Intracranial Pressure Monitoring in Patients with Severe Traumatic Brain Injury: A Cohort Study with Paired Analysis

Monitorização da pressão intracraniana em pacientes vítimas de traumatismo craniencefálico grave: Um estudo coorte com análise pareada

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Abstract

Introduction Intracranial hypertension continues to be the most frequent cause of death in patients with traumatic brain injury (TBI). Thus, invasive monitoring of intracranial pressure (ICP) is a very important tool in neurointensivism. However, there is controversy regarding ICP monitoring and prognosis.

Objectives To evaluate whether there is a difference in mortality between patients with severe TBI who underwent invasive ICP monitoring compared with those who did not undergo such procedure.

Methodology This is a unicentric study in the prospective cohort mode. A total of 316 patients with severe TBI were evaluated and, out of these 316 individuals, 35 were submitted to ICP monitoring. All clinical data were evaluated by the Tertiary Hospital Neurosurgery team in the city of São Paulo.

Results Of the total cohort, 35 (11%) patients underwent ICP monitoring, while 281 did not. Comparing the 2 groups, there was no difference in terms of early mortality between patients who were submitted to monitoring and those who were not (34.3 versus 14.3%; $p = 0.09$); there was also no difference in terms of hospital mortality (40 versus 28.5%; $p = 0.31$) or intensive care unit (ICU) length of stay (16.10 days, 95% confidence interval [CI]: 10.6–21.6; versus 20.60 days, 95%CI: 13.50–27.70; $p = 0.31$).

Conclusions In this cohort, we did not identify differences in mortality or in duration of hospitalization between patients with ICP monitoring and those exclusively with clinical-radiological evaluation. However, further national co-operative studies of services using ICP monitoring are needed to achieve results with greater generalization power.

Keywords
- intracranial pressure
- hospital mortality
- intracranial hypertension
- brain injuries
- traumatic

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Resumo

Introdução A hipertensão intracraniana continua a ser a causa mais frequente de morte em pacientes com traumatismo cranioencefálico (TCE). Assim, a monitoração invasiva da pressão intracraniana (PIC) é uma ferramenta de grande importância em neurointensivismo. No entanto, há controvérsias em relação à monitorização da PIC e sua relação com o prognóstico.

Objetivos Avaliar se há diferença de mortalidade entre pacientes com TCE grave submetidos à monitorização invasiva da PIC em comparação com aqueles não monitorizados.

Metodologia Trata-se de um estudo unicêntrico no modo de coorte prospectiva. Foram avaliados 316 pacientes com TCE grave e, desses 316 indivíduos, 35 foram submetidos à monitorização da PIC. Todos os dados clínicos foram avaliados pela equipe de Neurocirurgia de Hospital Terciário na cidade de São Paulo.

Resultados Da coorte total, 35 (11%) pacientes foram submetidos a monitorização da PIC, enquanto 281 não o foram. Comparando-se os 2 grupos, não houve diferença em termos de mortalidade precoce entre pacientes submetidos a monitorização e os que não foram submetidos (34,3 *versus* 14,3%; $p = 0,09$); não houve também diferença em termos de mortalidade hospitalar (40 *versus* 28,5%; $p = 0,31$) ou no tempo de internação na UTI (16,10 dias, intervalo de confiança [IC] 95%: 10,6–21,6 *versus* 20,60 dias, IC95%: 13,50–27,70; $p = 0,31$).

Conclusões Nesta coorte, não identificamos diferença de mortalidade ou de duração de tempo de internação entre pacientes com monitorização da PIC e aqueles com avaliação exclusivamente clínicorradiológica. Fazem-se, no entanto, necessários mais estudos cooperativos nacionais dos serviços que utilizam a monitorização da PIC para obtenção de resultados com maior poder de generalização.

Palavras-chave

- pressão intracraniana
- mortalidade hospitalar
- hipertensão intracraniana
- lesões encefálicas
- traumáticas

Introduction

Intracranial hypertension is the main cause of death in head trauma, due to changes in cerebral hemodynamics that generate catastrophic repercussions for the suffering brain. The normal values of intracranial pressure (ICP) in adults are between 3 and 15 mmHg, and values greater than this interval are normally filled with expansive intracranial processes, which in the context of polytrauma are mainly translated into subdural and epidural hematomas, traumatic subarachnoid hemorrhages, and diffuse injuries.

According to the Brain Trauma Foundation (BTF)[1] from the United States and to the European Brain Injury Consortium (EBIC), ICP monitoring is indicated in all patients with traumatic brain injury (TBI) with a score between 3 and 8 on the Glasgow Coma Scale (ECGl) and with abnormal skull computed tomography (CT).[2] In addition, it is also indicated in patients with normal skull tomography, but with at least two of the following criteria: arterial hypotension (SB$p < 90$ mmHg or DB$p < 60$ mmHg), age > 40 years old and decortication or decerebration posture. These indications are supported by the latest Brain Trauma Foundation guideline, where it is recommended to monitor the ICP to reduce in-hospital death within 2 weeks of the event.

Although these criteria are established in the literature, there are not enough studies to demonstrate whether there is a better prognosis in patients victims of TBI who are monitored compared with those evaluated only clinically. As an example, there is a study[3] performed by Bratton et al. in which he questioned the effectiveness of ICP monitoring, because when comparing patients with image monitoring with patients monitored by ICP monitor, they did not identify significant differences in the prognosis.

In our service, between 2011 and 2012 (Ferreira et al.),[4] a propensity score cohort analysis was performed, in which no difference was found in the outcomes hospital mortality, mortality in 14 days, and mortality in rehabilitation centers (after 14 days). Therefore, our objective is to assess whether there was a difference in terms of mortality in this more recent period of cohort analysis.

Material and Methods

This is a single-center study in the prospective cohort mode. The studied sample included individuals of both genders who were victims of severe cranioencephalic trauma (TBI) admitted consecutively to an intensive care unit (ICU) specialized in trauma at the Hospital das Clínicas of the Medical School of the Universidade de São Paulo (FMUSP, in the Portuguese acronym), São Paulo, state of São Paulo, Brazil, from March 2012 to January 2015. Patients > 14 years old with a clinical-radiological presentation of severe TBI admitted to the ICU and who needed a more substantial

assessment of ICP were included. Those with penetrating or open trauma, who had chronic subdural hematoma, or referred from external ICUs were excluded from the study. These patients were followed-up throughout the hospitalization period and their data were accounted for in a digital database to assess their mortality after 14 days, as well as to evaluate the length of hospital stay. The present study was approved by the Research Projects Analysis Commission (CAPPesq, in the Portuguese acronym) of the Hospital das Clínicas of the FMUSP under the protocol n° 00119/10.

The clinical predictors evaluated included:

- Pupillary reactivity (anisocoria, isocoria or fixed);
- International normalized ratio (INR)
- Activated partial thromboplastin time (APTT);
- Glasgow Coma Scale (GCS);
- Age;
- Male gender
- Simplified Acute Philosophy Score (SAPS) 3 score.

Possible confounding factors include:

- Time taken to transfer admitted patients to Intensive Care Unit from Emergency Department, categorized as < 24 h and > 24 h.
- Transfer mode, categorized as direct transport (transfer from the accident scene to the study hospital) or indirect transport (transfer after initial transport to less specialized hospitals).
- Kinetic energy involved in the trauma: high kinetic energy (running over, car accidents, falls from a high level) and low kinetic energy (physical aggression and falls from one's own level).

The GCS was evaluated in the extra-hospital and in-hospital environment; however, only the highest score was considered, due to the possibility of confounding factors such as sedation. Therefore, only individuals who scored < 9 on the scale were considered as having severe TBI.

Regarding the statistical analysis, the unpaired Student's *t*-test or the Mann-Whitney test for continuous variables were used to assess the association of the variables, and the chi-squared test or the Fisher exact test were used for the categorical variables. To assess the normality of continuous variables, the Shapiro-Wilk test was used. Categorical data are presented as absolute numbers (with percentages), parametric data as mean and standard deviation (SD), and nonparametric data as medians and interquartile range (IQR). Predictors that, in the univariate analysis, had $p < 0.10$ were selected for the multivariate analysis, which was done through logistic regression.

To determine the performance of the model, the discrimination was made by analyzing the area on the receiver operating characteristic (ROC) curves. The higher the area under the ROC curve (AUC), the better the prognostic discrimination. A model with an AUC of 0.50 has no discriminatory power, while an AUC of 1.0 reflects perfect discrimination. Calibration was assessed using the Hosmer-Lemeshow goodness of fit test, which assesses the ability of the model to correctly predict clinical outcomes. The internal validity was done with bootstraping procedures. This form of validation optimizes the prediction of clinical outcomes for similar populations. The data were analyzed using the STATA 11.0 software (StataCorp, College Station, TX, USA). Then, a "propensity score" type pairing was performed to enable the correlation between clinical outcomes and the use or not of monitoring, aiming, in this way, to reduce the heterogeneity of the compared groups.

Results

In total, 316 patients were included in the present study, of which 273 (86%) were male and 43 (14%) were female. The average age of the studied group was 38 ± 16 years old, and the main trauma mechanisms were falls (30.1%), followed by pedestrian accidents (26.1%) and motorcycle accidents (19.5%). Only 35 patients underwent ICP monitoring, in whom a paired propensity score analysis was performed. The most common associated extracranial injuries were facial trauma ($n = 165/32\%$), followed by orthopedic and thoracic trauma ($n = 143/25.9\%$, both), and spine trauma ($n = 80/15$, 4%). The 14-day mortality rate was 26.6% and the in-hospital mortality rate was 36.4% when the 316 patients were evaluated.

As noted in ►**Table 1**, the average age of the patients who underwent ICP monitoring was 43.94 ± 21.3 old, while the age of the clinically monitored patients was 37.62 ± 18.4 years old, which shows that the group clinically monitored was younger, although this age difference was not statistically significant ($p = 0.18$). In addition, 27 males were subjected to invasive monitoring, while those who were not totaled 32, which, even with this difference, allowed both compared groups to be homogeneous in this respect ($p = 0.188$). In all other clinical variables evaluated, such as GCS, SAPS3, APTT, INR, and pupils, there was no significant difference between the samples, allowing for a later comparison of the most reliable prognosis.

As described in ►**Table 2**, there was no significant difference between patients with ICP monitoring and those not monitored in terms of early mortality (34 versus 14%), hospital mortality (40 versus 28%), average length of stay in the ICU (20.82 versus 16.14 days), and mean length of hospital stay (28 versus 34.82 days). It is important to note that there were no adverse events (infection or intracranial hemorrhages) in the patients who underwent ICP monitoring.

Discussion

The present article exposed, as demonstrated above, a prospective analysis between groups of patients with TBI. Two groups of 35 individuals, 1 with invasively monitored patients and the other with patients submitted to clinical radiological evaluation, were obtained from a prospective cohort of 316 patients. Intracranial pressure monitoring is considered a fundamental pillar in the intensive monitoring of patients with severe TBI, whose basic principle is to

Table 1 Multivariate Analysis Type Propensity score

Variables	Patients followed up with an ICP monitor	Clinically monitored patients	*p-value*
Age	43.94 ± 21.3	37.62 ± 18.4	0.1899
Male	27	32	0.188
Glasgow Coma Scale (Median. p25-p75)	6 (4–8)	6 (3–8)	0.9241
SAPS, Simplified Acute Physiology Score 3	51.91 (95%CI: 47.6–56.1)	49.31 (95%CI: 44.1–54.4)	0.4335
APTT	1.18 (95%CI: 1.06–1.30)	1.20 (95%CI: 1.01–1.39)	0.8627
INR	1.40 (95%CI: 1.3–1.5)	1.56 (95%CI: 1.22–1.9)	0.3598
Pupil	3 Mid-position fixed 7 anisocoric 24 isochoric	2 Mid-position fixed 4 anisocoric 24 isochoric	0.756

Abbreviations: APTT, activated partial thromboplastin time; CI, confidence interval; ICP, intracranial pressure; INR, international normalized ratio.

Table 2 Assessment of prognostic variables

Variable	Patients followed up with an ICP monitor	Clinically monitored patients	*p-value*
Early mortality (before 14 days)	12 (34%)	5 (14%)	0.093
Hospital mortality	14 (40%)	10 (28%)	0.45
Length of stay in ICU	20.82 days (95%CI: 13.55–27.70)	16.14 days (95%CI: 10.62–21.65)	0.3132
Length of hospital stay	28 days (95%CI: 18.96–37.03)	34.82 days (95%CI: 20.55–49.15)	0.4155

Abbreviation: ICU, intensive care unit.

maintain an ICP < 22 mmHg.[1] However, based on the exposed data, no significant difference was demonstrated between the two groups regarding the studied variables. There are discrepancies in results obtained in the literature, and other studies have obtained similar results, such as those by Ferreira et a.l[5] and Biselli et al.,[4] in addition to the metanalysis performed by Yuan et al.[6] in 2015, which also did not found clinical evidence to indicate that ICP monitoring is superior to no ICP monitoring, although with the caveat that some studies included in this methanalysis indicated a reduction in the mortality. Although with the caveat, for the latter, that some studies indicate that there was a reduction in the mortality of patients submitted to invasive ICP monitoring. Yuan et al.,[7] McLaughlin et al.,[8] Dawes et al.,[9] and Agrawal et al.[10] obtained opposite results, demonstrating a benefit in the use of ICP monitoring.

As can be seen, this is a very controversial topic in the scientific community and there is still no clear consensus on the real benefits of using this form of monitoring. What we can see from the present study is that, most likely, the highest mortality rates in the invasive monitoring group do not result from the procedure itself, but from the fact that the individuals selected for this have more severe conditions than the other group due to the perception of the neurosurgery team that chose to monitor them. We can also exclude infections of the central nervous system, since no such case was reported in the monitored patients. Another disturbing factor is the possibility that there are other variables that were not considered during the propensity score pairing and that, in fact, may impair the final analysis of the data obtained.

The fact that the study was performed in a Brazilian public tertiary hospital may impair the external validation of the data, since the lack of resources and the often precarious pre-hospital care can be confusing bias. Only a few patients were monitored, which inevitably can lead to selection bias. A very controversial study[10] that caused repercussions in the scientific community was performed with 324 patients who were victims of severe TBI by a medical team in Bolivia, which showed similar results to ours.[11] However, several methodological errors were evident throughout its design, such as the inexperience of the Bolivian team in the approach of the patients, the nonconsideration of multisystemic trauma and length of stay, and, finally, the different approach for each group, in which unmonitored patients received more days of treatment. These listed factors make this study unfeasible to, separately, determine a change in the selection criteria in patients with post-traumatic intracranial hypertension. In the latest Brain Trauma Foundation (BTF) guidelines, the recommendation generated from this study was that the use of ICP monitoring determines lower mortality in 14 days (grade of recommendation IIb), since they had found a trend towards reduced mortality in the first 14 days in the group that was monitored with ICP. Regarding the previous study performed in our service, there was no difference in outcomes, showing that additional measures must be taken to improve the prognosis of these patients.

Conclusion

This cohort demonstrated, after adjustment by the propensity score method to minimize the possible biases inherent to

the study, there was no statistically significant difference between patients submitted to invasive ICP monitoring and those submitted only to clinical-radiological evaluation. Nevertheless, it is important to emphasize that, although some studies ratify such results, the theme is still not well-established and further studies with a larger number of individuals involved and with an analysis of multiple variables are necessary to, in fact, be able to establish the best role of ICP invasive monitoring in the management of patients with severe TBI.

Note

The present study was performed at the Hospital das Clínicas of the Medical School of the Universidade de São Paulo.

Conflict of Interests

The authors have no conflict of interests to declare.

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