INHALATION INJURY IN A BURN UNIT: A RETROSPECTIVE REVIEW OF PROGNOSTIC FACTORS

INHALATION DE FUMÉES DANS UN CTB: REVUE RÉTROSPECTIVE DES FACTEURS PRONOSTIQUES

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SUMMARY. Inhalation injury (InI) is known to seriously affect the prognosis of burn patients, as it is strongly associated with high morbidity and mortality. Despite major advances in the treatment of burn patients in the past years, advances in the treatment of smoke InI have been somewhat limited; mortality reduction mostly results from improvements in critical care. It is difficult to separate the contribution of InI from other mechanisms that also affect respiratory tract and lungs. The aim of this study was to compare patients with and without InI and to identify prognostic factors among patients with smoke InI. Patients with InI displayed higher total body surface area (TBSA) burned, higher incidence of pneumonia and acute respiratory distress syndrome (ARDS), a higher rate of positive blood cultures and a significantly higher death rate. We could conclude that older age, higher TBSA, ARDS and pneumonia were independent predictive factors for mortality in our global study population. Older age and higher TBSA were the only independent factors found to be predictive of mortality in patients with InI.

Keywords: burn, inhalation injury, smoke inhalation, prognosis, bronchoscopy

RÉSUMÉ. *L'inhalation de fumées (IF) est reconnue comme aggravant le pronostic des patients brûlés, étant fortement corrélée avec une morbidité et une mortalité élevées. Alors que des progrès majeurs ont été réalisés, ces dernières années, dans le traitement des brûlés, ils ont été plus limités dans celui de l'IF, les avancées étant surtout le fait des mesures générales de réanimation. Il est difficile de faire la part de l'IF et d'autres mécanismes touchant le système respiratoire. Le but de cette étude était de comparer les patients avec et sans IF pour identifier les facteurs pronostiques concernant les patients avec IF. Ceux – ci étant brûlés sur une plus grande surface, avaient plus fréquemment des pneumonies et des SDRA, plus d'hémocultures positives et mouraient plus souvent. Nous avons observé que l'âge plus élevé, la surface brûlée plus importante, le SDRA et la pneumonie étaient des facteurs pronostics de mortalité de la population globale, l'âge avancé et la surface brûlés étant les seuls critères pronostiques indépendants de mortalité des patients avec IF.*

Mots-clés: *brûlure, inhalation de fumées, pronostic, bronchoscopie*

Introduction

Inhalation injury seriously affects the prognosis of burn patients. Its incidence has been reported to be approximately 7 to 20% of patients with burns who need hospitalization and up to one third of patients with severe burns.[1-4] It is usually associated with burns on the head and neck, but it can occur without cutaneous lesion.[3]

The presence of InI is strongly associated with increased morbidity, an increase in mortality of up to 20% and incidence of pneumonia of up to 40%.[2,5] It involves damage to the respiratory tract and lungs by heat, smoke and toxicants.[1,6-8] Accurate diagnosis and treatment in the early stages is essential for achieving a better prognosis.[1,9]

Despite the advances seen in burn treatment in recent years, progress in the treatment of smoke InI has been limited.[6,7,10,11] Mortality reduction mostly results from improvements in critical care rather than specific interventions for inhalation injury.[10-12] Several factors account for this more protracted progress: burned skin can be debrided and substituted with skin grafts, but injured lungs can merely be supported and protected from secondary injury in the majority of cases.[10,12]

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The critically-ill burn patient displays multiple stress mechanisms in addition to InI that may contribute to pulmonary injury, such as systemic inflammation, ventilator-induced lung injury or sepsis.[10,12,13] Thus, InI has an important effect on the outcome of burn patients but it is difficult to separate it from the contribution of other intrinsic mechanisms that also have an impact on the lungs.[10]

Significant limitations for clinicians studying InI are the paucity of uniformity in diagnostic criteria, severity scales and lack of a common terminology to describe outcome. The need for standardized criteria for diagnosis and quantification of InI severity has been recognized.[10]

The best tools presently available to diagnose inhalation injury are clinical presentation and bronchoscopy findings. Serious difficulties arise in the attempt to predict which patients are vulnerable to resuscitation complications, increased pulmonary dysfunction, respiratory failure and mortality.[10]

The aim of this study was to compare patients with and without inhalation injury and to identify prognostic factors among patients with smoke inhalation.

Material and methods

This study includes all burn patients admitted to the Burn Unit (BU) of Centro Hospitalar São João (university and tertiary hospital) between January 2010 and December 2014 (only patients weighing over 30kg admitted). A retrospective review was performed.

Demographic characteristics, total body surface area (TBSA) burned, etiology of burn injury, length of admission, duration of mechanical ventilation, diagnosis of pneumonia, results of microbiological investigations, acute respiratory distress syndrome (ARDS)[14] and other BU-associated complications, mortality and cause of death were obtained from medical records.

Clinical diagnosis of InI was established in patients with smoke or flame-inhalation and one or more of the following: odynophagia and/or hoarseness, cough and bronchial irritation, expectorate containing soot, hypoxemia, laryngoscopy and bronchoscopy findings of lesions in the respiratory tract.[4,7,15,16]

Fibreoptic bronchoscopy findings were also documented. InI was divided into 4 categories based on severity of the epithelial injury: normal; mild injury, in which the airway epithelium exhibited slight hyperemia and edema; moderate, in which obvious epithelial hyperemia and edema, epithelial erosion, or petechial hemorrhage was observed; and severe, corresponding to airway epithelium necrosis and exfoliation.[10]

Patients were divided into two groups: non-inhalation injury (group A) and inhalation injury (group B); the latter group was further divided into upper airway and lower airway injury (B1 and B2, respectively).

Data analysis was performed using IBM SPSS Statistics version 20.0. All values are presented as mean ±SD for continuous variables and number and percentage for categorical values. Continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using the Chi-square or Fisher´s exact test. The Kaplan-Meier method was used for survival analysis. Factors significantly associated with survival were further analyzed and ranked using multivariate discriminate analysis. Hazard ratio (HR) with 95% confidence interval (CI) value was used to report the results. A p-value of < 0.05 was considered statistically significant.

Results

A total of 210 patients were admitted to the burn unit between January 2010 and December 2014. Mean age was 51.9 years (range 8 to 91); 61.4% of the patients were male (129 patients) and 38.6% female (81 patients); 82 (39%) patients were diagnosed with InI.

Mean TBSA was 20.3 (±19,9); group B exhibited a significantly higher TBSA than group A (29,9 ± 25,5 and 14,2 ± 11,9, respectively; p<0,001) (*Fig. 1*).

The main cause of burn in our study population was fire (76.2%), followed by hot liquid (12.4%), chemical (5.2%) and electrical (4.8%). In group B, 80 patients (97.6%) were injured by fire, and two had electric burns.

The majority of the burns occurred in a closed environment. No significant differences were found between group A and B in relation to the environment in which the burn injury occurred.

The superior half body surface was most frequently affected in both groups (*Fig. 2*), but head and neck, hands and trunk were significantly more frequent in group B

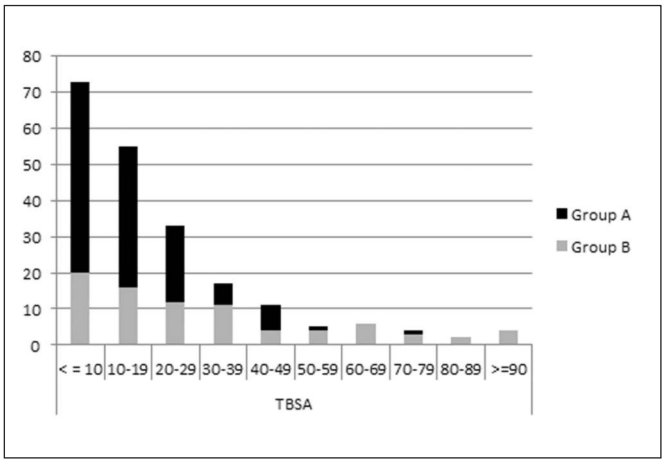

Fig. 1 - Distribution according to burn size (%TBSA) of patients with and without inhalation injury. Grey bars show the distribution of patients with inhalation injury, and black bars the patients without inhalation injury. Note the predominance of patients with inhalation injury exhibiting TBSA > 50%.

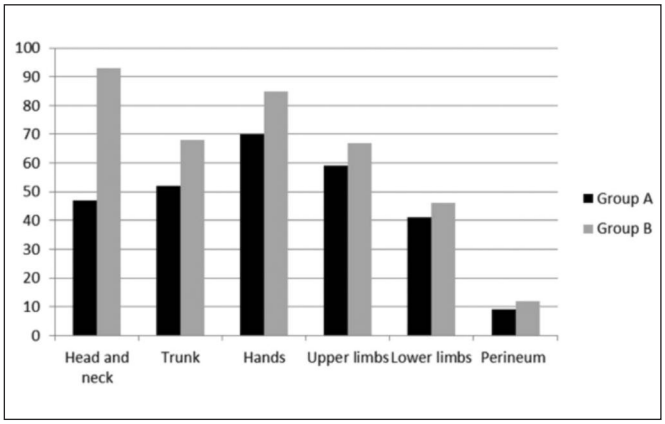

Fig. 2 - Anatomical distribution of burned areas in inhalation injury (group B) and non-inhalation injury (group A) patients. Grey bars show the distribution of patients with inhalation injury, and black bars patients without inhalation injury. Notice the predominance of head and neck, trunk and hand burns among the inhalation injury group.

Table I - Comparison between patients with and without inhalation injury. NS = non significant, SD = standard deviation.

	Group A No inhalation injury	Group B Inhalation injury	p value
Number of patients (%)	128 (61)	82 (39)	
Mean age (SD)	52.23 (± 21,04)	52.96 (±21,71)	NS
Male (%)	59.4	64.6	NS
Mortality rate	8.5	34.1	<0,001
Mean TBSA (SD)	14.2 (±11,9)	29.9 (± 25,5)	<0,001
Main burn cause (%)	Fire (63.3)	Fire (97.6)	<0,001
Closed environment (%)	74.5	68.6	NS
Burn distribution (%)	Head and neck (46.9) Hands (52.3) Trunk (69.5) Upper limbs (59.4)	Head and neck (92.7) Hands (85.4) Trunk (68.3) Upper limbs (67.1)	<0,001 0,008 0,019 NS
Mean length of stay – days (SD) Burn unit (BU) Hospital (BU + ward)	 34.4 (±25,6) 26.0 (±16,9)	 33.7 (±42,1) 26.7 (±27,5)	 NS NS

Table II - Comparison between patients with and without lower airway inhalation injury. NS = non significant, SD = standard deviation.

	Group A+B1	Group B2 (lower airway inhalation injury)	p value
Number of patients (%)	139 (66.2)	71 (33.8)	
Mean age (SD)	50.37 (20.7)	54.92 (22.1)	NS
Male (%)	84 (60.4)	45 (63.4)	NS
Mortality rate	12 (8.6)	27 (38)	<0,001
Mean TBSA (SD)	14.6 (12.4)	31.5 (26.4)	<0,001
Mechanical ventilation Number of patients (%)	 22 (23.7)	 68 (95.8)	 <0,001
Length of ventilation, days (SD)	11.62 (13.4)	13.39 (12.3)	NS
Pneumonia (SD)	22 (15.8)	34 (47.9)	<0,001
Positive blood cultures (SD)	19 (13.7)	34 (47.9)	<0.001
ARDS (SD)	3 (5.2)	10 (14.1)	0,014

(p<0,001; 0,009, 0,022 respectively). *Table I* summarizes patients with and without InI.

Of the 82 patients diagnosed with InI, 11 had displayed upper airway burns (group B1 – 13.4%) versus 71 with lower airway inhalation injury (group B2 – 86.6%).

Table II shows the analysis of patient data with lower airway InI (group B2), and comparison with the remaining patients (group A+B1).

Mean length of stay in the burn unit was 26.0 (±16,9) and 26.7 days (±27,5) for group A and group B, respectively. Mean hospital stay was 34.4 (±25,6) and 33.7 days (±42,1), respectively. No significant differences were found between the two groups.

Mortality rate in group B (34.1%) was significantly higher than in group A (8.5%) (p<0,001). Multiple organ dysfunction syndrome (MODS) was the main cause of death in both groups. In survival analysis using the Kaplan-Meier method, survival in group B was significantly lower (*Fig. 3*).

According to univariate analysis, inhalation injury, higher TBSA and age were found to have a significant impact on mortality (p<0,001).

Diagnostic and/or therapeutic bronchoscopy was performed in 63 patients (88.7%). The most frequent bronchoscopy finding was hyperemia (79.4%), followed by edema (46%), presence of soot (46%) and mucosal erosion (12.7%).

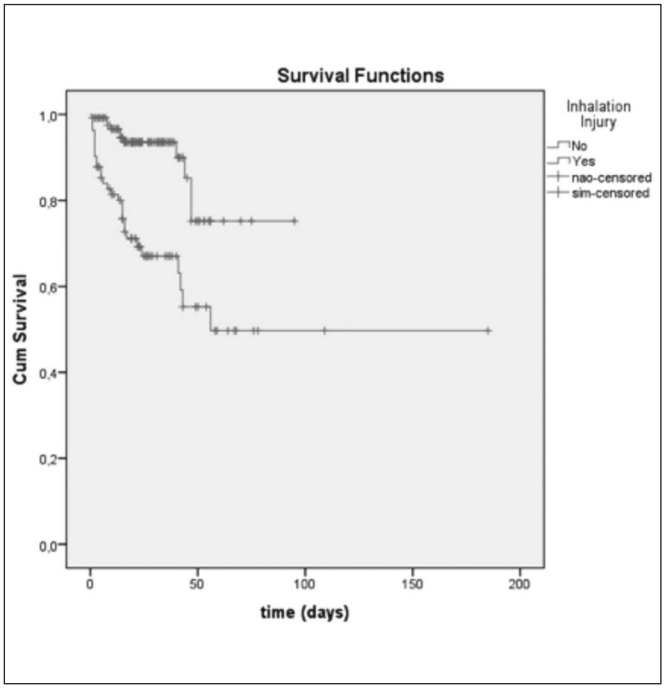

Fig. 3 - Survival analysis. Inhalation injury patients (group B - light grey line) always present lower survival when compared to patients without inhalation injury (group A – dark grey line).

Regarding InI severity based upon bronchoscopy findings, the majority of cases corresponded to mild injury (41 patients, 65.1%), followed by moderate cases (18 patients, 28.5%) and 3 severe cases (4.8%); the mortality group was 31.7% for mild injuries, 38.9% for moderate and 33.3% for severe, no significant differences being found between the 3 groups.

In group B2, 68 patients (95.8%) were mechanically ventilated (versus 19% in group A+B1; p<0,001; no difference was found regarding length of ventilation). Severity of inhalation injury also had no significant impact on length of ventilation.

Pneumonia and positive blood cultures were significantly higher in group B2 compared to the remaining patients (pneumonia, 49.3% versus 15.8%, p<0,001; positive blood cultures, 47.9% versus 13.7%, p<0,001).

The most frequently isolated agent in cases of pneumonia was *Pseudomonas aeruginosa* (31.2% in group B2, 45.5% in Group A+B1); no significant difference was found between the two groups. The most frequently isolated agent from blood cultures was again *Pseudomonas aeruginosa* (41.2% in group B2 and 31.6% in group A+B1); no significant differences were observed between the two groups.

According to univariate analysis, pneumonia did not show a significant impact on mortality of the patients in group B2, conversely the presence of positive blood cultures had a significant impact (p=0,88 and 0,028, respectively).

ARDS was significantly more prevalent in group B2 than group A+B1 (14.1% and 2.1%, respectively; p=0,007) with a significant impact on mortality (p=0,014).

A multivariate analysis was further performed using factors that demonstrated a significant impact on survival. In the global population (group A+B), older age (HR 1,087; 95% CI 1,034-1,144), higher TBSA (HR 1,072; 95% CI 1,040-1,104), pneumonia (HR 3,525; 95% CI 1,032-12,037) and ARDS (HR 4,318; 95% CI 1,529-12,193) were found to be independent predictors of mortality (*Table III*).

The same variables were analyzed separately for group B2; only age (HR 1,062; 95% CI 1,010-1,117) and TBSA (HR 1,057; 95% CI 1,028-1,087) were found to be independent predictive factors of mortality (*Table IV*).

Table III - Multivariate analysis for predictors of mortality in the global population (group A+B).

	p value	Odds ratio (95% confidence interval)
Age	0,002	1,082 (1,030-1,138)
TBSA	<0,001	1,076 (1,044-1,109)
Inhalation injury	0,958	1,045 (0,201-5,437)
Pneumonia	0,044	3,525 (1,32-12,037)
Positive blood cultures	0,736	1,365 (0,224-8,321)
ARDS	0,006	4,318 (1,529-12,193)

Table IV - Multivariate analysis for predictors of mortality among the lower airway inhalation injury group (group B2).

	p value	Odds ratio (95% confidence interval)
Age	0,02	1,062 (1,010-1,117)
TBSA	<0,001	1,057 (1,028-1,087)
Pneumonia	0,16	2,664 (0,680-10,433)
Positive blood cultures	0,491	0,502 (0,071-3,568)
ARDS	0,144	2,271 (0,755-6,831)

Discussion

Over the past 20 years, remarkable increases in the chance of survival of patients treated in burn centers have been registered. A simple, accurate system for the objective estimation of death probability would be extremely helpful for making medical decisions.[7]

According to our study, the presence of InI, a large burn area and advanced age were all associated with increased mortality (p <0,001). The incidence of InI among our patients was 38% (82 patients out of 210), which is in accordance with the literature. Overall mortality of patients with InI was 34.1%, compared with 8.5% for those without InI. This statistical analysis clearly indicates that InI is an important factor in burn patient mortality prediction.

Bronchoscopy is considered the gold standard test for the diagnosis of InI. Its limitations are mostly related to being observer dependent. Moreover, the absence of relevant bronchoscopy findings cannot rule out the possibility of lung parenchyma damage.[1,2,9,17] Bronchoscopy is also useful when clinical suspicion is low, allowing the diagnosis of cases that would otherwise be missed when based solely on clinical grounds.[16]

Hassan et al. analyzed mortality among 105 patients with InI following classification based on severity of bronchoscopy findings, and found significant correlation between such findings and mortality.[18] Interestingly, our results are not in accordance; this may be due to the small number of patients studied and to the inconsistent systematization of bronchoscopy descriptions.

Infection is a major cause of morbidity and mortality among burn patients. Although the incidence of pneumonia was significantly higher in lower InI patients, it did not turn out to have a significant impact on mortality, conversely to the significant impact it exhibited in the global population. Positive blood cultures were more prevalent among patients with lower airway injury and had a negative impact on mortality.

ARDS occurs in a substantial proportion of patients with burns and inhalational injury, and is a major factor associated with morbidity and mortality.[12] Alpard et al.[19] found a correlation between the incidence of ARDS and increasing doses of inhaled smoke in combination with cutaneous burns in sheep. Lifner et al.[15] were unable to identify a correlation between ARDS and inhalation injury, but they did not submit every patient to bronchoscopy. In our study a significant correlation was found between lower airway injury and development of ARDS (p=0,007), as well as between ARDS and mortality in the global patient population and among lower airway injury patients (p<0,001 and 0,014 respectively).

A study performed in Tokyo, Japan[4] to evaluate the impact of inhalation injury on burn patient mortality showed that 30.4% of the burn population studied had inhalation injury, and overall mortality among these patients was higher (33.6% versus 8.1%), similar to the values found in our study. However, they report that inhalation injury, full- and partial-thickness burn size and age were independent predictors of patient outcome, and that inhalation injury was the most important predictor of overall mortality. However, according to our data, inhalation injury was not an independent predictive factor for burn patient mortality. Our inhalation injury group had significantly higher TBSA, and higher prevalence of pneumonia, ARDS and sepsis, among other factors, making them a specifically critically-ill patient group. The combination of all these

factors and others that might not have been taken into account may be a plausible explanation for our results.

Older age, higher TBSA, development of ARDS and pneumonia were found to be independent predictive factors for mortality in our study; ARDS was the predictive factor with the biggest impact. Older age and TBSA were the single independent predictive factors of mortality among patients with lower airway InI.

Some potential limitations in this study must be highlighted: namely, its retrospective nature; the small number of patients and the lack of systematization criteria for bronchoscopy findings due to its observer dependency.

It should be stressed that patient outcome should not be viewed solely in terms of death or survival, with no consideration for the patients' short and long term quality of life; nevertheless our follow up time is still too short to allow the evaluation of long-term pulmonary sequelae of InI.

Conclusion

Inhalation injury is generally caused by steam and toxic inhalants. Major airway, pulmonary and systemic complications can develop, increasing patient mortality. Early detection and adequate management of inhalation-related injury is absolutely essential.

We could not correlate severity of bronchoscopy findings with mortality, pneumonia or mechanical ventilation. Bronchoscopy is currently the standard diagnostic procedure for InI. However there are no international standard criteria for assessing and describing bronchoscopy findings. Further studies and international collaborative surveys are mandatory.

No specific microorganism, either in blood cultures, bronchoalveolar lavage fluid or sputum was found to have a negative impact upon the survival of patients with or without InI.

InI did not correspond to longer length of stay in the BU or the hospital, according to our findings.

We can conclude that older age, higher TBSA, ARDS and pneumonia were independent predictive factors for mortality in our patient population. InI was not an independent predictive factor for mortality, probably due to high burn severity and ARDS development. In the lower respiratory tract InI group the independent predictive factors for mortality were older age and higher TBSA.

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