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ORIGINAL RESEARCH **NEUROANESTHESIA**

Comparing the effect of dexmedetomidine and metoprolol in reducing blood loss during craniotomies due to severe cerebral blunt trauma

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Abstract

Introduction: To control and reduce blood loss during craniotomy is one of the most important and significant goals of anesthesiologists and neurosurgeons. Numerous drugs including beta-blockers, calcium channel blockers, alpha-agonists, and narcotics have been used to achieve this goal. We compared the effects of dexmedetomidine and metoprolol in reducing blood loss during craniotomy due to severe cerebral blunt trauma.

Methodology: It was a randomized, double-blind clinical trial. Forty-four craniotomy candidates with severe head injuries were randomly divided into dexmedetomidine and metoprolol groups. For all groups, a questionnaire was completed so that data on MAP, pulse rate, mean blood loss score, mean number of packed cell units received, events of hypotension and bradycardia and the survival of the patients was recorded. Using SPSS-21 statistical software, the data obtained from the questionnaires were statistically inferred by the T-test and ANOVA test, and the results are expressed in tables.

Results: There was no significant difference in age and sex frequency in this study ($p = 0.6$). There was a significant difference between the two groups in terms of blood loss after the start of surgery, so that the average blood loss in patients at 15, 30, 45, 60, 90, 120 min after the start of the surgery in the dexmedetomidine group was less than in the metoprolol group ($p < 0.05$).

Conclusion: Dexmedetomidine and metoprolol could reduce blood loss during surgery and provide controlled hypotension during craniotomies due to severe cerebral blunt trauma. The effect is more pronounced with the use of dexmedetomidine compared to metoprolol.

Key words: Dexmedetomidine; Metoprolol; Craniotomy; Head trauma; Hypotension

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1. Introduction

Head trauma is one of the most common causes of hospital admissions. According to some studies, head injuries cause about 14% of hospitalizations.[1] Approximately, 70% of hospitalized patients with a concussion, will have a mild head trauma in which loss of consciousness is less than 30 min, there is no skull fracture and their Glasgow Coma Scale at the time of admission is 13 to 15.[2] Traumatic brain injury (TBI) is one of the major public health problems in the world. At least 10 million TBI cases cause death or hospitalization around the world annually.[3] The disease has reached 700 cases per 100,000 young people under the age of 25 in the United States. Therefore, it is called mature young disease.[4-6]

Based on the patient's level of consciousness with the Glasgow Coma Scale (GCS), traumatic brain injury is divided into three categories: mild, moderate and severe. Patients with mild TBI with a GCS score of 13 to 15 are often associated with complete neurological improvement, although most have temporary short-term memory and concentration problems. A TBI with GCS 9-13 leads to numbness in patients and severe TBI with GCS 3-9 leads to coma, high risk of hypotension, hypoxemia and cerebral edema.[7] Nerve damage from TBI will not occur immediately at the time of the accident (primary injury), rather it spreads over time (secondary injury). Most cases of secondary brain damage in these patients are due to cerebral edema and increased cerebrospinal fluid pressure, followed by ischemia.[8] In addition to disablement, TBI increases the risk of various other diseases, including epilepsy, depression and Alzheimer's disease, significantly higher than similar populations without TBI.[9]

One of the main reasons for the decline of head trauma patients' survival is intracranial hypertension management and it`s a big challenge for neurosurgeons. There are several ways to manage this problem in patients, including hyperventilation, barbiturate therapy, and hypothermia therapy.[10] Decompressive craniotomy is a surgical procedure in which the pressure on the brain tissue is reduced by removing part of the skull.[11] The period during surgery in craniotomy patients is frequently complicated by hypertensive episodes.[12] Many studies have indicated a correlation between the use of beta-blockers in patients with severe TBI and increased survival in these patients. Metoprolol, as a beta-blocker, is effective in creating controlled hypotension and reducing blood loss during surgery.[13,14] Dexmedetomidine is an α-2 agonist and in addition to its sedative effects, it is well used to control blood loss in patients undergoing craniotomy by creating appropriate hypotension.[15-16] The dexmedetomidine may affect hemodynamic stability in patients undergoing neurological and spinal surgery. [17] Therefore, we compared the effect of dexmedetomidine and metoprolol in reducing blood loss during surgery in craniotomy patients due to severe cerebral blunt trauma.

2. Methodology

It was a randomized, double-blind clinical trial and it was performed on 44 patients with severe head injury, who were candidates for craniotomy and referred to our hospital, and who fulfilled the criteria of the study. The patients were randomly divided into two equal groups; Group M (metoprolol) and Group D (dexmedetomidine) after getting informed consent. We set the time limit of their surgery to 150 min. The age limit was set to be 15 to 75 y.

Patients with an allergy to dexmedetomidine or metoprolol, or those who had other surgeries at the same time, or with a history of cardiovascular disease, pulmonary disease, uncontrolled diabetes, history of seizures and epilepsy, renal failure, liver failure, patients with coagulation disorders, and patients with a previous history of stroke or recent MI were excluded.

Sample size calculation formula used was:

$$n = \frac{(\delta 1 + \delta 2)^2 (z1 - \alpha/2 + z1 - \beta)^2}{(\mu 1 - \mu 2)^2}$$

$Z_{(1-\beta)}=2.33$ $Z_{(1-\alpha/2)}=1.96$

$\delta_2=29.4$ $\delta_1=45.7$

$\mu_2=274.6$ $\mu_1=342.6$

n = 22 n total= 44

Patients` heart rate, respiration rate, blood pressure, SpO_2, temperature, capnography and ECG were fully monitored at the time of entering the operating room. Each patient received Midazolam 1 mg with fentanyl 50-100 µg. Arterial line was taken from the non-dominant radial artery of the patients. At this stage, the patient was prepared for anesthesia by fentanyl 2 µg/kg, midazolam 0.3-0.5 mg/kg, atracurium 1-2 mg/kg, and propofol 2-3 mg/kg. The patient was intubated and connected to a ventilator; and after prepping and draping, prepared for craniotomy.

In Group D, dexmedetomidine was administered in a dose of 1 µg/kg and in Group M, metoprolol was administered at a dose of 2.5 mg/kg, the volume of which was increased to 5 ml in the two intervention groups. Then, after anesthesia and intubation, in Group D, dexmedetomidine infusion was started at 0.5 g/kg/h, and in Group M, metoprolol infusion was started at 0.5 mg/kg/h. The blinding procedure was performed in such a way that all patients were unaware of medications they were receiving. The medicines were prepared in each group by an anesthesiologist, and the initial doses were increased to 5 ml by normal saline. The medicines were given to anesthesia resident for injection by 5 ml syringes named A and B. Infusion doses were also prepared in 20 ml syringes by an anesthesiologist, named A and B and given to the anesthesia resident for injection. Therefore, the anesthesia resident was unaware of the type of injectable drug. Also, the medical intern in charge of

Table 1: Bleeding score

Blood loss	Score
0-50 ml	0
50-200 ml	1
200-500 ml	2
500-1000 ml	3
≤ 1000 ml	4

the project, who was responsible for completing the questionnaires and data recording, was not aware of the patients' placement in the study groups and the injectable solution. The anesthesiologist assigned A and B questionnaires in the operating room and medical intern merely completed them.

2.1. Data collection: For all groups, the questionnaire was completed using cardiac parameters monitored during surgery, so that data on MAP, PR, mean blood loss, episodes of hypotension, bradycardia and the survival of the patients.

Bleeding score was measured based on the following table (Table 1).

2.2. Data analysis: The data obtained from the questionnaires were statistically analyzed using SPSS-21 statistical software, ANOVA test and Student's T-test. The results are expressed in the form of tables and graphs.

2.3. Ethical considerations: In this study, individuals` identity was confidentially recorded. The cost was not imposed on the patient`s family and the hospital. Written consent was obtained from the patients. In all stages of the research, including writing a proposal, collecting samples, and data analysis, the researchers were required to consider ethical provisions in research approved by the Ministry of Health and the Helsinki Declaration.

3. Results

Mean age in dexmedetomidine group was 51.8 ± 2.7 y and in the metoprolol group was 52.2 ± 1.2 y. There were 57.9% male and 42.1% female in the dexmedetomidine group, and 58.3% male and 41.7% female in the metoprolol group ($p = 0.6$). The differences were not statistically significant.

There was a significant difference between the two groups in terms of estimated blood loss during surgery, so that the mean estimated blood loss at 15, 30, 45, 60, 90, 120 min after the start of surgery in the dexmedetomidine group was less than the metoprolol group ($p \leq 0.05$). Therefore, dexmedetomidine was significantly more effective in controlling blood loss (Table 2).

In Table 3 depict the comparative mean blood pressure during surgery at different times in two groups of dexmedetomidine and metoprolol. There was no significant difference between the two groups in terms of mean blood pressure of patients in 15, 30, 45, and 120 min after surgery ($p > 0.05$). However, 60 and 90 min the mean blood pressure in the dexmedetomidine group was significantly lower than in the metoprolol group ($p < 0.05$).

Table 2: Comparison of mean bleeding (ml)

Time after start of surgery	Dexmedetomidine Group	Metoprolol Group	p-value
15 min	70.45 ± 8.6	78.1 ± 5.9	0.04
30 min	77.3 ± 6.4	87.5 ± 7.7	0.03
45 min	90.9 ± 7.6	172.5 ± 8.9	0.01
60 min	159.2 ± 9.9	310.6 ± 8.8	0.01
90 min	377.3 ± 10.1	471.8 ± 11.3	0.001
120 min	438.6 ± 11.2	510.6 ± 12.2	0.01

Table 3: Comparison of mean blood pressure (mmHg)

Time after start of surgery	Dexmedetomidine Group	Metoprolol Group	p-value
15 min	75.8 ± 3.6	75.5 ± 2.9	0.6
30 min	73.2 ± 2.9	70.8 ± 3.6	0.4
45 min	72.1 ± 3.1	73.6 ± 2.9	0.4
60 min	68.1 ± 3.1	76.3 ± 3.7	0.03
90 min	65.5 ± 3.3	68.4 ± 2.9	0.04
120 min	68.1 ± 3.1	66.6 ± 2.8	0.6

Table 4: Comparison of mean heart rate (beats/min)

Time after start of surgery	Dexmedetomidine Group	Metoprolol Group	p-value
15 min	80.5 ± 4.1	81.1 ± 3.6	0.4
30 min	76.4 ± 3.8	74.4 ± 3.9	0.4
45 min	71.1 ± 3.1	73.5 ± 4.3	0.03
60 min	61.9 ± 2.9	72.2 ± 3.9	0.04
90 min	71.4 ± 3.3	74.8 ± 3.7	0.03
120 min	72.8 ± 3.3	76.9 ± 3.8	0.04

There was a significant difference between the two groups in terms of the patients` mean heart rates at 45, 60, 90, and 120 min after the start of surgery, being lower in the dexmedetomidine group ($p < 0.05$).

However, there was no significant difference between the two groups at 15 and 30 min after the start of surgery.

All patients in both groups completed the study uneventfully.

Discussion

To control and reduce blood loss during craniotomy is one of the most important goals of the anesthesiologist and the neurosurgeon. Various therapeutic agents have been used to achieve this goal, including beta-blockers, calcium channel blockers, alpha-agonists, and some narcotics.[18]

The results of our study indicated that the estimated blood loss, the mean blood pressure and the mean heart rates were lower at different times after the start of the surgery in patients of the dexmedetomidine group than in the metoprolol group, except at 45 min.

The results of our study are consistent with many previous studies. Zangbar and colleagues examined the effect of metoprolol on the survival of patients with TBI, and suggested that patients who received metoprolol had a better survival than the control group. There was a significant relationship between the use of beta-blockers (metoprolol) and improved survival of patients with brain trauma.[13] The results of this study are consistent with ours, since in our study, reduced blood loss during surgery in both groups had a positive effect on the patients` survival.

Two other researchers compared the effects of dexmedetomidine and magnesium sulfate on hemodynamics and recovery status of candidates for spinal surgery and sinus surgery, respectively. It was found that patients' mean heart rate and mean blood pressure in the two groups of dexmedetomidine and magnesium sulfate were significantly lower than those in the control group, which in turn reduced blood loss during surgery. The use of magnesium sulfate and dexmedetomidine, decreased patients` need for anesthetic medication during surgery. The need for anesthetic medications in dexmedetomidine and magnesium sulfate groups was significantly lower than in the control group. The results of these studies are consistent with ours.[17, 19]

In another study conducted by O Nazir and colleagues, the effect of dexmedetomidine and esmolol on the induced hypotension in spinal surgeries was investigated. It is worth mentioning that both drugs resulted in controlled hypotension and reduced blood loss during surgery, but the effect of dexmedetomidine was reported to be greater than esmolol. The results of this study are consistent with our study. Among these, the effect of dexmedetomidine in reducing blood loss during surgery and the creation of controlled hypotension in patients was reported to be greater than that of metoprolol.[20]

Finally, previous studies suggest the significant effect of dexmedetomidine and beta-blockers in creating a controlled hypotension for patients undergoing craniotomy and subsequently, reduction of blood loss during surgery and improving the surgical procedure of patients. In fact, episodes of hypertension during craniotomy always reduces visibility by the surgeon and impairs the conduct of craniotomy.[13]

Conclusion

According to the results of this study, we conclude that both dexmedetomidine and metoprolol reduce blood loss during patients' surgery and create a suitable controlled hypotension during craniotomy in patients with traumatic brain injury. This effect is more pronounced by dexmedetomidine compared to metoprolol.

Conflict of interest

None declared by the authors

Authors' Contribution

ANR: Concept, Design of the work, statistical analysis, drafting the work, final approval

AK :Design of the work, Data analysis, final approval

RR, SZ: Analysis, drafting the work

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