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ARTICLE

Hemotransfusion and mechanical ventilation time are associated with intra-hospital mortality in patients with traumatic brain injury admitted to intensive care unit

Hemotransfusão e tempo de ventilação mecânica estão associados à mortalidade intra-hospitalar em pacientes com lesão cerebral traumática, internados em unidade de terapia intensiva

Kelson James Almeida[1], Ânderson Batista Rodrigues[2], Luiz Euripedes Almondes Santana Lemos[2], Marconi Cosme Soares de Oliveira Filho[2], Brisa Fideles Gandara[2], Raissa da Rocha Lopes[2], Daniel Rocha e Silva Modesto[2], Irizon Klecio Pereira Rego[2]

ABSTRACT

Objective: To identify the factors associated with the intra-hospital mortality in patients with traumatic brain injury (TBI) admitted to intensive care unit (ICU). **Methods:** The sample included patients with TBI admitted to the ICU consecutively in a period of one year. It was defined as variables the epidemiological characteristics, factors associated with trauma and variables arising from clinical management in the ICU. **Results:** The sample included 87 TBI patients with a mean age of 28.93 ± 12.72 years, predominantly male (88.5%). The intra-hospital mortality rate was of 33.33%. The initial univariate analysis showed a significant correlation of intra-hospital death and the following variables: the reported use of alcohol (p = 0.016), hemotransfusion during hospitalization (p = 0.036), and mechanical ventilation time (p = 0.002). **Conclusion:** After multivariate analysis, the factors associated with intra-hospital mortality in TBI patients admitted to the intensive care unit were the administration of hemocomponents and mechanical ventilation time.

Keywords: craniocerebral trauma; intensive care units; hemotherapy service; ventilator weaning.

RESUMO

Objetivo: Identificar os fatores associados à mortalidade intra-hospitalar em pacientes com TCE internados em unidade de terapia intensiva (UTI). **Métodos:** A amostra incluiu pacientes com TCE internados na UTI em um período de um ano. Foi definido como variáveis as características epidemiológicas, os fatores associados ao trauma e variáveis decorrentes dos cuidados clínicos na UTI. **Resultados:** A amostra incluiu 87 pacientes com TCE, com idade média de 28,93 ± 12,72 anos, predominantemente do sexo masculino (88,5%). A taxa de mortalidade intra-hospitalar foi de 33,33%. A análise univariada inicial mostrou uma correlação significativa de morte intra-hospitalar e as seguintes variáveis: relato de uso de álcool (p = 0,016), hemotransfusão durante a internação (p = 0,036) e tempo de ventilação mecânica (p = 0,002). **Conclusão:** Após análise multivariada, os fatores associados à mortalidade intra-hospitalar em pacientes com TCE internados na unidade de cuidados intensivos foram a administração de hemocomponentes e tempo de ventilação mecânica.

Palavras-chave: traumatismos craniocerebrais; unidades de terapia intensiva; serviço de hemoterapia; desmame do respirador.

The traumatic brain injury (TBI) is one of the main problems of world public health because it generates strong economic impact and high mortality. In the United States, an average of 2.5 million people suffers TBI annually, which generates estimated spending by more than $ 76 billion/year[1]. About 10% of patients die before any medical care, other 4% die in hospital, and another 10% evolve with permanent neurological sequelae[2].

In an attempt to reduce the mortality rates by TBI, huge efforts have been done in order to determine treatment

[1]Unviersidade de São Paulo, Departamento de Neurologia, São Paulo SP, Brasil;

[2]Universidade Federal do Piauí, Centro de Ciências da Saúde, Teresina PI, Brasil.

Correspondence: Luiz Euripedes Almondes Santana Lemos; Conjunto São Raimundo, Quadra 02 / Casa 44; 64014-530 Teresina PI, Brasil; E-mail: luizalmondes@gmail.com

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protocols for these patients. The identification of epidemiological characteristics can guide intervention at primary prevention, as well as the determination of predictor factors of death can guide the medical conduct during the treatment. These interventions can promote cost reduction and promote reduction of secondary lesions that generate functional disability[1,3].

Based on this, the objective of this work is to identify the factors associated with the intra-hospital mortality in patients with TBI admitted to intensive care unit (ICU).

METHODS

This is an observational study, retrospective, held at the Intensive Care Unit (ICU) of the Teresina Urgency Hospital Dr. Zenon Rocha (HUT) in Teresina, Piauí, Brazil. It was included the medical records of patients with TBI admitted consecutively during a period of one year in an Intensive Care Unit (ICU), in which was possible to collect data from admission to the primary endpoint: intra-hospital death or hospital discharge. Patients with non-traumatic lesion were excluded, as the transferred patients, who the primary endpoint could not be known.

The following variables were collected: (A) Epidemiological variables: age, sex, causal factor of TBI, tomographic findings during ICU admission, systemic trauma associated with TBI. (B) Clinical variables associated with hospitalization and management in intensive care unit: Severity of TBI, initial procedure after admission to the urgency, use of mechanical ventilation in the ICU, use of vasoactive drugs, hemotransfusion, hemodialysis, and nosocomial infection. These variables were considered independent variables. The intra-hospital death was considered as the dependent variable.

The data collected were organized in Microsoft Excel 2010 Program database and, subsequently, exported to the software *IBM SPSS* version 20.0 for *Windows*, in which were analyzed. To test the normality of the study variables, it was used the statistical test of Kolmogorov-Smirnov. Continuous variables are presented as mean ± standard deviation (SD), and categorical in proportions. Univariate analysis was performed for evaluation association between the dependent variable and the other variables, It is used the chi-square test (X2) for categorical variables and the Student t test and Mann-Whitey test for continuous variables parametric and nonparametric, respectively. Multivariate analyses by logistic regression were used to evaluate the influence of the variables independently of the intra-hospital deaths. The level of statistical significance was determined by $p < 0.05$.

This project was approved by the Ethics Committee in Research of the Teresina Urgency Hospital Dr. Zenon Rocha (HUT) with protocol number 36/12.

RESULTS

It was selected 87 patients, with minimum aged of 15 years and maximum of 82 years, and average of 28.93 ± 12.72 years. From this total, 77 (88.5%) were men and 10 (11.5%) women. The most prevalent age group was 21-30 years, representing 39.1% of the sample. With regard to surgery before ICU admission, 53 patients (60.9%) were operated, and 34 (39.1%) received clinical treatment. About the severity of trauma, 64 patients (73.6%) received a diagnosis of severe TBI, with Glasgow coma scale (GCS) <= 8; 16 (18.4%) of TBI moderate; and 7 (8%) of mild TBI (Table 1).

Seventeen patients (19.5%) reported alcohol consumption prior to the event. The others 70 (80.5%) had not consumed alcoholic beverage or did not report the use of it. During the entire period of intensive care, 85 patients (97.7%) needed respiratory support. The use of vasoactive drugs occurred in 53 patients (60.9%). Thirty six patients (41.4%) received blood transfusion and 66 of the hospitalized (75.9%) acquired any nosocomial infection. One patient (1.1%) progressed with acute renal failure, requiring hemodialysis. Regarding to the intrahospital mortality, it was observed 22 deaths (25.3%); from these deaths, 18 (81.8%) were patients with severe TBI (Table 2).

Among the variables studied, in the univariate analysis, it was seen in association with intra-hospital deaths the use of alcohol ($p = 0.016$), the blood transfusion ($p = 0.036$) (Table 2), and the duration of mechanical ventilation ($p = 0.002$) (Table 3).

Table 1. Clinical and epidemiological characteristics of the studied sample (n = 87). Values presented in absolute frequency (n) and relative frequency (%).

Variables	n	%
Age		
0–20 years	25	28.7
21–30 years	34	39.1
31–40 years	15	17.2
41–50 years	7	8
51–60 years	2	2.3
> 60 years	4	4.6
Gender		
Male	77	88.5
Female	10	11.5
Comorbidities		
Yes	5	5.7
No	82	94.3
Severity of TBI		
Mild	7	8
Moderate	16	18.4
Severe	64	73.6
Treatment		
Clinical	34	39.1
Surgical	53	60.9
Time of stay in ICU (days)	20.23 ± 18.02	-
Total time of hospitalization (days)	40.36 ± 26.86	-

TBI: Traumatic brain injury. Source: Intensive Care Unit (ICU) of the Emergency Hospital of Teresina, Piauí, Brazil.

Table 2. Univariate analysis of categorical variables associated with intra-hospital death in patients victims of TBI admitted to the ICU of the Emergency Hospital of Teresina.

Variables	Death n (%)	Hospital discharge n (%)	Total n (%)	p
Gender				
Male	19 (31.1)	42 (68.9)	61(92.4)	0.202
Female	3 (60)	2 (40)	5 (7.6)	
Previous comorbidities				
Yes	1 (33.3)	2 (66.7)	3 (4.5)	0.701
No	21 (33.3)	42 (66.7)	63 (95.5)	
Alcohol use				
Yes	(7.1)	13 (92.9)	14 (21.2)	0.016 *
No	21 (40.4)	31 (59.6)	52 (78.8)	
Severe TBI				
Yes	18 (38.3)	29 (61.7)	47 (71.2)	
No	4 (21.1)	15 (78.9)	19 (28.8)	0.178
DAI at CT				
Yes	(16.7)	5 (83.3)	6 (9.1)	0.655
No	21 (35)	39 (65)	60 (90.9)	
Systemic trauma				
Yes	15 (37.5)	25 (64.5)	40 (60.6)	0.373
No	7 (26.9)	19 (73.1)	26 (39.4)	
Mechanical ventilation				
Yes	22 (33.8)	43(66.2)	65 (98.5)	0.667
No	-	1 (100)	1 (1.5)	
Use of vasoactive drugs				
Yes	18 (39.1)	28 (60.9)	46 (69.7)	0.130
No	4 (20)	16 (80)	20 (30.3)	
Hemotransfusion				
Yes	6 (20)	24 (80)	30 (45.5)	0.036*
No	16 (44.4)	20 (55.6)	36 (54.5)	
Nosocomial infection				
Yes	15 (31.25)	33 (68.75)	48 (72.7)	0.558
No	7 (38.9)	11 (61.1)	18 (27.3)	
Multidrug-resistant germ				
Yes	6 (27.3)	16 (72.7)	22 (33.3)	0.915
No	10 (28.6)	25 (71.4)	35 (66.7)	
ARF				
Yes	1 (100)	-	1 (1.5)	0.333
No	21 (32.3)	44 (67.7)	65 (98.5)	
Hemodialysis				
Yes	1 (100)	-	1 (1.5)	0.333
No	21 (32.3)	44 (67.7)	65 (98.5)	

Source: Intensive Care Unit (ICU) of the Emergency Hospital of Teresina, Piauí, Brazil. TBI: traumatic brain injury; DAI: diffuse axonal injury; CT: computed tomography; ARF: acute renal failure; *statistical significance.

In multivariate analyses by logistic regression, blood transfusion (p = 0.021) and duration of mechanical ventilation (p = 0.01) remained as independent predictors of mortality.

The most common cause of TBI was motorcycle accident in 66 cases (75.9%), followed by automobile accident in eight cases (9.2%) and running over in five cases (5.7%), (Table 4). In relation to the tomographic findings in ICU admission, 19 cases (21.8%) of extradural hematoma, 10 (11.5%) subdural hematoma, and nine (10.3%) diffuse axonal injury (DAI), while 31% of patients had combination of two or more lesions (Table 5).

Regarding the presence of systemic trauma associated with TBI, 24 patients (27.6%) had chest trauma; 11 (12.6%) musculoskeletal trauma; and 35 (40.2%) showed no associated trauma.

Table 3. Univariate analysis of the continuous variables associated with intra-hospital death in patients victims of TBI admitted to the ICU of the Emergency Hospital of Teresina.

Independent variable	Death yes	Death no	p-value
Age	27.90 ± 14.48	30.72 ± 12.83	0.267
Time of trauma to admission to ICU	44.00 ± 49.79	43.32 ± 40.09	0.982
Trauma time CT	3.90 ± 5.52	2.98 ± 3.66	0.734
MV time	22.19 ± 20.04	13.18 ± 17.52	0.002*
Total hospital stay	32.07 ± 28.77	44.69 ± 28.52	0.065

Source: Intensive Care Unit of the Emergency Hospital of Teresina, Piauí, Brazil. CT: computed tomography; ICU: intensive care unit; MV: mechanical ventilation; *statistical significance.

Table 4. Distribution of causes of traumatic brain injury (TBI) treated at the Emergency Hospital of Teresina.

Trauma mechanism	n	%
Automobile accident	8	9.2
Motorcycle accident	66	75.9
Running over	5	5.7
Firearm projectile	0	0
Beating	3	3.4
Fall	1	1.1
Fall of own height	2	2.3
Others	2	2.3

Source: Intensive Care Unit of the Emergency Hospital of Teresina, Piauí, Brazil.

Table 5. Distribution of the main tomographic findings in patients victims of traumatic brain injury (TBI) treated at the Emergency Hospital in Teresina (n = 87).

Changes	n	%
Brain injury	8	9.2
Extradural haemorrhage	19	21.8
Subarachnoid hemorrhage	4	4.6
Subdural hematoma	10	11.5
Intraparenchymal hemorrhage	4	4.6
Diffuse axonal injury	9	10.3
Multiple injuries	27	31
Others	6	6.9

Source: Intensive Care Unit of the Emergency Hospital of Teresina, Piauí, Brazil.

DISCUSSION

The TBI is the main cause of mortality as result of trauma in all age groups[3]. In 2010, about 2.5 million people suffered some form of TBI, which represented an estimated expenditure of 76.5 billion dollars for the US government[1]. In Brazil, every year, a half million people require hospitalization as a result of head trauma. In the city of Teresina, capital of the state Piauí, with an estimated population of 814,230 inhabitants, and reference to approximately 2 million people in the middle North of Brazil, this was the first study related to the topic.

In the studied sample, there was a predominance of young adult males, which is corroborated by other series described[4,5,6,7,8]. There was a higher prevalence of severe TBI, due to the research scenario: the intensive care unit. Due to higher lethality observed in patients with severe TBI, it is justified to conduct studies that seek death predictor variables in intensive care environment.

It was observed that motorcycle accidents were the leading cause of TBI, but there was disagreement with other researchers about the same theme. According to a series of Spain, automobile accidents represented 55% of the causes of TBI from 2005 to 2012. Of these, 22.5% were with cars, 17.1% with pedestrians, 12.3% with motorcycles, and 3.6% with bicycles[9]. In similar studies conducted in Brazil, the leading cause of TBI was collision between vehicles, followed by running over[10,11]. In another study conducted in Bahia, the highest prevalence was fall from height, followed by running over[8].

Regarding the tomographic findings for ICU admission, it was predominated the extradural hematoma (EDH), followed by acute subdural hematoma (SDH). A study conducted in Europe, published in 2014 correlated tomographic findings in the initial hospital admission to the causal factor of TBI. It was observed that victims of traffic accidents presented more intracerebral hemorrhages, followed by traumatic subarachnoid hemorrhage, cerebral contusions, SDH, contusion and subdural hematoma, and less commonly, EDH[9].

Gender did not constitute variable associated with mortality (p = 0.202), which is consistent with literature data[12,13]. This means that despite more men have been victims of TBI, the males do not progress to death independently.

However, it should be mentioned that the ratio M / F present in the study is high (7.7: 1). In other studies that also observed this high ratio, the indexes appear as 3.47: 1[12], and 4.8:1[8].

In univariate analysis, there was no significant association (p = 0.178) between the scores equal to or less than 8 on the Glasgow coma scale (GCS) and lethality. A study of 2014 found that GCS<=8 is more associated with rapid neurological deterioration, and that these patients progressed more rapidly to death, especially because of complications such as hypovolemic shock and hypoxia[9].

There was no correlation between the presence of systemic lesions associated with TBI and lethality resulting from TBI in this casuistic (p = 0.373), as also demonstrated by other studies[14,15,16].

The need for mechanical ventilation during ICU stay did not correlate with intra-hospital mortality in univariate analysis (p = 0.667). Ventilatory support in the acute phase of TBI is critical to prevent secondary lung injury as comorbidity,

and it can promote the stabilization of parameters of cerebral perfusion and adequacy of brain hemodynamics[17]. However, it should be mentioned that the mechanical ventilation time was an independent predictor for intra-hospital mortality after multivariate analysis (p = 0.002).

These findings are in accordance with Gumus et. al.[17], that evaluated 830 patients in the postoperative period of cardiovascular surgery. It was observed that in the group in which there was need for mechanical ventilation for a prolonged period (> 24 hours), there was a higher intra-hospital mortality (p = 0.001). The rate of neurological complications in patients with prolonged mechanical ventilation (PMV) was 34.8%, while in the group without PMV was 5.4% (p = 0.001). The rate of nosocomial infection in patients with PMV was 34.8%, while in the remaining was 7.5%[17].

It was found a high proportion of patients admitted to the ICU who acquired nosocomial infection (75.9%). However, there was no correlation between this variable and mortality (p = 0.558). These findings are discordant with the study of Lia et. al., that associated the diagnosis of nosocomial infection with high rates of clinical complications and high mortality rate in patients admitted to intensive care unit for neurological and no neurological causes[18].

In univariate analysis there was a correlation between reported use of alcohol and intra-hospital mortality (p = 0.016). However, the use of alcohol was not an independent variable predictor of mortality after multivariate analysis. Pandit et. al.[20], pointed that intoxication with ethanol in patients victims of severe TBI is not directly related to mortality. However, there is a higher frequency of hospital complications in the group of patients that made use of alcohol[19]. One possible explanation would be the fact of prior exposure to ethanol intensifies neuroinflammatory response after TBI[20].

Another variable considered as a predictor of mortality in an independent way after multivariate analysis was the realization of hemotransfusions (p = 0.036). Blood transfusion has undesirable effects such as aggravation of acute inflammatory response, which contributes to the increased incidence of multiple organ failure[21,22,23]. Duane et al.[24], showed that, although most patients victims of TBI alone do not require blood transfusion, those who need it have higher mortality rates, and these patients are more likely to undergo some surgical intervention. In addition, the most seriously injured patients require more frequently blood transfusion, which leads to maintenance of systemic inflammatory response[25]. In this study, the criteria used for hemotransfusions were presence of inadequate tissue oxygenation signals, such as angina, electrocardiographic changes, hemodynamic instability, cardiac decompensation and altered state of consciousness. In the absence of clinical symptoms, blood transfusion was performed in patients whose hemoglobin concentration was below 7 g/dL.

In conclusion, the predictive factors of intra-hospital mortality in patients with TBI under intensive care were: mechanical ventilation time and hemotransfusions.

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