PROGNOSTIC SIGNIFICANCE OF INTRACRANIAL PRESSURE MONITORING AND INTRACRANIAL HYPERTENSION IN SEVERE BRAIN TRAUMA PATIENTS

PROGNOSTIČKI ZNAČAJ MONITORINGA INTRAKRANIJALNOG PRITISKA KOD BOLESNIKA S TEŠKIM KRANIOCEREBRALNIM POVRĐENAMA

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Summary – Since without prospective randomized studies it is not possible to have a clear attitude towards the importance of intracranial pressure monitoring, this study was aimed at examining the prognostic effect of the intracranial pressure monitoring and intracranial pressure oriented therapy in severe brain trauma patients, and at defining optimal intracranial pressure values for starting the treatment. Two groups of patients were treated in the study, one consisted of 32 patients undergoing intracranial pressure monitoring and the second group of 29 patients without intracranial pressure monitoring in the control group. The study was prospective with groups randomized. There were 53% survivals in the intracranial pressure monitored patients and 34% in the control group, with no significant difference in the survival rate between the two groups ($\chi^2=2.11; p=0.15; p>0.05$). The average intracranial pressure in the patients with intracranial hypertension who died was 27 mm Hg, while in the patients who survived the average intracranial pressure was significantly lower (Student’s $t$ test: $t=2.91; p=0.008; p<0.01$) and it was 18 mm Hg. We recommend starting intracranial pressure oriented therapy when the patient’s intracranial pressure exceeds 18 mmHg during 2 hours of monitoring.

Key words: Intracranial Pressure + physiology; Intracranial Hypertension; Craniocerebral Trauma; Brain Injuries; Prognosis; Monitoring, Physiologic

Introduction

Up to now, all assessments of prognostic and therapeutic significance of intracranial pressure (ICP) monitoring in severe brain trauma patients had no prospective and randomized character and were based on two main modes. One of the modes compared the survival rate of patients treated before introducing ICP monitoring with patients’ survival after the ICP monitoring had become the routine method in an intensive care unit. Another mode compared the survival of brain trauma patients between two intensive care units, one practicing ICP monitoring with the other one that did not. Introduction of routine ICP monitoring during 1980’s enabled clinicians to apply ICP and/or cerebral perfusion pressure (CPP) oriented therapies, which resulted in outcomes better than those achieved in previously applied therapies [1]. The Brain Trauma Foundation officially recommended routine ICP monitoring after severe craniocerebral trauma in 1995 and 2000.

After the severe brain trauma, numerous secondary ischemic insults „enrich” the initial brain injury in the hours and days that followed [2]. Earlier studies emphasized the reduced perfusion in order to explain ischemia after severe brain trauma (SBT), and used the classical mechanisms of cerebrovascular insult (CVI) for the explanation of irreversible tissue damage. However, cerebral metabolism is often reduced after SBT [3], not only because of the trauma itself [4] but also because of the additional application of sedatives. The applicability of mechanisms of tissue damage during CVI on the damage during SBT is questionable. Unlike stroke, pathophysiological mechanisms responsible for the death of neurons are not well understood in SBT. In patients with SBT and persistent intracranial hypertension (ICHHTN), cerebral blood flow (CBF), which is required to preserve the tissue, must be higher than in stroke, because of a low threshold for metabolic vulnerability of the traumatized brain. Therefore, the treatment of patients with SBT either by increasing CPP or decreasing the ICP imposes a difficult and uncertain task, considering the altered cerebrovascular auto-regulation capacity, on the one hand, and resistant cases of ICHHTN on the other.

This study was aimed at examining the prognostic importance of ICP monitoring and consecutive ICP oriented therapy for patients with severe head trauma, and at finding out the optimal values of ICP to start appropriate treatment.

Material and methods

The study included 61 patients who were treated and followed in the period from the 16th February 2008 to the 15th February 2010. The study was prospective and the sample was randomized depending on which day of the week the patient was admitted to hospital (one group of patients consisted of those admitted on e.g., Monday, Thursday and Friday and the other one on the rest of the days). The study group consisted of two subgroups of patients: 32 patients with ICP monitoring performed and 29 patients without intracranial pressure monitoring in the control group.
patients with no ICP monitoring done. Seventeen patients had ICP monitor implanted subdurally, 11 intraparenchymally and 4 intraventricularly.

According to the inclusion criteria, the study sample consisted of patients with brain trauma and with: GCS ≤ 8 or abnormal CT scan of the brain in terms of present mass lesions. Mass effects that had been shown in the CT with midline shifting bigger than 5 mm were surgically explored (external or internal decompression). The patients with CT findings of no mass effect large enough and with ICHTA were treated conservatively.

The values of patient’s ICP were recorded each hour in the medical charts after readings from display device (Codman ICP Express). The average values of ICP were calculated for each patient by adding the readings of all values and dividing with number of measurements. Neurological assessments were quantified in Glasgow Coma Score (GCS) in time interval of 4 hours, or 30 min in case of initiating ICHTN. ICP monitoring was performed in patients with ICHTN until the values of ICP got normal and after that for another 48 to 72 hours, and in cases resistant to therapy usually until death occurred. ICP monitoring was done for another 48 hours in the patients with no ICHTN during the first two days after the injury. The treatment outcome was estimated on the basis of the data obtained by outpatient examination or telephone interviews 6 months after the hospitalization.

ICP values in patients who had undergone monitoring were designated as normal or hypertensive. We defined ICHTN as the values of ICP over 20 mm Hg for more than 2 hours. In the control group, intracranial hypertension criteria were: 1. Brain CT findings with the present diffuse or focal edema around the lesion with evident displacement of surrounding intracranial structures; 2. neurological examination exhibiting newly found decerebration or decortication, or GCS less than 9; 3. Fundus examination with findings of edema or papilla stasis of 0.5 diopters. Based on the last two criteria, it was possible to note the deterioration in patients and to indicate the control brain CT.

We applied general, special and ultimate measures of treatment of ICHTN. The following general treatment measures were used in cases of ICHTN: 1. raising the headboard at 30 degrees, 2. avoidance of the neck flexion, 3. avoidance of hypotension (SAP <90 mm Hg), 4. controlling hypertension, if present (nitropresside, beta blockers), ventilation to normocarbia (pCO2 = 35-40 mmHg), light sedation (e.g. codeine). The specific measures included: 1. deep sedation and/or relaxation (fentanyl, vecuronium), 2. Drainage of 3 to 5 ml of CSF (in cases of intraventricularly placed systems), 3. mannitol bolus at first and then application intravenously for 6 hours, 4. Hyperventilation to pCO2 = 30-35 mmHg. The following ultimate treatments were applied: 1. treatment with high doses of barbiturates (barbituric coma) 2. Hyperventilation to pCO2 = 25-30 mmHg, 3. operation: internal or external decompression. Appropriate nutritional support, glycemia control, and peptic ulcer prophylaxis was provided to all of the patients in the study. Internal decompression of traumatic mass lesions was done in 22 patients according to general neurosurgical indications.

The quantitative statistical analysis was performed on the computer. Excel program from Microsoft Office 2003 software package was used for entering, rating, grouping, tabular and graphical presentation of data. The calculations were performed using the SPSS program version 10.0. In all analysis, the limit of statistical significance as the default error was considered to be 0.05 or 5%. The Student’s t test for independent samples was used to compare numerical values between the two groups. The comparison of representation of certain modes of attribute characteristics between the two groups was performed by Mantel Haenszel Chi square test or Fisher’s test.

Results

Age and GCS homogeneity of the groups

The vast majority of study participants (86.89%) were male, accounting for 90.62% in the group of ICP monitored patients and 82.76% in the control group.

There was no statistically significant difference between ICP monitored patients and control group by age (Fisher’s test: p> 0.05). The average age of the patients in our study was 42.15±22.02 years. In the ICP monitored patients it was 40.97±21.70 and in the control group 43.41±22.31, and no significant difference between ICP monitored patients and control group was found (T test: t=0.43 and p>0.05).

The average initial GCS was 6.25±2.11 and 6.29±2.16 in the ICP monitored patients and in the

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**Abbreviations**

ICP – intracranial pressure
CPP – cerebral perfusion pressure
SBT – severe brain trauma
CVI – cerebrovascular insult
ICHTN – intracranial hypertension
CBF – cerebral blood flow
CT scan – computer tomography scan
GCS – Glasgow Coma Score

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**Graph 1.** Average GCS during hospitalization of ICP monitored patients and in the control group.
control group, respectively (Student’s T test: t=0.06; p>0.05). Two of the patients had initial GCS 3, each from one group of the patients. On the 8th day, the average GCS was 6.60±4.21, and 8.00±3.38 for the ICP monitored group and the control group, respectively (Student’s t test: t=1.05 p>0.05). On the 15th day, the average GCS was 9.00±4.36, and 10.00±3.89 for the ICP monitored group and the control group, respectively (Student’s t test: t=0.32 p>0.05). On the 21st day, the average GCS was 9 both in the control group and in the group with ICP monitoring (t test: t=0.06; p>0.05). Two of the patients had initial GCS 3, each from one group of the patients. On the 8th day, the average GCS was 6.60±4.21, and 8.00±3.38 for the ICP monitored group and the control group, respectively (Student’s T test: t=2.91; p=0.008; p<0.01). Those tests did not confirm statistically significant differences between the two groups in all four measurements.

Survival of the patients in relation to the application of the ICP monitoring

The total survival rate in our study was 44% of patients, namely 34 died out of 61.

The survival rate in the ICP monitored group and in the control group was 53% and 34%, respectively (Table 1).

<table>
<thead>
<tr>
<th>ICP monitoring</th>
<th>N</th>
<th>Died</th>
<th>% Died</th>
<th>Survived</th>
<th>% Survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Done/Ispitivana grupa</td>
<td>32</td>
<td>15</td>
<td>46.87%</td>
<td>17</td>
<td>53.13%</td>
</tr>
<tr>
<td>Not done/Kontrolna grupa</td>
<td>29</td>
<td>19</td>
<td>65.52%</td>
<td>10</td>
<td>34.48%</td>
</tr>
<tr>
<td>Total/UKupno</td>
<td>61</td>
<td>34</td>
<td>55.74%</td>
<td>27</td>
<td>44.26%</td>
</tr>
</tbody>
</table>

The Mantel Haenszel Chi square tests did not confirm that the percentage of surviving patients was significantly higher in the group where the ICP was monitored ($\chi^2=2.11$ and $p=0.15$; $p>0.05$).

Survival of patients in relation to the presence of ICHTN

Elevated values of ICP were found for more than two hours in 22 ICP monitored patients (68.75%), and in ten patients (31.25%) there were no criteria of ICHTN. In the group with ICHTN, the survival rate was lower than in the group without ICHTN, being 41% and 80%, respectively (Table 2).

<table>
<thead>
<tr>
<th>ICP monitored</th>
<th>N</th>
<th>Died</th>
<th>% Died</th>
<th>Survived</th>
<th>% Survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With ICHTN/Sa ICHTN</td>
<td>22</td>
<td>13</td>
<td>59.10%</td>
<td>9</td>
<td>40.90%</td>
</tr>
<tr>
<td>Without ICHTN/Bez ICHTN</td>
<td>10</td>
<td>2</td>
<td>20.00%</td>
<td>8</td>
<td>80.00%</td>
</tr>
<tr>
<td>Total/UKupno</td>
<td>32</td>
<td>15</td>
<td>46.75%</td>
<td>18</td>
<td>53.25%</td>
</tr>
</tbody>
</table>

Fisher’s test showed that the percentage of survival was statistically significantly lower in the group of patients having ICHTN (Fisher’s test, $p=0.04$; $p<0.05$).

**Discussion**

Until this study, we could not find any randomized controlled study in literature trying to demonstrate the effectiveness of therapy of SBT directly and which would be guided by values of ICP obtained by monitoring. Even in the current studies [5] there is still uncertainty about the prognostic significance of ICP monitoring in patients with SBT and even clinicians treating SBT have divided opinions about its real importance [6]. By reviewing the literature, papers can be found that either confirm [7] or neglect [8,9] ICP monitoring as an expedient method in treating SBT. This dilemma, widely present in the world’s professional and scientific circles, constrained us to try to help in shaping an answer to the question: "is there any effect of ICP monitoring and consequently ICP oriented therapy in SBT patient’s outcome?"

It seems that the Brain Trauma Foundation recommendations for the routine monitoring of ICP after SBT are applied in a rather facultative manner in the neurosurgical intensive care units around the world. Approximately 25% [10] of these centers in economically developed societies do not use ICP monitoring, while in poorer countries this percentage is certainly higher. The starting attitude of the centers which practice ICP monitoring is that it may help early detection of mass lesions, restrict use of some interventions which may harm the patient (such as hyperventilation), influence the reduction of ICP by cerebrospinal fluid drainage (and thereby increase cerebral blood perfusion). Other centers are skeptical about the ultimate benefits of the patients [11], or point out a specific type of serious complication [12], the frequency of...
Is it possible to treat hypertension without measuring blood pressure? A parallel to this question would be: is it possible to treat increased ICP without monitoring it? Of course, noninvasive placement of the inflatable cuff around the upper arm is not equal to invasive intracranial placement of ICP catheter which is, as outlined above, coupled with a certain percentage of serious complications. However, if we know that the probability of occurrence of ICHTN in mild (GCS 15 to 13) and in moderate (GCS 12 to 9) brain trauma is, respectively 3% and 10 to 20% [15], that being approximately the percentage of perioperative complications related to ICP monitoring, it is clear why ICP monitoring could be justified only in cases of severe brain trauma, where over 50% [16] of injured have elevated ICP.

Heterogeneity of cranioencebral injuries [17], of their pathophysiology and outcomes in different investigated groups of patients, is attempted to be compensated by homogenization of the groups according to Glasgow Coma Score (GCS), which correlates with the outcome very well [18,19]. In our study, two groups of patients were homogeneous by the initial and during hospitalization state of consciousness. The average initial GCS in the control group and ICP monitored patients was 6.3 and 6.2, respectively, which clearly indicates the depth of altered states of consciousness. Some authors [20] doubt the justification of routine use of this type of monitoring, especially when it comes to patients with an initial GCS 3, due to early and irreversible brain damage. The experience from our study confirms this.

A recent study [21] showed almost twice lower mortality in neurosurgery centers where ICP was usually monitored comparing to the intensive care unit where it was not. Also, Lane [22] found significantly better survival after insertion of ICP monitors in a large group of 541 patients with SBT. In his study, Saul [23] had monitored ICP in 127 patients with SBT and found mortality 46%, which is a very similar result to our own. Still, there are some studies that showed no difference in survival of SBT patients no matter whether ICP monitoring was undertaken or not [24,25]. In our study, almost 20% of ICP monitored patients survived more than non ICP monitored (mortality ratio 66%/47%), yet no statistically significant difference was found (p = 0.15; p>0.05). We believe that final evaluation of importance of the ICP-oriented therapy requires a much larger sample size, which, on the other hand, may be coupled with significant logistical and financial difficulties. A similar view can be found in Joseph’s paper [15], who has quoted a figure of 750 required patients according to the official estimates of the Brain Trauma Foundation from year 2000.

According to the reports from the Brain Trauma Foundation data bank based on 654 patients with SBT, 72% of them had ICP>20 mm Hg for a significant period of time [26]. This is similar to the results from our study, where ICHTN was found in 69% of patients. In ICHTN patients, the average ICP in patients who died was 27 mmHg, while it was 18 mmHg in those patients who survived, that being a significantly lower value (t test: t = 2.91 and p = 0.008; p<0.01). Thus, the average ICP in the ICHTN patients correlates with survival and its borderline values should be looked for in the range from 18 to 27 mmHg. In our opinion, it seems less reasonable that some authors [23] take the value of 25 mmHg as the limit in defining ICHTN, compared to the others [16,27] who take 20 mmHg. The reason for this is the necessity to introduce the adequate ICHTN treatment as soon as possible. The major significance of the mean values of ICP in survival of SBT patients was found in Nga study [28] as well in McGraw’s [29]. It is possible not only to monitor and treat ICP peaks on the basis of ICP monitoring, but also to calculate the mean ICP. The predictive value of mean ICP is demonstrated by correlating the values of ICP in the deceased and surviving ICHTN patients.

Conclusion

The results of the our study suggest that intracranial pressure monitoring is a useful method in the treatment of patients with severe cranioencebral injuries, although a statistically significant by better survival of intracranial pressure monitored group has not been confirmed. The value of intracranial pressure, which requires appropriate treatment, begins with 18 mm Hg.

References

Uvod
Bez prospektivnih randomizovanih studija ne postoji jasan stav prema značaju monitoringa intrakranijalnog pritiska kod bolesnika s teškim kraniocerebralnim povredama. Cilj rada bio je da se ispitaj prostog kliničkog značaja monitoringa intrakranijalnog pritiska i posledično orijentisane terapije kod bolesnika s teškim povredama mozga.

Materijal i metode
Ispitivana grupa činila su 32 bolesnika kod kojih je meren intrakranijalni pritisak, a kontrolnu grupu 29 bolesnika kojima nije meren. Studija je bila prospektivna i randomizovana.

Ključne reči: Intrakranijalni pritisak + fiziologija; Povišeni intrakranijalni pritisak; Kraniocerebralna trauma; Povrede mozga; Prognoza; Monitorirnog


Rezultati
Preživljavanje u ispitivanoj grupi bolesnika iznosilo je 53%, a u kontrolnoj 34%. Nema bitne razlike u preživljavanju (x²=2,11; p=0,15; p>0,05). Prosečni intrakranijalni pritisak kod umrlih bolesnika s intrakranijalnom hipertenzijom iznosio je 27 mmHg, dok je kod preživelih iznosio 18 mmHg (p=0,008; p<0,01).

Zaključak
Rezultati naše studije sugeriše da monitoring intrakranijalnog pritiska u bolesnika sa teškim intrakranijalnim povredama je potrebno. Evo da se u bolesnim sa teškim intrakranijalnim povredama izvede prospektivna i randomizovana studija.

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