deterioration in nutritional status score evaluated by Self-Generated Subjective Global Assessment (p=0.02). NI group showed smaller decrease and faster recovery in global Quality of Life (p=0.009) and in physical function (p=0.012). Note: Nutritional intervention comprehended nutritional counseling and OS for up to 3 months, though authors don't leave clear how many patients received OS.
Supportive Care Cancer 2010;18:837-845	66 patients Intervention Group (IG): 33 Control Group (CG): 33	6 months	Retrospective study	Weight changes in 6 months: IG = -2.35 ± 8.15 kg CG = -9.55 ± 8.10 kg (p=0.0077) There were no differences in the percentage of patients who completed treatment for grades 3 to 4 mucositis. RT break for more than 5 days due to toxicity: IG = 30.3% CG = 63.3% (p<0.01) Unplanned hospital admissions: IG = 16.1%

			CG = 41.4% ($p<0.05$) Median length of enteral nutrition = 100 days (14-586). 2 patients continued until death; 5 remained at month 6 (4 in use of PEG and 1 in use of NGT). There was found a linear correlation between weight loss and days of radiation treatment delayed for toxicity ($r=-0.35$, $p<0.01$). Note: intervention group included nutritional counseling for adequate nutritional status, with or without OS or EN, according to nutrient intake and/or weight loss. At week 4, 36.6% of patients needed EN, whereas at the end of CRT, 60.6% (n=20, from which 16 NGT and 4 PEG).

OR: PEG = Percutaneous Endoscopic Gastrostomy tube, NGT = NasoGastric Tube, HNC = Head and Neck Cancer, GIC = Gastrointestinal Cancer, RT = Radiotherapy, OS = Oral Supplements, EN = Enteral Nutrition, CRT = Chemoradiation Therapy.

Table 4. Enteral nutrition outcomes in patients with head and neck cancer – data extracted from prospective articles (n=3)

Reference Nº	Patients	Follow up	Study Design	Outcomes
Head Neck 2009; 31:867-876	105 patients 32 PEG 73 NGT	6 weeks after treatment 6 months	Prospective study	Weight changes after 6 weeks – PEG: + 0.8 kg* NGT: - 3.7 kg* At 6 months: no differences on weight, dysphagia grade or performance status, but weight loss from tube insertion: PEG = 1.0 kg* and NGT = 4.3 kg* No differences between groups in circumferences, skin folds, gastrointestinal symptoms and nutritional requirements. Self assessed general physical condition and overall Quality of Life scores were similar between groups at 6 weeks, but not 6 months. Median duration of use: PEG = 146 days (55-617)* NGT = 57 days (5-396)* PEG-associated costs were almost 10 times NGT ones.
Journal of Medical Imaging and Radiation Oncology	Patients of this study were included in the sample of the previous one, published in Head and Neck, 2009. For this reason, only the previous study was considered for the purposes of the present review. Authors claim as a reason to choose a prospective design than a randomized controlled one, the fact that patient population refused to allow the randomization process to determine their type of feeding tube.			

2008;52:503-510				
J Pain Palliat Care Pharmacother 2012;26:226-232	94 patients 50 PEG 44 NGT	6 weeks after tube insertion	Prospective randomized controlled study	Weight changes: PEG = -1.88 ± 0.59 kg* NGT = -6.68 ± 0.88 kg * PEG: better performance in terms of Hemoglobin (mean differences from the beginning of the study: PEG = -1.23% and NGT = -6.51%) and Mid Arm Circumference (mean differences: PEG = -3.79% and NGT = -8.07%)*. Local site infection: PEG = 4%* NGT = 64%* Tube dislodgement: PEG = none* NGT = 36%* Patients satisfaction (in terms of scores of pain, difficulty in learning to use the tube, inconvenience, uncomfortable feeds, altered body image, effect on family life and interference with social activities): PEG = 100% of patients scored 1 to 2* NGT = 100% of patients scored 3 to 4* Scores: 1 = not at all, 2 = a little, 3 = quite a bit, 4 = very much

OR: PEG = Percutaneous Endoscopic Gastrostomy tube, NGT = NasoGastric Tube

* $p<0.001$

Table 5. Enteral nutrition outcomes in patients with head and neck cancer – data extracted from retrospective articles (n=3)

Reference Nº	**Patients**	**Follow up**	**Outcomes**
J Medical Imaging and Radiation Oncology 2009; 53:494-499	71 PEG = 7 Control = 64: 28 NGT 36 OS	6 to 7 weeks (from the beginning of the study to the final week of radiotherapy)	Median absolute weight loss and mean percentage weight loss between groups did not reach statistical significance. After adjusting for risk factors (linear regression), weight loss reached a significant difference (p=0.016): PEG lost 5.2% less weight than control group. There were no statistical differences in the Odds Ratio for hospital admission for nutritional reasons and for treatment interruptions.
J Hum Nutr Diet 2010; 23:277-284	196 patients: Induction CT:24 CCRT: 76 RT: 96 For each group OS was compared to EN	6 weeks	Prophylactic PEG lost the least amount of weight during treatment period, ranging from -4.6% to +1.4%, according to treatment modality. No values of p were available. PEG installed during treatment period showed the most weight loss, ranging from -9.4% to -4.3%, according to treatment modality. There were no significant differences between methods of enteral feeding. There was found no relationship between final weight and disease stage or treatment interruptions.

British Journal of Oral and Maxillofacial Surgery 2012;50:601-605	144 patients 120 PEG, from which 5 pre-operatory and 115 intra-operatory 24 NGT	Not clear	Mean duration of use: PEG = 212 days (27-733) to the date of actual removal. NGT = 13 days (5-63) Complications: PEG = 18% (2% from major complications and 16% for minor ones). No major complications were found in the 5 patients who received PEG pre-surgery. NGT = 8% of major complications. No numeric data on minor complications were available. Mean of tubes per patient = 1.9 (1-5).

OR: PEG = Percutaneous Endoscopic Gastrostomy tube, NGT = NasoGastric Tube, OS = Oral Supplements, CT = Chemotherapy, CCRT = Chemoradiation Therapy, RT = radiotherapy.

* $p<0.001$

4 ARTIGO ORIGINAL

Planificación funcional de una unidad de nutrición enteral de un hospital de Brasil, para la atención en el domicilio del paciente – Salomon ALR, Novaes MRCG. Nutr Hosp 2013, 28(6):2027-2032

4 ARTIGO ORIGINAL

PLANIFICACIÓN FUNCIONAL DE UNA UNIDAD DE NUTRICIÓN ENTERAL DE UN HOSPITAL DE BRASIL, PARA LA ATENCIÓN EN EL DOMICILIO DEL PACIENTE.

Resumen

Introducción: Con el objeto de garantizar la calidad del producto ofrecido a los clientes en sus domicilios, las unidades hospitalarias necesitan adecuar sus áreas físicas para poder desarrollar todas las actividades especializadas que conlleva la nutrición enteral.

Objetivo: Proporcionar una planificación funcional y las herramientas para la reorganización del espacio físico de una unidad de nutrición enteral, describiendo el proceso de preparación, la descripción de sus características y funciones laborales.

Métodos. Estudio descriptivo, retrospectivo y documental, proporcionando las herramientas para la planificación funcional y de gestión de calidad en una unidad de preparación de la nutrición enteral en un hospital público del Distrito Federal, Brasil. Los datos fueron recolectados en el período comprendido entre los años 2000 y 2010.

Resultados. A través de la creación de un programa de nutrición enteral en el Departamento de Salud Pública del Distrito Federal y según lo dispuesto por la legislación nacional, se efectuó un plan de alta complejidad respecto de la nutrición enteral en atención al perfil demográfico y epidemiológico de la población. Este trabajo consiste en una propuesta de implementación de terapia nutricional dentro de un plan de alta complejidad, y de acuerdo a lo prescrito por la legislación del Ministerio de Salud Brasileño. El número de pacientes atendidos por esta modalidad terapéutica se ha ido incrementando, por consiguiente se hace necesario garantizar la calidad del servicio, por medio de la organización de los espacios funcionales.

Conclusión. Por medio de la planificación funcional de un Laboratorio de Nutrición Enteral, se puede garantizar la asistencia nutricional especializada y de calidad, a la población hospitalaria o domiciliaria, tomando las precauciones necesarias en la manipulación de las fórmulas enterales.

Palabras clave: Consejos de planificación en salud, nutrición enteral, asistencia médica, servicios de atención de salud a domicilio.

THE FUNCTIONAL PLANNING OF A ENTERAL NUTRITION UNIT FOR HOME CARE AT A HOSPITAL IN BRAZIL

Abstract

Introduction: In order to warrant the quality of the products offered to their clients at home, hospitalar units need to adequate their physical structures to develop their specialized activities on enteral nutrition.

Objective. The present article aims to provide a functional planning and tools for the reorganization of the physical space of an enteral nutrition preparation unit describing its features and function.

Methods. A descriptive, prospective and documental study was undertaken, providing the tools for the functional planning and quality management at a unit of enteral nutrition preparation in a public hospital in the Federal District, Brazil. Data were collected in the period from 2000 to 2010.

Results. Through the establishment of a Home Enteral Nutrition Program in the Public Health Department of the Federal District and as determined by the publication of national legislation, a District Plan of High Complexity in Enteral Nutrition was conducted, according to the demographic and epidemiological profile of the population.This plan consisted of the proposal for implementation of the high complexity in nutritional therapy, according to the Health Ministry legislation. The number of patients assisted by this therapeutical modality has increased, which indicates the need to ensure the quality of dispensed formulas through the planning of functional spaces.

Conclusion. The functional planning of an Enteral Nutrition Laboratory ensures assistance for the needs of the population enrolled at the hospital and at home, allowing the proper training of caregivers aiming at the adequacy of necessary precautions in manipulating enteral formulas.

Key words. Health planning counsils, enteral nutrition, medical assistance, home care services.

Introducción

Para garantizar la calidad del producto ofrecido a sus clientes, las empresas prestadoras de servicios, incluyendo las unidades hospitalarias, necesitan adecuar las áreas físicas para desarrollar sus atividades[1]. En el caso de servicios de alta complejidad como la Terapia de Nutrición Hospitalaria (TNE) en Brasil[2], la legislación sanitaria establece las condiciones mínimas estructurales para resguardar la calidad y seguridad de los productos ofrecidos[3].

La planificación funcional permite la adecuación de los espacios físicos, asegurando incluso la flexibilidad y adaptabilidad a nuevas demandas, en conformidad con la capacidad económica de los gestores en salud y la disponibilidad espacial para la implementación de tales adecuaciones[1].

La nutrición enteral es una modalidad terapéutica aplicada a los pacientes que sufren enfermedades que los imposibilitan de recibir alimentos por la vía oral o de satisfacer sus necesidades nutricionales por esta vía. Para evitar o minimizar los efectos deletéreos de la desnutrición, esos pacientes consumen los alimentos a través de sondas naso gástricas o entéricas, o aún de estomias (gastrostomias o jejunostomias) en localizaciones específicas del sistema digestivo[4,5]. En Brasil, se incluyen también las fórmulas especializadas químicamente definidas, administradas por la vía oral para la mantención o recuperación del estado nutricional[3].

Para los pacientes en Nutrición Enteral (NE) dados de alta hospitalaria y que requieren seguir con el tratamiento de nutrición enteral en su domicilio,la manipulación de la dieta artesanal se vuelve una tarea difícil sin el apoyo logístico y técnico del equipo de la institución, pues el uso de dietas artesanales en sondas de calibre inadecuado o muy delgado pueden ocasionar la obstrucción de las sondas, haciendo que el paciente abandone el tratamiento y empeore su pronóstico clínico y nutricional[4].

Se observó que un laboratorio de nutrición enteral de un hospital público de Brasilia, presentó señales de desgaste asociadas al aumento en la demanda de nutrición enteral hospitalaria y domiciliaria, requiriendo de mejorías en el espacio físico para asegurar la calidad de los servicios prestados.

Fue publicado, en Brasil, por la Agencia Nacional de Fiscalización Sanitaria, en el año de 1999 y revisado en 2000, el primer reglamento técnico para el funcionamiento de la NE[3,6], que constituye en la definición de la estructura mínima para la terapia de nutrición enteral para que esta sea viable en los hospitales, garantizando la seguridad

microbiológica de las fórmulas que se le proporcionan a los pacientes. En 2004 fue publicado por el sistema de salud público del Gobierno de Brasilia, Distrito Federal (SES-DF), el primer reglamento técnico para el suministrode la nutrición enteral domiciliaria (NED), lo que beneficiaa todos los pacientes atendidos por el Sistema Único de Salud (SUS) en Distrito Federal, Brasil[7,8].Este reglamento visa garantizar la continuidad del fornecimiento de las fórmulas enterales industrializadas después del alta hospitalaria, siendo totalmente pago por el Gobierno de Brasilia, Distrito Federal, Brasil. En el año 2005, el Ministerio de la Salud Brasileño incluyó los procedimientos de nutrición enteral de Alta Complejidad[2], con el objetivo del pago de los presupuestos de los procedimientos relativos a la terapia de nutrición enteral. Eso exigió la planificación de los espacios hospitalarios para atender las nuevas exigencias de la legislación nacional y el aumento en las atenciones de los pacientes con indicación de nutrición enteral[9,10].

El Hospital Regional de Asa Norte (HRAN) pertenece la Secretaria de Salud de Distrito Federal, que es constituida de 16 (dieciséis) hospitales públicos en Brasilia, Distrito Federal, y atiende a una demanda estimada de 10.706 pacientes para hospitalizaciones/año (año base 2012). HRAN es un hospital terciario, general y público que pertenece a la Secretaria de Salud de Distrito Federal (SES/DF), del Gobierno de Brasilia, objeto de este trabajo. La demanda mensual del Hospital HRAN se estima en cerca de 893 pacientes, con 359 lechos en las especialidades de emergencia adulto e infantil, clínica médica, pediatría, cirugía general, terapia intensiva adulta y neonatal, ginecología y obstetricia, quemados y cirugía plástica[11,12].

El objetivo de este trabajo es presentar el desempeño de una planificación funcional como herramienta de organización en los espacios físicos de una unidad de preparación de nutrición enteral para la atención hospitalaria y domiciliaria de un hospital general y público de Brasilia, Brasil.

Métodos

Este estudio es retrospectivo, descriptivo de la situación de la NE en el HRAN, y presenta una propuesta de Unidad de NE para solucionar mejor los problemas derivados del incremento del número de pacientes con NE a los pacientes que tiene que atender el hospital. Fueron aplicadas herramientas para la planificación funcional conteniendo elementos vinculados a la gestión de calidad en una unidad de preparación de nutrición

enteral que efectúa la atención hospitalaria y domiciliaria en un hospital terciario, público y general de Brasilia.

Los métodos para planificación funcional incluyeron: a) el planeamiento organizacional para atendimiento de la misión institucional en terapia de nutrición enteral en acuerdo al Plano de Alta Complexidad de Distrito Federal, Brasil; b) el diagnóstico situacional de las condiciones físicas que garanticen la seguridad microbiológica de las fórmulas producidas en conformidad a las normas técnicas presentadas en la Resolución RDC 63 (2000); c) la implementación de las adecuaciones estructurales; d) el control del proceso por medio de evaluaciones microbiológicas periódicas de las fórmulas; e) establecimiento de un plan de acciones correctivas mediante los desvíos en la producción de la nutrición enteral.

El desarrollo de la planificación funcional del LNE de HRAN siguió el modelo recomendado por Udobro[1], basado en procesos y flujos que garantizan la circulación (material y personal) libre de contaminación, con controles de acceso y presencia (Figura 1).

Los datos fueron recolectados en el período de 2000 hasta 2009 y analizados en un sistema informático.

Resultados

Los aspectos organizativos de la nutrición enteral en la institución

Si realiza la prescripción de la fórmula de NE a los pacientes durante el período de hospitalización y en domicilio después de alta hospitalaria por medio de informes médico, nutricional y social para la continuidad en la asistencia integral y gratuita por el equipo de terapia nutricional. El paciente en domicilio recibe el entrenamiento para la continuidad de los procedimientos de Nutrición enteral en domicilio.

Diagnóstico epidemiológico de los pacientes en terapia nutricional enteral en el Hospital Regional de Asa Norte (HRAN)

Conforme presentado en las Figuras 2 y 3, en el período de 2000 a 2009 las atenciones constituidas por niños (45.9%), adultos jóvenes (19.2%) y adultos mayores (34.9%), se mantiene el perfil epidemiológico. El número de óbito en Brasilia, en lo mismo período, correspondió a las enfermedades del aparato circulatorio, neurológicas, accidentes vasculares cerebrales y cáncer[13], lo que conllevó a un aumento del consumo

de nutrición enteral domiciliaria, lo que sugiere la necesidad de una planificación funcional de la unidad para atender al aumento en la utilización en pacientes.

Implementación de las alteraciones estructurales -Planificación funcional acorde a la estrategia de la institución

Un diseño organizativo depende de la orientación estratégica para el alcance de la misión institucional: (1) satisfacer las demandas directas de la población que surgen de la organización de los servicios básicos; (2) satisfacer la demanda epidemiológica de la población (Figura 1); (3) satisfacer la demanda de nutrición enteral en la institución (Figura 2); (4) incorporar las posibles adaptaciones a la evolución en el tiempo considerando la comparación de los investimentos en nutrición enteral hospitalaria y domiciliaria, siendo que la primera fue cerca de 2,65 veces superior a la segunda, presentando resultados estadísticamente significativos[4].

El esquema básico del proceso de gestión fue adoptado en la secuencia: (1) identificación de la estrategia, (2) Fijación y priorización de los objetivos, (3) Desarrollo e implementación del modelo organizativo, (4) Establecimiento del sistema de control, (5) Evaluación.

En la evaluación del proceso de planificación funcional se debe considerar la propuesta en términos de espacios, ordenación de los mismos en el ámbito espacial, enlaces, interrelaciones y calidades. Por esto, es importante que el plan funcional no se considere un documento acabado cuando se termina su redacción y se entrega para su transformación en un proyecto, sino que en este momento se evalúe el seguimiento de su aplicabilidad y funcionalidad.

La evaluación fue desarrollada en términos de (1) criterios organizativos (misión institucional), (2) plan de acción, (3) diagnóstico situacional (estructura, procesos, resultados), (3) dimensión y elementos de la planificación funcional, (4) funcionalidad de la propuesta, en conformidad a los criterios establecidos en la legislación sanitaria nacional[3]. Después de la evaluación, en el año de 2010, fueron concluidas las modificaciones estructurales en el local de manipulación de la NE en el Hospital HRAN, local en que si pasó este estudio.

Propuesta de diseño para la Unidad de Nutrición Enteral

Espacios físicos planeados para la Unidad de Nutrición Enteral

El espacio físico de la Unidad de Nutrición Enteral es el elemento básico de la planificación funcional. De la superficie destinada a cada uso se siguen las condiciones de habitabilidad y funcionalidad. El dimensionado previsto y sus características dependen de la ordenación prevista de los flujos internos y circulaciones; las calidades de ambiente deseables; la función básica en se tratando de una área muy técnica y específica.

A continuación se relacionan las condiciones básicas, en el rango de mínimos de los espacios más relevantes de una instalación para la unidad de preparación de nutrición enteral para la atención hospitalario y domiciliario. Estos fueran adecuados a las normas técnicas brasileñas de la Agencia Nacional de Vigilancia Sanitaria (ANVISA), presentadas en la Norma Técnica RDC/ANVISA 63[3], de un Laboratorio de Nutrición Enteral (LNE):

1. Área de Almacenamiento – El área puede ser compartida con otras áreas de la unidad hospitalaria. Para mejorar el control ambiental de la temperatura fue instalado un termómetro y un sensor para el control de la humedad, evitándose también la exposición directa a la luz del sol de las formulaciones de NE, insumos y envases. Además el área de almacenamiento debe recibir los insumos y materiales de NE reprobados o devueltos, para una evaluación correctiva posterior.

2. Área de Recepción de Prescripciones y Dispensa de la Nutrición Enteral (NE) – el área puede ser compartida con otras áreas de la unidad hospitalaria. La evaluación de las prescripciones es documentada en esta área por el Equipo Multidisciplinario de Terapia Nutricional (EMTN), donde están los farmacéuticos, nutricionistas y nutriólogos, médicos de distintas especialidades y enfermeros.

3. Área de Limpieza y Sanitización de los Insumos para la manipulación de la nutrición enteral - el área está integrada con otras áreas de la unidad hospitalaria. Posee un área exclusiva para la entrada de los insumos higienizados, incluyendo el local para la limpieza de los materiales e equipamientos para la limpieza de los envase de los insumos.

4. Área de Sanitización de los funcionarios y vestimentas– Se constituye con una barrera entre el Área de Limpieza y Sanitización de los Insumos y el Área de Manipulación y Envase de NE, siendo la única entrada para la sala de manipulación. Se destina una instalación especial para la manipulación de las fórmulas y lavado de las manos.

5. Área para la preparación de alimentos "in natura" – se trata- de un área importante cuando se utiliza la nutrición enteral artesanal, para la limpieza de los alimentos ‘’in natura’’, evitándose la contaminación microbiológica en la manipulación de la nutrición enteral. En HRAN esta área actualmente es inexistente por no utilizar alimentos "in natura".

6. Área para Manipulación y Envase de NE –Área cerrada, libre del acceso y circulación de personas y materiales no sanitizados. Dispone de local para la limpieza de los materiales de apoyo para la manipulación de las formulaciones, entrada para los insumos y salida para las fórmulas manipuladas y envasadas, ambas independientes. En esta área es vedada la existencia de desagües. Él agua utilizada debe ser potable y exenta de bacterias. Todos los utensilios y equipos (calefactores, heladera, microondas y *freezer*) deben permitir la fácil higienización. En esta área es posible observar y entrenar a los manipuladores y al equipo de trabajo, pues se permite la visualización de todos los procedimientos que se realizan en el proceso de manipulación debido a la presencia de ventanas de vidrios en las paredes de la sala. Dentro de esta área hay un espacio independiente reservado para el equipo, reduciendo al mínimo el riesgo de contaminación.

7. Sanitarios de los funcionarios (masculino y femenino) – Esta área tiene acceso independiente del área de manipulación y de almacenamiento, que fueron adecuadas después de la planificación funcional.

8. Área para el almacenamiento de material de limpieza – área destinada a guardar los materiales de limpieza y sanitización aislados de los ambientes externos, adecuadas después de la planificación funcional.

9. Revestimiento e Iluminación del Laboratorio de Nutrición Enteral - Los materiales de revestimiento del ambiente son de colores claros, permiten la mantención de una superficie plana y con revestimiento lavable para facilitar y garantizar la higienización del local. Las tuberías de energía eléctrica y de agua son protegidas y embutidas en la pared.

En la planificación funcional de la Unidad de Nutrición Enteral para la atención domiciliaria y en alta hospitalaria se consideró también el tiempo de dedicación laboral de los técnicos, la privacidad, el número creciente de los usuarios y características del hospital. De esta forma el diseño organizativo, los flujos de trabajo, el apoyo logístico, considerando los presupuestos y los espacios disponibles en la institución para la planificación de la Unidad de Nutrición Enteral, fueron planeados con una orientación estratégica. Todos los procedimientos realizados en el laboratorio de nutrición enteral - LNE fueran empadronados y registrados en formularios específicos. La planta física del laboratorio de nutrición enteral esta presentada en la Figura 4.

Discussion e Consideraciones Finales

Despues de la implantación de la planificación funcional fue mantenida la manutención de la área adecuada y la licenza sanitaria de funcionamento del Laboratório de Nutricion Enteral de HRAN por la Agencia Nacional de Vigilância Santinária de Distrito Federal, Brasil, conforme descrito previamente por Haack el al[14]. No fueran registrados casos de infeccion hospitalaria o contaminación bacteriana debido a contaminacion de fórmulas enterales en la unidad.

Una limitación de este estudio se relaciona a escasez de estudios brasileños que permitan la comparación de la experiencia presentada con otras estrategias bien sucedidas en Brazil.

La planificación funcional posibilitó la obtención de espacios físicos dimensionados para responder a la misión de preparación de la nutrición enteral. La adecuación de las áreas de manipulación de la nutrición enteral en las unidades hospitalarias, obtenidas a través de la planificación funcional, fue de gran importancia para garantizar la calidad y la demanda de los productos ofrecidos a los pacientes, que se encuentran muchas veces con problemas graves de salud y expuestos a menudo a infecciones que conllevan al agravamiento de su estado clínico y nutricional.

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Figuras

Figura 1. Utilización de nutrición enteral domiciliaria x enfermedades prevalentes en HRAN, Secretaria de Salud de Brasilia, Distrito Federal, Brasilia, Brasil. Período de 2000 -2005 [5].

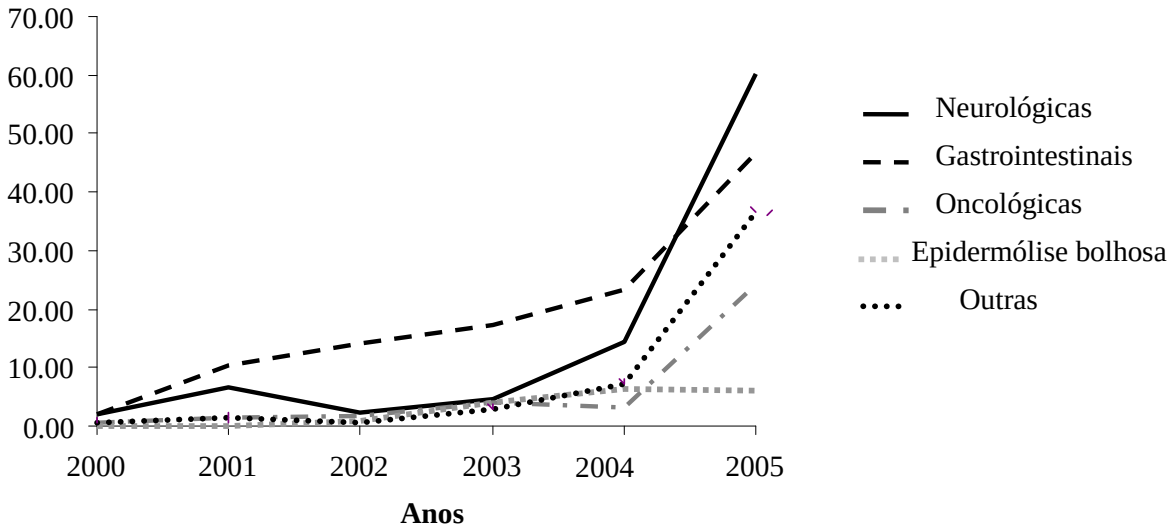


Figura 2. Utilización de nutrición enteral domiciliaria en HRAN, Secretaria de Salud de Brasilia, Distrito Federal, Brasilia, Brasil. Período de 2000 - 2009.

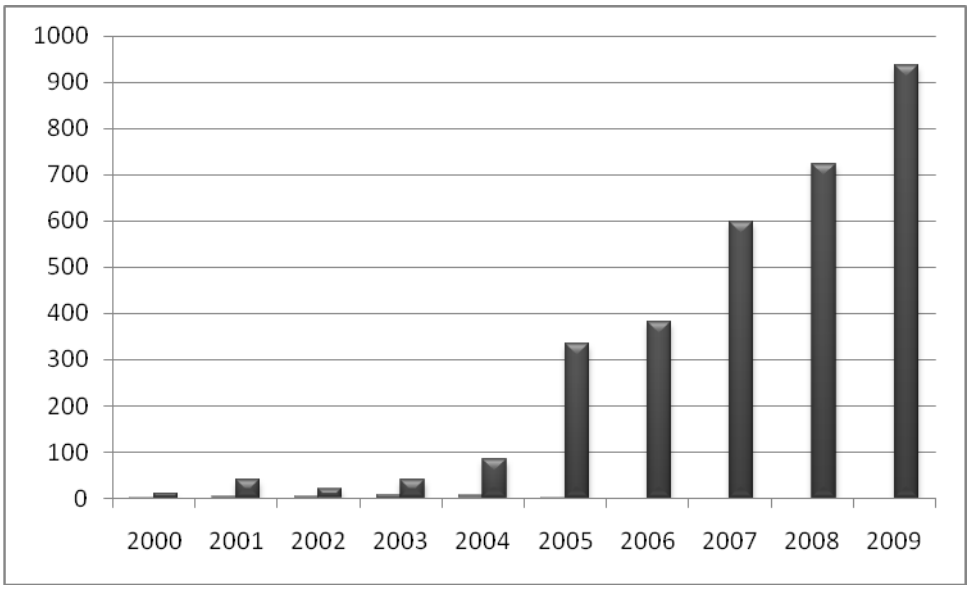


Figura 3. Etapas da planificación funcional del Laboratorio de Nutrición Enteral del Hospital Regional da Asa Norte – HRAN, Brasilia, Brasil.

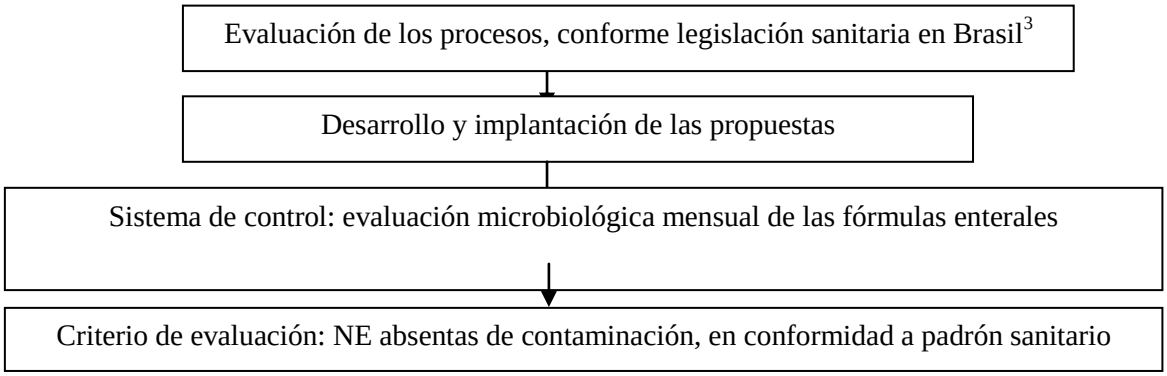
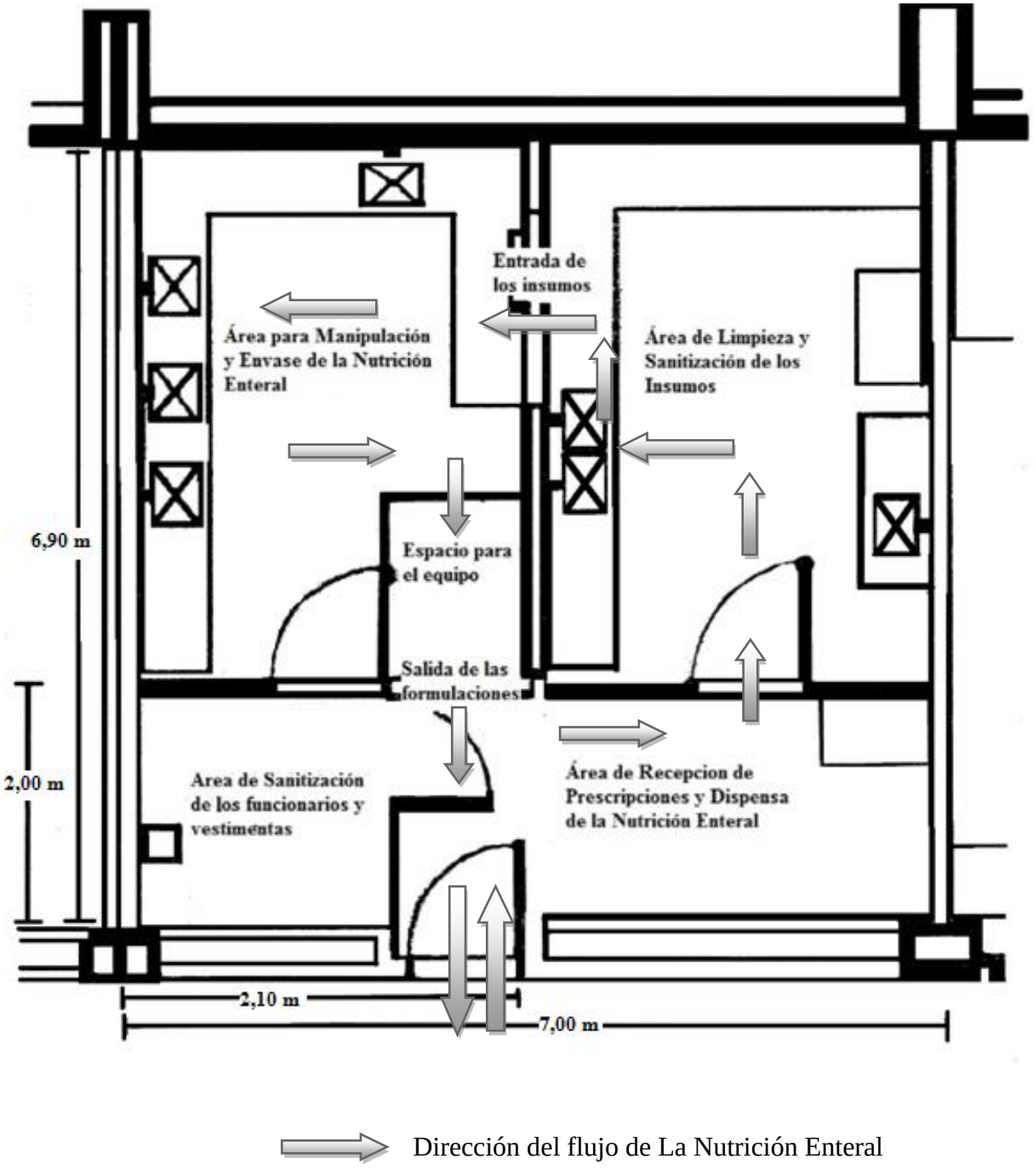


Figura 4. Planta física del Laboratorio de Nutrición Enteral del Hospital Regional da Asa Norte – HRAN, Brasilia, Brasil.



5 ARTIGO ORIGINAL

Does socioeconomic status influence survival for patients with neurological impairment and cancer in home enteral nutrition? A Brazilian study – Salomon ALr, Novaes MRC. Submetido ao periódico ***Health Economics***

5 ARTIGO ORIGINAL

DOES SOCIOECONOMIC STATUS INFLUENCE SURVIVAL FOR PATIENTS WITH NEUROLOGICAL IMPAIRMENT AND CANCER IN HOME ENTERAL NUTRITION? A BRAZILIAN STUDY

Abstract

The main leading causes of home enteral nutrition are neurological diseases and cancer. The aim of the present study was to assess clinical and nutritional evolution of patients diagnosed with neurological impairment and head and neck and gastrointestinal cancers in home enteral nutrition therapy in the Federal District of Brazil, according to their socioeconomic status. This was a prospective, observational and comparative study, with two groups of patients constituted from the Human Development Index, classified as medium or high. Nutritional evolution was assessed through body weight changes in a 1-year follow-up. Clinical evolution was assessed through a scoring system in a 1-year follow-up, and also through survival analysis during the 35 months of the research (from January 2010 to December 2012). An amount of 247 patients were selected for the present study. 164 were demented patients and 83 were patients with head and neck or gastrointestinal cancers. 144 patients lived in a region considered to be of high socioeconomic level. Patients with diagnosis of neurological impairment had a mean age of 74.87 ± 13.38 years and there was a higher frequency of women in this group of disease. In the cancer group, mean age was of 58.8 ± 11.2 years and males were predominant. For the group of patients with neurological impairment, socioeconomic status was positively associated with survival. For the group of patients with gastrointestinal or head and neck cancers, a medium socioeconomic status was associated to a higher weight loss, but also to an improvement on clinical scores.

Key words: home care services, enteral nutrition, socioeconomic status, dementia, cancer, outcomes.

Introduction

Home Enteral Nutrition (HEN) is applied to patients who have no indication for remaining hospitalized exclusively to maintain nutritional therapy (1, 2). International studies demonstrate that the main indications for HEN are neurological diseases and cancer (3-5), data that are in accordance to a study conducted in Brazil (6).

The prevalence of dementia among Brazilian elders (people over 60 years old) who live in the community, reaches levels of 7,1% and the main responsible for these cases is Alzheimer's disease (AD), which responds for 55% of them (7). The disease prevalence increases exponentially with aging from 1% at 60-65 years to 30-35% aged 80 or more(8). Dementia also represents an important cause of death in the United States of America(9). In Brazil, the leading cause of death is cardiovascular diseases, from which Cerebrovascular diseases are the most prevalent. The second major cause of death is cancer (10, 11).

Malnutrition is often associated with advanced cases of neurological impairments and some types of cancer, like ones of head and neck and gastrointestinal areas, due to dysphagia secondary to these diseases or their treatment, and is associated with poorer outcomes (12-15). A Brazilian study with elderly patients in which neurological diseases were the most prevalent ones, levels of 70% of malnutrition were identified, justifying the need for nutritional intervention(16). Between 35 and 60% of HNC patients are malnourished and optimal nutritional support is vital for their post-treatment recovery (17).

Poverty tends to worsen the outcome of patients with these diseases, since the restricted access to food hinders them to get a complete nutrition. However, studies that deal with socioeconomic impact on people's health are usually conducted with pediatric population. A recent review from Cochrane Library states that there is a strong and consistent relationship between relative poverty and poor child health and well-being even among rich nations (COCHRANE). This raises a special concern towards governmental programs that deal with supplying any form of nutritional support to poor families, on behalf of deviating this support from the patient who is unable to receive oral feeding to the care of the whole family.

The objective of this study was to assess clinical and nutritional evolution, in terms of nutritional status recovery and of survival, of patients diagnosed with neurological impairment and head and neck and gastrointestinal cancers, according to

their socioeconomic status, treated with home enteral nutrition therapy in the Federal District of Brazil.

Materials and Methods

Study Design

This is a prospective, observational and comparative study with two groups of patients constituted from the Human Development Index (HDI)(18, 19). The study variables include age, gender, clinical diagnosis, nutritional status, HDI, and survival.

The research project was approved by the Ethics Committee of the Public Health Department of the Federal District of Brazil, according to Protocol number 425/2009, which was extended until 2012.

Patients

The State Health Department of the Federal District of Brazil issued in 2004 the first regulation of HEN supply, which consists on providing patients with industrialized enteral nutrition and its administration system. The costs of this program are completely funded by the government of the Federal District. Patients are admitted to the program after their hospital discharge and are followed by a multidisciplinary team, who reevaluates them every three months.

A clinical sample from patients admitted to HEN Program from January 2010 to March 2012 was selected. Patients were followed-up until December 2012. The inclusion criteria of patients comprehended adults (aged 20 to 59 years) and elders (aged 60 or up) (20) with a primary diagnosis of neurological impairment made according to validated diagnostic criteria such as ICD-10(7) or a diagnosis of cancer of head and neck or gastrointestinal areas. Data were collected in patients' records of HEN Program. A data extraction form was used which included the variables mentioned before.

Patients were followed-up for 1 year, according to the following study times: Time 0 = prior to HEN initiation, Time 1 = at three months of therapy beginning, Time 2 = at six months, Time 3 = at nine months and Time 4 = at 12 months. The whole study period was from January 2010 to December 2012, totalizing 35 months, time that was considered for survival estimates.

Nutritional Status Assessment

Nutritional diagnosis was made on basis of combination of subjective and objective methods, in order to assess clinical evolution. Subjective methods included the application of validated formularies according to age. For adults, Detsky's Subjective Global Assessment was applied (21), whereas for elders, Guigoz and Vellas' Mini Nutritional Assessment was used (22). Nutritional evolution was assessed through body weight changes at each time of the study (T0-T1-T2-T3-T4).

Clinical Assessment

This evaluation was collected from patients' records, through patients' clinical history, where their status was classified into three scores: 1 = clinical/nutritional worsening; 2 = clinical/nutritional maintenance; 3 = clinical/nutritional improvement. The diagnostics were formulated at each time of the study (T0-T1-T2-T3-T4).

Human Development Index (HDI)

In 1998, the concept of the Human Development Index (HDI) was created by Mahbub ul Haq with the cooperation of the Indian economist Amartya Sen, a Nobel prize winner. This index corresponds to a summarized measure of long term progress that involves three basic dimensions of the human being: income, education and health (19). In 2012 Brazil occupied the 85th position on the global HDI ranking. The index varies from zero to one and is classified in four categories: low –values ranging from 0 to 0.499 - medium – from 0.500 to 0.799 – high – from 0.800 to 0.899 – and very high – values equal or higher than 0.900.

In 2005, the last published edition of the Federal District data, the average Brazilian index was of 0,792, which kept Brazil among the nations of medium human development (HDI between 0.500 and 0.799). The best Brazilian index corresponds to the one of the Federal District of 0.874 (19).

For this study purposes, data on HDI calculated by each administrative region of the Federal District, Brazil, were used. HDI was divided into two categories: higher than 0.800, considered good, and lower or equal to 0.800, considered medium. Regions with a medium HDI are: Brazlândia, Planaltina, Paranoá, Ceilândia, Sambaia, Santa Maria and Recanto das Emas (18).

Survival

Survival was assessed from time of patient's admission to HEN Program until the occurrence of one of the following events: death or discharge of program due to oral rehabilitation or waiver or continuation on the Program until the end of the study.

Sample size

Calculated sample size comprised a total of 204 participants, divided in two groups: (i) high HDI (n = 102) and (ii) medium HDI (n = 102)(19), who were followed from January 2010 to December 2012, according to the datum of their admission in the Program.

Sample size was calculated on basis of an observational study that comprehended 401 patients(23) in which from patients initially diagnosed as malnourished, 5.75% presented a nutritional recovery at the end of the study and 4.10% had a worsening in their nutritional status as compared to the initial status (unpublished data). A level of significance of 5% and a power of test of 80% were considered. The software GPower version 3.0.5 was applied for this purpose.

Statistical Analysis

Data analysis included descriptive statistics – mean and standard deviation for quantitative variables and percentages for qualitative ones (gender, clinical diagnosis and clinical assessment, which were all converted into quantitative variables, by attributing a numeric category to them).

Measures of weight were observed in Times 0-1-2-3-4. Longitudinal measures inter and intra groups were tested using models of mixed-effects to repeated measures and matrix of non-structured variance and covariance, adjusting for sex and age. Main focuses on analysis were changes at 3, 6, 9 and 12 months (T1-2-3-4) compared to baseline (T0). A residual analysis was conducted to verify if residues of the model presented a Gaussian distribution with constant variance and it was verified that both suppositions of normality and of homogeneity of residues were accomplished.

Clinical assessment scores were observed on times 0-1-2-3-4. Longitudinal measures inter and intra groups were tested with the model of proportional chances with generalized estimation equations (GEE), adjusting for sex and age. Main focuses on analysis were changes at 3, 6, 9 and 12 months (T1-2-3-4) compared to baseline (T0). A level of significance of 5% was considered.

Survival functions for patients divided in two groups according to HDI were estimated by Kaplan-Meier curves and compared with the log-rank test.

The software Statistical Analysis System (SAS) version 9.2 was used for all analysis mentioned above.

Demographic differences intra-groups were assessed by the Chi-square test, with Statistical Package for Social Sciences (SPSS), version 18.0.

Results

An amount of 247 patients were selected for the present study. 164 were patients with neurological impairments (NI), which represented 56% of all patients with same diagnosis enrolled on the Program in the study period, and 83 were patients with head and neck or gastrointestinal cancers, representing 83% of all cancer patients of the Program. 144 patients lived in a level 1 HDI region. From NI patients, distribution of HDI was the following: 64.6% (n=106) corresponded to HDI 1 and 35.4% (n=58) to level 2, whereas, from cancer patients, 45.8% (n=38) lived in a level 1 HDI region and 54.2% (n=45) in a level 2. When both groups of diseases were compared in terms of HDI levels, a statistical difference was found (p=0.005).

When groups of diseases were separated in order to perform an analysis of clinical and nutritional evolution intra-group, patients with diagnosis of NI had a mean age of 74.87 ± 13.38 years and there was no statistical difference for age in terms of HDI (p=0.086). There was a higher frequency of women in this group of disease, which didn't differ in terms of HDI (HDI 1 = 63.2% and HDI 2 = 51.7% of females, p=0.153). When it comes to the cancer group, mean age was of 58.8 ± 11.2 and there was no difference of age for HDI (p=0.321). In this group of disease, males were predominant (HDI 1 = 81.6% and HDI 2 = 64.5%), without statistical differences inter-subgroups (p=0.082). The appointed facts lead to the conclusion that there were no demographic differences intra-groups which could harm the HDI comparison.

Group of patients with neurological impairments

According to World Health Organization (WHO), dementia, classified through the International Code of Diseases version 10 (7) with the codes from F00 to F03, can be defined as a syndrome due to disease of the brain, which occurs in Alzheimer disease, in cerebrovascular disease, and in other conditions primarily or secondarily affecting the brain.

In the present study, the patient population presented either a cerebrovascular disease with neurological impairment or dementia and corresponded to 66.4% of all enrolled patients, and the main diseases that were involved were cerebrovascular accidents (58.5%) and Alzheimer's disease (25.6%).

Figure 1 presents weight evolution according to HDI, for NI patients.

Both in the subgroup with HDI ≤ 0.80 as in the subgroup with HDI > 0.80 there were no significant changes in average weight at three, six, nine and 12 months compared to the baseline. There was not a significant difference inter subgroups either when the same moments were compared to baseline.

Figure 2 shows clinical evolution according to HDI status.

Both for HDI ≤ 0.80 as for HDI > 0.80 subgroups there was not a significant change of medium scores of clinical evolution at three, six, nine and 12 months compared to baseline. When one subgroup was compared to the other, there was not a statistical difference in alterations of clinical evolution in relation to baseline.

Figure 3 presents survival functions according to socioeconomic subgroups of demented patients.

From the result of log-rank test it is possible to affirm that NI patients with a higher socioeconomic status (HDI > 0.80) survive longer than the ones with HDI ≤ 0.80, with statistical significance (p=0.0176).

Group of patients with gastrointestinal or head and neck cancers

Head and neck cancer (HNC) comprises a variety of malignant tumors that can develop in the upper respiratory and digestive tracts, including cancers of the lip, oral cavity, tongue, salivary glands, pharynx, larynx, nasal cavity, ear and skull base (14). Gastrointestinal Cancer (GIC) is a term for the group of cancers that affect the digestive system. This includes cancers of the esophagus, gallbladder, liver, pancreas, stomach and bowel (the bowel includes the small intestine, large intestine or colon and rectum) (24).

In the present study, the patient population presenting gastrointestinal or head and neck cancers corresponded to 33.6% of all enrolled patients. GIC comprehended 49.4% of all cancers (n=41), whereas NHC, 50.6% (n=42). The main types of cancers that involved GIC in the present study were esophagus, with 70.7% of cases and gastric,

with 24.4%. When it comes to HNC, the main types of cancer were larynx with 33.3% of cases, lips with 16.6%, oropharynx with 12% and oral cavity with 9.5%.

Figure 4 presents weight evolution according to HDI, for patients diagnosed with cancer.

In the subgroup with HDI ≤ 0.80 there was a significant reduction of average weight at three and six months when compared to baseline and there was no significant change in months nine and 12. The subgroup with HDI > 0.80 there was no significant alterations on average weight at three, six, nine and 12 months in relation to baseline. There was no statistical difference inter subgroups concerning weight changes in the same periods compared to baseline.

Figure 5 reveals clinical evolution of patients according to their socioeconomic status, measured by HDI levels.

For HDI ≤ 0.80 subgroup there was a significant raise of clinical evolution medium score at six months in comparison to baseline. After six months of follow up patients were 3.02 times more likely to present a clinical improvement than at the study beginning. At the other months of follow-up there were no significant changes in medium score of clinical evolution. For the subgroup with HDI > 0.80, no changes were observed at three, six, nine and 12 months in relation to baseline. There was no statistical difference between subgroups when study times 1, 2, 3 and 4 were compared to baseline.

Figure 6 shows survival probabilities according to HDI subgroups for patients with GIC and HNC.

From the results of the log-rank test, it is possible to notice that survival time of patients with HDI > 0.80 did not differ significantly from the one of patients with HDI ≤ 0.80 (p=0.1228).

Discussion

When it comes to analyzing how socioeconomic status influences the outcomes for patients in home enteral nutrition, a literature search was conducted on PubMed/MEDLINE, Brazilian Health Virtual Library (BVS), Embase and PROQUEST with the use of Medical SubHeading (MeSH) Terms “enteral nutrition” AND “socioeconomic status” and no articles were found that addressed to the same assessment as the one conducted in the present study. Only articles involving pediatric

population in oral nutrition, costs of enteral nutrition procedures and perspectives of caregivers on enteral nutrition were found. Only one article addressing sepsis, as a complication of parenteral nutrition, related to socioeconomic status was retrieved, which showed no statistical differences. For this reason, no comparison was possible to be made among this study's findings and other studies' ones, except for survival, which is a theme often explored by some authors, which led to the decision to leave an apart section to discuss this outcome.

Group of patients with neurological impairements

Dementia is a complex syndrome whose frequency varies from 3% at age of 70 years old to 20% to 30% at age of 85, doubling every five years with increasing age (25). This was also observed in the present study, where a higher frequency (85.4%) of elders was observed in this group of patients, with mean age of 74.87 years and a median age of 79 years. The higher prevalence of females (59.1%) is also in accordance with other studies (9, 16). A systematic review published in Cochrane Database with seven observational controlled studies, involving a total sample of 1821 patients found a mean age of 82 years, close to the present study, and that subjects were predominantly female(13).

It is worth noticing that no differences were found between subgroups of HDI (HDI $\leq$ 0.80 and HDI > 0.80) in terms of nutritional or clinical evolution, but for survival, which will be addressed in a posterior topic. Despite this finding, 22.5% of patients of this group presented some complications, that could be related to clinical worsening, of which the main one corresponded to development of a pressure sore (24.3%), followed by supply shortage of enteral formulas (16.2%), lack of adherence to prescription (13.5%), infections (13.5%), diarrhea (5.4%), decline on kidney function (5.4%) and others. No statistical differences were found in complications incidence between HDI subgroups (p=0.845). In a thirty five- months follow-up, 20.12% of patients died.

Group of patients with gastrointestinal or head and neck cancers

As stated by some researchers, head and neck cancer incidence is higher in men, which also occurs with the most common forms of gastrointestinal cancers, that comprehend gastric and colorectal ones (26-28). In accordance to these studies, the

present one found a higher frequency of men in this group of patients (72.3%), with a median age of 57 years old.

This study found no statistical differences for either nutritional or clinical evolution for HDI > 0.80 subgroup. However, a significant association between a lower socioeconomic status (HDI ≤ 0.80) and a reduction in body weight at three and six months of follow-up. Despite this finding, a higher medium score of clinical evolution was found for the same subgroup, who also presented, after six months of treatment, a 3.02 times greater chance to present a clinical improvement. A possible explanation for that would be that patients with a higher socioeconomic level could present a more severe form of the disease. However, cancer staging was not evaluated in the present study, since this data wasn't available in patients' charts. 14.5% of all patients of this group presented complications mainly associated with the disease or with its treatment (33.3% of frequency of each). Nevertheless, the incidence of complications did not differ between subgroups (p=0.533), despite the low number of cases (n=12). No statistical differences on tumor site or route of enteral nutrition administration were found between subgroups. In the study period (35 months), 18.1% of patients of this group died.

Survival

Three studies addressing this subject were found: two dealing with elderly patients(9, 29)and one with several kinds of diseases, involving elders, adults and children(30). Two studies assessed survival with Kaplan-Meier curves and the log-rank test like the present research(9, 30). The other study used Cutler-Ederer curves(29). None of these studies dealt with socioeconomic status.

Schneider et al. worked with 417 patients from whom 380 were adults and elders. Main diagnoses for these patients were neurological disorder (38.9%), digestive disease (20%), head and neck cancer (16.8%) and dementia (14.2%). The authors found that mortality was positively associated to dementia, head and neck cancer and age higher than 70 years. They mainly assessed survival at 1month, 1 year and 5 years(30).

Martins et al. dealt with 79 elderly patients who had neurological diseases, from whom 49.4% presented dementia. They assessed mortality rates at 3, 6 and 11 months(9). Kumagai et al. worked with 261 demented patients, divided into two groups – one with percutaneous endoscopic gastrostomy (PEG) and other with nasogastric

tubes. They evaluated survival at 3, 6, 9, 12, 15, 18, 21, 24, 27 and more months but found a higher survival with PEG at 27 months(29).

In the present research, no differences were found in terms of survival probability for patients with GIC or HNC concerning socioeconomic status. However, for NI patients, a significant difference was found for patients with a higher status.

When findings of this study were compared to the ones which also used Kaplan-Meier method, a higher survival was observed for this study. When Schneider found a 1-month survival of 80%, the present study found a 2 –months survival that varied from 88% (for cancer patients) to 97.09% (NI patients with higher HDI). The first authors also found a 24-months survival of 41.70%, while the present study showed a 23-months survival of 71.68% for NI patients with higher socioeconomic levels (no data was available for cancer patients at this time). Finally, Schneider et al describe a 60-months survival of 25%. The present study didn't follow-up patients for as long as five years, but 35 months. The last available survival probability for this study was calculated for months 28 (NI patients with lower HDI) and 29 (NI patients with higher HDI) and it corresponded, respectively to 29.18% and 35.84%(30).

Martins et al. found a 3, 6 and 11-months survivals of respectively 84.80%, 77.20% and 57%. For the same period of follow-up the present study found an average of 86,81% (ranging from 74% for cancer patients with HDI 1 to 94% for the same group of patients with HDI 2) at three months, of 81.11% (ranging from 69% for cancer patients with HDI 1 to 90,35% for NI patients with the same HDI level) at six months, and of 75.56% (ranging from 65.67% for NI patients with HDI 2 to 85.45% for the same group of patients with HDI 1)(9). In the present study the highest follow-up time for cancer patients was of 16 months (survival of 55%).

The study of Kumagai et al, despite the methodological difference for survival estimates showed an approximate survival percentage at months 3, 6, 9, 15 and 21 of respectively 88%, 80%, 80%, 75% and 68%, which were lower than percentages presented by the present study, considering the same group of patients, this is NI ones, with higher socioeconomic level. For this group of patients, the following values were found for the correspondent months (except for the 21st, since this time period didn't show in the present study, which led to comparison to month 23): 91.70%, 90.35%, 87.35%, 82.60% and 71.68%. The only period in which Kumagai et al. study showed a higher survival time than the present one was the one comprehending months 27 and 30,

which presented a survival of 65.6% for the PEG group (44.4% for nasogastric one), while the present study showed a 29-months survival of 35.84%(29).

One aspect that is worth mentioning about the present study is that the subgroup of NI patients who presented the highest survival rate (HDI 1) was also the one with a higher use of PEG (59.4%), a result similar to the one found by Kumagai et al(29), that showed a significantly higher survival rate by 27 months when using PEG tube than when using a nasogastric one. Although this comparison was not an objective of the present study, it raises the concept that PEG may be beneficial for NI patients, contrary to studies that contraindicate this route of administration for these patients(31, 32). Cochrane's systematic review itself mentions that there is insufficient evidence to suggest that enteral tube feeding is beneficial in patients with advanced dementia(13), which highlights the importance of this finding.

Limitations of the present study specially relate to the fact that its sample wasn't randomized, which allows occurrence of selection bias, although the sample comprised more than 50% of all patients (NI, HNC and GIC) enrolled on the Program in the study period, and that information was collected from patients' charts, which may induce information bias and harms the complete control of some variables like cancer staging. Some authors state that a randomized design for this type of study may raise ethical conflicts, since it is not ethical to allow a group of patients to starvation for purposes of having a control group (13, 31, 33), which difficult controlling selection bias.

Considerations

In the present work, clinical evolution was assessed through a score system and also through survival analysis, while nutritional evolution, by body weight in the studied times. For the group of patients with NI, socioeconomic status was not associated either to nutritional or clinical scores evolution. However, it was positively associated with survival, which was found to be even higher than in other studies. This subgroup of NI patients with higher survival was also the one who presented an increased use of percutaneous endoscopic gastrostomy tubes.

For the group of patients with gastrointestinal or head and neck cancers, a medium socioeconomic status was associated to a higher weight loss, but also to an improvement on clinical scores. This may be due to the severity of the disease in the other subgroup of patients (higher socioeconomic status), which could not be evaluated

in the present work. No association between survival and socioeconomic status was found for this group.

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Conflict of interests

The authors declare no conflict of interests.

Authorship

ALRS has participated on the acquisition of data and the drafting the article.

MRCGN has participated on revising the article critically for important intellectual content.

Both authors have participated on the conception, design and interpretation of data, as well as on the final approval of the version to be published.

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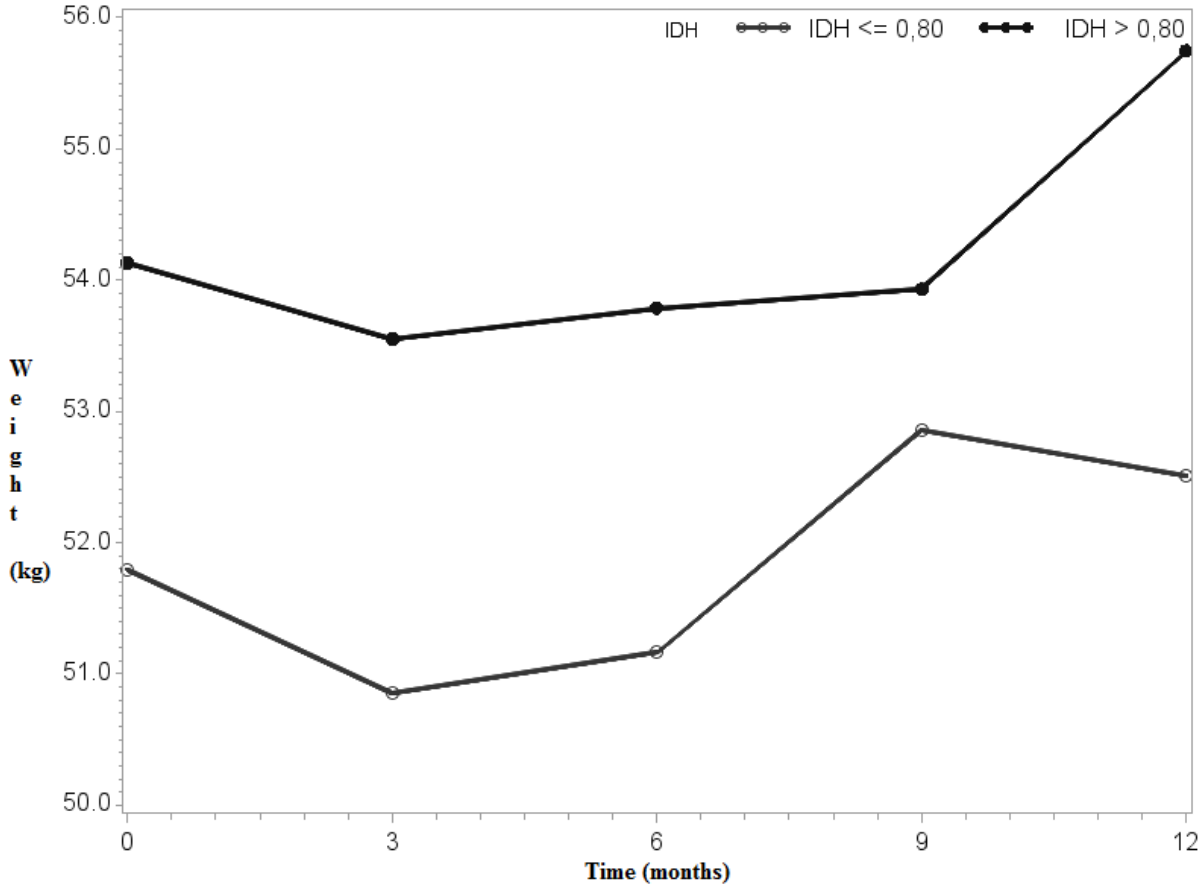

Figure 1. Weight evolution according to socioeconomic subgroups for demented patients (n=164) ($p>0.05$)

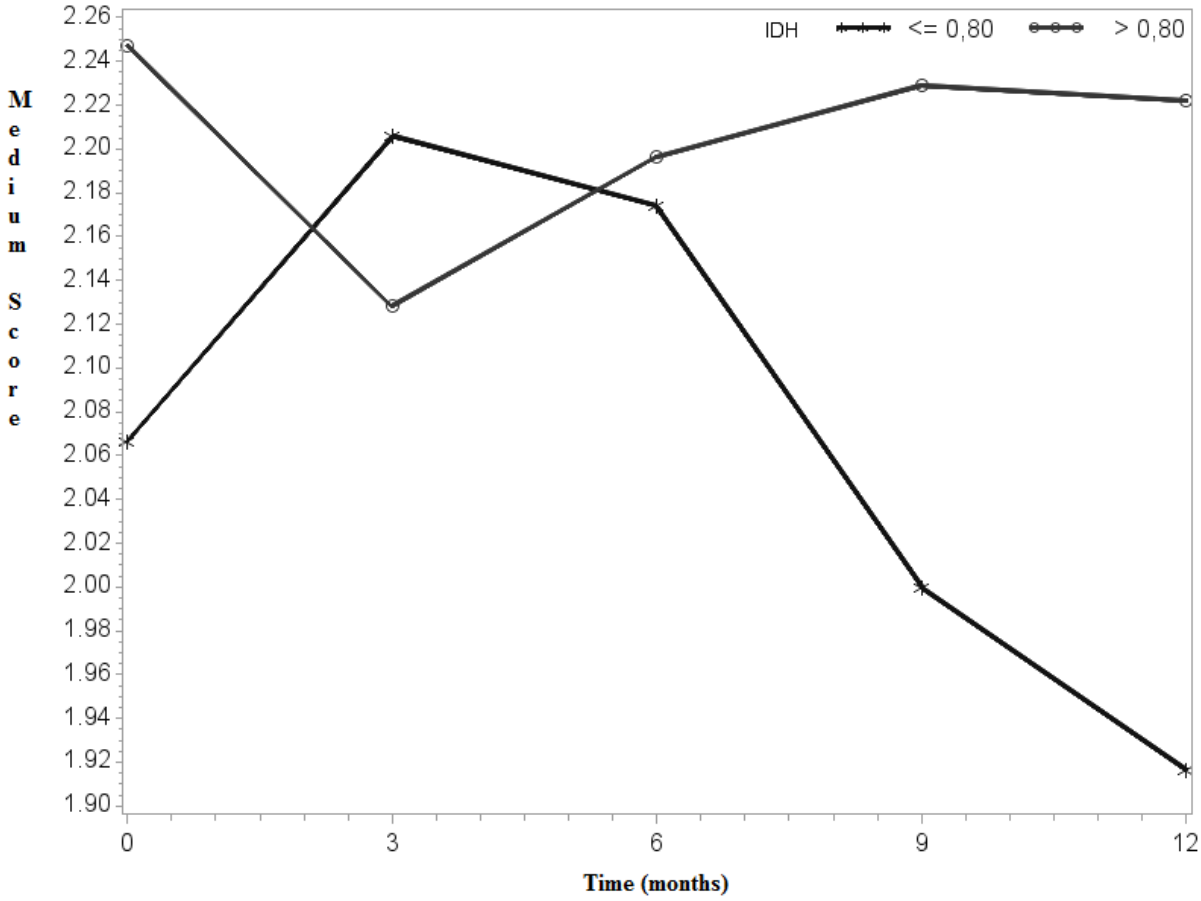

Figure 2. Clinical evolution of demented patients according to socioeconomic status (n=164) (p>0.05)

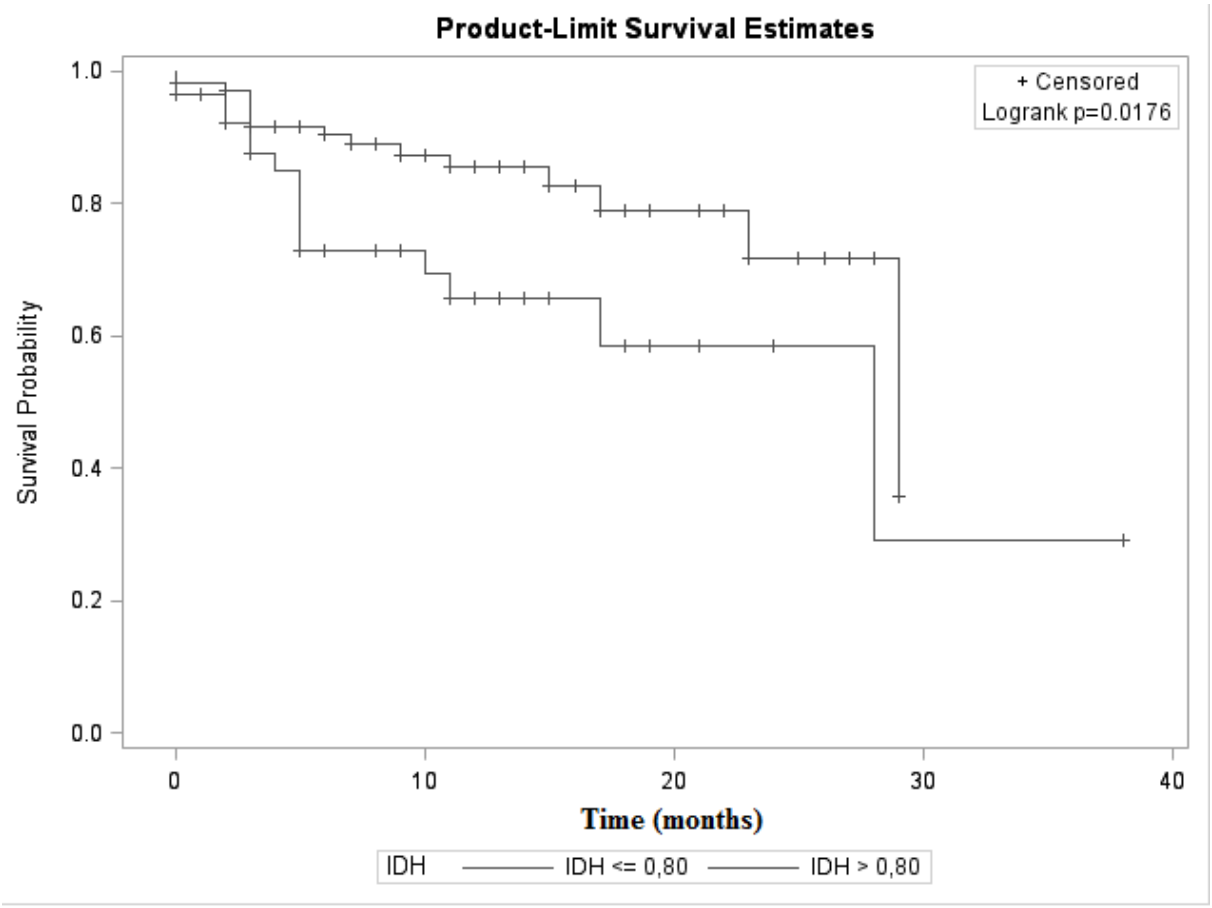

Figure 3. Survival in time, according to socioeconomic status of patients with dementia (n=164)

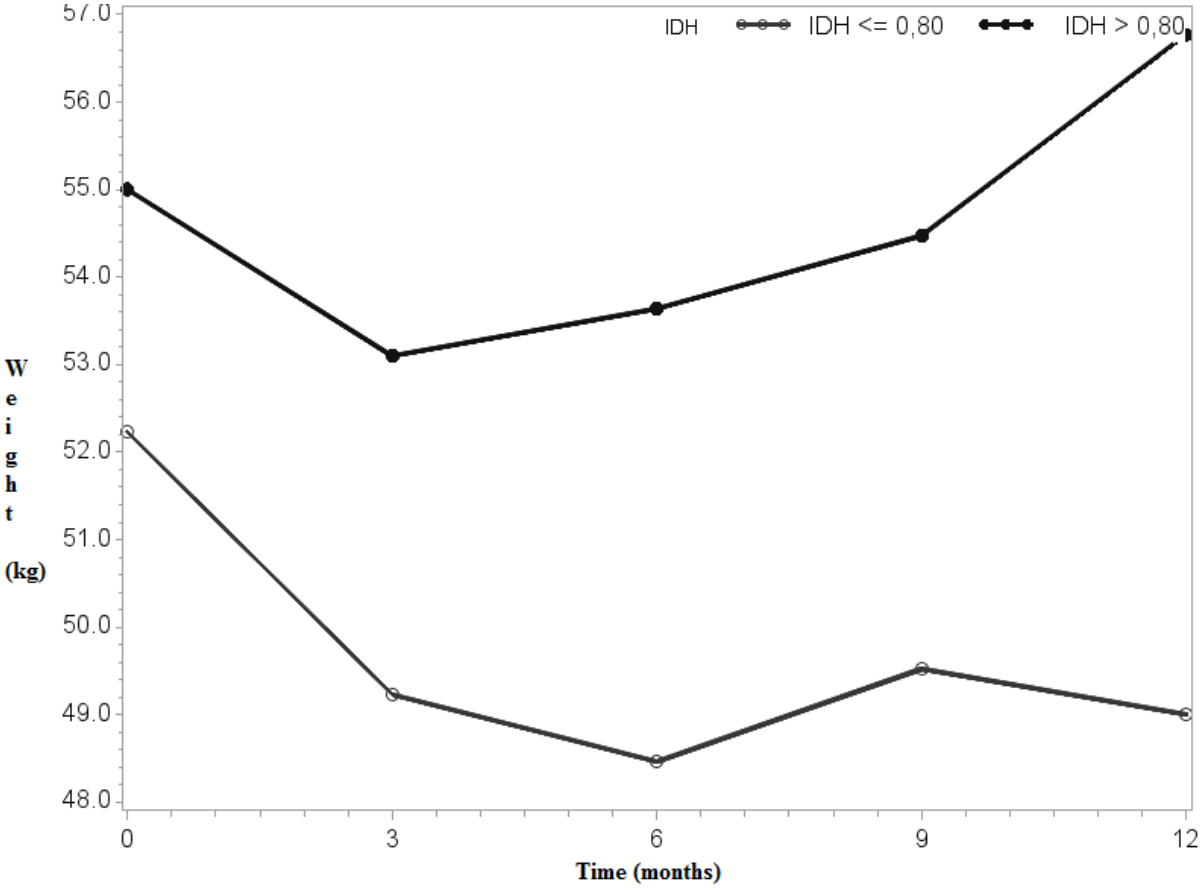

Figure 4. Weight evolution according to socioeconomic subgroups in patients with gastrointestinal or head and neck cancers (n=83) (p>0.05)

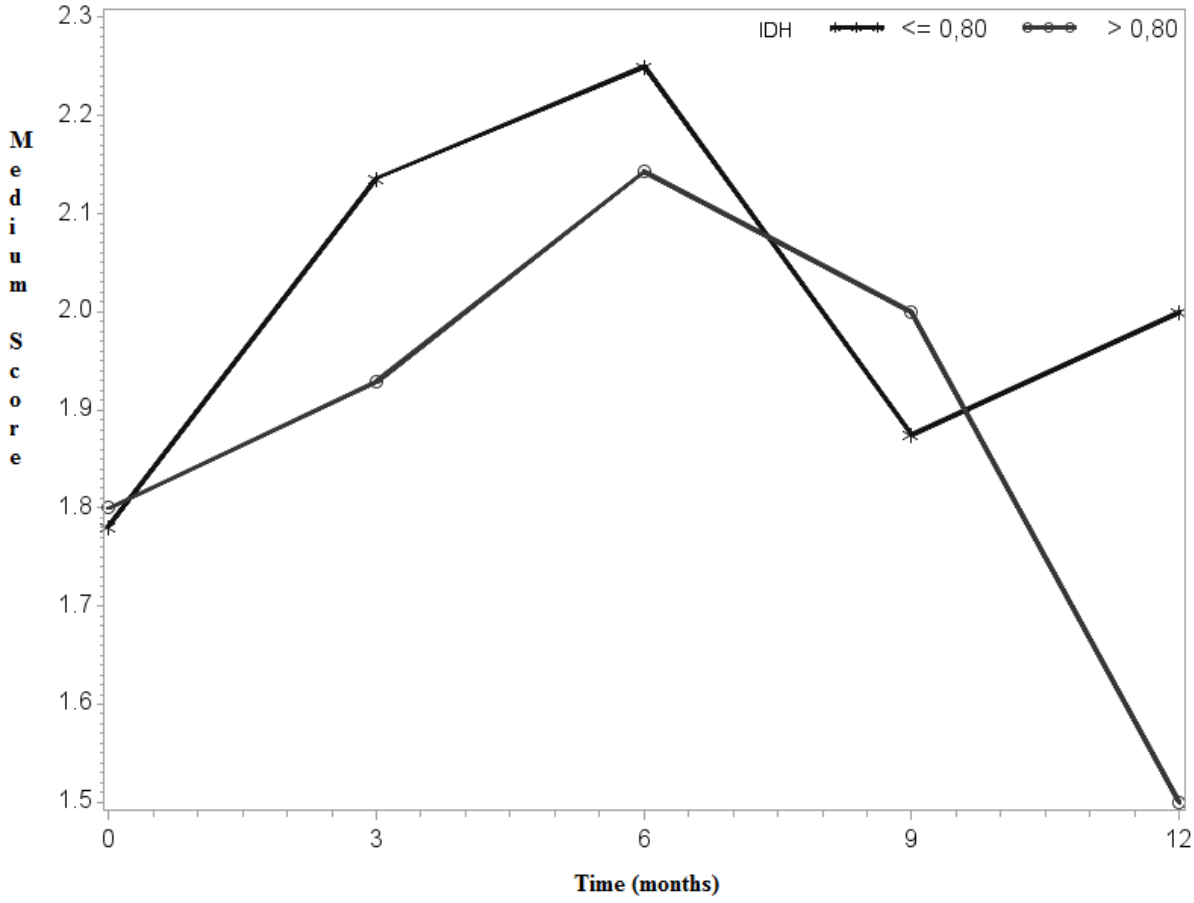

Figure 5. Clinical evolution of patients with gastrointestinal or head and neck cancers according to their socioeconomic status (n=83) (p>0.05)

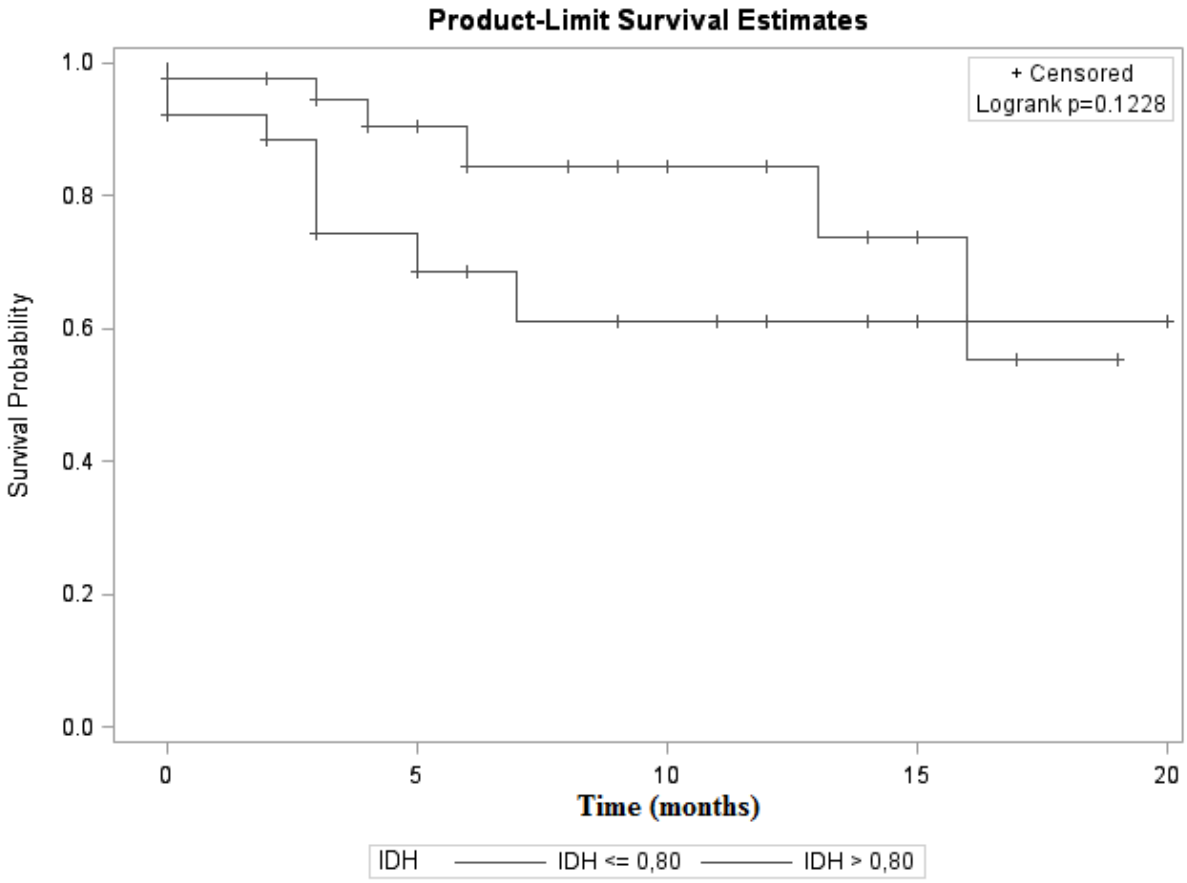

Figure 6. Survival in time, according to socioeconomic status of patients with gastrointestinal or head and neck cancers (n=83)

6 ARTIGO ORIGINAL

Does route of feeding influence clinical and nutritional outcomes for patients with neurological impairment? A Brazilian study – Salomon ALR, Novaes MRCG – artigo submetido ao periódico ***Current Alzheimer Research***

6 ARTIGO ORIGINAL

DOES ROUTE OF FEEDING INFLUENCE CLINICAL AND NUTRITIONAL OUTCOMES FOR PATIENTS WITH NEUROLOGICAL IMPAIRMENT? A BRAZILIAN STUDY

Abstract

At present there is insufficient evidence to support administration of enteral feeding for patients with neurological impairments, including advanced dementia. The aim of the present study was to examine whether enteral nutrition is an effective tool in improving survival, nutritional and clinical parameters in patients with neurological impairment treated with home enteral nutrition therapy in the Federal District of Brazil. This was a prospective, observational and comparative study, with three groups of patients according to feeding method (oral route, nasal routes and ostomies). Patients were followed-up from January 2010 to July 2013. An amount of 165 patients were selected for the present study. Patients had a mean age of 74.73 ± 13.46 years and there was a higher frequency of women. Enteral nutrition was positively associated with weight evolution, maintenance of clinical status and of laboratorial parameters, improvement of pressure sores and survival, which showed to be higher than the one presented in other studies. A favorable nutritional status is a decisive factor for nutritional therapy success in improving patients' outcomes as survival, pressure ulcer healing and lowering complications rates. Industries that produce enteral formulas should revise the content of micronutrients in order to prevent interactions, which might be responsible for maintenance of most patients' anemia status. Other studies approaching a long term follow-up of demented patients in nutritional therapy, with a comparison group are needed in order to clear all the doubts left around the efficacy of this treatment, ensuring an adequate follow-up by specialized health professionals.

Key words: home care services, enteral nutrition, socioeconomic status, dementia, outcomes.

Introduction

Home Enteral Nutrition (HEN) is applied to patients who have no indication for remaining hospitalized exclusively to maintain nutritional therapy (1, 2). International studies demonstrate that neurological diseases are the main indication for HEN (3-5), which is also in accordance to a study conducted in Brazil (6). Among neurological diseases, cerebrovascular one and advanced dementia are highly associated to artificial feeding due to dysphagia (7, 8)

In Brazil, the leading cause of death is cardiovascular diseases, from which Cerebrovascular diseases are the most prevalent. (9, 10). The prevalence of dementia among Brazilian elders (people over 65 years old) who live in the community, reaches levels of 7,1% and the main responsible for these cases is Alzheimer's disease (AD), which responds for 55% of them (11). Dementia also represents an important cause of death in the United States of America(12).

Cerebrovascular accident-associated dysphagia reached frequencies of 91% when evaluated by fluoroscopy and imposes the need for an alternative feeding and hydration route for patients when the degree of dysphagia is advanced (severe), which often leads to an enteral nutrition indication. However, very little evidence is available to demonstrate the clinical benefits from enteral tube feeding for advanced dementia patients.(13, 14)

A small scale study was conducted to assess self-feeding dependency and self-feeding behaviour in individuals with early stage of AD. Though the majority of studies well document eating impairment in the late stage of AD (50% of patients lose the ability to feed themselves 8 years after diagnosis), this one documented a significant difference in self-feeding dependence in mild AD, as subjects demonstrated significantly prolonged swallow durations for the oral transit duration for solid consistency and pharyngeal response duration for liquids, as well as total swallowing duration for liquids, which may increase the risk for aspiration pneumonia(8). Dysphagia is an important cause of weight loss in nursing home residents with neurodegenerative diseases with a prevalence ranging between 40-60%(15)

That is a widely held belief that enteral feeding is harmful for patients with advanced dementia (14, 16-19). Criticisms of artificial nutrition are based on a failure to show a favourable outcome or to lengthen survival (20). However, there are also several studies that stand against this belief affirming that there is not evidence that favours the decision of withholding artificial nutrition from these patients (20, 21).

The purpose of this study was to examine whether enteral nutrition is an effective tool in improving survival, nutritional and clinical parameters in patients with neurological impairment treated with home enteral nutrition therapy in the Federal District of Brazil, and to associate the method of feeding to these outcomes.

Materials and Methods

Design and Setting

This was a prospective and observational study with three comparison groups in terms of feeding method: Oral Supplements (OS), Nasal Route (NR – nasogastric and nasoenteric tube feedings) and Gastrostomy (GT) groups. The study variables included age, gender, clinical diagnosis, nutritional status, laboratorial parameters (hemoglobin, haematocrict, total proteins, albumin and globulin, as well as albumin/globulin (A/G) ratio) , presence of pressure sores, occurrence of complications, length of hospital stay (when readmitted) and survival.

The study was conducted between January 1, 2010 and July 31, 2013 in the Public Health Department of the Federal District (PHD/FD) of Brazil, which involves all the17 public hospitals of this Federal Unit, with a medium hospital admission of 11.260 patients in a month (22).

The research project was approved by the Ethics Committee of the PHD/FD, according to Protocol number 425/2009.

Subjects

The PHD/FD issued in 2004 the first regulation of HEN supply, which consists on providing patients with industrialized enteral nutrition and its administration system. The costs of this program are completely funded by the government of the Federal District. Patients are admitted to the program after their hospital discharge and are followed by a multidisciplinary team, who reevaluates them every three months.

Calculated sample size comprised a total of 136 participants. Sample size was calculated on basis of an observational study that comprehended 401 patients (23) in which from patients initially diagnosed as malnourished, 5.75% presented a nutritional recovery at the end of the study and 4.10% had a worsening in their nutritional status as compared to the initial status (unpublished data). A level of significance of 5% and a power of test of 80% were considered. The software GPower version 3.0.5 was applied for this purpose.

A clinical sample from all patients enrolled on the HEN Program from January 1, 2010 to March 31, 2012 was selected. Patients were followed-up until July 31, 2013. The inclusion criteria of patients comprehended adults (aged 20 to 59 years) and elders (aged 60 or up) with a primary diagnosis of neurological impairment made according to validated diagnostic criteria such as ICD-10(11). Data were collected from patients' charts of HEN Program. A data extraction form was used which included the variables mentioned before.

Patients were followed-up for 3 and a half years, according to the following study times: Time 0 = prior to HEN initiation, Time 1 = at three months of therapy beginning, Time 2 = at six months, Time 3 = at nine months, Time 4 = at 12 months, Time 5 = at 15 months, Time 6 = at 18 months, Time 7 = at 21 months, Time 8 = at 24 months, Time 9 = at 27 months, Time 10 = at 30 months, Time 11 = at 33 months, Time 12 = at 36 months, Time 13 = at 39 months and Time 14 = at 42 months.

Nutritional Status Assessment

Nutritional status was assessed by weight evolution on different study periods. At first there was the intention of collecting data on every nutritional evolution through body weight changes at each time of the study (from T0 to T-14). However, due to the high mortality rates associated to the lying disease, it was not possible to obtain statistical significance for all the period. Intra-group evolution for NR and GT was assessed from times 1 to 8 (24 months follow-up) in relation to baseline. For OR this was reached only at times 0, 3 and 6. For the purpose of comparing the three routes of administration, only assessments at 0, 3 and 6 months reached statistical significance ($p = 0,0447$).

Clinical Assessment

This evaluation was collected from patients' records, through patients' clinical history, where their status was classified into three scores: 1 = clinical/nutritional worsening; 2 = clinical/nutritional maintenance; 3 = clinical/nutritional improvement. For the same reasons considered for nutritional assessment, comparisons of the three routes of feeding were only possible at times 3 and 6, since at baseline it was not possible to assess patients' evolution. Intra-group evolution for NR and GT was assessed from times 1 to 8 (24 months follow-up)

Pressure sores and other complications

From patients clinical records data on presence or occurrence of Pressure Sores (PS) and their evolution, occurrence of complications - as reduction of formulas supply, hospital readmission and the length of hospital stay (in number of days) and occurrence of comorbidities - were also collected.

Pressure sores' evolution at the end of the study was divided into three categories: 1 – PS worsening, 2 – PS in healing process and 3 – PS completely healed.

Reductions of formulas supply was assessed according to the leading causes for it and were categorized into: 1 – occurrence of gastrointestinal symptoms, 2 – attempt of artesanal feeding, 3 – lack of products in the PHD/FD, 4 – GT complications, 5 – lack of carer, 6 – lack of following professionals' guidance, 7 – hyporexia (for patients using oral route), 8 – formula intolerance, 9 - tube feeding accidental removal and 10 – professional planning of reducing the amount of calories offered to patients.

Comorbidities were divided into four categories: 1 – thrombosis, 2 – sepsis, 3 – lowering of renal function and 4 – severe disease.

Laboratorial parameters

As it was not the intention of this study to propose changes in the routine of patients' follow-up, patients' laboratorial data were also collected from their charts, whenever available. Blood samples were collected and analyzed by the crew of the Clinical Analysis Laboratory of PHD/FD and interpreted according to the parameters adopted by this laboratory.

Survival

Survival was assessed from time of patient's admission to HEN Program until the occurrence of one of the following events: death or discharge of program due to oral rehabilitation or waiver on continuation on the Program until the end of the study.

Statistical Analysis

Data analysis included descriptive statistics – mean and standard deviation for quantitative variables and percentages for qualitative ones (gender, clinical diagnosis and clinical assessment, which were all converted into quantitative variables, by attributing a numeric category to them).

Longitudinal changes inter groups were tested with the model of mixed effects for repeated measures with non-structured variance and covariance matrixes, and adjustment for basal weight, gender and age. Main focuses of comparative analysis (OR x NR x GT) were changes at 3 and 6 months compared to baseline values. When the p-value was lower than 0.05, pre-specified contrasts were applied to test the following three hypothesis: whether changes presented by patients treated with NR are different from those presented by patients treated with GT; whether changes presented by patients treated with NR are different from those presented by patients treated with OR; and whether changes presented by patients treated with OR are different from those presented by patients treated with GT. Bonferroni's correction was used to adjust this three pre-specified comparisons.

For NR and GT, longitudinal changes intra-groups were also tested with the model of mixed effects for repeated measures with non-structured variance and covariance matrixes, and adjustment for basal weight, gender and age. Main focuses of intra-group analysis (NR and GT) were changes at 3, 6, 9, 12, 15, 18, 21 and 24 months compared to baseline values.

For all tests mentioned above, a residual analysis was conducted to verify if residues of this model presented a Gaussian distribution with constant variance and it was verified that suppositions of both normality and homogeneity of residues were attended.

Clinical assessment scores were observed on times 1 and 2. In order to compare whether marginal proportions of patients' conditions at 3 months differ from marginal proportions at 6 months, contrasting inter-group assessment of the three routes of feeding, it was applied the test of marginal homogeneity.

Intra-groups longitudinal measures (for NR and GT) were tested by applying the model of proportional chances with generalized estimation equations (GEE), adjusting for age and gender. Main focuses of analysis were comparisons at months 3, 6, 9, 12, 15, 18, 21 and 24 in relation to baseline.

A level of significance of 5% was considered.

Survival functions for patients submitted to treatments by three routes of feeding were estimated by Kaplan-Meier curves and compared with the log-rank test. Multiple comparisons were adjusted by Bonferroni method.

The software Statistical Analysis System (SAS) version 9.2 was used for all analysis mentioned above.

In order to evaluate the effect of laboratorial changes through the follow-up period, a before and after analysis was conducted applying paired-sample T-test. Statistical Package for Social Sciences (SPSS), version 18.0 was used for this purpose.

Complications and co-morbidities incidences were evaluated by descriptive statistics (frequencies).

Results

An amount of 165 patients with neurological impairments (NI) were selected for the present study. Patients' sample represented 56% of all patients with same diagnosis enrolled on the Program in the study period.

Patients with diagnosis of NI had a mean age of 74.73 ± 13.46 years. Only 14,6% of patients were younger than 60 yrs. There was a higher frequency of women (59.4%). The main diseases that were involved were cerebrovascular accidents (58.8% - n=97) and Alzheimer's disease (26.06% - n=43). Dementia on Parkinson's disease and non specified dementia corresponded to 5.45% (n=9) of cases, each. Other cases of dementia were related to multiple sclerosis (n=3), Huntington corea (n=2), amiotrofic lateral sclerosis (n=1) and dementia of Lewy's body (n=1). Total cases of dementia comprehended 68 patients (41.2%).

Nutritional Status Assessment

When analyzing the different methods of nutrient administration to patients, only follow-up periods 1 and 2 allowed an inter-group statistical analysis concerning weight evolution, which included 157 patients: 51 in NR, 87 in GT and 19 in OR. The other patients either died or waivered on the program continuation.

Figure 1 presents weight evolution according to feeding route.

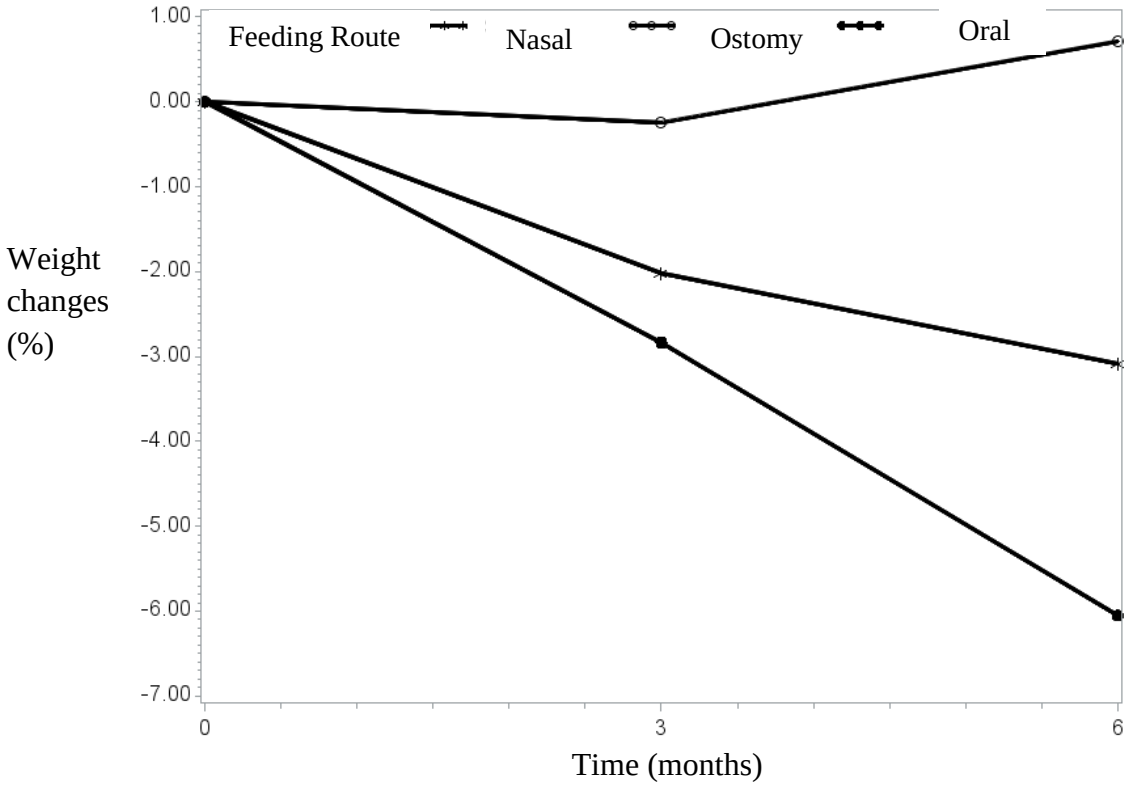

Figure 1 Percentage of medium weight changes during 6 first months of follow-up (n=157) (p>0.05)

Intra-group analysis, conducted for patients treated by NR and GT, presented the following results: patients treated by ostomy (GT), presented weight gains from months 6 to 24, which reached statistical significance at 12, 15, 18, 21 and 24 months, corresponding to 2.64 ± 0.74 kg (a 4.8% change in relation to baseline), 2.52 ± 0.77 kg (a 4.6% change), 3.09 ± 0.82 kg (a 5.6% change), 3.15 ± 0.88 kg (a 5.7% change) and to 4.18 ± 0.95 kg (a 7.6% of change), respectively ($p<0.05$). Patients treated by NR, presented a non-significant weight loss from months 3 to 15, and started gaining weight at month 18, with statistical significance only for month 24, when there was an increasing of 4.04 ± 2.02 kg (a 7.8% in relation to baseline) ($p<0.05$).

For OR, since patients number was low (n=19) and there were deaths during the follow-up period, the only possible evaluation were at months 3 and 6 compared to baseline. Contrary to the enteral feeding routes, those treated by OR presented a weight loss at the end of six months, an average loss of -2.69 ± 1.39 kg (a 6% change in relation to baseline), with marginal significance ($p=0.0548$).

When comparing feeding routes, mean weight was significantly higher, by 6 months, for patients treated with GT when compared to the ones with OR – an average weight gain of 3.08 kg (p=0,0455). Contrasting NR to GT, the differences reached statistical significance for months 12 and 15, where there was a weight loss of respectively -3.66 ± 1.58 (p=0.0214) and -3.81 ± 1.67 (p=0.0228) for patients treated by NR in relation to the ones treated by GT, favoring this feeding method.

As mentioned before a statistical analysis for a longer follow-up period was not viable due to patients' deaths. At time 6, 53.36% of patients with OR were alive, which corresponded to 10 patients. At a 22 months follow-up, 36.01% of patients of NR group were alive, comprehending 19 patients. At month 23, 60.1% of patients of GT group were alive, which equals 52 patients. This way, an amount of 80 patients would compose the sample for statistical purposes (48.8% of the total sample), and especially for OR the number of patients would not be enough to reach significance.

Despite the fact the number of patients that reached this follow-up period was insufficient to make any statistical inferences, for patients who survived until Time 8, those treated by oral route presented an average weight loss of -4.96 ± 2.42 kg (an 11.1% change in relation to baseline).

When comparing feeding routes at time 5, average weight of patients treated with GT was higher than 4 kg in comparison to the ones treated by OR. At time 8, this increasing reached the difference of 9 kg higher for GT group. Patients treated with NR also presented a higher weight gain in comparison to OR group at the end of 24 months, which corresponded to 9 kg.

Clinical Assessment

When applying the marginal homogeneity test to assess patients' clinical evolution, both for NR as for GT groups, it was not possible to reject the hypothesis of marginal equality which means that patients' clinical conditions at 6 months follow-up didn't differ from their condition at 3 months - χ^2 = 1,352; df = 2; p = 0,5086 and χ^2 = 0,3259; df = 2; p = 0,8496, respectively. Nevertheless, when applying the model of proportional chances with GEE, patients treated by NR presented a 5.98 higher chance (CI 95 1.14; 31;47) of presenting an improvement in clinical status at month 21 in relation to base line. For patients treated by a GT, there were no significant changes in the first 24 months of follow-up.

However, as one can observe in Table 1, for OR patients' clinical condition at 6 months was statistically different from their condition at 3 months (χ^2 = 8,3178; df = 2; p = 0.0156). The difference consisted of the following: the proportion of patients at 6 months who presented a clinical worsening (38,5%) was significantly higher than the one of patients at the same clinical category at month 3 (7,7%). The proportion of patients who showed clinical improvement at 6 months (23.1%) was significantly lower than the one of patients at the same clinical category at 3 months (53.9%). This allows the conclusion that patients in OR had a clinical worsening from 3 months of follow-up to 6 months.

Table 1 Marginal homogeneity of clinical evolution from patients with neurological impairment receiving oral supplements at 3 and 6 months (n=13) (p=0.0156)

	Clinical status at 6 months			
Clinical Status at 3 months	**Worsening**	**Maintenance**	**Improvement**	**Total**
Worsening	1 (7,7)	0 (0,0)	0 (0,0)	1 (7,7)
Maintenance	2 (15,4)	3 (23,1)	0 (0,0)	5 (38,5)
Improvement	2 (15,4)	2 (15,4)	3 (23,1)	7 (53,9)
Total	5 (38,5)	5 (38,5)	3 (23,1)	13 (100,0)

Pressure Sores and Other Complications

During the course of the study 87 patients (53%) presented pressure sores. Of these, 54% (n=47) presented information concerning pressure sores evolution registered on their charts. At the end of the study, 8.5% (n=4) had a worsening of the ulcer (though the degree was not mentioned), 34% (n=16) were in the process of ulcer healing and the remaining 57.4% (n=27) had a complete healing of the pressure sore. Considering that both categories of "in healing process" and "complete healing" are positive outcomes, it is possible to affirm that the great majority of patients (91.4%) presented a positive outcome concerning to ulcer healing.

Reduction in formula supply happened to 18.8% (n=31) patients, and the main cause was the occurrence of gastrointestinal symptoms in 9 patients (29%). The most frequent gastrointestinal symptom presented by these patients was diarrhea (n=4), followed by gastroesophageal reflux and upper digestive hemorrhage (n=2, each) . The

other symptom was abdominal distension, which was referred by one patient. Second main cause of reduction in formula supply was the lack of following professional's guidance (22.6% - n=7). Third main cause of this complication was lack of products in the PHD/FD which happened in 19.3% of cases (n=6). This may have underestimated the real improvement from which patients in HEN might benefit, though there was a significant weight gain when comparing GT route of feeding to oral route.

Co-morbidities were presented by 28 patients (16.9%) during the course of the study and the higher incidence corresponded to infection (n=24). Pneumonia was the leading cause of infection (n=12), but no difference was pointed in relation to occurrence of aspiration. Second cause of infection was urinary tract one, which was presented by 6 patients. Other causes of infection were pressure sore infection (n=3), multi-resistant infection, sepsis and septic shock (n=1, each). 2 patients developed kidney failure, one presented thrombosis and another one had a worsening of the lying disease, needing oxygen-therapy at home.

A total of 55 patients (33.3%) had to be readmitted to hospitals mainly due to the presence of the mentioned co-morbidities and other complications. Mean duration of hospital stay was of 31.3 days, ranging from 1 to 180 days. Patients who remained in hospital settings for lower periods usually were readmitted to convert from NR to GT (n=8). One patient was readmitted due to lack of formula supply.

Laboratorial Parameters

As mentioned before, it was not the intention of this study to propose changes in the routine of patients' follow-up. For this reason, patients' laboratorial data were collected from their charts whenever available. Since a small number of patients had their laboratorial data available on their charts, a before and after analysis was conducted, comparing the baseline results with the ones of the end of the study.

Data on patients' heamoglobin and hematocrit results were available for 60 patients (36,37% of total sample). Data on patients' results of total proteins, albumin, globulin and albumin/globulin ratio were available for 43 patients (26,06% of total sample).

Results for laboratorial tests are presented in Table 2.

Table 2 Laboratorial results of hemoglobin and hematocrit (n=60) and total proteins, albumin, globulin and albumin/globulin ratio (n=43) of patients with neurological impairments treated with home enteral nutrition – a before and after analysis

Laboratory Test	Before	After	Mean difference	95% CI	t	df	p-value
Hemoglobin (Hg)	11.83 ± 2.04g/dL	11.64 ± 2.85 g/dL	0,19 ± 2.90	-0.56; 0.94	0.511	59	0.611
Hematocrit (Htc)	35.47 ± 6.16%	34.98 ± 8.54%	0,49 ± 8.83	-1.79; 2.77	0.431	59	0.668
Total Proteins (TP)	6.39 ± 0.86g/dL	6.09 ± 1.13g/dL	0.30 ± 1.04	-0.013; 0.63	1.934	42	0.060
Albumin (Alb)	3.43 ± 0.54g/dL	3.21 ± 0.67g/dL	0.22 ± 0.63	0,029; 0.41	2.327	42	0.025
Globulin (Glb)	2.95 ± 0.65g/dL	2.86 ± 0.68g/dL	0.08 ± 0.67	-0.12; 0.29	0.865	42	0.392
Albumin/Globulin Ratio	1.22 ± 0.33	1.15 ± 0.27	0.07 ± 0.26	-0.008 ± 0.15	1.816	42	0.077

From the results presented at Table 2, it is possible to conclude that values of hemoglobin, hematocrit, total proteins, globulin and albumin/globulin ratio didn't change through the study follow-up time. The only value that reached statistical significance was of albumin which showed a mean reduction of 0.22 g/dL.

Survival

At the end of the study 61 (about 37%) patients had died.

Figure 2 shows the Kaplan-Meier survival curve of patients with neurological impairments according to the route of feeding.

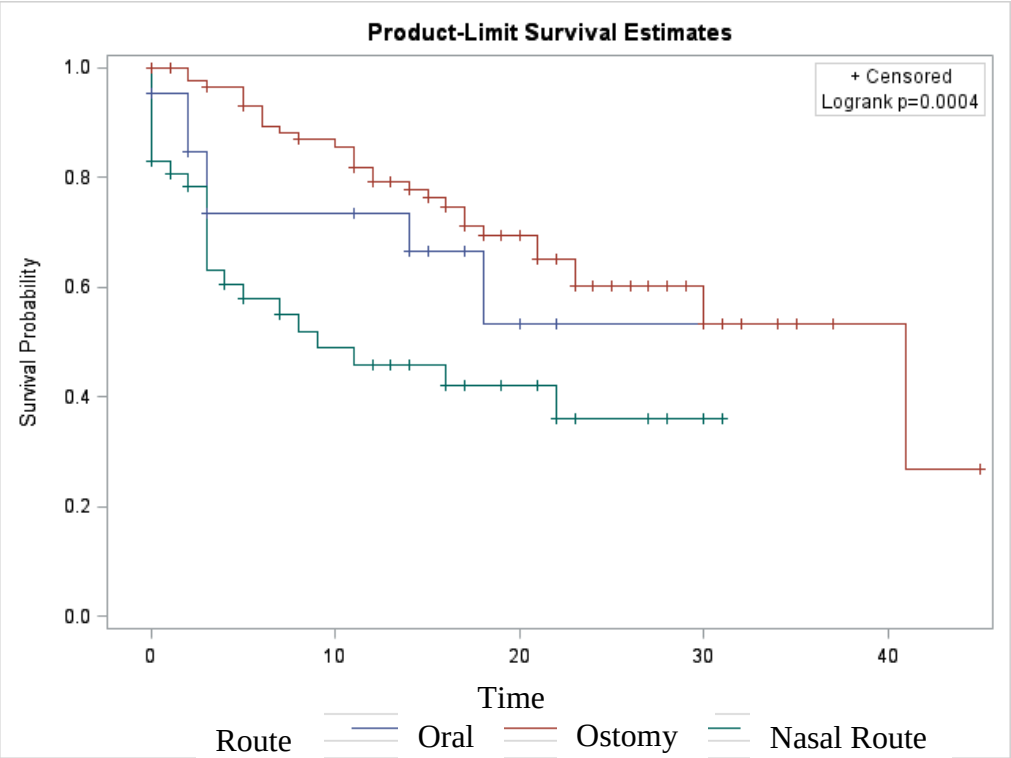

Figure 2 Survival probability in time according to route of feeding of patients with neurological impairments in home enteral nutrition (n=165)

From the result of log-rank test it is possible to conclude that patients' survival time differs at least between two routes of feeding (p=0.0004).

Table 3 shows the results of multiple comparisons with the adjustment of Bonferroni.

Table 3 Adjustment for Multiple Comparisons for the Logrank Test with Bonferroni's adjustment

Strata Comparison		Chi-square	p-Values	
Route	Route		Raw	Bonferroni
Oral	Ostomy	5.4866	0.0192	0.0575
Oral	Nasal	7.7290	0.0054	0.0163
Ostomy	Nasal	15.1607	<.0001	0.0003

From the result of multiple comparisons with the adjustment of Bonferroni, it is possible to draw the following conclusions: survival time of patients treated by OR and

GT didn't differ significantly (p=0.0575); survival time of patients treated by OR is significantly higher than the one of patients treated by NR (p=0.0163); survival time of patients treated by GT is significantly higher than the one of patients treated by NR (p=0.0003).

Discussion

The main indications for PEG in the literature are dysphagia, cerebral contusion, Parkinson's disease, head malignancy, among others (24). Dysphagia often presents at an advanced stage of dementia (20). Dementia is a complex syndrome whose frequency varies from 3% at age of 70 years old to 20% to 30% at age of 85, doubling every five years with increasing age (25). This was also observed in the present study, where a higher frequency (85.4%) of elders was observed in this group of patients, with mean age of 74.73 years and a median age of about 79 years. This median age approaches the age of elders followed-up by other authors (12, 18, 24, 26-29), with exception of the study conducted by Gaines et al (21), in which patients' median age was of 64 yrs. The higher prevalence of females (59.4%) is also in accordance with other studies (12, 30). A systematic review published in Cochrane Database with seven observational controlled studies, involving a total sample of 1821 patients found a mean age of 82 years, close to the present study, and that subjects were predominantly female(14).

Nutritional Status Assessment

In the present study mean weight by 6 months was significantly higher for patients treated with GT when compared to OR. The study of Jaul et al (26), on the other hand, didn't find any clinical or nutritional differences among the groups treated with OR or Enteral Nutrition (EN). However, the Hazard Ratio for mortality was higher for the OR 2.86 in relation to EN (95% CI 1.50;5.45). In the study conducted by Arinzon and co-workers (27), there was a significant reduction on Body Mass Index (BMI) for both OR and EN. However, more patients of the EN group have had an increase in body weight by 5%, when compared to the control group. Of the EN group, 37% (n=21) presented a weight increase while 7% (n=4) presented a decrease. On the other hand in the control group (OR), 5% (n=5) presented an increase while 28% (n=31) faced a decrease. In the present study, the GT group presented a weight increase of 7.6% by the end of 24 months in comparison to baseline, which was higher than found by these authors.

The study of Martins et al (12), compared two groups of patients – with dementia and with other neurological diagnosis – both on EN and found no improvements in nutritional status.

In the present study, though it did not reach statistical significance, when analyzing patients' weight evolution during the course of 24 months, both for GT and NR there was a higher weight gain of about 9 kg in comparison to OR group, which reinforces the efficacy of EN (either through a GT or a NR), in relation to OR. This opposes to the study of Teno et al (17) that states that tube-feeding is of questionable benefit for patients with advanced dementia and also to the proposal of comfort feeding through oral route for these patients (16).

Clinical Assessment

Like nutritional status, clinical evolution of patients with OR showed signs of worsening during the 6 first months of follow-up. Clinical status of patients treated with EN (either GT or NR) didn't show any significant changes during this period.

Pressure Sores and Other Complications

Though it was not possible to conduct statistical or even stratified analysis concerning the presence of Pressure Ulcers (PU), data from 54% (n=47) of patients with PU that had information on evolution, showed that for the great majority (91.4%) there was a positive improvement on PU status, and of these, 57.4% presented a complete ulcer healing. In the study conducted by Martins et al (12), 43% of patients presented a PU at the beginning of the study (versus 53% in the present one). 41.2% presented healing and 20% developed a new ulcer. Data of the present study (though there was no information for all patients), showed a better result. The study of Arinzon et al (27) failed to demonstrate any improvements on pressure sore development with EN. In fact, patients with EN presented a higher proportion of PU – 30% (n=17) – when compared to the control group – 14% (n=15). The study of Teno et al (18) also revealed that Percutaneous Endoscopic Gastrostomy (PEG) was related to an increased risk of developing a PU as well as to a higher risk of developing a pressure ulcer stage 4.

When it comes to reduction on formula supply, main reasons related to this occurrence in the present study were gastrointestinal symptoms, lack of following professionals' recommendations and lack of products in the PHD/FD, which may all have underestimated the real impact of HEN on patients' evolution. As mentioned by

Regnard et al (20), there is no mention of problems such as refeeding syndrome or gastric stasis in the gastrostomy-dementia literature, which difficult comparison of the present results with other studies. Occurrence of refeeding syndrome was not reported in the present study, but the presence of gastroesophageal reflux and abdominal distension which were reported in 3 cases may be linked to gastric stasis and contributed to the reduction of the amount of formulas used by the patients, lower than their needs. Martins et al (12) also stated the occurrence of vomiting and reflux in 16.2% (n=11) and 4.4% (n=3) of cases, respectively, which may also be linked to gastric stasis. Arinzon et al (27) stated the occurrence of refeeding syndrome in 4% (n=2) of the patients treated with EN.

Concerning the occurrence of co-morbidities, infections were the leading cause of this complication and took place in 24 of the 28 cases that had this presentation, which represents 14.5% of total cases. There was not sufficient data to separate pneumonia of aspiration pneumonia, but 12 patients developed this infection. In the study of Higaki et al (24), the difference between pneumonia and aspiration pneumonia was also not performed and total incidence of this disease reached 115 from 311 patients (36.9%). Martins et al (12) showed an incidence of 55.9% of pneumonia presented by patients in enteral nutrition within a 6 months follow-up. In the study of Arinzon et al (27), patients fed by EN presented a higher incidence of pneumonia of 47% (n=27), when compared to the control group – 24% (n=26). Gaines et al (21) state that acute illness increase mortality after PEG.

When it comes to hospital readmission, only the study of Venturini et al (31) dealt with this subject and the authors stated that there were no differences between the groups (with and without dementia) for the number of hospital readmissions. However they don't mention the number of readmissions and neither the length of hospital stay.

Laboratorial Parameters

Patients' laboratorial parameters didn't reach statistical significance when comparing the values between baseline and the end of the study, except for albumin levels which showed a 0.22 g/dL reduction. Values of hemoglobin and hematocrit remained below normal values (11.64 ± 2.85 g/dL and 34.98 ± 8.54%), and anemia was a common occurrence related by health professionals. When analyzing Iron amounts of enteral formulas, it was found to be within recommendations (according to Dietary Recommended Ingestion). However, Copper amount is over recommendations and this

mineral may compete with Iron for intestinal absorption, which may result in Iron deficiency (data not published). Total Proteins, Globulin and Albumin/Globulin ratio were among normal values, but Albumin levels were below normal parameters (3.21 ± 0.67 g/dL).

The study of Arinzon et al (27) found an improvement in Albumin levels both for OR and EN, which ended in normal values. The study of Kumagai et al (28) didn´t find any differences in albumin levels in a before and after analysis, within a period of 6 months, but levels were below normal (2.9 ± 0.6 g/dL). Likewise, the study of Martins et al (12) didn't find any improvements on albumin levels , which remained between normal values.

Higaki et al (24) claim that among the predictors of poor survival after PEG are low levels of serum albumin (lower than 2.8 g/dL), with a hazard ratio of 2.081 (95% CI 1.490-2.905). This is reinforced by the study of Gaines et al (21) when the authors point out among the factors associated with a 30-day mortality after PEG, the decreasing serum albumin, with a hazard ratio of 0.45 (95% CI 0.22;0.84).

Survival

Five studies addressing this subject were found: four dealing with elderly patients (12, 24, 26, 28) and one with several kinds of diseases, involving elders, adults and children(32). Four studies assessed survival with Kaplan-Meier curves and the log-rank test like the present research (12, 24, 26, 32). The other study used Cutler-Ederer curves (28).

Schneider et al. worked with 417 patients from whom 380 were adults and elders. Main diagnoses for these patients were neurological disorder (38.9%), digestive disease (20%), head and neck cancer (16.8%) and dementia (14.2%). The authors found that mortality was positively associated to dementia, head and neck cancer and age higher than 70 years. They mainly assessed survival at 1month, 1 year and 5 years (32).

Martins et al. dealt with 79 elderly patients who had neurological diseases, from whom 49.4% presented dementia. They assessed mortality rates at 3, 6 and 11 months(12). Kumagai et al. worked with 261 demented patients, divided into two groups – one with percutaneous endoscopic gastrostomy (PEG) and other with nasogastric tubes. They evaluated survival at 3, 6, 9, 12, 15, 18, 21, 24, 27 and more months but found a higher survival with PEG at 27 months(28).

Jaul et al dealt with 88 demented patients of whom 26 were fed orally and 62 by nasogastric tube. Patients were followed-up by 17 months and 47.7% died during follow-up, 65.4% of the OR and 40.3% of NR groups. The crude hazard ratio for mortality comparing patients with OR versus NR was 2.86 (95% CI 1.50-5.45). The conditions that were associated with mortality were having dementia, stroke or persistent vegetative state and peripheral vascular disease (26). In the study of Higaki et al, 311 consecutive patients were followed-up, 143 with dementia and 168 without dementia. Survival was not significantly different between groups at 12 months (p=0.62) (24).

In the present research, survival was higher for patients fed orally and through a GT than of the ones fed by NR. There was no difference between OR and GT groups.

When findings of this study were compared to the ones which also used Kaplan-Meier method, a higher survival was observed for this study. When Schneider found a 1-month survival of 80%, the present study found a 2 –months survival that varied from 84.6% (for OR) to 97.7% (GT). Only the group who presented the smallest survival in the present study (NR) had a similar survival at 1 month (80.7%).The first authors also found a 24-months survival of 41.70%, while the present study showed a 23-months survival of 60.1% for GT group and a 30-months survival of 53.43% (no data was available for OR at this time), while for NR group survival at 22 months equaled 36%. Finally, Schneider et al (32) describe a 60-months survival of 25%. The present study didn't follow-up patients for as long as five years, but 42 months. The last available survival probability for this study was calculated for month 41 (GT group) and it corresponded to 26.71%.

Martins et al. found a 3, 6 and 11-months survivals of respectively 84.8%, 77.2% and 57% (12). For the same period of follow-up, considering the group of higher survival (GT group), the present study found respective values of 96.5% (3 mo), 89.4% (6 mo) and 79.3% at 12 months.

The analysis conducted by Jaul et al was different from other studies where Kaplan-Meier method was used. Instead of applying the survival probability according to time evolution, the authors used a cumulative survival according to feeding modality which didn't allow a comparison to the present study. Despite of this, the median survival time of patients receiving oral feeding was 40 days, while the one of patients receiving EN was 250 days, showing that EN was positively associated to patients' survival (26).

Higaki et al (24) analyzed survival at 6 months, 1 and 3 years. The results of this study revealed that survival at 6 months varied from 57% for patients without dementia (WD) to 66% for demented (D) ones. Comparing these data to the ones of the present study related to the GT group (same analysis as Higaki et al performed), the present study showed a higher survival at 6-months, which corresponded to 89.4%. The authors also found a 1-yr survival ranging from 49% (WD) to 51% (D) and a 3-yrs survival varying from 24% (D) to 29% (WD). The present work found a 12-mo survival of 79.3%, higher than the one found by the authors, but the 36-mo analysis was not assessed in the present study, but only analysis of 30 and 41 months, which were respectively 53.4% and 26.7%. Higaki et al also state that many studies with demented patients report a 12-month mortality of 50 to 60%, which reinforces the fact that survival in the present study was higher than the other studies.

The study of Kumagai et al, despite the methodological difference for survival estimates, showed an approximate survival percentage at months 3, 6, 9, 15 and 21 of respectively 88%, 80%, 80%, 75% and 68%, which were lower than percentages presented by the present study, considering the same group of patients, this is NI ones, treated with GT. For this group of patients, the following values were found for the correspondent months (except for the 9^{th}, since this time period didn't show in the present study, which led to comparison to month 10): 96.5%, 89.4%, 85.7%, 76.3% and 65.1%. The only period in which Kumagai et al.'s study (28) showed a higher survival time than the present one was the one comprehending month s 21 (shown earlier) and 27, which presented a survival of 65.6% for the PEG group, while the present study showed a 30-months survival of 53.4%.

One aspect that is worth mentioning about the present study is that Cochrane's systematic review mentions that there is insufficient evidence to suggest that enteral tube feeding is beneficial in patients with advanced dementia(14), which highlights the importance of this study's findings.

Limitations of the present study specially relate to the fact that its sample wasn't randomized, which allows occurrence of selection bias, although the sample comprised more than 50% of all patients enrolled on the Program in the study period. Other concern refers to the fact that information was collected from patients' charts, which may induce information bias and harms the complete availability of data (like laboratorial parameters and data on PU evolution for some patients). Some authors state that a randomized design for this type of study may raise ethical conflicts, since it is not

ethical to allow a group of patients to starvation for purposes of having a control group (14, 18, 26), which difficult controlling selection bias.

Conclusion

In the present study it was observed that enteral nutrition was an effective tool in improving survival, which was found to be even higher than in other studies. Patients treated with enteral nutrition also showed more favorable outcomes related to nutritional evolution, assessed by body weight in the studied times, with weight gain for patients fed by a gastrostomy and a nasal route, while patients fed orally presented weight loss. Clinical evolution, assessed through a score system, showed maintenance of clinical status for patients treated with enteral nutrition, while patients that kept oral feeding presented a clinical worsening in the first 6 months of follow-up.

In a non-stratified analysis (due to low number of patients), the available data on pressure ulcer evolution showed an improvement in 91.4% of cases. Laboratorial data on hemoglobin, hematocrit, total proteins, globulin and ratio albumin/globulin also showed maintenance in a before and after analysis. Despite adequate amounts of iron supplied by enteral formulas, values of hemoglobin and hematocrit remained below normal values. When analyzing the micronutrient profile of standard enteral formulas, it is possible to identify values of copper that exceed recommendations. This may explain why anemia was not recovered, since copper may compete with iron for intestinal absorption. Industries that produce enteral formulas should revise the content of micronutrients in order to prevent interactions.

Values of total proteins, globulin and albumin/globulin ratio remained between normal ranges. A favorable nutritional status is a decisive factor for nutritional therapy success in improving patients' outcomes as survival, pressure ulcer healing and lowering complications rates.

There is a lot of controversy on enteral feeding patients with neurological impairments, especially ones with advanced dementia. For this reason, other studies approaching a long term follow-up of demented patients in nutritional therapy, with a comparison group are needed in order to clear all the doubts left around the efficacy of this treatment. It is important, nevertheless, to ensure an adequate follow-up by specialized health professionals in order to minimize the occurrence of bias.

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Conflict of interests

The authors declare no conflict of interests.

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7 ARTIGO ORIGINAL

How home enteral nutrition influences survival, nutritional and clinical outcomes for patients with gastrointestinal, head and neck cancers? A Brazilian study – Salomon ALR, Noves MRCG – artigo submetido ao periódico ***World Journal of Gastroenterology***

7 ARTIGO ORIGINAL

HOW HOME ENTERAL NUTRITION INFLUENCES SURVIVAL, NUTRITIONAL AND CLINICAL OUTCOMES FOR PATIENTS WITH GASTROINTESTINAL, HEAD AND NECK CANCERS? A BRAZILIAN STUDY

Abstract

The aim of the present study was to assess the role of home enteral nutrition in improving survival, nutritional and clinical outcomes in patients with gastrointestinal or head and neck cancers treated with home enteral nutrition therapy in the Federal District of Brazil. This was a prospective and observational study with three comparison groups in terms of feeding method: Oral Supplements, Nasal Route and Gastrostomy. Outcomes that were assessed included nutritional and clinical evolution and survival. An amount of 82 patients were followed-up for three and a half years, mean age of 58.8 ± 11.2 years. There were no significant differences in weight variations among feeding methods through the follow-up period. Nasal route was associated to a higher chance of presenting a clinical improvement at nine months of follow-up. 15.8% of patients presented complications that caused reduction in formula intake and 8.5% presented co-morbidities during the follow-up period. 28% had to be readmitted to hospitals. No differences were observed in a before and after analysis for laboratorial parameters. Survival time of patients treated by oral and nasal routes didn't differ significantly, but was higher than the one of patients treated by a gastrostomy. Timing on enteral route implementation may be decisive for these results. It is important to assure an adequate follow-up by a health team, monitoring nutritional status of patients, granting the achievement of nutritional requirements and planning adequate nutritional intervention needed to maintain nutritional status.

Key words: home care services, enteral nutrition, cancer, outcomes

Introduction

Colorectal Cancer (CRC) is the most common forms of Gastrointestinal Cancer (GIC) and is the third and most commonly diagnosed cancer in males and females, respectively. CRC were responsible for 8% of all cancer deaths in 2008 (1). Gastric Cancer (GC), is currently the fourth most common malignancy in the world (2) and is the second leading cause of cancer deaths in both sexes worldwide (736,000 deaths, 9.7% of the total) (3).

Malnutrition occurs frequently in patients with cancers of the gastrointestinal (GI) or head and neck (HN) area due to factors other than cancer itself, such as limitations on oral intake and poor dietary habits. Side effects from antineoplasic therapy also play an important role in malnutrition development (4). Between 35 and 60% of HNC patients are malnourished and optimal nutritional support is vital for their post-treatment recovery (5). Free fat mass loss is the determinant factor of malnutrition consequences: increasing the risk of infections and treatment toxicity, decreasing response to treatment, quality of life (QoL) and life expectancy (4, 6-8).

Risk of malnutrition increases with the use of multi-modality treatments (Induction Chemotherapy and Chemoradiation) and 75-85% of patients present with significant weight loss during treatment. And a higher proportion of patients require enteral feeding (66-71% for combined modality treatment versus 12% for radiotherapy) (9, 10). The use of enteral nutrition, and prophylactic gastrostomy tubes has been proposed as a way of improving nutritional outcomes for these patients (7) and it has also been touted to be essential to meet the nutritional needs of HNC patients (8).

The aim of the present study was to assess the role of home enteral nutrition in improving survival, nutritional and clinical outcomes in patients with GIC and HNC treated with home enteral nutrition therapy in the Federal District of Brazil, as well as to associate the feeding method to these outcomes.

Materials and Methods

Design and Setting

This was a prospective and observational study with three comparison groups in terms of feeding method: Oral Supplements (OS), Nasal Route (NR – nasogastric and nasoenteric tube feedings) and Gastrostomy (GT) groups. The study variables included age, gender, clinical diagnosis, nutritional status, laboratorial parameters (hemoglobin, hematocrict, total proteins, albumin and globulin, as well as albumin/globulin (A/G)

ratio), occurrence of complications, length of hospital stay (when readmitted) and survival.

The study was conducted between January 1, 2010 and July 31, 2013 in the Public Health Department of the Federal District (PHD/FD) of Brazil, which involves all the17 public hospitals of this Federal Unit, with a medium hospital admission of 11.260 patients in a month(11).

The research project was approved by the Ethics Committee of the PHD/FD, according to Protocol number 425/2009.

Subjects

The PHD/FD issued in 2004 the first regulation of HEN supply, which consists on providing patients with industrialized enteral nutrition and its administration system. The costs of this program are completely funded by the government of the Federal District. Patients are admitted to the program after their hospital discharge and are followed by a multidisciplinary team, who reevaluates them every three months.

Calculated sample size comprised a total of 68 participants. Sample size was calculated on basis of an observational study that comprehended 401 patients (12) in which from patients initially diagnosed as malnourished, 5.75% presented a nutritional recovery at the end of the study and 4.10% had a worsening in their nutritional status as compared to the initial status (unpublished data). A level of significance of 5% and a power of test of 80% were considered. The software GPower version 3.0.5 was applied for this purpose.

A clinical sample from all patients enrolled on the HEN Program from January 1, 2010 to March 31, 2012 was selected. Patients were followed-up until July 31, 2013. The inclusion criteria of patients comprehended adults (aged 20 to 59 years) and elders (aged 60 or up) with a primary diagnosis of GIC and HNC made according to ICD-10 criteria (13). Data were collected from patients' charts of HEN Program. A data extraction form was used which included the variables mentioned before.

Patients were followed-up for 3 and a half years, according to the following study times: Time 0 = prior to HEN initiation, Time 1 = at three months of therapy beginning, Time 2 = at six months, Time 3 = at nine months, Time 4 = at 12 months, Time 5 = at 15 months, Time 6 = at 18 months, Time 7 = at 21 months, Time 8 = at 24 months, Time 9 = at 27 months, Time 10 = at 30 months, Time 11 = at 33 months, Time 12 = at 36 months, Time 13 = at 39 months and Time 14 = at 42 months.

Nutritional Status Assessment

Nutritional status was assessed by weight evolution on different study periods. At first there was the intention of collecting data on every nutritional evolution through body weight changes at each time of the study (from T0 to T-14). However, due to the high mortality rates associated to the lying disease, it was not possible to obtain statistical significance for all the period. Intra-group evolution for NR and GT was assessed from times 1 to 4 (12 months follow-up) in relation to baseline. For OR this was reached only at times 0, 3 and 6. For the purpose of comparing the three routes of administration, only assessments at 0, 3 and 6 months were considered, though statistical significance was not reached (p = 0,1653).

Clinical Assessment

This evaluation was collected from patients' records, through patients' clinical history, where their status was classified into three scores: 1 = clinical/nutritional worsening; 2 = clinical/nutritional maintenance; 3 = clinical/nutritional improvement. For the same reasons considered for nutritional assessment, comparisons of the three routes of feeding were only possible at times 3 and 6, since at baseline it was not possible to assess patients' evolution. Intra-group evolution for NR and GT was assessed from times 1 to 4 (12 months follow-up)

Complications

From patients' clinical records data on occurrence of complications - as reduction of formulas supply, hospital readmission and the length of hospital stay (in number of days) and occurrence of co-morbidities - were also collected.

Reductions of formulas supply was assessed according to the leading causes for it and were categorized into: 1 – occurrence of gastrointestinal symptoms, 2 – attempt of artisanal feeding, 3 – lack of products in the PHD/FD, 4 – GT complications, 5 – lack of carer, 6 – lack of following professionals' guidance, 7 – radio or chemotherapy, 8 - hyporexia (for patients using oral route), 9 – formula intolerance, 10 - tube feeding accidental removal and 11 – professional planning of reducing the amount of calories offered to patients.

Co-morbidities were divided into five categories: 1 – thrombosis, 2 – sepsis, 3 – lowering of renal function, 4 – CA reoccurrence and 5 - severe disease.

Laboratorial parameters

As it was not the intention of this study to propose changes in the routine of patients' follow-up, patients' laboratorial data were also collected from their charts, whenever available. Blood samples were collected and analyzed by the crew of the Clinical Analysis Laboratory of PHD/FD and interpreted according to the parameters adopted by this laboratory.

Survival

Survival was assessed from time of patient's admission to HEN Program until the occurrence of one of the following events: death or discharge of program due to oral rehabilitation or waiver on continuation on the Program until the end of the study.

Statistical Analysis

Data analysis included descriptive statistics – mean and standard deviation for quantitative variables and percentages for qualitative ones (gender, clinical diagnosis and clinical assessment, which were all converted into quantitative variables, by attributing a numeric category to them).

Longitudinal changes inter groups were tested with the model of mixed effects for repeated measures with non-structured variance and covariance matrixes, and adjustment for basal weight, gender and age. Main focuses of comparative analysis (OR x NR x GT) were changes at 3 and 6 months compared to baseline values. When the p-value was lower than 0.05, pre-specified contrasts were applied to test the following three hypothesis: whether changes presented by patients treated with NR are different from those presented by patients treated with GT; whether changes presented by patients treated with NR are different from those presented by patients treated with OR; and whether changes presented by patients treated with OR are different from those presented by patients treated with GT. Bonferroni's correction was used to adjust this three pre-specified comparisons.

For NR and GT, longitudinal changes intra-groups were also tested with the model of mixed effects for repeated measures with non-structured variance and covariance matrixes, and adjustment for basal weight, gender and age. Main focuses of intra-group analysis (NR and GT) were changes at 3, 6, 9 and 12 months compared to baseline values.

For all tests mentioned above, a residual analysis was conducted to verify if residues of this model presented a Gaussian distribution with constant variance and it was verified that suppositions of both normality and homogeneity of residues were attended.

Clinical assessment scores were observed on times 1 and 2. In order to compare whether marginal proportions of patients' conditions at 3 months differ from marginal proportions at 6 months, contrasting inter-group assessment of the three routes of feeding, it was applied the test of marginal homogeneity.

Intra-groups longitudinal measures (for NR and GT) were tested by applying the model of proportional chances with generalized estimation equations (GEE), adjusting for age and gender. Main focuses of analysis were comparisons at months 3, 6, 9 and 12 in relation to baseline.

A level of significance of 5% was considered.

Survival functions for patients submitted to treatments by three routes of feeding were estimated by Kaplan-Meier curves and compared with the log-rank test. Multiple comparisons were adjusted by Bonferroni method.

The software Statistical Analysis System (SAS) version 9.2 was used for all analysis mentioned above.

In order to evaluate the effect of laboratorial changes through the follow-up period, a before and after analysis was conducted applying paired-sample T-test. Statistical Package for Social Sciences (SPSS), version 18.0 was used for this purpose.

Complications and co-morbidities incidences were evaluated by descriptive statistics (frequencies).

Results

An amount of 82 patients with GIC and HNC were selected for the present study. Patients' sample represented 82% of all patients with cancer enrolled on the Program in the study period.

Patients with diagnosis of GIC and HNC had a mean age of 58.8 ± 11.2 years. There was a higher frequency of men in the sample (73.2%). HNC comprised 51.2% (n=42) of all cases, among which larynx cancer was the most frequent – 33.3% of cases (n=14), followed by lip and pharynx cancers, 14.3% each (n=6, each). GIC cancers were represented in the great majority of cases by esophagus ones – 70% (n=28),

followed by gastric cancers, which accounted for 25% of cases (n=10). The other 5% (n=2) were bowel cancers.

Nutritional Status Assessment

When analyzing the different methods of nutrient administration to patients, only follow-up periods 1 and 2 allowed an inter-group statistical analysis concerning weight evolution, which included all patients: 34 in NR, 41 in GT and 7 in OR.

Figure 1 presents weight evolution according to feeding route.

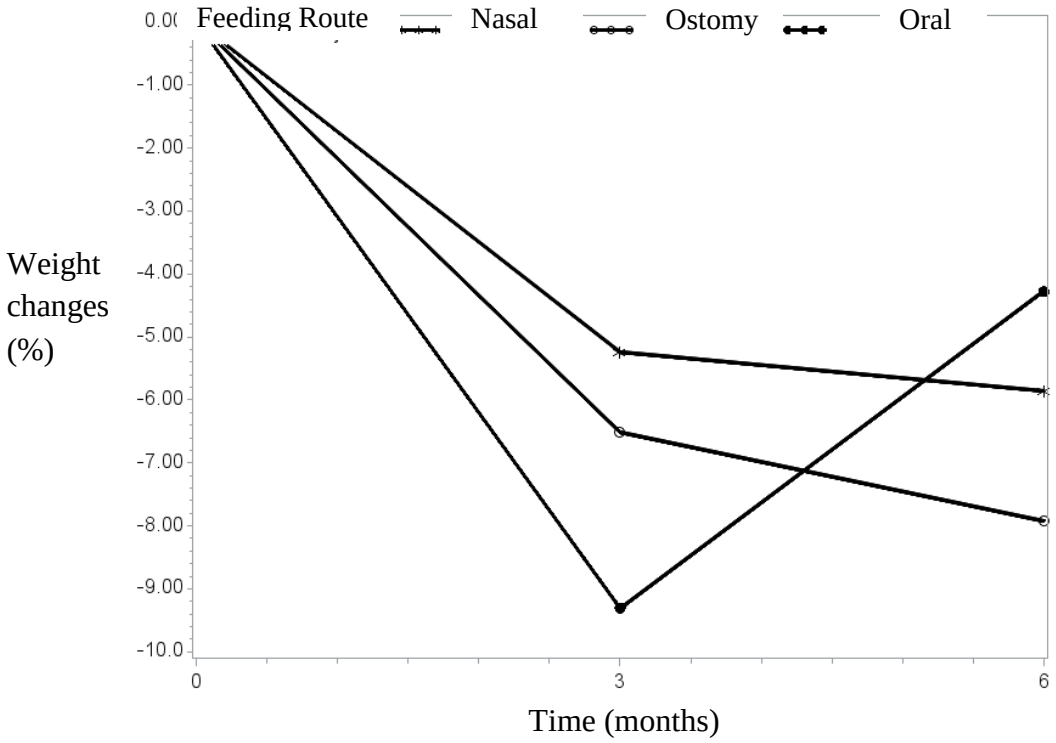

Figure 1 Percentage of medium weight changes during 6 first months of follow-up (n=82) ($p>0.05$)

Both patients treated by a NR, as the ones with GT presented weight losses during the twelve first months of follow-up. These losses reached statistical significance at months 3, 6, 9 and 12 for NR group and corresponded to -3.32 ± 1.14 kg (a 6% change in relation to baseline), -3.55 ± 1.24 kg (a 6.4% change), -3.11 ± 1.40 kg (a 5.6% change) and -3.62 ± 1.66 kg (a 6.5% change), respectively. For the GT group, weight losses reached statistical significance at months 3, 6 and 9 and were, respectively of -3.64 ± 1.25 kg (a 6.6% change in relation to baseline), -4.43 ± 1.54 kg (a 7.9% change) and -5.66 ± 2.15 (a 6.5% change). At 12 months of follow-up there was no

statistical difference in relation to baseline, which could indicate the beginning of weight recovery. On the other hand, those treated by OR presented the lowest amount of weight loss and by the end of six months had lost an average of -2,30 ± 2,39 (a 4.3% change in relation to baseline), without statistical significance (p=0.1653).

When comparing methods of feeding, there were no significant differences in weight variations through the follow-up period.

Clinical Assessment

When applying the marginal homogeneity test to assess patients' clinical evolution, both for NR as for GT groups, it was not possible to reject the hypothesis of marginal equality which means that patients' clinical conditions at 6 months follow-up didn't differ from their condition at 3 months- χ^2 = 2.7641; df = 2; p = 0,2511 and χ^2 = 2.7726; df = 2; p = 0,2500, respectively. It was not possible to apply this test for patients treated by OR due to insufficient data. Nevertheless, when applying the model of proportional chances with GEE, patients treated by NR presented a 4.12 higher chance (CI 95 1.10; 15.39) of presenting an improvement in clinical status at month 9 in relation to base line. For patients treated by a GT, there were no significant changes in the first 12 months of follow-up.

Complications

Reduction in formula supply happened to 15.8% (n=13) patients, and the main cause was the occurrence of adverse effects of chemo and radiotherapy in 6 patients (46.1%). Two patients (15.4%) presented gastrointestinal symptoms, which corresponded to vomiting, which also might be related to chemo and radiotherapy adverse reactions. Other two patients (15.4%) referred hyporexia, which might be related to cachexia syndrome. One patient (7.7%) presented weight loss due to the absence of a carer, other presented intolerance to enteral formula and another referred lack of formula supply.

Co-morbidities were presented by 7 patients (8.5%) during the course of the study and the higher incidence corresponded to infection (n=4, 57.1%), which was related to the occurrence of pneumonia for all these patients (n=4). No difference was pointed in relation to occurrence of aspiration. The other present co-morbidity corresponded to cancer relapse.

A total of 23 patients (28%) had to be readmitted to hospitals due to the presence of the mentioned co-morbidities and other complications. Mean duration of hospital stay was of 13.9 days, ranging from 1 to 60 days. One patient was readmitted due to lack of formula supply.

Laboratorial Parameters

As mentioned before, it was not the intention of this study to propose changes in the routine of patients' follow-up. For this reason, patients' laboratorial data were collected from their charts whenever available. Since a small number of patients had their laboratorial data available on their charts, a before and after analysis was conducted, comparing the baseline results with the ones of the end of the study.

Data on patients' hemoglobin and hematocrit results were available for 31 patients (37.8% of total sample). Data on patients' results of total proteins, globulin and albumin/globulin ratio were available for 13 patients (15.8% of total sample). Albumin was available for 16 patients (19.5%).

Results for laboratorial tests are presented in Table 1.

Table 1 Laboratorial results of hemoglobin and hematocrit (n=31) and total proteins, globulin and albumin/globulin ratio (n=13) and albumin (n=16) of patients with gastrointestinal, head and neck cancers treated with home enteral nutrition – a before and after analysis

Laboratory Test	Before	After	Mean difference	95% CI	t	df	p-value
Hemoglobin (Hg)	11.97 ± 2.43g/dL	11.70 ± 2.37 g/dL	0,27 ± 2.46	-0.63; 1.17	0.605	30	0.550
Hematocrit (Htc)	36.33 ± 7.2%	35.10 ± 6.56%	1.23 ± 7.45	-1.50; 3.96	0.919	30	0.366
Total Proteins (TP)	5.93 ± 1.12g/dL	5.71 ± 1.02g/dL	0.21 ± 1.37	-0.61; 1.04	0.567	12	0.581
Albumin (Alb)	3.44 ± 0.57g/dL	3.28 ± 0.53g/dL	0.15 ± 0.77	-0,26; 0.56	0.777	15	0.449
Globulin (Glb)	2.41 ±	2.50 ±	-0.08 ±	-0.58;	-0.368	12	0.719

	0.73g/dL		0.70g/dL		0.83		0.42				
Albumin/Globulin	1.53	±	1.38	±	0.15	±	-0.13	±	1.193	12	0.256
Ratio	0.29		0.46		0.46		0.43				

From the results presented at Table 2, it is possible to conclude that values of hemoglobin, hematocrit, total proteins, albumin, globulin and albumin/globulin ratio didn't change through the study follow-up time.

Survival

At the end of the study 33 patients (40.24%) had died.

Figure 2 shows the Kaplan-Meier survival curve of patients with gastrointestinal, head and neck cancers according to the route of feeding.

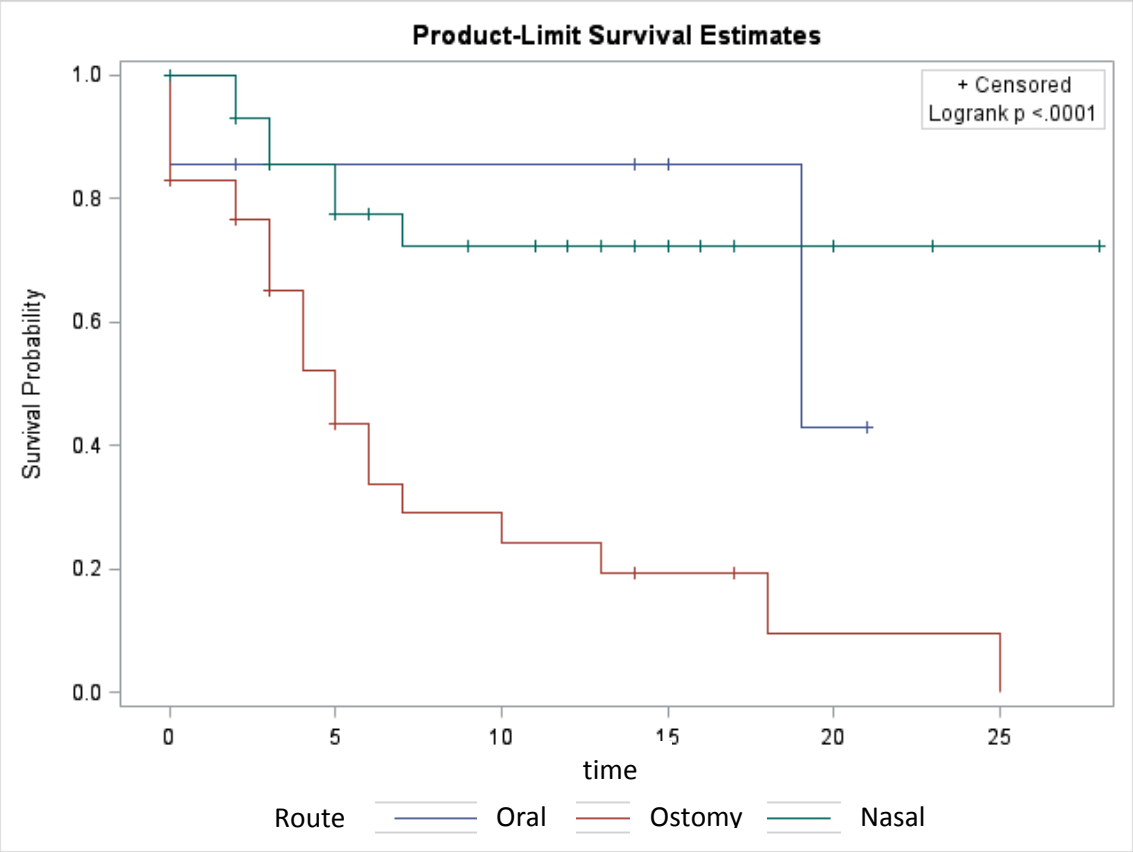

Figure 2 Survival probability in time according to route of feeding of patients with gastrointestinal, head and neck cancers in home enteral nutrition (n=82)

From the result of log-rank test it is possible to conclude that patients' survival time differs at least between two routes of feeding (p=0.0004).

Table 2 shows the results of multiple comparisons with the adjustment of Bonferroni.

Table 2 Adjustment for Multiple Comparisons for the Logrank Test with Bonferroni's adjustment

Strata Comparison		Chi-square	p-Values	
Route	Route		Raw	Bonferroni
Oral	Ostomy	13.9846	0.0002	0.0006
Oral	Nasal	4.5241	0.0334	0.1003
Ostomy	Nasal	17.3125	<0.0001	<0.0001

From the result of multiple comparisons with the adjustment of Bonferroni, it is possible to draw the following conclusions: survival time of patients treated by OR or NR didn't differ significantly (p=0.1003); survival time of patients treated by OR is significantly higher than the one of patients treated by GT (p=0.0006); survival time of patients treated by NR is significantly higher than the one of patients treated by GT (p<0.0001).

Discussion

The main indications for PEG in the literature are dysphagia, cerebral contusion, Parkinson's disease, head malignancy, among others (14). Besides to the direct involvement of the digestive tract in gastrointestinal or head and neck cancers, the treatments of these tumors (chemotherapy, radiotherapy and surgery) burdens the organism, with the result that patients are usually unable to meet their nutritional needs (15), which leads to nutritional therapy indication.

Researchers state that head and neck cancer incidence is higher in men, which also occurs with the most common forms of gastrointestinal cancers, that comprehend gastric and colorectal ones (1, 3, 16). In accordance to these studies, the present one found a higher frequency of men in this group of patients (73.2%), with a median age of 58 years old, which is also in accordance to the mean age of around 60 years found in other studies (5, 6, 15, 17).

Nutritional Status Assessment

In the present study mean weight by 6 months didn't reach statistical significance when comparing different feeding methods. All feeding routes showed a weight loss, which was smaller for the OR group and higher for GT group. These findings are different from those found by Corry et al (17), where the authors found a greater weight loss for NR in comparison to GT both at 6 weeks (mean weight loss for NR = -3.7kg, while there was a median weight gain for GT = 0.8kg; $p<0.001$) as at 6 months, where NR experience a weight decrease in relation to baseline of 4.3kg, and this decrease for GT group was of 1.0kg ($p=0.04$). It is worth mentioning that baseline weights between groups didn't differ ($p=0.11$). The authors also found that at 6 months a greater proportion (35%) of patients of NR group presented an important weight loss of more than 10%, than patients of GT group (13%) ($p=0.09$).

In a study with a small sample conducted by Anwander et al (15), 15 patients who received a prophylactic PEG were compared to 15 patients who underwent post-operatory nasogastric feeding. The PEG group experienced greater improvements on nutritional status. In the study of Nugent et al (9) Prophylactic PEG (PPEG) was also compared to nasogastric feeding, a conventional PEG (placed after surgery) and oral route and PPEG group was the one who presented the least amount of weight loss, though there were no statistical difference for feeding methods. Another small study sample (7) also showed by multivariate analysis that patients who received a PPEG ($n=7$) lost less weight than the control group ($p=0.016$).

The study conducted by Sadasivan et al (4) compared 44 patients with Nasogastric Tube (NGT) to 50 patients fed by a PEG and the authors concluded that PEG patients performed better than NGT ones in terms of hemoglobin levels and of weight gain at a 6-weeks analysis. When comparing PEG to NGT weight losses were of $-3.31\pm0.97\%$ and $-11.0\pm1.8\%$, respectively. They weren't able to perform a 6-months analysis since all NGT patients converted to PEG at this time. The authors concluded that PEG is more efficacious than NGT as a channel for nutrition in advanced head and neck cancer patients over a short duration.

Paccagnella et al (18) investigated whether early nutrition intervention had a positive impact on weight and cancer treatment tolerance, in relation to a conventional nutritional treatment (after the beginning of therapy). Each group comprehended 33 patients and the intervention group (early nutrition), at the end of four weeks, received either oral supplements (36.6%) or enteral nutrition (60.6%), the great majority through

a NGT. The Intervention Group (IG) presented significant less weight loss, which accounted in the 6 months of treatment for -2.35 ± 8.15kg in the intervention group and -9.55 ± 8.10 kg in the Control Group (CG) (p=0.0077). Considering the whole treatment period, IG also presented a lower weight loss in comparison to CG (p=0.024).

In the present study, the timing of enteral routes insertion was not established, though it is believed that this happened after the beginning of patients' treatment, since they were discharged to their homes with enteral nutrition. Time 0 of this study corresponds to patients' admission to the HEN Program of the PHD/DF. This way the results found in the present study concerning GT groups might be a consequence of a late availability of this feeding method. As observed in most of the studies, despite of the small sample of some, a prophylactic insertion of a GT was associated to better nutritional outcomes and is claimed to significantly reduce weight loss and the rate of hospitalization during radiotherapy (7, 9, 15). Nugent et al (9) also state that the method of feeding should reflect the anticipated length of feeding required, since malnutrition is significantly associated as a poor prognosis indicator for cancer treatment.

In relation to nutritional status, some authors refer that weight maintenance leads to beneficial outcomes and suggest that this, rather than weight gain, may be a more appropriate aim of nutritional support during radiotherapy (6, 18).

Clinical Assessment

The scoring system applied in the present work wasn't used in any other article which hinders comparisons. Some of the scientific literatures assess clinical evolution through the incidence of complications which was also conducted in this article and will be discussed below. Due to the small number of patients treated by oral route in the present study (n=7) it was not possible to draw any conclusions for this group of patients. Patients who were submitted to a NR feeding showed a clinical improvement that reached statistical significance only at month 9 of follow-up. GT group didn't present significant changes through the first year of the study.

Complications

Complications assessed in the present study included ones that could hinder the achievement of nutritional requirements, leading to reduced formula intake, as well as complications related to worsening of disease burden (co-morbidities) that would lead to patients' clinical decay. Total complications (due to formula reduction and co-

morbidities) took place in 24.4% of cases (n=20). Main reasons presented in this research concerning reduction on formula supply were related to adverse effects of cancer treatments (chemo and radiotherapy) in six of 82 patients, the incidence of vomiting in two patients and hyporexia referred by other two. The main co-morbidity was pneumonia in 4 patients. There were no reports on tube-related complications such as leakage, infection or accidental removal, which were also investigated by the present study.

Eley et al (5) also assessed the occurrence of minor complications in patients treated either with a PEG or a NGT. The amount of the reported complications was of 16% of patients (n=19), who presented minor complications, and 8.3% (n=10) presented major complications, totalizing 24.3% complications, similar to the present study. Main causes of minor complications were overgranulation of stoma (n=7) and abdominal pain (n=4), both not referred in the present research. The main cause of major complications was significant abdominal pain in 5 cases, 3 of which were not related to the gastrostomy.

The study of Sadasivan et al (4) also assessed complications occurrence, related to local site infections and tube dislodgement. NGT patients had significant local site infections (64% - n=28) while PEG patients presented only 4% (n=2). The authors found no tube dislodgement in the PEG group while the NGT group had 36% (n=16) tube dislodgements that required reinsertion.

When it comes to hospital readmission, 28% of patients had to be readmitted due to mentioned complications. The only study that dealt with this subject was published by Paccagnella et al (18), though no mention is made concerning length of hospital stay. The authors claim that control group had significantly more unplanned hospital admissions (41.4%) in relation to intervention group that dealt with early nutritional support (16.1%) ($p<0.05$). Though this study didn't analyze subgroup differences concerning hospital readmission, the value found approaches the mean found by these authors (28.75%).

Laboratorial Parameters

Patients' laboratorial parameters didn't reach statistical significance when comparing the values between baseline and the end of the study. Values of hemoglobin, hematocrit, total proteins and albumin remained slightly below normal ranges at the end of the study (11.70 ± 2.7 g/dL, 35.10 ± 6.56%, 5.71 ± 1.02 g/dL and 3.28 ± 0.53 g/dL

respectively). Anemia was a common occurrence related by health professionals. When analyzing Iron amounts of standard enteral formulas, it was found to be within recommendations (according to Dietary Recommended Ingestion). However, Copper amount is over recommendations and this mineral may compete with Iron for intestinal absorption, which may result in Iron deficiency (data not published). Globulin and Albumin/Globulin ratio were among normal values.

Sadasivan et al (4) also assessed laboratorial parameters in two groups of HNC patients, one fed by PEG and the other by NGT. In a 6-weeks follow-up the authors found that PEG group performed better than NGT one in terms of Hemoglobin levels, but not Albumin – for this parameter there was no statistical significance in relation to baseline levels. Changes on hemoglobin levels corresponded to -1.23 ± 1.0% for PEG group and -6.51 ± 2.94% for NGT group ($p<0.001$). Hemoglobin levels at baseline were similar to the ones found in the present study (11.79 ± 1.14 g/dL for PEG group and 11.3 ± 1.08 g/dL for NGT group in relation to 11.97 ± 2.43 g/dL found at baseline of this study). Albumin levels at baseline were also similar between studies (3.2 ± 0.11 g/dL for PEG group and 3.2 ± 0.07 g/dL for NGT group in relation to 3.44 ± 0.53 g/dL found at baseline of this study).

The study of de Luis et al (19) also approached laboratorial analysis. The authors studied a group of 102 patients, from whom 69.6% were diagnosed with HNC. Patients were distributed in two groups according to feeding method: group I for OR, with 79.4% (n=81) of patients, and group II for EN (NGT, PEG and Jejunostomy (JT)). In a 3-years follow-up, the authors found that albumin, prealbumin, transferring and lymphocytes improved in all the groups when comparing the first review to the last.
In group I albumin levels went from 3.1 ± 0.7 g/dL at baseline to 4.18 ± 0.9 g/dL at last revision. In group II the levels went from 2.9 ± 0.7 g/dL at baseline to 4.18 ± 0.9 g/dL at last revision ($p<0.05$ for all analysis). This is different from the findings of the present study where no improvements on albumin levels were observed in a similar follow-up period. However, it is worth mentioning that since this study didn't propose any changes on routine follow-up of patients the amount of available data may have influenced final results (ranging from 15.8 to 37.8% of patients).

Since the number of patients that presented laboratorial results in the present study was small (ranging from 13 to 31 patients), a subgroup analysis was not possible to be conducted.

Survival

Three studies addressing this subject were found, dealing with several kinds of diseases (20). All assessed survival with Kaplan-Meier curves and the log-rank test like the present research. No studies that worked exclusively with cancer patients were found for comparison purposes to the present one.

Schneider et al. worked with 417 patients from whom 380 were adults and elders. All patients were discharged from the hospital on HEN. Main diagnoses for these patients were neurological disorder (38.9%), digestive disease (20%), head and neck cancer (16.8%) and dementia (14.2%). The authors found that mortality was positively associated to dementia, head and neck cancer and age higher than 70 years. They mainly assessed survival at 1month, 1 year and 5 years (20).

The study conducted by de Luis et al (19) involved 102 adult patients, whose characteristics were mentioned above. The authors state that all patients were discharged from the hospital on HEN, although 79.4% were able to receive HEN through oral route – the authors referred them as having oral intake conserved. Concerning HNC patients no mention was made related to whether these patients received cancer therapies (radio or chemotherapy). Though they state Kaplan-Meier curves with log-rank test were applied in order to analyze survival, these results are not shown in the text. They also calculated hazard ratio for mortality according to study groups.

Leeds et al (21) dealt with a survival analysis after two techniques of gastrostomy insertion, radiological (PIG) and endoscopic ones (PEG). They included patients with dysphagic stroke (n=36), oropharyngeal cancer (n=175), neurological cancer (n=116), cognitive impairment (n=5) and other (n=71). Of all 403 patients, 170 patients were in the PIG group and 233 in the PEG. The authors found similar mortalities for a 30-day and a 1-year analysis. They also assessed mortality at 90 days.

In the present research, survival was higher for patients fed orally and through a NR than of the ones fed by GT. There was no difference between OR and NR groups.

Schneider (20) found a 1-month survival of 80%, while the present study found a 3-months survival of 85.6% for NR. GT group, which had the worst survival in the present study, was lower – of 65.3%. The first authors also found a 24-months survival of 41.70%. In the present study there were no data on survival higher than 19 months (for the OR), which was of 42.86%. For GT group the higher follow-up considered for survival analysis corresponded to 18 months – 9.7% (this was the group that presented the worst survival), while for NR, 7 months only, of 72.3%. This fact hinders any other

comparisons to these authors' study. It is worth mentioning that the authors found as a result of a multivariate analysis with patients between 16 and 70 years old, that among independent factors associated with death at the end of follow-up was head and neck cancer with a Relative Risk (RR) of 2.14 (95% CI: 1.03-4.67).

De Luis (19) state that a 3-years survival was of 90.2%. They also affirm that poor prognosis was associated to HNC at an advanced stage, but there is no mention of mortality in this subgroup of patients. Authors claim that survival probability was influenced by the access route, with the worse outcome in patients without oral nutrition. In a multivariant analysis, oral nutrition was associated with the best prognosis, with a hazard ratio of 24.9% (95% CI: 4.1-52), adjusted by age, sex and diagnosis. In the present study the mortality rates after a 42-months follow-up was of 40.24%, but it is not possible to compare this finding to the one presented by the authors, since in the present study only 7 patients (8.5%) presented a conserved oral intake.

In the study conducted by Leeds et al (21), the 1-month survival for the PEG group corresponded to 89.3% which was similar to the 3-months survival for NR group in the present study – 85.6%. The 2-months survival for GT patients of the present study was smaller, corresponding to 76.8%. The 3-months survival found by the authors was of 82.4%, similar than the one found for NR in the present study, but higher than the GT group (65.3%). In the analysis of the authors, the 1-year survival was of 43.3%. In the present study the 13-months survival for the GT group was of 19.3%, smaller than the one presented by the authors, but the 19-months survival for the OR was of 42.8%, though there was a small number of patients in this group.

Due to the difference of studied groups conducted by the other authors (20) on survival, comparisons to the present study become distorted.

Limitations of the present study specially relate to the fact that its sample wasn't randomized, which allows occurrence of selection bias, although the sample comprised 82% of all patients enrolled on the Program in the study period. Other concern refers to the fact that information was collected from patients' charts, which may induce information bias and harms the complete availability of data (like laboratorial parameters). Some authors state that a randomized design for this type of study may raise ethical conflicts, since it is not ethical to allow a group of patients to starvation for purposes of having a control group (22, 23), which difficult controlling selection bias. Other limit refers to the fact that though nutritional parameters were monitored, the

calorie intake was not recorded, but it is important to enlighten the fact that all patients were followed-up by a health team, including the nutritionist, who granted the meeting of nutritional requirements.

Conclusion

In the present study it was observed that enteral nutrition was an effective tool in improving survival, which was found to be similar than oral route. In terms of nutritional recovery, there was found no difference among feeding routes, which all presented weight losses. This is a different finding from other studies that claim percutaneous endoscopic gastrostomy is effective in recovering weight, even in a short time duration. Timing on enteral route implementation may be decisive for these results, since a prophylactic insertion is related to better outcomes, including improved cancer treatment tolerance.

Clinical evolution, assessed through a score system, showed maintenance of clinical status for patients treated with gastrostomy while patients treated by nasal routes presented a significant improvement at nine months of treatment.

In a non-stratified analysis, laboratorial data on hemoglobin, hematocrit, total proteins, albumin, globulin and ratio albumin/globulin also showed maintenance in a before and after analysis. Despite adequate amounts of iron supplied by enteral formulas, values of hemoglobin and hematocrit remained below normal values. When analyzing the micronutrient profile of standard enteral formulas, it is possible to identify values of copper that exceed recommendations. This may explain why anemia was not recovered, since copper may compete with iron for intestinal absorption. Industries that produce enteral formulas should revise the content of micronutrients in order to prevent interactions.

Values of total proteins and albumin showed slightly below normal ranges since the study beginning, while globulin and albumin/globulin ratio remained between normal ranges. A favorable nutritional status is a decisive factor for nutritional therapy success in improving patients' outcomes as survival and tolerance of cancer therapies.

There is a lot of controversy on applying enteral nutrition for long term in patients with cancers, especially because of the high costs associated to a percutaneous endoscopic gastrostomy. In fact, oral route should be encouraged for every patient whose oral integrity is preserved. However, whenever a nutritional risk is anticipated due to cancer treatments, early introduction of a nutritional support must be considered

in order to prevent malnutrition and to improve tolerance to these treatments. Most important is to assure an adequate follow-up by a health team, monitoring nutritional status of patients, granting the achievement of nutritional requirements and planning adequate nutritional intervention needed to maintain nutritional status.

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Conflict of interests

The authors declare no conflict of interests.

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8 CONCLUSÕES

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A população acompanhada nos 42 meses desta pesquisa foi representativa do total de pacientes em terapia de nutrição enteral domiciliar vinculados à rede pública de saúde do Distrito Federal, correspondendo a 56% dos pacientes portadores de disfunções neurológicas admitidos no Programa de Terapia de Nutrição Enteral Domiciliar da Secretaria de Estado de Saúde do DF, no período do estudo, e 82% dos portadores de câncer gastrointestinal ou de cabeça e pescoço, admitidos no mesmo período. Deste modo, os achados da pesquisa podem ser extrapolados à mesma população de pacientes do Distrito Federal.

Da mesma forma que encontrado em literatura científica internacional, as doenças neurológicas, incluindo as demências, têm sua prevalência aumentada com o avanço da idade dos pacientes, sendo o perfil demográfico destes pacientes correspondente à faixa etária idosa com predominância do sexo feminino. Em relação aos portadores de neoplasias gastrointestinais ou de cabeça e pescoço, sua prevalência se refere à faixa etária adulta próxima ao início da terceira idade, com maior frequência do sexo masculino.

Mediante os achados do presente estudo demonstrou-se que a terapia de nutrição enteral domiciliar, quando adequadamente indicada e implementada sob o acompanhamento rotineiro de equipe especializada, possui efetividade na reabilitação nutricional, na manutenção de parâmetros clínicos e laboratoriais dentro dos valores de normalidade ou muito próximos aos mesmos (exceto para hemoglobina e hematócrito), na recuperação (cicatrização) de úlceras de decúbito e no aumento da sobrevida dos pacientes, o que se relacionou proporcionalmente ao status socioeconômico dos mesmos.

Contrapondo-se à literatura internacional, que contraindica a nutrição enteral para portadores de disfunções neurológicas, em especial as demências, o presente estudo verificou como via mais favorável a um melhor prognóstico, a gastrostomia, com maior sobrevida, inclusive em relação à apresentada por outros autores. Tal melhoria não se referiu apenas ao aspecto de prolongamento da vida, mas prolongamento com qualidade, que se evidencia pela melhora clínica dos pacientes, sobretudo no que se refere à capacidade de cicatrização das úlceras de decúbito, que se constituem grande porta de entrada para infecções e aumento de mortalidade nesta população.

No tocante aos portadores das neoplasias, reforça-se a importância da implementação precoce da terapia nutricional (sobretudo aquela prevista por longo prazo, através das estomias), no sentido de se prevenirem as complicações relacionadas aos efeitos adversos das terapias antineoplásicas, que foram observadas no presente estudo. Entretanto, não existe consenso em literatura ou diretrizes, que estabeleçam o tempo ideal de introdução da nutrição enteral profilática para tais pacientes – somente se reforça a necessidade de início desta terapia antes do estabelecimento das terapias antineoplásicas. Para este grupo de pacientes, não houve diferenças entre a suplementação oral e as vias nasais de alimentação enteral, quanto à sobrevida, que se mostrou menor para o grupo das estomias. Vale lembrar que todos os pacientes portadores dessas doenças, independente da via de acesso, apresentaram perda ponderal em relação ao tempo basal do estudo, o que indica o uso da nutrição enteral de forma tradicional e não profilática. A manutenção de peso para esta população, ao invés do ganho, tem sido apontada como fator favorável à adequada resposta terapêutica.

Reforça-se a necessidade de treinamento adequado dos pacientes e/ou seus cuidadores, quanto à técnica de manipulação das fórmulas enterais, no sentido de se garantir o sucesso e inocuidade da terapia. Mesmo com os desfechos favoráveis encontrados no presente estudo, ainda se verificou, entre os pacientes portadores de disfunções neurológicas, a ocorrência da redução do fornecimento de fórmulas aos pacientes por não seguimento da prescrição feita pelos profissionais de saúde, por parte dos cuidadores. Tal fato pode ter contribuído para um subdimensionamento dos resultados aqui apresentados, mas reforça a necessidade de uma abordagem mais efetiva dos pacientes e/ou seus cuidadores quanto ao entendimento das orientações passadas, sobretudo para aqueles com nível socioeconômico mais reduzido, o que está intimamente relacionado a um menor grau de instrução e menor compreensão da importância da terapia nutricional.

Enfatiza-se que o estado nutricional é um fator decisivo para o sucesso terapêutico e para melhora de sobrevida, cicatrização de úlceras de pressão e redução das taxas de complicação, o que em termos de políticas públicas, implica redução dos gastos com o cuidado de portadores de doenças crônicas. Ao se contemplar a situação precária do sistema de saúde público nacional, com demandas cada vez mais crescentes por leitos hospitalares, paralelas à exaustão dos recursos disponíveis para resolução, deve-se considerar a atenção domiciliar como uma alternativa para gestão dos recursos de saúde.

Desta maneira, pretende-se que a presente tese venha sensibilizar os gestores em saúde pública, quanto à adoção de políticas nacionais que contemplem o fornecimento de fórmulas especializadas para nutrição enteral domiciliar, uma vez que a manutenção de um bom estado nutricional reduz os custos com a reinternação de pacientes crônicos, viabilizando a liberação de leitos para atendimento de quadros agudos de doenças, além de melhorar a qualidade de vida dos pacientes, relacionada à sua reinserção em seu ambiente familiar. É fundamental que tais políticas contemplem o adequado acompanhamento destes pacientes por profissionais especializados, para que o sucesso do tratamento domiciliar seja garantido, bem como que haja uma interface entre os serviços de atendimento ao paciente (hospitalar, ambulatorial e domiciliar), propiciando o fortalecimento da rede assistencial de saúde, com sistemas de referência e contra-referência. Além disso, considerando-se o aspecto da humanização do atendimento ao paciente, é essencial a inclusão de estratégias que abordem a atenção à saúde do cuidador, havendo necessidade de estudos sobre este tema.

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10 ANEXOS

GOVERNO DO DISTRITO FEDERAL
SECRETARIA DE ESTADO DE SAÚDE
Fundação de Ensino e Pequisa em Ciências da Saúde

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BRASÍLIA

COMITÊ DE ÉTICA EM PESQUISA/SES-DF

Carta Nº 366/09 - CEP/SES. Brasília, 11 de dezembro de 2009.

Ilmº (a) Senhor(a)

Diretor(a) Do: DAE/SES-DF

Assunto: aprovação projeto de pesquisa – 425/09 - CEP/SES/DF

Senhor(a) Diretor(a),

Participamos a V. Sa. que o projeto **Terapia de Nutrição Enteral domiciliar - uma alternativa eficaz para a recuperação nutricional?** em conformidade com a Resolução 196/96 Conselho Nacional de Saúde/Ministério da Saúde - CNS/MS e suas complementares.

Data da aprovação: 11/12/09.
Período da pesquisa: 11/209 A 05/2010
Pesquisador responsável : ANA LÚCIA R.S. ZABAN - 34368068

Os dados serão coletados no (a) DAE/SES-DF o pesquisador deverá observar as responsabilidades que lhe são atribuídas na Resolução 196/96 CNS/MS, incisos IX.1 e IX.2, em relação ao desenvolvimento do projeto.

Ressaltamos que a conduta do pesquisador, assim como o seu acesso à Unidade de Saúde deve seguir as normas e os procedimentos preconizados pela Secretaria de Estado de Saúde do Distrito Federal. O pesquisador deve se apresentar ao Diretor da Unidade de Saúde para os procedimentos administrativos necessários.

Atenciosamente.

Maria Rita Carvalho Garbi Novaes
Comitê de Ética em Pesquisa/SES-DF
Coordenadora

Ângela Maria /CEP/SES/DF

Fundação de Ensino e Pesquisa em Ciências da Saúde - SES
Comitê de Ética em Pesquisa
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Recebi em 16/12/09
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Fundação de Ensino e Pesquisa em Ciências da Saúde

COMITÊ DE ÉTICA EM PESQUISA/SES-DF

EMENDA A PROJETO **Projeto nº 425/09**

I – IDENTIFICAÇÃO
Título: Terapia de Nutrição Enteral domiciliar – uma alternativa eficaz para a recuperação nutricional?
Pesquisador responsável: Profissional de saúde
Data de entrada no CEP: 26/03/2012
Data de Distribuição: 28/03/2012 - Redistribuído

II – INTRODUÇÃO: MOTIVO(s) DA EMENDA

Considerando minha aprovação no processo seletivo para Doutorado em Ciências da saúde da Universidade de Brasília, com a mesma linha de pesquisa apontada no Projeto de pesquisa acima referenciado: - Venho solicitar a prorrogação da validade do protocolo de pesquisa número 425/09, para um ano adicional, ou seja, até dezembro de 2012.

Justificativa: adequação aos dados disponíveis na instituição. Mudança da metodologia (consulta a prontuário) e a inclusão de um questionário que será aplicado à chefia da UTI.

III – PARECER DO CEP FRENTE ÀS RESOLUÇÕES 196/96 CNS/MS E COMPLEMENTARES

Considerando o acima exposto no item II – Motivo da emenda – estamos de acordo com a prorrogação solicitada, desde que o Projeto acima referido siga a mesma linha do que estava proposto.

IV – EMENDA:

Aprovada

Brasília, 09 de abril de 2012.
(data da reunião do CEP)

Atenciosamente,

Luiz Fernando Galvão Salinas
Comitê de Ética em Pesquisa/SES-DF
Vice-Coordenador

AL-CEP/SES/DF