

A randomized control trial comparing the efficacy of intravenous Dexmedetomidine infusion versus scalp block with 0.5% Levobupivacaine and fentanyl to attenuate the hemodynamic response to skull pin insertion in Craniotomies

Dr. AISHWARYA SRINIVASAN

Dr. SHRADDHA NAIK

HOD & PROFESSOR

DEPARTMENT OF ANAESTHESIOLOGY, KRISHNA INSTITUTE OF MEDICAL SCIENCES, KRISHNA VISHWA VIDYAPEETH (Deemed to be University) KARAD – 415 539, MAHARASHTRA, INDIA

KEYWORDS

Dexmedetomidine,
Levobupivacaine,
Craniotomies

ABSTRACT

Introduction: This study compares the efficacy of intravenous dexmedetomidine, fentanyl, and 0.5% levobupivacaine scalp block in attenuating the hemodynamic response to skull pin insertion in craniotomies. The aim is to improve patient outcomes and safety in neurosurgery by refining perioperative management strategies. **Aims:** The study investigates the efficacy of intravenous dexmedetomidine infusion and scalp block with fentanyl and 0.5% levobupivacaine in attenuating the hemodynamic response to skull pin insertion in craniotomies. **Methodology:** The study at Krishna Institute of Medical Sciences involved 80 patients aged 18-65 for elective and emergency craniotomies with skull pins under general anesthesia, measuring parameters at baseline, induction, and pinning. **Results:** The study found no significant differences in age, sex, height, weight, ASA status, MAP measurements, bradycardia, hypotension, or rescue medication requirements between two groups. **Discussion:** The study compared anesthesia methods in patients with varying heights, weights, and ASA statuses, finding dexmedetomidine effective in maintaining oxygenation, lower heart rates, and attenuating hemodynamic changes during skull pin insertion. **Conclusion:** The study found scalp block with fentanyl-levobupivacaine and IV dexmedetomidine effectively reduces skull pin insertion hemodynamic response, but provides better analgesia, requiring caution due to potential adverse effects.

INTRODUCTION

A craniotomy is a surgical procedure that creates a bone flap in the skull to access the brain. It is commonly used to treat conditions like brain tumors, hematomas, aneurysms, head injuries, foreign objects, brain swelling, or infections. The procedure can range in size and complexity, with smaller openings used for specific purposes and larger "keyhole" openings providing broader access. Techniques like stereotactic frames, image-guided computer systems, or endoscopes can guide instruments through smaller openings. Craniotomies present unique challenges due to their invasive nature and potential hemodynamic responses, such as increased

blood pressure and heart rate. The skull pin head holder is crucial for maintaining head stability during neurosurgical procedures. [1-3]

Skull pins applied during craniotomy can cause tachycardia, brain oedema, elevated intracranial pressure, and intracerebral haemorrhage, even under general anesthesia, and trigger noxious stimuli and sympathetic activation. [4]

Skull pin placement can increase cerebral blood flow and intracranial pressure, and various anesthesia and pharmacological methods have been used to reduce the hemodynamic response.[5]

To reduce surgical reactions, various methods like deepening anesthesia, administering opioids, using β -blockers, scalp blockade, and local anesthetic infiltration have been used, including dexmedetomidine and fentanyl. [6]

Levobupivacaine and Dexmedetomidine are effective pain relievers and central sympatholytic agents during pin insertion, reducing hemodynamic and stress responses to anesthesia stimuli.[9]

This study compares the efficacy of intravenous dexmedetomidine, fentanyl, and 0.5% levobupivacaine scalp block in attenuating the hemodynamic response to skull pin insertion in craniotomies. The aim is to improve patient outcomes and safety in neurosurgery by refining perioperative management strategies.

Aims & Objectives

This study compares the effectiveness of intravenous dexmedetomidine infusion and scalp block with fentanyl and 0.5% levobupivacaine in attenuating hemodynamic response to skull pin insertion in craniotomies.

The study aims to investigate the effects of I.V Dexmedetomidine and scalp block of fentanyl with 0.5% Levobupivacaine on attenuating the hemodynamic response of skull pin insertion in craniotomies.

MATERIALS AND METHODS

The study was conducted at Krishna Institute of Medical Sciences, Karad, Maharashtra, from August 2022 to February 2024, involving Anesthesiology and Neurosurgery departments.

STUDY DESIGN- This is a prospective, randomized clinical study that was conducted at Department of Anesthesiology, Krishna Institute of Medical Sciences in Karad, Maharashtra. Randomization was performed according to computer-generated random numbers.

STUDY DURATION- This study was conducted over a period of 18 months.

PLACE- The study was conducted in the Neurosurgical operation theatre of Krishna hospital, Karad.

SOURCE OF DATA- Patients were included in the study after taking written informed consent by applying the necessary inclusion and exclusion criteria

INCLUSION CRITERIA: Neurosurgical patients aged 18-65, scheduled for elective and emergency craniotomies with skull pins under general anesthesia, with American Society of Anaesthesiologists physical status grading 1 and 2.

EXCLUSION CRITERIA: Patients with severe brain injury, preoperative heart rate below 50 beats per minute, known allergies, beta-blockers, comorbidities, pregnant or lactating patients, refusal/inability to give consent, and redo craniotomies are excluded.

The study calculates a sample size of 80 patients based on four parameters: heart rate, arterial pressure, systolic blood pressure, and diastolic blood pressure. The sample size is increased to 40 due to a 10% drop rate, and all patients are randomly divided into two groups.

The study involved a pre-anesthetic evaluation and consent process for elective surgeries. Patients were given a detailed physical examination and systemic examination before surgery, and informed consent was obtained from the patient and their relatives. Patients were kept non-opioid for 6 hours before surgery. Laboratory investigations included blood tests, blood sugar, renal function tests, coagulation profile, serum electrolytes, ECG, and chest radiogram. Patients were randomly divided into two groups, Group D (Dexmedetomidine infusion) and Group S (Scalp block). The pre-induction procedure involved connecting standard monitors, recording baseline readings, and initiating general anesthesia. Anaesthesia was maintained with 1.2 MAC. Patients were given a loading dose of 0.5mcg/kg/hr after 10 minutes of loading dose. After induction, a bilateral scalp block was performed, covering six scalp nerves. The study duration was 10 minutes. Parameters measured at baseline, after induction, 1 minute before skull pin insertion, and after pinning were recorded.

Observations & Results

Table 1: Table showing age distribution of the subjects between the group

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Age	D	40	41.25	13.930	2.202	T value-0.016, p value- 0.98, non-significant
	S	40	41.20	14.084	2.227	

The mean age of group D is 41.25 years, while group S has 41.20 years, with no significant difference in age distribution between the two groups.

			Group		Total
			D	S	
Sex	F	Count	20	21	41
		% within Group	50.0%	52.5%	51.2%
	M	Count	20	19	39
		% within Group	50.0%	47.5%	48.8%

Total	Count	40	40	80
	% within Group	100.0%	100.0%	100.0%
Chi-sq value- 0.05, p value- 0.82				

Table 2: Distribution of sex of subjects within the group

The study found no significant difference in sex distribution between two groups, with 41 females (51.2%) and 39 males (48.8%) in the overall distribution, based on a chi-square test.

Table 5: Table showing mean comparison of Height of the subjects between the group

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Height	D	40	159.07	5.465	.864	T value- 0.17, p value- 0.86, non-significant
	S	40	158.88	4.603	.728	

The table shows height distribution of 40 participants in two groups, D and S. The mean height is 159.07 cm for D and 158.88 cm for S, with no significant difference in height distribution between the two groups.

Table 3: Table showing mean comparison of weight of the subjects between the group

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Weight	D	40	56.13	8.847	1.399	T value- 0.81, p value- 0.41, non-significant
	S	40	54.40	10.025	1.585	

The table shows weight distribution in two groups, D and S, with no significant difference between the two groups, with the mean weight of D being 56.13 kg and the standard error of S being 54.40 kg.

Table 4: Distribution of ASA status of subjects within the group

			Group		Total
			D	S	
ASA status	I	Count	17	19	36
		% within Group	42.5%	47.5%	45.0%
	II	Count	23	21	44
		% within Group	57.5%	52.5%	55.0%
Total		Count	40	40	80
		% within Group	100.0%	100.0%	100.0%
Chi-sq value- 0.20, p value- 0.65, non-significant					

The table shows the ASA status distribution of subjects in groups D and S, with 42.5% in group D and 57.5% in group S. No significant difference was found in ASA status distribution between the two groups.

Table 5: Table showing mean comparison of SPO2 at different time points between the group

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Baseline(BI)	D	40	98.50	1.132	.179	0.10
	S	40	98.08	1.163	.184	
After Induction (AI)	D	40	98.40	1.057	.167	0.67
	S	40	98.50	1.038	.164	
(T-1)1 min before skull pins insertion	D	40	98.85	1.122	.177	0.37
	S	40	98.63	1.148	.181	
(T1)1 min after skull pins	D	40	98.65	1.099	.174	0.19
	S	40	98.33	1.141	.180	
3 min after skull pins(T3)	D	40	98.15	1.051	.166	0.22
	S	40	98.45	1.154	.182	
5 min after skull pins(T5)	D	40	98.53	1.154	.183	0.11
	S	40	98.13	1.090	.172	
10 min after skull pins(T10)	D	40	98.53	1.062	.168	0.74
	S	40	98.45	1.011	.160	

The table compares Spo2 saturation between D and S groups during skull pin insertion procedures. No significant difference was found at baseline or after induction, all $p > 0.05$.

Table 6: Table showing mean comparison of heart rate at different time points between the group

	Gro up	N	Mean	Std. Deviation	Std. Error Mean	P value
Baseline	D	40	90.60	11.261	1.781	0.02
	S	40	83.85	14.080	2.226	
After Induction (AI)	D	40	76.28	8.640	1.840	0.03
	S	40	82.60	12.791	1.706	
(T-1)1 min before skull pins insertion	D	40	79.08	10.184	1.610	0.61
	S	40	82.30	11.078	1.752	
(T1)1 min after skull pins	D	40	86.28	10.105	1.598	0.51
	S	40	84.70	10.922	1.727	
(T3)3 mins after skull pins	D	40	92.15	10.475	1.656	0.01
	S	40	88.38	8.587	1.674	
(T5)5 mins after skull pins	D	40	85.10	11.675	1.846	0.04
	S	40	91.78	8.401	1.803	
(T10)10 mins after skull pins	D	40	89.83	12.590	1.991	0.35
	S	40	91.35	11.251	1.779	

The table compares heart rates of individuals in groups D and S during a skull pin insertion procedure. At baseline, group D had higher blood pressure than the Standard group. After induction, heart rates dropped significantly, but not significantly at subsequent time points. At 3 and 5 minutes, group D had lower heart rates than group S. Heart rates stabilized 10 minutes after insertion.

Table 7: Table showing mean comparison of Systolic Blood Pressure at different time points between the groups

	Grou p	N	Mean	Std. Deviation	Std. Error Mean	P value
baseline	D	40	125.25	15.142	2.394	0.80
	S	40	124.40	15.219	2.406	
After Induction (AI)	D	40	106.18	12.430	1.965	0.028
	S	40	115.73	8.155	1.289	
(T-1)1 min before skull pins insertion	D	40	105.33	12.970	2.051	0.042
	S	40	114.60	7.665	1.212	
(T1)1 min after skull pins	D	40	114.13	12.527	1.981	0.16
	S	40	117.33	6.900	1.091	
3 min after skull pins	D	40	119.65	11.902	1.882	0.17
	S	40	122.65	6.573	1.039	

5 min after skull pins	D	40	124.08	11.911	1.883	0.20
	S	40	126.85	6.845	1.082	
10 min after skull pins	D	40	123.60	10.782	1.705	0.08
	S	40	127.35	7.957	1.258	

The study compares systolic blood pressure (SBP) between group D and group S at different time points. Initial SBP was similar, but after induction and T-1 intervals, SBP decreased significantly. At subsequent time points, group D showed lower SBP, but not statistically significant. Overall, similar effects were observed.

Table 8: Table showing mean comparison of Diastolic Blood Pressure at different time points between the groups

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
baseline	D	40	75.15	11.731	1.855	0.1
	S	40	71.60	6.808	1.076	
After Induction (AI)	D	40	70.40	7.417	1.173	0.003
	S	40	76.00	8.803	1.392	
(T-1)1 min before skull pins insertion	D	40	72.93	8.401	1.328	0.03
	S	40	77.65	10.633	1.681	
(T1)1 min after skull pins	D	40	72.28	7.693	1.216	0.09
	S	40	75.88	10.964	1.734	
3 min after skull pins	D	40	71.70	6.779	1.072	0.29
	S	40	73.88	10.999	1.739	
5 min after skull pins	D	40	72.60	6.412	1.014	0.17
	S	40	75.13	9.595	1.517	
10 min after skull pins	D	40	72.47	6.710	1.061	0.052
	S	40	75.75	7.462	1.180	

The table compares Diastolic Blood Pressure (DBP) between group D and group S during a skull pin insertion procedure. At baseline, no significant difference was found. After induction and one minute before insertion, DBP was significantly lower in group D. However, no significant differences were found at subsequent time points.

Table 9: Table showing mean comparison of Mean Atrial Pressure (MAP) at different time points between the groups

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Baseline(BI)	D	40	90.38	4.216	.667	0.17
	S	40	89.23	3.214	.508	
After Induction (AI)	D	40	77.28	9.175	2.241	0.021

	S	40	82.47	14.888	2.354	
(T-1)1 min before skull pins insertion	D	40	74.10	4.235	.670	0.043
	S	40	84.30	9.910	.776	
(T1)1 min after skull pins	D	39	84.56	4.844	.776	0.37
	S	40	88.45	6.156	.973	
3 min after skull pins(T3)	D	40	81.47	9.717	2.011	0.036
	S	40	89.03	11.417	1.805	
5 min after skull pins(T5)	D	40	84.20	4.717	.746	0.02
	S	40	90.10	7.653	.736	
10 min after skull pins(T10)	D	40	85.20	4.121	.652	0.047
	S	40	90.40	5.518	.873	

The table compares Mean Arterial Pressure (MAP) measurements between group D and group S during a skull pin insertion procedure. At baseline, no significant difference was found. After induction and one minute before insertion, MAP was significantly lower in group D.

Table 10: Table showing adverse effect among the subjects between the groups

			Group		Total
			D	S	
Adverse effect	Bradycardia	Count	1	2	3
		% within Group	2.5%	5.0%	3.7%
	Bradycardia+ Hypotension	Count	15	0	15
		% within Group	37.5%	0.0%	18.5%
	Hypotension	Count	22	11	33
		% within Group	55.0%	27.5%	40.7%
	No	Count	2	27	30
		% within Group	5.0%	67.5%	37.0%
Total		Count	40	40	81
		% within Group	100.0%	100.0%	100.0%
Chi-sq value- 42.05, p value- <0.05, significant					

The table shows that bradycardia was present in 2.5% of group D participants, while hypotension was observed in 55.0% of group D participants, and only 27.5% of the Standard group experienced hypotension without bradycardia.

Table 11: Table showing the need of rescue dose among the subjects between the groups

			Group		Total
			D	S	
Rescue dose needed	NO	Count	34	37	71
		% within Group	85.0%	92.5%	88.8%
	YES AT T10	Count	2	1	3
		% within Group	5.0%	2.5%	3.8%
	YES AT T5	Count	4	2	6
		% within Group	10.0%	5.0%	7.5%
Total		Count	40	40	80
		% within Group	100.0%	100.0%	100.0%
Chi-square value- 1.13, p value- 0.57 , non-significant					

The table shows that most subjects in group D and group S did not require rescue medication, with a small percentage needing rescue doses at different time points. The Chi-square test showed no significant difference between the groups, indicating similar rates of needing rescue medication between IV Dexmedetomidine infusion and Scalp block treatment.

DISCUSSION

The study found that demographic parameters such as age, gender, heights and weights, and ASA status were comparable between two groups. The mean age for group D was 41.25 years, while for group S it was 41.20 years. This suggests that age-related biases are unlikely to affect the study's outcomes. The overall distribution of participants was 41 females (51.2%) and 39 males (48.8%), with no statistically significant difference in sex distribution between the two groups. These findings highlight the importance of ensuring comparable age distributions across treatment groups to mitigate potential biases and provide more robust and generalizable conclusions in clinical studies. [8]

The study aimed to compare the effectiveness of different anaesthesia methods in patients with varying heights, weights, and ASA statuses. The results showed that both groups maintained comparable SPO2 levels throughout procedural stages, indicating their effectiveness in maintaining adequate oxygenation. However, there was a transient difference observed in K. Mohana Akshaya's 2023 study immediately after pinning, which did not persist in subsequent readings. [9]

The mean height for both groups was similar, with no statistically significant differences observed between the two groups. This suggests that the methodological rigor in patient selection and outcome assessment is crucial in ensuring the reliability of findings related to anaesthesia method comparisons.

The mean weight for both groups was similar, with no significant difference observed between the two groups. This highlights the importance of maintaining comparable weight distributions across treatment groups in clinical research to minimize potential biases and enhance the robustness and generalizability of their findings.

In terms of ASA status, there were no significant differences observed between the two groups at baseline or after induction. However, the transient difference observed in K. Mohana Akshaya's study immediately after pinning highlights potential short-term effects that may not necessarily impact overall oxygenation stability over time. Overall, the study found that both groups maintained comparable SPO2 levels throughout procedural stages, indicating their effectiveness in maintaining adequate oxygenation.[9]

The study found that patients receiving IV dexmedetomidine (Group D) had significantly lower heart rates compared to those receiving Scalp block with fentanyl and Levobupivacaine (Group S) at various time intervals during and after skull pin insertion. At baseline, group D had a significantly higher mean blood pressure (90.60bpm) compared to the Standard group (83.85bpm). However, after induction, group D showed a drop in heart rates (mean-76.28bpm) and a statistically significant difference between both groups.

After 10 minutes after skull pin insertion, heart rates between both groups stabilized, suggesting that any initial differences in heart rate modulation between group D and group S likely normalized as anaesthesia deepened or stabilized during the procedure. The study suggests that both methods effectively manage heart rate dynamics during medical procedures.

Systolic blood pressure (SBP) showed comparable effects between Dexmedetomidine and Scalp block across the measured time intervals. Most patients in group D exhibited lower SBP after induction but was not significant enough to require intervention. In contrast, in N. Thakuria et. all study conducted in 2020, mean systolic blood pressure increased but these increase was not statistically significant in both the groups. However, later at 10 minutes and 15 minutes after scalp pin insertion, group D showed a significantly lower mean SBP compared to Group S, indicating a more pronounced reduction in SBP with Dexmedetomidine.

Overall, these studies highlight the importance of selecting anaesthesia methods based on their specific effects on SBP and overall hemodynamic stability.

The study compares diastolic blood pressure (DBP) between IV Dexmedetomidine and scalp block with Fentanyl + Levobupivacaine during medical procedures. The results show that Dexmedetomidine consistently lowers DBP levels compared to scalp block-based regimens during certain procedural phases. This highlights the importance of selecting anaesthesia protocols tailored to individual patient needs, procedural requirements, and desired hemodynamic goals.

Mean arterial pressure (MAP) was also found to be lower in the group D group after induction and at one minute before skull pin insertion. However, there was a significant decrease in MAP values from T5-T20 compared to baseline in both groups, with a decrease more in group D than group R. This decrease can be attributed to hypotension caused by dexmedetomidine.

In conclusion, the study highlights the influence of anaesthesia choice on cardiovascular parameters during procedures involving skull pin insertion. Dexmedetomidine's potential to lower MAP may offer benefits in certain contexts, such as reducing intraoperative bleeding and

optimizing surgical conditions, but careful titration is essential to mitigate risks of excessive hypotension.

The study compared the adverse effects of IV Dexmedetomidine infusion and scalp block with fentanyl and levobupivacaine in attenuating hemodynamic changes during skull pin insertion in patients requiring craniotomies. Individuals in Group D showed more adverse effects than those in Group S, with hypotension and bradycardia observed in 55% of individuals. These effects were mostly seen in Group D after induction and generally at 1 minute before skull pin insertion.

In a similar study, group D showed hypotension in 31.8% of patients receiving dexmedetomidine infusion, while group S had lower heart rates and blood pressure than baseline rates. However, none of the groups warranted use of any management for these effects.

The majority of subjects did not require rescue medication, with 85.0% in Group D and 92.5% in Group S. A small percentage required rescue doses at different time points. Scalp block is effective in attenuating the hemodynamic response and providing adequate analgesia. Levobupivacaine is an ideal drug for nerve blocks requiring large volumes and in areas like the scalp, which are highly vascularized.

Dexmedetomidine is a highly selective α -2 agonist that provides hemodynamic stability during periods of stress by inhibiting noradrenaline release from the presynaptic neuron. IV infusion of low doses decreases the HR and systemic vascular resistance, indirectly decreasing cardiac output and SBP. It does not alter ICP, maintains the oxygen supply-demand relationship, and decreases cerebrovascular dilatation produced by volatile anaesthetics, making it an ideal drug for intracranial surgery.

Conclusion

The study found that scalp block with fentanyl-levobupivacaine and IV dexmedetomidine effectively attenuate skull pin insertion hemodynamic response, but scalp block provides better analgesia, requiring caution due to adverse effects.

Reference

1. Misra S, Koshy T, Unnikrishnan KP, Suneel PR, Chatterjee N. Gabapentin premedication decreases the hemodynamic response to skull pin insertion in patients undergoing craniotomy. *J NeurosurgAnesthesiol*. 2011;23(2):110-117.
2. Mizrak A, Erkutlu I, Alptekin M. Efficacy of fentanyl and/or lidocaine on total antioxidants and total oxidants during craniotomy. *Clin Med Res*. 2011;9(2):82-87.
3. Bithal PK, Dash HH, Chauhan RS, Mohanty B. Haemodynamic changes in response to skull-pins application: comparison between normotensive and hypertensive patients. *Indian J Anaesth*. 2002;46:381-383.
4. 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.

5. Nanjundaswamy NH, Marulasiddappa V. Attenuation of hemodynamic response to skull pin head holder insertion: Intravenous clonidine versus intravenous lignocaine infusion. *Anesth Essays Res.* 2017;11:129-33.
6. Uyar AS, Yagmurdu H, Fidan Y, Topkaya C, Basar H. Dexmedetomidine attenuates the hemodynamic and neuroendocrinal responses to skull-pin head-holder application during craniotomy. *J NeurosurgAnesthesiol.* 2008;20(3):174-9.
7. Geze S, Yilmaz AA, Tuzuner F. The effect of scalp block and local infiltration on the haemodynamic and stress response to skull-pin placement for craniotomy. *Eur J Anaesthesiol.* 2009;26(4):298-303.
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 Oct 8;17(3):463-9. doi: 10.1055/s-0042-1757221. PMID: 36398172; PMCID: PMC9665997.
9. **Akshaya KM, Saravanan J, Arul J, Vijayanand K, Mala R.** Intravenous dexmedetomidine versus bupivacaine scalp block in attenuating the hemodynamic response to skull pin head holder application in patients posted for neurosurgery: a randomized clinical trial. *Int J Acad Med Pharm.* 2023;5(6):1187-92.
10. **Stachtari C, Stergiouda Z, Koraki E, Sifaki F, Bagntasarian S, Chatzopoulos S.** Dexmedetomidine as an adjuvant to scalp block in patients undergoing elective craniotomy: A prospective randomized controlled trial. *Clin NeurolNeurosurg.* 2023 Apr;227:107669. doi: 10.1016/j.clineuro.2023.107669. Epub 2023 Mar 11. PMID: 36924695.
11. **Sahana BN, Radhapuram SD, Samantaray A, Hemanth N, Pasupuleti H, Mangu HR.** Comparison of effects of dexmedetomidine added to ropivacaine versus ropivacaine alone infiltration scalp block for attenuation of the haemodynamic response to skull pin placement in neurosurgical procedures: A double-blind, randomised clinical trial. *Indian J Anaesth.* 2021 Nov;65(11):782-8.
12. **Singh G, Ganesamoorthi A, Karen Ruby L, Smita V, Bijesh Y, Appavoo A, Sethuraman M.** 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 Neuroanaesthesiol Crit Care.* 2020;7(1):10-5.
13. **Konwar C, Thakuria N.** The effects of levobupivacaine scalp block versus dexmedetomidine infusion on hemodynamic response to skull pin insertion in patients undergoing elective craniotomy: a randomized blinded clinical comparative study. *Indian J Appl Res.* 2020 Feb;10(2):40-3.
14. **Arunashree S, Hosagoudar P.** Intravenous fentanyl 4 µg per kg administered before scalp pin application is inferior to scalp block in preventing hemodynamic changes. *Anesth Essays Res.* 2019 Oct-Dec;13(4):625-30. doi: 10.4103/aer.AER_107_19. Epub 2019 Dec 16. PMID: 32009706; PMCID: PMC6937886.
15. **Nasr YM, Waly SH, Morsy AA.** Scalp block for awake craniotomy: lidocaine-bupivacaine versus lidocaine-bupivacaine with adjuvants. *Egypt J Anaesth.* 2020;36(1):7-15. doi: 10.1080/11101849.2020.1719301.
16. **Bharne S, Bidkar PU, Badhe AS, Parida S, Ramesh AS.** Comparison of intravenous labetalol and bupivacaine scalp block on the hemodynamic and entropy changes

following skull pin application: a randomized, open label clinical trial. *Asian J Neurosurg.* 2016 Jan-Mar;11(1):60-5. doi: 10.4103/1793-5482.165801. PMID: 26889282; PMCID: PMC4732245.

17. **Mizrak A, Erkutlu I, Alptekin M, Sen E, Geyik M, Gok A, Oner U.** Efficacy of fentanyl and/or lidocaine on total antioxidants and total oxidants during craniotomy. *Clin Med Res.* 2011 Jun;9(2):82-7. doi: 10.3121/cmr.2010.884. Epub 2011 Jan 24. PMID: 21263058; PMCID: PMC3134437.
18. **Yildiz K, Madenoglu H, Dogru K, Kotanoglu MS, Akin A, Boyaci A.** The effects of intravenous fentanyl and intravenous fentanyl combined with bupivacaine infiltration on the hemodynamic response to skull pin insertion. *J NeurosurgAnesthesiol.* 2005 Jan;17(1):9-12. PMID: 15632536
19. Dawlatly AB, Abdullah K, Watidy SA, Jamjoom Z, Murshid WR, Delvi B. Effect of small dose intravenous dexmedetomidine and/or local anesthetic infiltration on hemodynamic responses to skull pin placement. *Pan Arab J Neurosurg* 2006;10(1):29–33 29