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Intravenous Esmolol for Intracranial Pressure Reduction After Traumatic Brain Injury

Tayebeh Zarei [1], Arzoo Ahmadi [2], Atabak Najafi [2], Mojtaba Mojtahedzadeh [3], Kamal Basiri [4], Somayeh Mehrpour [5,*], Khalil Komlakh [6] and Kaveh Hedayati Emami [2]

[1]Department of Anesthesiology & Critical Care, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[2]Department of Anesthesiology & Critical Care, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Clinical Pharmacy, Pharmaceutical Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[4]Prehospital and Hospital Emergency Research Center, Tehran University of Medical Sciences, Tehran, Iran
[5]Department of Anesthesiology & Critical Care, Qom University of Medical Sciences, Qom, Iran
[6]Department of Neurosurgery, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[*]*Corresponding author*: Department of Anesthesiology & Critical Care, Qom University of Medical Sciences, Qom, Iran. Email: somayeh.mehrpour@gmail.com

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Abstract

Background: Several studies have examined the possible role of beta-blockers, including esmolol, in controlling intracranial pressure (ICP). This study aimed to evaluate the effect of esmolol on ICP in patients with severe traumatic brain injury.
Methods: In this case-control study, all TBI patients with ICP > 20 cmH_2O, who were admitted to ICU during the study period, were included. Some patients received standard treatment plus esmolol (500 μg/kg and then 50 mg/kg/min for 24 hours), and some others just received standard treatment with no esmolol. The patients were monitored, and the ICP measurement was performed via inserted intra-ventricular catheter. The ICP and vital signs were measured and recorded before, 8, 16, and 24 hours after starting the treatment in the two groups, and the findings were then compared.
Results: Twenty-two patients (13 males and 9 females) were included in this study, of whom 12 patients received esmolol, and 10 patients were in the control group. The mean age of those who received esmolol was smaller than those who did not receive it (46.6 $\pm$ 18.5 vs. 62.3 $\pm$ 19.1 years; P = 0.08). Moreover, the mean length of the ICU stay was smaller in the esmolol receivers than the control group (5.6 $\pm$ 1.1 vs. 17.3 $\pm$ 7.7 days; P = 0.04 (there was no significant difference between the two groups in terms of mortality rates (P = 0.30). The variations of the vital signs over time was not significantly different between the two groups (P > 0.05); however, the mean of ICP was lower in those who received esmolol compared to the control group at all checkpoints (P < 0.05).
Conclusions: Those patients with TBI who received esmolol as part of their ICP control management in ICU had lower ICP than those who received no esmolol.

Keywords: Esmolol, Intracranial Pressure, Traumatic Brain Injuries, Physiologic Monitoring, Adrenergic Beta-Antagonists

1. Background

Monitoring and controlling intracranial pressure (ICP) is a critical issue in patients with severe traumatic brain injury (TBI), As patients with higher ICP are at higher risk for occurance of sever complications (1-3). In adult patients with ICP > 15 CmH20, the most common symptoms are nausea and vomiting, while symptoms such as decreased consciousness, motor paralysis, papillary edema, hypertension, bradycardia, respiratory depression usually appear in those with ICP > 20 CmH20 (4-7). Brain herniation and death may occur following the complete failure of the compensatory mechanisms and brain autoregulation (1).

Several studies have assessed the possible role of beta-blockers, including propranolol, in patients with a head injury and rising ICP, and their findings documented the significant positive effects of such beta-blockers on the patients' outcomes (8-11). Esmolol is a short-acting, water-soluble, and selective beta1-adrenergic receptor antagonist drug with a 9-minute half-life. Esmolol is also likely to reduce intracranial pressure in patients with head trauma.

2. Objectives

Due to its short half-life, esmolol can be a suitable drug to reduce ICP (12-16); however, this issue has been less investigated. Accordingly, the present study aimed to evaluate the effect of esmolol on ICP in patients with severe TBI.

3. Methods

3.1. Study Design and Setting

A case-control study was conducted at the Sina Hospital (Tehran, Iran) from June to November, 2017. The investigators did not interfere with patients' management protocol considered by the in-charge intensivist and just observed the patients and recorded the variables. The proposal of the present study was approved by the Ethics Committee of the Tehran University of Medical Sciences (Code: IR.TUMS.MEDICINE.REC.1396.4641)

3.2. Study Population

All TBI patients aged above 18 years with ICP > 20 cmH_2O, who were admitted to the ICU during the study period, were included in this study. Patients with each of the following criteria were excluded from this study: patients aged above 80 years old, Glasgow Coma Scale (GCS) > 8, reactive airway diseases, recent infectious and inflammatory diseases, underlying heart, kidney, liver, and neurologic diseases, coagulation disorders, previous head injury requiring surgery, hemodynamically unstable (systolic blood pressure (SBP) < 90 mmHg, pulse rate (PR) < 60/min, mean arterial pressure (MAP) < 65 mmHg), treated with high dose vasopressors, normal initial CT scan not requiring invasive ICP monitoring.

3.3. Patients' Management Protocol

All Patients received standard treatment, including intravenous (IV) mannitol, hyperventilation, sedation, and surgical intervention, if needed. According to the in-charge intensivist's prescription, some patients also received esmolol orphan (manufactured by Orpha-Devel factory in Austria with serial number pl30414/0001) with an initial dose of 500 μg/kg and then 50 mg/kg/min for 24 hours (case group), and some other patients just received standard treatment without esmolol (control group). The patients were fully monitored with standard electrocardiogram (ECG) monitoring, continuous pulse oximetry, invasive blood pressure monitoring through the intra-arterial line, central venous pressure through the intra-jugular line, and ICP measurement via an intraventricular catheter. In the two groups, the ICP, PR, MAP, and SPO2 variations were measured before, 8, 16, and 24 hours after starting the treatment. All data were collected by an intensive care fellowship and recorded in a pre-prepared sheet.

3.4. Outcome

The outcomes were recorded as the length of ICU stay and mortality rates.

3.5. Statistics

The data were analyzed using SPSS software version 24. Frequency was reported for the qualitative variables, and mean, and standard deviation were calculated for the quantitative variables. Moreover, $P < 0.05$ was set as the significance level.

4. Results

Fifty-nine patients with severe TBI were admitted to ICU during the study period, of whom 37 patients were excluded from the study regarding the exclusion criteria. Finally, 22 patients (13 males and 9 females) were included in this study, of whom 12 patients received esmolol, and 10 patients were in the control group. The mean age of those who received esmolol was smaller than those who did not receive it (46.6 ± 18.5 vs. 62.3 ± 19.1 years; P = 0.08).

The mean age of those receiving esmolol was lower than those who did not receive it (46.6 ± 18.5 vs. 62.3 ± 19.1 years; P = 0.08). Moreover, the mean length of the ICU stay was smaller in the esmolol receivers than the control group (5.6 ± 1.1 vs. 17.3 ± 7.7 days; P = 0.04). The mortality rate was 5 (22.7%); there was no significant difference between the two groups in terms of mortality rates (P = 0.30). Respiratory compromise because of bronchospasm was noticed in none of the patients.

Table 1 shows the mean values of ICP and vital signs of the patients at various checkpoints. The variations in vital signs over time were not statistically significant between the two groups ($P > 0.05$); however, the mean of ICP was lower in the esmolol group than the control group at all checkpoints ($P < 0.05$). Figure 1 also shows ICP variations over time in the two study groups. It should be mentioned that the mean of ICP before starting the management was not significantly different in the two groups (P = 0.141).

5. Discussion

In the present study, the mean of ICP over time was lower in those receiving esmolol than those undergoing the standard treatment without esmolol. Moreover, the ICU length of stay was shorter in the esmolol group than the control group. While, the variations in vital signs, including PR, MAP, and SPO2, was not different over time in the two groups.

TBI is one of the most common indications of intracranial pressure measurement. Increased intracranial pressure in patients with TBI leads to most deaths. Sometimes,

Table 1. Mean Values of ICP and Vital Signs of the Patients at Various Checkpoints [a]

Variable	Case (N = 12)	Control (N = 10)	P-Value
Intracranial pressure (CmH_2O)			
Before	28.03 ± 0.82	29.75 ± 3.52	0.141
8 h	21.20 ± 2.53	25.83 ± 3.04	0.001
16 h	19.30 ± 1.64	22.25 ± 3.02	0.012
24 h	18.10 ± 0.99	20.58 ± 3.55	0.045
Pulse rate (beat/min)			
Before	82.31 ± 6.46	82.42 ± 8.24	0.971
8 h	80.60 ± 8.57	85.75 ± 12.86	0.293
16 h	82.43 ± 8.97	83.58 ± 10.80	0.785
24 h	80.11 ± 7.55	81.02 ± 8.87	0.803
Mean arterial pressure (mmHg)			
Before	99.71 ± 12.01	102.82 ± 25.95	0.729
8 h	90.93 ± 11.78	100.30 ± 16.36	0.148
16 h	92.50 ± 11.70	94.73 ± 14.01	0.699
24 h	92.54 ± 8.71	88.03 ± 17.07	0.463
Blood oxygen saturation (%)			
Before	96.61 ± 2.59	98.30 ± 1.78	0.078
8 h	96.03 ± 2.68	97.33 ± 2.57	0.248
16 h	95.70 ± 2.63	96.92 ± 2.68	0.297
24 h	97.13 ± 2.08	96.67 ± 2.06	0.63

[a] Values are expressed as mean ± SD.

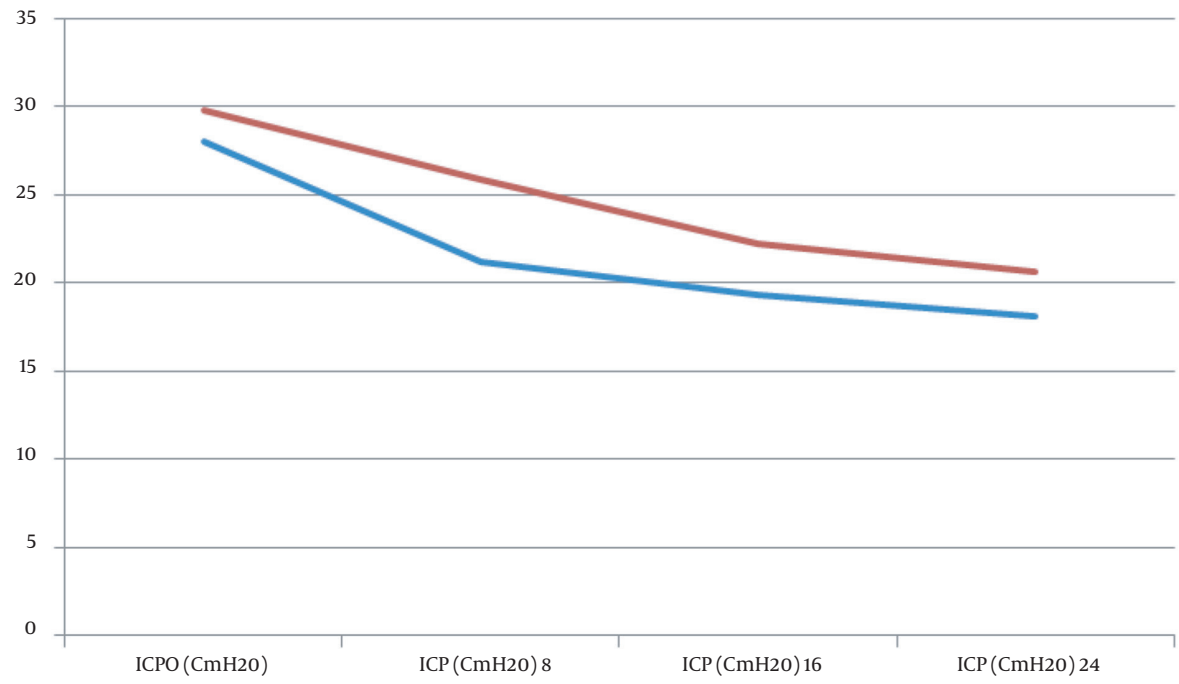

Figure 1. Intracranial pressure (ICP) variations over time in two groups

the best treatment may not be possible to eliminate the underlying cause of intracranial pressure. Esmolol is a selective beta1-adrenergic antagonist specific to the cardiovascular system, with the rapid onset of action and the short duration of action with few effects on bronchial receptors. Esmolol seems to decrease intracranial pressure by reducing blood pressure. Due to its short half-life, this drug is efficient in reducing intracranial pressure in patients with trauma (17).

The beta-blocker agents have a significant therapeutic effect on reducing blood pressure and intracranial pressure in patients with traumatic brain injuries. In most studies, Propranolol is a competitive β1 and β2 adrenergic receptor blocker, with a 5-10 minute onset of action and a half-life of 2 - 5.5 hours after the IV administration. Such a long half-life raised some concerns regarding its suitablity for managemnet of ICP raising in TBI patients. However, the findings of the present study revealed that esmolol as a short-acting selective beta1-adrenergic receptor blocker with a short half-life (it has about 10-30 minutes' duration of action and 9 minutes' half-life) has significant therapeutic effects on the ICP control in the setting of TBI and is associated with no respiratory and hemodynamic complication. Esmolol was selected to be examined in this study because of the shorter duration of action and the absence of side-effects compared to other beta-blockers.

5.1. Limitations

The small sample size was the main limitation of the present study. This was not an interventional study, and a randomized clinical trial is definitely required to follow this preliminary observational study.

5.2. Conclusions

The patients with TBI who received esmolol as part of their ICP control in ICU had lower ICP compared to those not receiving this agent.

Footnotes

Authors' Contribution: It was not declared by the authors.

Conflict of Interests: The authors have no conflict of interest.

Ethical Approval: The proposal of this study was approved by the Ethics Committee of the Tehran University of Medical Sciences (Code: IR.TUMS.MEDICINE.REC.1396.4641).

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