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Sepsis in burned patients

Sepse em pacientes queimados

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Abstract *A prospective study was conducted from June 2001 to May 2002 at the Burns Unit of Hospital Regional da Asa Norte, Brasília, Brazil. During the period of the study, 252 patients were treated at the Burns Unit, 49 (19.4%) developed clinically and microbiologically proven sepsis. Twenty-six (53.1%) were males and 23 (46.9%) females with a mean age of 22 years (range one to 89 years) and mean burned body surface area of 37.7 ± 18.4% (range 7 to 84%). Forty-three patients had flame burns, five a scald and one an electric burn. These 49 patients had a total of 62 septic episodes. Forty (81.6%) patients had only one and nine (18.4%) had up to three episodes of sepsis. Thirty (61.2%) patients had their first septicemic episode either earlier or by one week postburn. Out of 62 septic episodes, 58 were due to bacteria and four due to* Candida *sp. The most common bacteria isolated from blood culture were* Staphylococcus aureus*, coagulase-negative* Staphylococcus, Acinetobacter baumannii, Enterobacter cloacae *and* Klebsiella pneumoniae*. Eleven (18.9%) episodes were due to oxacillin resistant* Staphylococcus aureus. Acinetobacter baumannii *was sensitive to ampicillin/sulbactam in 71.4% and to imipenem in 85.7% of the cases. The primary foci of sepsis were the burn wound in 15 (24.2%) episodes. The most common clinical findings of sepsis in these patients were fever, dyspnea, hypotension and oliguria. The most common laboratory findings of these patients were anemia, leukocytosis, hypoalbuminemia and thrombocytopenia. Twelve (24.5%) patients died. The appropriate knowledge of clinical, epidemiological, laboratorial and microbiological aspects of sepsis in burned patients permits an adequate diagnosis and treatment of this complication.*

Key-words*: Burn. Sepsis. Hospital infection.*

Resumo *Um estudo prospectivo foi realizado de junho de 2001 a maio de 2002, na Unidade de Queimados do Hospital Regional da Asa Norte, Brasília, Brasil. Durante o período do estudo, 252 pacientes foram tratados na Unidade de Queimados, 49 (19,4%) desenvolveram sepse clinicamente e microbiologicamente provada. Vinte e seis (53,1%) eram homens, 23 (46,9%) eram mulheres, com uma média de idade de 22 anos (variação de um a 89 anos) e superfície corporal queimada total de 37,7 ± 18,4% (variação de 7 a 84 %). Quarenta e três pacientes tiveram queimaduras por chama aberta, cinco por escaldamento e um por queimadura elétrica. Esses 49 pacientes tiveram um total de 62 episódios septicêmicos. Quarenta (81,6%) pacientes tiveram somente um episódio de sepse e nove (18,4%) tiveram até três episódios. Trinta (61,2%) pacientes tiveram seu primeiro episódio septicêmico dentro da primeira semana após a queimadura. Dos 62 episódios de sepse, 58 foram bacterianos e quatro por* Candida *sp. As bactérias mais comumente isoladas das hemoculturas foram* Staphylococcus aureus*,* Staphylococcus *coagulase-negativo*, Acinetobacter baumannii, Enterobacter cloacae *e* Klebsiella pneumoniae*. Onze (18,9%) episódios foram devido a* S. aureus *resistentes à oxacilina.* A. baumannii *era sensível a ampicilina/sulbactam em 71,4% e ao imipenem em 85,7% dos casos. O foco primário da sepse foi a queimadura em 15 (24,2%) episódios. Os achados clínicos mais comuns da sepse foram a febre, dispnéia, hipotensão e oligúria. As alterações laboratoriais mais comuns foram a anemia, leucocitose, hipoabuminemia e trombocitopenia. Doze (24,5%) pacientes morreram. O conhecimento apropriado dos aspectos clínicos, epidemiológicos, laboratoriais e microbiológicos da sepse no paciente queimado favorecem um adequado diagnóstico e tratamento dessa complicação.*

Palavras-chaves: *Queimadura. Sepse. Infecção hospitalar.*

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Despite advances in the use of topical and parenteral antimicrobial therapy, and the practice of early tangential excision, sepsis remains a major cause of death in burn victims today. Few patients are as susceptible to the development of systemic infections as burn patients. Severe dysfunction of the immune system, a large cutaneous colonization, the possibility of gastrointestinal translocation, a prolonged hospitalization and invasive diagnostic and therapeutic procedures, all contribute to sepsis[1 2 7 9 19 20 21 30].

The experience accumulated over the past three decades, in the early interventional treatment of burns patients has dramatically changed the cause of death; it is now estimated that about 75 percent of the mortality following burn injuries is related to infections, rather than to osmotic shock and hypovolemia. Therefore, knowledge of the responsible microflora, together with its prevalence and bacterial resistance, is of crucial importance for fast and reliable therapeutic decisions.

The present study was undertaken to analyze 49 clinically diagnosed and blood culture positive sepsis patients who were treated during a one-year period. The identification of the microorganisms and the susceptibility of all bacteria isolated were studied.

PATIENTS AND METHODS

Our analysis was based on a prospective study which was conducted from June 2001 to May 2002 at the Burns Unit of Hospital Regional da Asa Norte, Brasília, Brazil.

Since 1980, patients having partial thickness skin burns covering less than 25 percent of the body surface area, were not generally admitted to the Burns Unit if they were adults, or less than 10 per cent if they were children. Patients with full thickness skin burns of small extent (≤5% of the body surface area), were also treated as outpatients until the wound was ready for excision and grafting by members of plastic surgery team. Commonly admission to the Burns Unit only occured with severely burned patients (>25-30% of the body surface area).

All patients who were admitted to the Burns Unit were resuscitated based on the Parkland formulae guidelines using crystalloids, except in few cases where there was either delayed or difficult resuscitation and colloids were used earlier than 24h postburn[15].

Silver sulfadiazine (1% flamazine) was used topically and the dressings were changed daily. The wound was inspected daily during dressing and swabs for culture from the burn wounds were taken weekly or when an infection was suspected.

Sepsis was suspected when a patient showed signs of disorientation, hyperthermia or hypothermia, circulatory embarrassment, hemorrhages, leukocytosis, thrombocytopenia and/or oliguria. A blood culture was always done for confirmation and the results of all microbiological cultures of the burn wound, urine, tracheal secretion and vascular catheter were considered.

A set of two blood cultures was taken with an interval of one hour in patients with clinical sepsis. Blood samples were not taken through the central venous catheters, but through another central vein. The immediate institution of empirical antibiotic therapy in such cases was done after consultation with the microbiologist reviewing the previous burn wound swab cultures. The bacteriological isolation was carried out in the microbiology laboratory of the Hospital Regional da Asa Norte, Brasília. The blood specimens were processed in a Bact Alert 120® and in a MicroScan 96® machine which is known for quick detection of bacterial growth leading to an early diagnosis. Repeated specimens were collected if cultures were negative after 24h. If positive, the microbiologist immediately contacted the clinician with the Gram stain results and antibiotic therapy was modified whenever necessary. The specific isolation of pathogen was made using a specific culture medium for bacteria (blood agar for gram positive and MacConkey for gram negative) or fungus (Sabouraud's dextrose agar).

The criteria for determining the source of sepsis were: a) finding of the same pathogen as in the blood culture in burn wound, urine, tracheal exudates, or vascular catheter; b) Clinical and bacteriological evidence of infection: discoloration and odor from the wounds > 10^5 organisms/g tissue; urinary tract infection with 10^5 cfu/ml urine; respiratory tract infection; catheter-related infection were defined as those giving >15cfu. On removal of the vascular or urinary catheter, the distal tip (about 20mm long) was cut and investigated in the microbiology laboratory using roll plate method[13].

RESULTS

Two hundred and fifty-two cases were treated as in-patients at the Burns Unit of Hospital Regional da Asa Norte during the period of the study, 49 (19.4%) developed clinically and microbiologically proven sepsis during their stay in the hospital. Twenty-six (53.1%) were males, 23 (46.9%) females, with a mean age of 22 years (range one to 89 years) and mean total body surface area burn of 37.7 ± 18.4% (range 7 to 84%).

The flame burn was the predominant cause of burns amongst patients who had sepsis. Forty-three had flame burns, five a scald and one had a electric burn. These 49 patients had a total of 62 septic episodes. Forty (81.6%) had only one and nine (18.4%) had up to three episodes of sepsis.

Thirty (61.2%) patients had their first septic episode between 3 – 7 days postburn, 14 (28.6%)

between 8 – 14 days and five (10.2%) after 15 days postburn.

Out of the 62 septic episodes, 34 (54.8%) were due to gram positive, 11 (17.7%) due to gram negative, four (6.5%) due to fungi and 13 (21%) due to mixed organisms. Out of the 62 episodes, 58 (93.5%) were due to bacteria and four (6.5%) due to fungus (*Candida* sp). The most common bacteria isolated from blood culture were *Staphylococcus aureus*, coagulase-negative *Staphylococcus, Acinetobacter baumannii, Enterobacter cloacae* and *Klebsiella pneumoniae*. Eleven (18.9%) episodes were due to oxacillin resistant *Staphylococcus aureus* (Table 1).

Table 1 - Microbial etiology of 58 bacteraemic episodes of sepsis in 49 burned patients treated at the Burns Unit of Hospital Regional da Asa Norte, Brasília, from June 2001 to May 2002.

Isolate	Number	Percentage
Staphylococcus aureus		
oxacillin susceptible	16	27.6
oxacillin resistant	11	18.9
Coagulase-negative		
Staphylococci	12	20.7
Acinetobacter baumannii	7	12.1
Enterobacter cloacae	7	12.1
Klebsiella pneumoniae	5	8.6
Pseudomonas aeruginosa	4	6.9
Serratia marcescens	1	1.7
Citrobacter freundii	1	1.7
Providencia rettgeri	1	1.7
E. coli	1	1.7
Enterococcus faecalis	1	1.7
Stenotrophomonas maltophilia	1	1.7

The source of the 62 septic episodes were burn wound in 15 (24.2%) episodes, lung in four (6.1%), vascular catheter in three (4.8%) and the source remained undetermined in 40 (64.5%) episodes.

Table 2 presents the antimicrobial susceptibility of the gram-positive bacteria isolated from blood culture of burned patients with sepsis. The incidence of oxacillin resistance among staphylococci were high (40.7% for *Staphylococcus aureus* and 50% for coagulase-negative *Staphylococcus)*. The oxacillin resistant *Staphylococcus aureus* showed low susceptibility to gentamicin, ciprofloxacin, co-trimoxazole, clindamycin and imipenem. However all staphylococci were susceptible to vancomycin. The oxacillin susceptible *Staphylococcus aureus* showed high susceptibility to a wide range of antibiotics. Coagulase-negative *Staphylococcus* showed low to moderate susceptibility to amoxicillin/ clavulanic acid, cephalothin, cefuroxime, imipenem, oxacillin, gentamicin, amikacin and co-trimazole, but its susceptibility was high to ciprofloxacin, clindamycin and vancomycin.

Table 3 presents the antimicrobial susceptibility of the gram-negative bacteria isolated from blood culture of burned patients with sepsis. More than 70% of *Acinetobacter baumannii* isolated were susceptible only to ampicillin/sulbactam and imipenem. More than 70% of *E. cloacae* and *K. pneumoniae* were sensitive to imipenem, gentamicin, amikacin and ciprofloxacin. All strains of *P. aeruginosa* were sensitive to imipenem, amikacin and ciprofloxacin.

The most common clinical findings of sepsis in these patients were fever, dyspnea, hypotension and oliguria. On the other hand, the most common laboratory findings of these patients were anemia, leukocytosis, hypoalbuminemia and thrombocytopenia (Table 4).

Table 2 - Antimicrobial susceptibility (%) of gram-positive bacteria isolated from patients treated at the Burns Unit of Hospital Regional da Asa Norte, Brasília, from June 2001 to May 2002.

Antibiotic	Oxacillin susceptible *S. aureus* n= 16	Oxacillin resistant *S. aureus* n= 11	Coagulase-negative staphylococci n= 12
Amoxicillin/ Clavulanic acid	87.5	0	50.0
Cephalothin	87.5	0	50.0
Cefuroxime	ND	0	50.0
Imipenem	93.8	0	50.0
Oxacillin	100	0	50.0
Gentamicin	100	0	66.7
Amikacin	100	ND	66.7
Ciprofloxacin	100	27.3	83.3
Clindamycin	87.5	0	83.3
Co-trimoxazole	93.8	45.5	66.7
Vancomycin	100	100	100

ND = not done

Table 3 - Antimicrobial susceptibility (%) of gram-negative bacteria isolated from patients treated at the Burns Unit of Hospital Regional da Asa Norte, Brasília, from June 2001 to May 2002.

Antibiotic	*A. baumannii* N = 7	*E. cloacae* N = 7	*K. pneumoniae* N = 5	*P. aeruginosa* N = 4
Ampicillin/Sulbactam	71.4	42.9	80.0	ND
Aztreonan	ND	57.1	60.0	ND
Cephalothin	0	0	60.0	ND
Cefoxitin	ND	0	ND	ND
Ceftriaxone	0	ND	ND	25.0
Ceftazidime	14.3	ND	ND	50.0
Cefuroxime	0	ND	ND	0
Ticarcillin/clavulanic acid	28.6	42.9	80.0	25.0
Piperacillin	14.3	42.9	20.0	0
Imipenem	85.7	100	100	100
Gentamicin	14.3	71.4	80.0	25.0
Amikacin	14.3	85.7	80.0	100
Ciprofloxacin	14.3	85.7	100	100
Co-trimoxazole	ND	42.9	60.0	ND

ND = not done

Table 4 - Clinical and laboratory findings of sepsis of the 49 patients treated at the Burns Unit of Hospital Regional da Asa Norte, Brasília, from June 2001 to May 2002.

Data	Number	Percentage
Clinical findings		
fever	48	98.0
dyspnea	26	53.1
hypotension	17	34.7
oliguria	17	34.7
mental disorientation	11	22.4
icterus	7	14.2
anasarca	6	12.2
hemorrhages	6	12.2
hypothermia	1	2.0
Laboratory findings		
hemoglobin < 10 g/dl	35	71.4
leukocytosis > 12,000 cells/ml	33	67.3
serum albumin < 2.5 g/dl	24	49.0
thrombocytopenia < 100,000/ml	18	36.7
total bilirubin > 2 mg/dl	7	14.2
serum creatinine > 2 mg/dl	6	12.2

Twelve (24.5%) septicemic patients died during the study period, with a mean age of 33 years (range one to 89 years). Their burned body surface area varied from 17 to 84% (mean 50%) and seven (58.3%) had over 50% burned body surface area. There were 17 septic episodes among these 12 patients during their stay in the hospital until the time of their deaths (Table 5).

DISCUSSION

Thermal injury is associated with anatomic, physiologic, endocrinologic, and immunologic alterations, which require specialized care. Cutaneous injury results in significant fluid loss as well as the release of multiple inflammatory mediators. When disseminated by the circulation, bacteria and inflammatory mediators can cause sepsis, and, ultimately, multiple organ failure[3].

The majority of septic episodes ocurred in the first two weeks postburn, which confirms the earlier

Table 5 - Details of the burned patients who died due to septicemia.

No.	Age (years)	Burn (%)	No. septicemic episodes	Last-organism(s) detected	Death postburn day	Organ (s) affected in necropsy
1	29	50	2	*Candida* sp	49th	lung
2	57	35	3	*S. marcescens*	9th	lung
3	89	17	3	*E. cloacae*	22nd	lung
4	37	84	1	*A. baumannii*	9th	heart, lung
5	1	70	1	*P. aeruginosa, E. cloacae*	8th	**
6	24	19	1	*A.. baumannii*	15th	lung
7	42	63	1	*A.. baumannii*	8th	lung
8	29	72	1	*E. coli, E. cloacae*	5th	lung, liver
9	20	42	1	*S. aureus*	13th	lung, peritoneum
10	3	54	1	*S. aureus*	7th	lung
11	17	50	1	*E. cloacae*	10th	lung
12	46	40	1	CNS*	6th	**

* CNS= coagulase-negative *Staphylococcus.* ** There was not any organ affected significantly in necropsy.

observation by Bang et al[1]. This early detection was possible probably because of continuous observation for the clinical signs of sepsis, regular inspection of burn wounds for any change, and timely culture of blood specimens.

The main source of sepsis in these groups of patients was the burn wound. One reason for this might have been the fact that multiresistant nosocomial organisms present in the Burn Unit form the normal flora of the burned patient within a few days of admission, replacing the original endogenous flora. However in the majority of septic episodes, the source of sepsis was not identified. Our results are similar to those of other authors[1 13 19 22 26].

The flame burn was the predominant cause of burn amongst patients who had sepsis due to the fact that this agent produces deeper and more extensive lesions than other agents, leading to more colonization of burn wound and sepsis[10 15 20 24].

The majority of septic episodes being due to *Staphylococcus* might reflect the fact that Burns Units are a major source of this bacteria, as confirmed by other authors[1 4 6 14 16]. The incidence of oxacillin resistance among *Staphylococcus* was high (40.7% for *S. aureus* and 50% for coagulase-negative *Staphylococcus).*

Furthermore, coagulase negative *Staphylococcus* should be considered an important pathogen for sepsis in burns. The organism, being ubiquitous in a hospital environment, and burn wounds being the ideal medium for its multiplication, it is hardly surprising that this bacteria would be the cause of 20.7% of septic episodes. The possibility of contamination was excluded by collecting specimens from different sites with appropriate aseptic procedures as well as repeated cultures of blood specimens and clinical correlation.

The low incidence of *Pseudomonas* sepsis (only 6.9%) in burned patients indicates a decline of septic episodes due to this organism as confirmed by other authors[5 8 11 18 21 25 27] . The reasons for this decline may be effective topical and systemic antibiotics, as well as the competition by other more adaptable bacteria. All strains of *P. aeruginosa* were sensitive to imipenem, amikacin and ciprofloxacin, although other workers have demonstrated low susceptibility of *P. aeruginosa* to aminoglycosides and to ciprofloxacin[12 13 14 17 28].

Burn sepsis due to *Acinetobacter* deserves attention, though this organism was rarely implicated in sepsis until 1970. However, this organism had been isolated more frequently from blood cultures and is frequently multi-resistant[5 23 25]. This bacteria was the third most common organism isolated in our patients after *S. aureus* and coagulase-negative *Staphylococcu*s. More than 70% of *Acinetobacter baumannii* isolated were susceptible only to ampicillin/sulbactam and imipenem. The observation made in this study that 12.1% of the septic episodes were due to *Acinetobacter baumannii* is important because its emergence might have been linked to the extensive use of broad-spectrum antibiotics, resulting in its classification as a nosocomial pathogen[5 27 29].

Septicemia due to *Candida* sp is not uncommon in burned patients and four patients in this study developed sepsis due to this fungi. Most of these episodes were associated with patients having burns of > 50% burned total body surface area, prolonged hospital stay (> four weeks), use of multiple antibiotics and delay in surgery for the closure of the wounds[8 18 26].

The lethality rate of 24.5% in septic patients was lower compared to those reported in earlier studies. The reduced mortality rate in these patients may probably be attributed to adequate resuscitation together with continuous clinical and microbiological surveillance leading to quick detection of etiology, institution of appropriate antibiotics, care over nutrition, early excision and wound coverage.

The appropriate knowledge of clinical findings, epidemiological, laboratorial and microbiological aspects of sepsis in burned patients permits an adequate diagnosis and treatment of this complication.

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