Original Article • นิพนธ์ต้นฉบับ

Therapeutic Efficacy of Dexmedetomidine on Hemodynamic Response to Skull Pin Holder Placement: a Randomized, Double-Blind Controlled Study

Sittiporn Deetayart[1], Weerawat Thangthum[2]

[1] *Department of Anesthesiology, Ratchaburi Hospital, Ratchaburi, 70000*

[2] *Boromarajonani College of Nursing, Changwat Nonthaburi, Faculty of Nursing, Praboromarajchanok Institute, Nonthaburi, 11000*

Abstract

Background: The skull pin holder placement in neurosurgery is the strong stimuli that produced the intense sympathetic response. Dexmedetomidine is one of many drugs that have been used to attenuate this response. We evaluate the effective intravenous dose of dexmedetomidine 0.5 µg/kg and 0.75 µg/kg infusion that can blunt hemodynamic response.

Methods: This study is a prospective, randomized controlled double-blinded study. A total of one hundred and twenty patients were selected and randomized into three groups of forty patients each: group 1 received an infusion of dexmedetomidine 0.5 µg/kg, group 2 received an infusion of dexmedetomidine 0.75 µg/kg, and group 3 received an equivalent quantity of normal saline. Hemodynamic parameters were monitored regularly of skull pin holder placement.

Result: There was no significant difference in the monitored hemodynamic parameters among the three groups from baseline until intubation time. Heart rate (HR) and mean arterial pressure (MAP) increased significantly in group 3, whereas the values decreased in group 1 and 2 ($P<0.001$). Group 2 showed a higher and sustained attenuation of HR and MAP. Group 3 had a higher incidence of tachycardia and hypertension that need medication to treat the response.

Conclusion: Dexmedetomidine in both doses (0.5 µg/kg and 0.75 µg/kg infusion) was effective in attenuating hemodynamic response to skull pin holder placement.

Keywords: dexmedetomidine, hemodynamic response, intracranial surgery, skull pin holder placement

Introduction

In a neurosurgical procedure, a skull pin head holder is necessary for the steady positioning of the patient's head. It helps to prevent the displacement of the surgical area. This device has pins that take place through the scalp and the pericranium into the external layer of skull. The skull pins are applied after induction of general anesthesia. These stimuli produced an intense sympathetic response (hemodynamic change including tachycardia, and increased blood pressure) resulting in an increase in the intracranial pressure from the increase of cerebral

Correspondence to: Sittiporn Deetayart, E-mail: doxterer@hotmail.com

Received April 12, 2023, Revised August 25, 2023, Accepted August 25, 2023

blood flow and subsequently the intracranial pressure (ICP).[1,2] It can lead to producing brain herniation and intracranial hemorrhage. Various techniques can produce blunt sympathetic responses, such as giving more anesthetic agents to dept the level of anesthesia[3], analgesic drugs[4,5], calcium channel blocker[6], beta-blocker[7], scalp nerve blocks[8], infiltration of local anesthetic agents of the pin sites[9], and alpha-agonist.[10]

Dexmedetomidine is an alpha-2-adrenergic receptor agonist drug that is well-known in Thailand. It has been used as a sedative agent with analgesic properties, for hemodynamic stability from decreases the sympathetic outflow, and preservation of respiratory function.[11] Dexmedetomidine in the dose of 1 µg/kg infusion over 15 min before induction has been used to attenuate the hemodynamic response to endotracheal intubation[12] and response to skull pin head holder.[1,5,6] However, this dose is a maximal dose that causes bradycardia and hypertension. We have proposed a hypothesis that the dose of 0.5 µg/kg and 0.75 µg/kg may be effective in attenuating hemodynamic responses to skull pin head holders with fewer adverse events.

Methods

This study is a prospective, randomized, double-blind controlled trial, reviewed and approved by the Institutional Ethical Committee Ratchaburi Hospital (No. COA-RBHEC 001/2021) and informed consent from the patient. Patients aged 18-65 years, with the American Society of Anesthesiologists physical status I-III, undergoing the elective neurosurgical procedure under general anesthesia and requiring the application of skull pins were included in the study. The patients who have cardiac problems (shock, bradycardia, uncontrolled hypertension, heart failure, myocardial infarction or conduction defect) respiratory disease (respiratory failure, acute respiratory distress syndrome), renal disease, hepatic disease or the other causes effects hemodynamic instability were excluded from the study.

All of the patients had been asked for a pre-anesthetic evaluation. Routine preoperative laboratory investigations were done. Patients fasted for 8 hours before surgery. In the operating room, monitoring was established regarding blood pressure (BP), electrocardiogram, pulse oximetry, end-tidal carbon dioxide ($ETCO_2$), and arterial blood pressure. Baseline heart rate (HR), BP, and oxygen saturation were recorded. Patients were randomly allocated to one of the three groups using the computer-generated table for random numbers. Patients in each group were stipulated to receive either dexmedetomidine or a placebo. Group 1 received dexmedetomidine 0.5 µg/kg, group 2 received dexmedetomidine 0.75 µg/kg, and group 3 received 0.9% saline as a placebo. The test drugs were infused over 15 min before induction.

After all, patients received 100 % oxygen for 3 minutes before induction with fentanyl 3 µg/kg, and propofol 2-3 mg/kg until patients had a loss of verbal response. Rocuronium of 1 mg/kg was used for muscle relaxation ; mask ventilation was continued for 3 minutes. Patients were intubated with the appropriate size oral endotracheal cuff tube and connected to the anesthetic circuit with controlled ventilation. Anesthesia was maintained after intubation with

desflurane in oxygen/air mixture (FiO_2 = 0.6) ventilation controlled to target end-tidal carbon dioxide between 30-35 mmHg. The radial artery was cannulated with a 20-gauge catheter for continuous invasive arterial blood pressure monitoring. The pin insertion sites were marked by the neurosurgeon, and each pin site was not filtrated with local anesthetic drugs. The patient's head was fixed on the frame head holder with four-point pins by applying constant pressure on the scalp until the pins were firmly tightened 15 minutes after the start of the study infusion.

Blood pressure, mean arterial pressure (MAP) and heart rate were recorded at the following time intervals baseline value, after intubation time, P0 at pin insertion and P1, P2, P3, P5, P10, P15, P20, P25, P30 as 1, 2, 3, 5, 10, 15, 20, 25, 30 min after pin insertion respectively. Rescue drugs were prepared for adverse events such as tachycardia, and a heart rate greater than 120 beats/min was treated with esmolol 5 mg titration. Bradycardia, heart rate lower than 50 beats/min, was treated with atropine 0.3 mg. The titration of 6 mg of ephedrine treated blood pressure lower than 90/60 mmHg. If blood pressure rose higher than 160/90 mmHg, a rescue dose of fentanyl 1 ug/kg was intravenously administered.

Statistical analysis

A sample size of 35 subjects in each group was used compact program G*power 3.1.9.2 [t-test: mean difference of HR between two independent means (two groups)] effect size = 0.95, α = type I error = 0.05, power 95%.

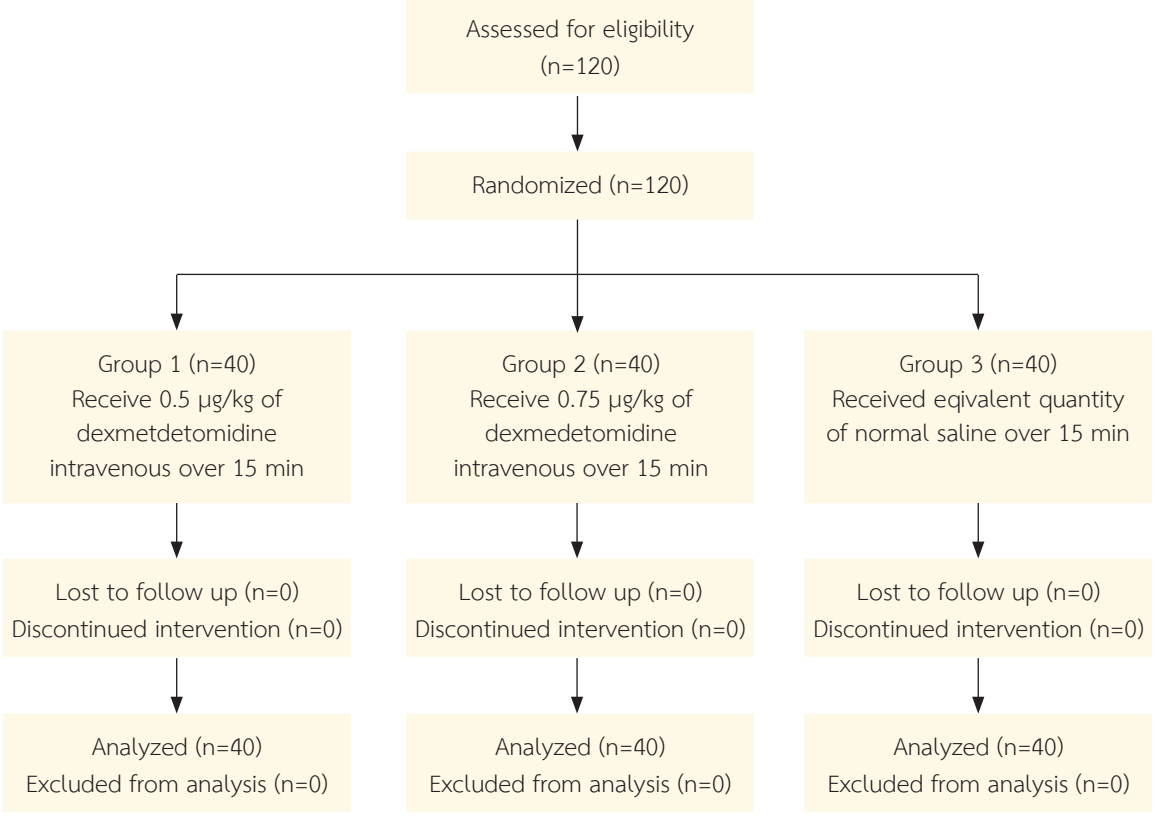


Figure 1 Flow diagram of study

Assuming a few dropouts, the final sample size was set at 40 subjects in each group. Mauchly's test of sphericity has been carried out in the present study. The result on continuous measurements was presented as mean+standard deviation, and the result on categorical measurements is presented in number (%). A one-way ANOVA test was used to find the significance of study parameters on a continuous variable between the three groups. An Independent sample t-test was used to find the significance of study parameters on the continuous scale within the group on metric parameters. The significance is assessed at a 5% level of significance. A $P < 0.05$ was considered statistically significant.

Result

Patient demographic data was displayed in Table 1. No statistically significant difference was observed in these three groups. There were no significant differences in means of HR and MAP among the three groups at baseline and intubation, they are comparable. Both groups 1 and 2 produced a significant reduction in HR and MAP but higher in group 3 at pining time until 30 minutes (T30) with statistical significance between 3 groups. (Table 2) They are comparable values of HR and MAP increasing when skull pin insertion was placed in group 3 and decreased in group 1 and 2. (Table 2 and 3) The two doses of dexmedetomidine in this study are showing higher HR and MAP in group 3 more than group 2. (Figure 1 and 2)

The number of cases of group 3 has more intraoperative tachycardia and hypertension than group 1 and 2. There were no differences between the two doses of dexmedetomidine with intraoperative hemodynamics variations. It has 3 cases (7.5%) in group 1 and 1 case (2.5%) in group 2 developed tachycardia and received esmolol bolus, 16 cases (40.0%) in group 3 received esmolol bolus to treat tachycardia, and 9 cases (22.5%) in group 3 was received fentanyl 1 µg/kg bolus for hypertensive condition after not respond with esmolol titration.

Table 1 Patients' characteristics

	Group 1	Group 2	Group 3	*P*-value
Age (yr), mean±SD	55.2+8.2	52.7+8.4	52.3+12.2	0.413
Sex, n (%)				
Male	14 (35.0)	16 (40.0)	18 (45.0)	
Female	26 (65.0)	24 (60.0)	22 (35.0)	
Body mass index (kg/m^2), mean±SD	26.2+3.6	25.7+4.3	24.0+2.9	0.258
ASA physical status, n (%)				
I	2 (5.0)	6 (15.0)	4 (10.0)	
II	13 (32.5)	21 (52.5)	17 (42.5)	
III	25 (62.5)	13 (32.5)	19 (47.5)	

Table 2 Hemodynamic parameters

		Group 1	Group 2	Group 3	*P*-value
Baseline	HR MAP	80.1±8.0 96.8±9.6	77.0±10.2 100.5±8.5	72.9±8.5 95.5±8.4	0.244 0.075
Stop loading	HR MAP	75.6±10.7 96.0±10.1	77.8±10.7 100.6±9.6	78.3±7.5 100.5±9.2	0.282 0.053
Intubation	HR MAP	74.2±8.3 93.4±8.7	72.8±8.8 96.0±8.9	77.0±7.5 95.9±8.5	0.069 0.308
Pining	HR MAP	78.6±7.4 93.5±11.3	70.0±7.3 88.9±7.7	90.3±8.9 109.1±7.5	<0.001* <0.001*
P1	HR MAP	78.0±8.7 94.2±10.8	68.0±13.0 87.8±7.7	97.5±10.6 113.0±9.2	<0.001* <0.001*
P2	HR MAP	75.9±8.3 91.7±10.0	68.3±6.6 86.3±6.3	88.9±8.2 105.3±7.0	<0.001* <0.001*
P3	HR MAP	73.2±7.4 88.6±10.1	67.6±6.4 84.9±6.2	82.9±5.8 101.5±5.7	<0.001* <0.001*
P5	HR MAP	71.5±7.8 85.7±10.6	67.1±6.5 84.5±6.2	80.2±4.6 100.5±17.0	<0.001* <0.001*
P10	HR MAP	70.1±7.8 84.7±9.8	66.5±6.4 84.3±5.7	78.9±4.5 96.5±4.7	<0.001* <0.001*
P15	HR MAP	69.9±7.7 84.2±9.9	66.4±6.4 83.8±5.7	78.1±4.3 95.6±5.2	<0.001* <0.001*
P20	HR MAP	69.3±7.2 84.5±9.2	64.5±12.3 83.4±6.3	77.2±3.7 94.9±4.5	<0.001* <0.001*
P25	HR MAP	69.3±7.2 84.2±8.2	66.1±6.7 82.2±6.1	76.8±3.8 94.9±4.3	<0.001* <0.001*
P30	HR MAP	69.5±6.7 84.6±7.7	66.2±6.8 83.2±6.2	76.6±3.4 94.3±4.7	<0.001* <0.001*

* $P < 0.05$

Table 3 Complications

	Group 1	Group 2	Group 3	*P*-value
Tachycardia, n (%)	3 (7.5)	1 (2.5)	16 (40.0)	0.206
Hypertension, n (%)	0	0	9 (22.5)	0.001*

*$P < 0.05$

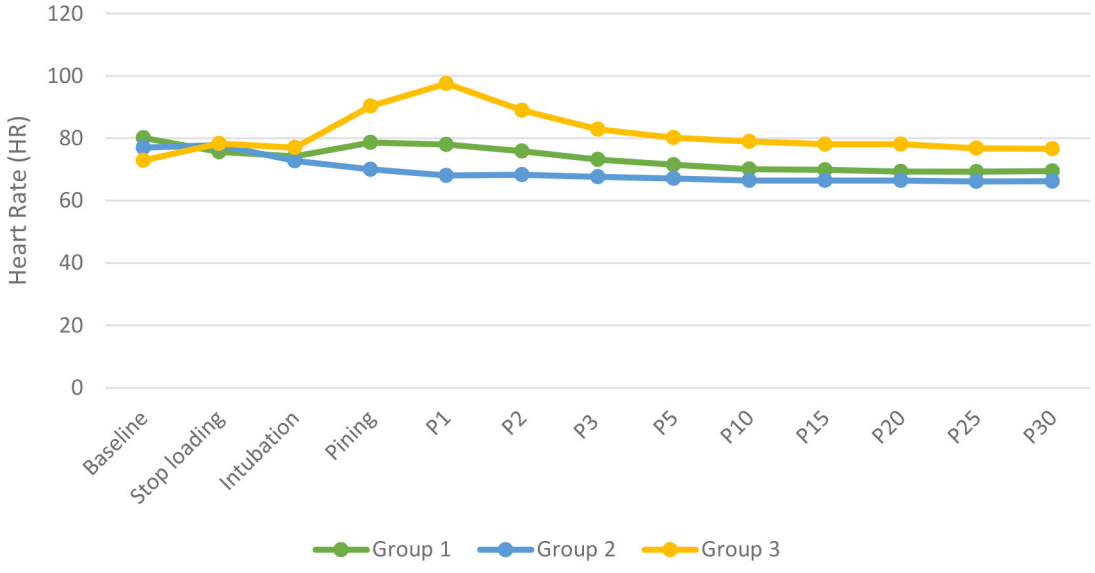


Figure 2 Heart rate

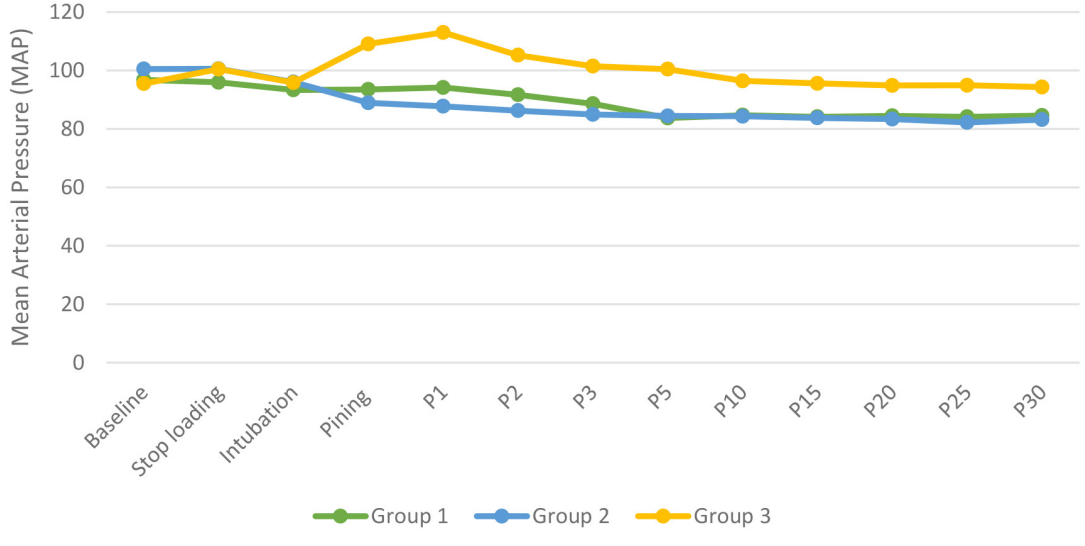


Figure 3 Mean arterial pressure

Discussion

In this study, we compared the effect of intravenous dexmedetomidine at 0.5 µg/kg and 0.75 µg/kg drip 15 minutes before induction, to observe on hemodynamic response to skull pin holder application in ASA I-III patients under general anesthesia and balanced technique. We found that dexmedetomidine in both dosages has effective in attenuating the hemodynamic response in skull pin holder placement. Maintaining hemodynamic stability during intracranial surgery is the one of the most important tasks because hypertension may lead to hemorrhage and vasogenic edema and low blood pressure may result in cerebral ischemia in areas of impaired

autoregulation.[12] An adjuvant liked dexmedetomidine can give multiple benefits to the anesthesiologist such as attenuation of hemodynamic response to skull pin holder application, opioid, and anesthetic sparing effect that make optimal cerebral perfusion pressure. The prevention and hemodynamic control of Anesthesia maintained at adequate depths by inhalation or narcotic agents cannot often reliably ablate the response to various surgical stimuli leading to raise ICP and ultimately reducing cerebral perfusion pressure in susceptible patients.

Dexmedetomidine is an α_2-adrenergic agonist, located on sympathetic presynaptic terminals where the inhibit epinephrine and norepinephrine release. It decreases central sympathetic outflow by acting on locus coeruleus. It has an onset of action at about 5 min at a dosage of 1 μg/kg and has a peak effect which occurs within 15 minutes. Its elimination half life is about 2-3 hours. We use in neuroanesthesia because its sympatholytic and antinociceptive properties that may improve hemodynamic stability at critical moment of surgery.[13] Dexmedetomidine reduces the intraoperative anesthetic and opioid requirements.[14] Patients undergoing craniocerebral operation receiving dexmedetomidine, hemodynamic was more stable and there was a higher survival rate compound with patients in the control group. The use of dexmedetomidine did not increase the incidence of hypotension or bradycardia, common side effects of the drug.[15] Dexmedetomidine at dose 1 μg/kg attenuated the hemodynamic response to skull pin holder placement.[6,16] When we use this dosage or over, it may be making bradycardia and hypertension that disturbs ICP and cerebral perfusion pressure.[17]

In this study, we find the dose of dexmedetomidine below dose of 1 μg/kg that can preserve hemodynamic when placement of skull pin holder. We have compared two doses of 0.5 and 0.75 μg/kg intravenous over 15 minutes. Finally, we found that both of dosage were effective to control hemodynamic response from skull pin holder placement, the dose of 0.75 μg/kg was more effective than 0.5 μg/kg when we focused on number of patients needed esmolol or fentanyl. There were no episodes of hypotension and bradycardia that needed medication treatment.

Our study had some limitations. In depth of anesthesia, we use only clinical observation. If we use the bispectral index, it can make a better accurate depth of anesthesia before skull pin holder placement. According to the duration from intubation time to skull pin holder placement time, when we wait for a long time, the efficacy of dexmedetomidine is too low, and HR and MAP at that time are not the real values.

Conclusion

We concluded that both doses of dexmedetomidine 0.5 μg/kg and 0.75 μg/kg intravenous over 15 minute are effective in attenuating the HR and MAP response to skull pin holder placement.

Financial support and sponsorship

None

Conflicts of interest

There are no conflicts of interest.

References

1. Paul A, Krishna HM. Comparison between intravenous dexmedetomidine and local lignocaine infiltration to attenuate the haemodynamic response to skull pin head holder application during craniotomy. Indian J Anaesth. 2015;59: 785-8.
2. Lin N, Vutskits L, Bebawy JF, Gelb AW. Perspectives on dexmedetomidine use for neurosurgical patients. J Neurosurg Anesthesiol. 2019;31:366-77.
3. Nguyen A, Mandavalli A, Diaz MJ, et al. Neurosurgical anesthesia: optimizing outcomes with agent selection. Biomedicines. 2023;11:372.
4. Demartini Jr Z, Gatto LAM, da Rocha TC, et al. Is the Mayfield head holder obligatory for intracranial aneurysm clipping? Pediatr Neurosurg. 2018;53:360-3.
5. Singh G, Arimanikam G, Lionel KR, et al. Comparison of dexmedetomidine infusion versus scalp block with 0.5% ropivacaine to attenuate hemodynamic response to skull pin insertion in craniotomy: a prospective, randomized controlled trial. J Neuroanaesth Crit Care. 2021;8:180-6.
6. Smith FJ, van de Merwe CJ, Becker PJ. Attenuation of the haemodynamic response to placement of the Mayfield skull pin head holder: alfentanil versus scalp block. Southern Afr J Anaesth Analg. 2014;8:4-11.
7. Masoudifar M, Amini-Tehrani MH, Kashefi P. Comparison of the hemodynamic indices during skull-pin head-holder insertion in neurosurgeries in two groups receiving dexmedetomidine and midazolam. J Isfahan Med School. 2020;38:790-7.
8. Bala R, Arora V, Anshul A, Arora R, Kamal K, Malhan S. A comparative study of intravenous Dexmedetomidine with local infiltration of ropivacaine in attenuation of stress response to skull pin insertion in craniotomies. Asian J Neurosurg. 2022;17:463-9.
9. Nasr YM, Waly SH, Morsy AA. Scalp block for awake craniotomy: lidocaine-bupivacaine versus lidocaine-bupivacaine with adjuvants. Egypt J Anaesth. 2020;36:7-15.
10. Blue R, Alexis M, Mensah-Brown K, et al. Endoscopic microvascular decompression without the use of rigid head fixation. J Clin Neurosci. 2022;106:213-6.
11. Ahmed MNU, Afifa M, Salim M, Asaduzzaman M, Rahman AF. Dexmedetomidine for sedation and analgesia in mechanically ventilated patients. Sch J App Med Sci. 2021;9:149-55.
12. Venkatesh S, Karthik RM. Prospective randomized study to compare between intravenous dexmedetomidine and esmolol for attenuation of hemodynamic response to endotracheal intubation. Anesth Essays Res. 2016;10:343-8.
13. Bruder NJ, Ravussin P, Schoettk P. Cottrell's and Young's Neuroanesthesia, Sixth edition, USA, Elsevier, 2017;p190-208.
14. Castillo RL, Ibacache M, Cortínez I, et al. Dexmedetomidine improves cardiovascular and ventilatory outcomes in critically ill patients: basic and clinical approaches. Front Pharmacol. 2020;10:1641.
15. Senapati LK, Samanta P. Effect of dexmedetomidine on dose requirement of propofol and thiopentone induction in patients under general endotracheal anesthesia. Asian J Pharm Clin Res. 2018;11:262-5.
16. Wu J, Li B, Ma K, Li H, Shao X. A systematic review and meta-analysis of the clinical efficacy of the intravenous injection of dexmedetomidine in ICU patients with hyperactive brain syndrome. Ann Palliat Med. 2022;11:299-308.
17. Kondavagilu SR, Pujari VS, Chadalawada MV, Benvinguddaiah Y. Low dose dexmedetomidine attenuates hemodynamic response to skull pin holder application. Anesth Essays Res. 2017;11:57-61.