EPIDEMIOLOGY OF PNEUMONIA IN A BURN CARE UNIT: THE INFLUENCE OF INHALATION TRAUMA ON PNEUMONIA AND OF PNEUMONIA ON BURN MORTALITY

EPIDEMIOLOGIE DE LA PNEUMONIE DANS UNE UNITE DE SOINS AUX BRULES : L'INFLUENCE DES TRAUMATISMES D'INHALATION SUR LA PNEUMONIE ET DE LA PNEUMONIE SUR LA MORTALITE CHEZ LES BRULES

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SUMMARY. The aim of this study is to determine the epidemiological characteristics of burn patients developing pneumonia, as well as the predisposing factors and the mortality of these patients. Infectious complications present serious problems in severely burned patients. Pneumonia, in particular, is a major cause of morbidity and mortality in burn patients. Patients with inhalation injuries are exposed to a greater risk due to the possible development of infectious complications in the lower respiratory tract. During their stay in our Burn Care Unit, 22.9% of our burn patients developed pneumonia and 10.9 % of these patients died. Risk factors for the development of pneumonia in burn patients were found to be inhalation trauma, high ABSI score, the Baux and modified Baux index, and high ASA score ($p<0.01$). Age and gender showed no significant correlation to the incidence of pneumonia. In this study we were able to determine the incidence of pneumonia in burn patients, their mortality and the strong correlation of the presence of inhalation injury with the development of pneumonia.

Keywords: pneumonia, inhalation trauma, burn patients, prophylactic antibiotic therapy

RÉSUMÉ. *Le but de cette étude est de déterminer les caractéristiques épidémiologiques des patients brûlés qui développent une atteinte pulmonaire , ainsi que les facteurs prédisposants et le taux de mortalité . La pneumonie est une cause majeure de morbidité et de mortalité chez les patients gravement brûlés. Les patients atteints de lésions par inhalation sont exposés à un risque plus élevé en raison de l'évolution possible de complications infectieuses dans les voies respiratoires inférieures. Au cours de leur séjour dans notre unité de soins aux brûlures, 22,9% de nos patients brûlés ont développé la pneumonie et 10,9% de ces patients sont décédés. Les facteurs de risque pour le développement de la pneumonie chez les patients brûlés retrouvés sont le traumatisme de l'inhalation, le score élevé de ABSI, l'incice de Baux et l'indice Baux modifié, et le score ASA élevé ($p <0,01$). L'âge et le sexe des patients n'ont montré aucune corrélation significative à l'incidence de la pneumonie. Dans cette étude, nous avons pu déterminer l'incidence des complications pulmonaires du fait des lésions par inhalation .chez les patients brûlés, ainsi que sur le taux de mortalité.*

Mots-clés: *pneumonie, traumatisme inhalation, patients brûlés, traitement antibiotique prophylactique*

Introduction

Advances in the treatment of severely burned patients have led to reduced mortality rates and modification of the causes of death. In the past, burn shock, which typically develops in patients with a total burn surface area (TBSA) of over 20%, was the predominant cause of death, especially during the 1930s and 40s.[1] Sophisticated fluid resuscitation helps avert this complication and reduce mortality.[1]

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Infection, in particular pneumonia, is a major cause of morbidity and mortality in burn patients.[2] Cutaneous burns activate the complement cascade and induce intrapulmonary leukocyte aggregation and release of free oxygen radicals, causing pulmonary damage, possibly adding further respiratory insult to patients with inhalation injury. This pathophysiological response is accompanied by global immunosuppression, proportional to the extent of the burn injury.[3] In patients with extensive burns (>25-30% TBSA) increased capillary permeability occurs, not only at the injured site but also in remote organ systems.[4]

Apart from the immunocompromising effects of the burn trauma, burn patients are also at high risk of infection due to the prolonged hospital stay, intensive diagnostic and therapeutical procedures and broad-spectrum antibiotic therapy.[5,6]

Prospective studies conducted between 1992 and 1998 on burn patients requiring mechanical ventilation show infection rates of up to 50%, with a pneumonia rate of 65%.[2,7] The expected increase in mortality due to pneumonia has been estimated to be 25%.[2]

Burn injury is a strong predictor of ventilator-associated pneumonia (VAP) and the intubation process itself contributes to the risk of infection. Moreover, as previously mentioned, cutaneous thermal injury can also cause pulmonary dysfunction.[4]

The aim of our study is to determine the epidemiological characteristics of patients developing pneumonia in a Burn Care Unit and to study the predisposing factors for the development of pneumonia and the mortality of these patients.

Material and methods

A retrospectively maintained institutional database containing all patients in our Burn Care Unit, consisting of four one-patient rooms, was reviewed. From this database, we selected all the patients who were diagnosed with pneumonia during their stay.

All patients enrolled in the study were aged older than 16 years, had been admitted to the Burn Care Unit between January 2008 and December 2012 and fulfilled the Burn Centre referral criteria to a Burn Care Centre, according the German Burn Association. Exclusion criteria were immunosuppression, pregnancy and ICU admission 48 h after burn trauma.

All patients were resuscitated using the modified Parkland formula. Enteral nutrition was commenced within 24 h of injury and gradually increased during the first 3 days. At direct patient contact, a protective sterile gown and disposable gloves were used.

At this point, we would like to refer to the diagnosis of pneumonia and inhalation trauma and the Burn Centre referral criteria according to the German Burn Association Guidelines.[8]

The diagnosis of pneumonia was made using standard Centers for Disease Control criteria, including new or changing infiltrate on chest radiograph, leukocytosis, temperature > 38.5°C (100.4°F) or hypothermia < 35.0°C (95°F), and the presence of purulent tracheal aspirates.[2] In order to prevent a ventilor associated pneumonia, the following measures are taken in our Burn Care Unit: elevating the head of bed, oral decontamination, subglottal suctioning, early beginning of the physiotherapy and regular alveolar recruitment maneuver.

As far as the fluid management for burns is concerned, there is always a fine line between an adequate resuscitation and overresuscitation leading also to pulmonary complications. In our Burn Care Unit, we use the Parkland formula, which advocates the guideline for total volume of the first 24 hours of resuscitation at approximately 4mL/kg body weight per percentage burn TBSA. With this formula, half the volume is given in the first eight hours postburn, with the remaining volume delivered over 16 hours. In the first 24 hours only, Ringer lactate solutions and no colloids were used. Moreover, our patients receive a haemodynamic monitoring allowing us to estimate the fluid volume required in the best possible way. Heamodynamic monitoring includes blood pressure monitoring with target parameter mean arterial pressure (MAP) ≥65mmHg, urine output monitoring with target ≥0,5ml/kg/h and pulse contour cardiac output (PiCCO) measurement system with target volumetric parameters extravascular lung water (EVLW) 3-7ml/kg, global end-diastolic volume index (GEDI) 600-800ml/m^2 and right ventricular end-diastolic volume index (RVEDVI) 60-100ml/m^2.

Inhalation injury is suspected in patients with facial and neck burn injuries and in patients who suffered burns in an enclosed space. All suspected patients underwent bronchoscopy at their submission to our burn unit. The diagnosis of inhalation injury was made by manifestation of inflammatory changes in the respiratory tract, such as mucosal erythema, edema, ulceration or submucosal hemorrhages.[9]

In patients with diagnosed inhalation injury, we always use prophylactic antibiotic treatment with piperacillin and tazobactam, starting on the admission day and administrated for a minimum of 5 days.

The Burn Centre referral criteria according to the German Burn Association Guidelines conclude:

i) Partial thickness burns greater than 20% total body surface area (TBSA)
ii) Burns that involve the face, hands, feet, genitalia, perineum
iii) Third degree burns in any age group
iv) Electrical burns, including lightning injury
v) Chemical burns
vi) Inhalation injury

The following data were registered for each patient: age, sex, comorbidities, total body surface area (TBSA) burned, American Society of Anesthesiologists (ASA) score, Abbreviated Burn –Severity Index (ABBSI), Baux index, modified Baux index, length of hospital stay, mortality, time of intubation, mobilization, extreme obesity, bacteremia, presence of tracheostoma, length of mechanical ventilation, microbiology of pneumonia and burn wound infections, antibiotic therapy of the pneumonia and its length. The TBSA was calculated by adding percentages of dermal and subdermal burns using the BurnCase® Software (RISC Software GmbH, Hagenberg, Austria). The ABSI was used in order to assess the injury severity for each patient. The index is a scoring system based on sex, age group, presence of inhalation injury and full thickness burn, and percentage of TBSA involvement.

All patients in our Burn Care Unit were intubated before their admission or by their admission for blister removal. Debridement and grafting at the earliest possible opportunity is a principle of our Burn Unit. The duration of each surgery and consequently the extent of the debridement and grafting are related to the haemodynamic stability and the temperature of the patient. Burn wounds less that 60% TBSA may be closed with split thickness skin grafts taken from unburned areas. As the size of injury increases, there is less donor site for autografting, so alternate techniques are required such as keratinocyte transplantation.

In our Burn Care Unit the patients are mobilized as soon as they are haemodynamic stable and the skin grafts tolerate it. The physiotherapy begins from the first day of their stay. In order to evaluate the mobilization of the burn patients, the time point of independent transfer was classified into three groups: up to Day 7, between Days 7 and 15, and after Day 16 of hospitalization.

The group of the extreme obese population includes all patients with BMI>35kg/m^2.

Enteral nutrition begins within few hours after the accident and parenteral nutrition 24h after the admission to improve the nutritional profile. The daily caloric needs were calculated by the following equation: 25kcal/ kg weight+ 40kcal/%TBSA.

The Baux index represents a prognosis in lethality and is calculated by adding TBSA in % with the age of the patients, in the modified Baux index the inhalation injury is calculated as 17 points.

Antimicrobial therapy was instituted with the help of an infectious disease consultant ("antibiotic stewardship") from the Department of Microbiology.

The retrospective study did not have to be approved by the institutional committee according to the regulation of our institution at the point the study was conducted.

SPSS version 20 (SPSS GmbH Software, Illinois, USA) was used for the statistical analysis of the data. Variables were analyzed using contingency tables, Chi-Square test and logistic regression. p-values lower than 0.05 were regarded as statistically significant.

Results

201 patients fulfilling the Burn Centre referral criteria, with a mean age of 47.3 years, were treated in our Burn Care Unit between 2008 and 2012 (male: female 151:50). The mean TBSA was 18.7% , the mean ABSI score 6.4 and the mean length of hospital stay 21.3 days (*Table I*). The mortality rate in our Burn Care Unit was 10.9%. Forty-six of these patients were diagnosed with pneumonia during their hospital stay, giving a pneumonia incidence of 22.9%. The mean age of the patients acquiring pneumonia was 47.2 years, the mean TBSA 24.8, the mean ASA score 1.9, the mean ABSI score 6.9 (*Table II*).

Table I - Characteristics of all burn patients cared in our Burn Care Unit between 2008 and 2012

Variables	Range	Mean ± SD
Age (yr)	16- 90	47.3 ± 19.08
Length of stay (d)	1- 95	21.3 ± 16.00
Total burn area (%)	1- 95	18.7 ± 16.63
ABSI	2- 16	6.4 ± 2.90
Baux-Index	20-167	65.8 ± 25,90
Modified Baux index	23-184	70.5 ± 28,77

Table II (a) - Univariate analysis (t-test) of continuous factors in the pneumonia and the non-pneumonia group

Variables	Mean of the pneumonia group	Mean of the non-pneumonia group	P
Age (yr)	47.2 ± 15.9	47.3 ± 19.97	0.86
Total burn area (%)	24.8 ± 15.8	16.9 ± 16.52	<0.01
ASA	1.9 ± 0.79	1.5 ± 0.80	0.04
ABSI	6.9 ± 2.40	6.2 ± 3.02	<0.01
Baux-Index	71.9 ± 22.08	64.0 ± 26.72	<0.01
Modified Baux- Index	81.4 ± 24.85	67.1 ± 29.14	<0.01
Length of tracheostoma (d)	25.2 ± 17.88	16.45 ± 5.72	<0.01
Length of stay (d)	36.0 ±20.78	17.1 ± 11.21	<0.01

Table II (b) - Univariate analysis (chi-square test) of categorical factors in the pneumonia and the non-pneumonia group

Variables	Number of patients of the pneumonia group (n=47)	Number of the patients of the non pneumonia group (n=154)	P
Sex (M: F)	38: 9	113: 41	0,74
Mechanical ventilation	36	20	< 0.01
Inhalation injury	26	32	< 0.01
Deaths	5	12	0.51

The average length of hospital stay in the pneumonia group was 36 days, while burn patients without pneumonia stayed an average of 17 days (p<0.01). The TBSA is also correlated as statistically significant with the length of stay of the burn patients (p<0.01). A total of 73.9% of the pneumonia patients needed a tracheotomy with the mean duration of mechanical ventilation of 25.2 days.

In the tracheal secretions of 25 patients (>50%) more than one microbial factors was isolated. The commonest (*Table III*) were Staphylococcus species (19.8%), Haemophilus species (12.3%) and Candida species (30.8%). Overall, 92% of the microbial factors were pansensitive. In 30.8% of the pneumonia patients Candida albicans and non-albicans species were isolated in their tracheal secretions. Twelve of the 25 patients with isolated Candida in their tracheal aspirate required systemic antifungal therapy, as the Candida antigen titer in serum in the remaining 13 patients not requiring systemic therapy was negative. Only 46% of the patients with isolated Candida in their tracheal aspirate required systemic antifungal therapy. Candida infections were not a great problem in this study, as the mortality of all our burn patients with Candida infections was only 0.9%.

Bacteremia was detected in 6 % of our patients and there was no correlation to pneumonia (p=0,088). Thirty-five of our patients were intubated prior to admission and 12 upon admission. The time point of intubation did not influence the development of pneumonia (p=0.115). Pneumonia rates were not higher in extreme obese patients (p=0.198).

In 19.8% of the patients with infection of the lower respiratory tract, the pathogenic factor was also isolated in the burn wounds. An escalation of the antibiotic therapy (in terms of addition of one or more new antimicrobial agents or change in antibiotic to one with a broader spectrum) was necessary in 76.1% of these. In 25.7% of these patients the antibiotic therapy was changed to imipenem. The second most commonly used antibiotic in that group of patients was meropenem (17.1%), followed by moxifloxacin (8.6%) and ciprofloxacin (8.6%).

In our study, the mortality of burn patients with pneumonia was shown to be 10.9%.

Risk factors for the development of pneumonia in burn patients, in a statistically significant way, were found to be inhalation trauma, high ABSI score, Baux index, modified Baux index and high ASA score (p<0.01). Age and gender showed no correlation with the incidence of pneumonia (*Table II*).

In the logistic regression, the odds of the development pneumonia are higher in patients with tracheostoma, longer duration of mechanical ventilation and longer duration of stay (*Table IV*). The odds of mortality are higher in patients with inhalation injury, pneumonia, tracheostoma, longer duration of hospital stay, higher ABSI score and in female patients (*Table V*).

The incidence of inhalation injury in our pneumonia group was 56.5% (*Fig. 1*).

The pneumonia rate was 3.2 (44.8% : 14%) times higher in patients with inhalation injury compared to those without inhalation injury.

Table III - Microorganisms isolated in the tracheal secret of pneumonia patients

pathogenic germs	N	F
Staphylococcus sp.	16	19.8%
Haemophilus sp.	10	12.3%
Streptococcus sp.	9	11.1%
Enterobacter sp.	7	8.6%
Escherichia coli	6	7.4%
Klebsiella sp.	5	6.2%
Pseudomonas sp.	2	2.5%
Bacillus sp.	1	1.3%
Neisseria sp.	1	1.3%
Candida albicans	18	22.2%
Candida non-albicans	7	8.6%

Table IV - Logistic regression analysis of pneumonia and the independed variables (sex, age, inhalation injury, duration of stay, TBSA, tracheostoma, length of mechanical ventilation)

Parameter	Significance	Odds ratio (95% CI)
Sex	0,832	0,762 (0,062; 9,437)
Age	0,430	0,889 (0,858; 1,050)
Inhalation injury	0,098	0,054 (0,002; 1,720)
Duration of stay	<0,01	1,093 (1,050; 1,138)
TBSA	0,663	0,938 (0,704; 1,250)
Tracheostoma	0,07	2,614 (1,306; 5,231)
Length of mechanical ventilation	0,028	1,356 (0,670; 0,980)
Model adjusted R^2=0,513		

Table V - Logistic regression analysis of mortality and the independed variables (sex, age, inhalation injury, duration of stay, TBSA, tracheostoma, length of mechanical ventilation, ABSI, pneumonia)

Parameter	Significance	Odds ratio
Sex	0,032	3,347 (1,110; 10,087)
Age	0,312	0,970 (0,913; 1,030)
Inhalation injury	0,498	1,857 (0,310; 11,139)
Duration of stay	0,294	1,023 (0,981; 1,067)
TBSA	0,151	0,940 (0,863; 1,023)
Tracheostoma	0,677	1,267 (0,417; 3,847)
Length of mechanical ventilation	0,983	0,999 (0,951: 1,050)
ABSI	0,046	1,623 (1,009; 2,613)
Pneumonia	0,895	1,112 (0,229; 5,392)
Model adjusted R^2=0,138		

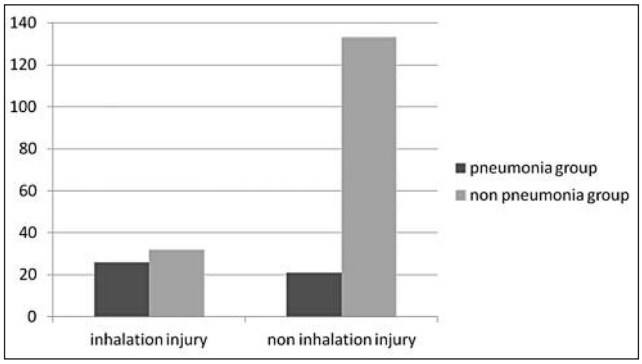

Fig. 1 - The number of patients in inhalation and non-inhalation injury group is divided in the patients having pneumonia or not. The development of pneumonia is statistically significant associated with the presence of inhalation injury ($p<0.001$).

Discussion

Depending on the diagnostic criteria used, inhalation injury is reported in 0.3-43% of the patients with severe burn injuries.[10] It is one of the major (independent) risk factors for mortality of burn patients, as it is associated with increased mortality of up to 8-10 fold.[10]

Although mortality from smoke inhalation alone is low (0-11%), smoke inhalation in combination with cutaneous burns is fatal in 30-90% of patients.[11]

According to Trupkovic, 40-70% of patients with cutaneous burns and inhalation injury developed pneumonia during their stay[12] and 27% of the patients in the study of Edelman.[13] On the other hand, 34% of our patients with inhalation trauma developed pneumonia during their stay. This percentage is higher in the study by Eckert, reaching 74%.[14]

In the prospective study by Appelgren, this mortality rate of burn patients was 14.3% , and in the retrospective study by Shirani 25% respectively [3, 15], rates that are higher in comparison to the mortality rate of 10.9% in our Burn Care Unit.

In their study, de la Cal et al. reported that the pneumonia rate was also much higher in patients with inhalation injury compared to those without inhalation injury (n= 56, $p<0.001$).[2]

Mlcak et al. found a 40% mortality rate in severely burned patients with pneumonia. However, if the pneumonia occurred in patients with inhalation trauma the mortality rate went up to 60%.[11] Edelman et al. refer to a mortality rate of 19% in patients with inhalation injury and pneumonia, double the mortality rate of 9% found in patients with inhalation injury and no pneumonia.[13]

In our study, as well as in the study by Appelgren,[15] no such differences were found. The mortality rate in severely burned patients with pneumonia was 10.9% , in patients with inhalation injury and no pneumonia 9.7% and in patients with inhalation injury and pneumonia 12.1% .

Pham stated in his study that burn patients > 55 years old who developed pneumonia were more likely to be male ($p<0.01$) in contrast to our results. He also showed a statistical significant correlation between higher TBSA ($p<0.01$), inhalation injury ($p<0.01$), comorbid condition ($p<0.01$) and the incidence of pneumonia.[16]

Inhalation injury also seemed to contribute to the microbiology of the VAP. In the absence of an inhalation injury, the predominant organisms cultured (89%) were pansensitive Haemophilus influenza, Staphylococcus, and Streptococcus series.[14]

As also stated in the American Burn Association Practice Guidelines for prevention, diagnosis, and treatment of VAP in burn patients, isolation of Candida from endotracheal aspirates is common, but unusually represents colonization of the airway and rarely requires treatment with antifungals.[4] In our study, less than the half patients with isolated Candida in their endotracheal aspirates needed systemic antifungal treatment.

As can be seen in the results, in 19.8% of the patients with infection of the lower respiratory tract, the pathogenic factor was isolated in the burn wounds as well. This percentage allows us to make the hypothesis that the contamination of the burn wound is a possible pathway of the pulmonary infection, but unfortunately there are no references to similar epidemiological data and possible pathophysiological paths in the literature.

TBSA is a matter of controversy as a risk factor for developing pneumonia. In the study by Edelman, an increase in TBSA was associated with a higher pneumonia rate.[13] The assessment of TBSA is very important in the critical care management of a burn patient, as the calculation of Parkland formula is based on TBSA. It is very important in that case to avoid overresuscitation following pulmonary capillary leakage and further pulmonary complications. In the Japanese study of Tanizaki, VAP rate did not differ with increasing TBSA in burn patients with inhalation trauma.[7] We found no statistically significant correlation between TBSA and pneumonia incidence ($p=0.27$) either.

In patients with diagnosed inhalation injury, we always use prophylactic antibiotic treatment. The first choice antibiotic is piperacillin and tazobactam. Administration of prophylactic antibiotics is also a controversial matter. Because there are no clear recommendations, it is up to the experience of the team of burn surgeons and microbiologists to make the choice of what, if any prophylactic antibiotic should be given.[1] In our department, we will continue with the prophylactic antibiotic treatment because of the lower mortality rate of pneumonia patients in comparison to the mortality rates described in the international literature.

In the metanalysis of Anvi, the use of systematic antibiotics in the general or perioperative setting showed a significant reduction in pneumonia. It was stated that a dis-

crepancy was shown between the current guidelines not recommending antibiotic prophylaxis for the management of burn patients and the evidence showing a reduction in pneumonia of about 50%.[17]

A limitation of our study is the possible overdiagnosis of pneumonia, as the criteria defining a pneumonia are not specific enough to distinguish it from tracheobronchitis or a colonization of the respiratory tract.

Conclusion

To sum up, 22.9% of our burn patients developed pneumonia during their stay in our Burn Care Unit and 10.9 % of these patients died. We also found a statistically significant correlation between developing pneumonia and inhalation injury, tracheostoma, higher ASA score, longer duration of mechanical ventilation and longer duration of hospital stay.

The choice of antibiotics is piperacillin and tazobactam. Administration of prophylactic antibiotics remains a subject of controversy. Given that there are no clear recommendations, it is up to the experience of the team of burn surgeons and microbiologists to make the choice of what, if any, prophylactic antibiotic should be given.

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