ORIGINAL RESEARCH PAPER

Volume-7 | Issue-7 | July-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF THE EFFECTS OF DEXMEDETOMIDINE AS AN ADJUVANT TO BUPIVACAINE IN SCALP BLOCK FOR SUPRATENTORIAL CRANIOTOMY PROCEDURES.

Anesthesiology

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ABSTRACT

Background: Scalp block combined with general anaesthesia reduces pin and incision response, along with providing stable perioperative haemodynamics and analgesia. Dexmedetomidine has proved to be a valuable additive in peripheral nerve blocks. We studied the efficacy and safety of addition of Dexmedetomidine to scalp block for supratentorial craniotomies.

Materials and Methods: 60 ASA grade1 patients were randomly divided into and two groups. All the patients received fentanyl, propofol, sevoflurane based general anaesthesia. Followed by scalp block with 0.25% bupivacaine added either with Dexmedetomidine 1mcg/kg (Group BD) or normal saline (Group B). Haemodynamic parameters, requirement of sevoflurane, postoperative pain score and sedation scores were recorded.

Results: Both the groups showed blunted response to initial noxious stimuli like pin insertion and scalp incision due to local anaesthetic effects but group BD demonstrated excellent haemodynamic stability thereafter throughout intraoperative and postoperative period. Dexmedetomidine significantly reduced Sevoflurane requirement (mean 15.30 + 1.90 ml in group BD and 25.10 + 1.86 in group BD, $p<0.05$). potentiated the block action with analgesia lasting more than 300 minutes postoperatively. Sedation level was also comparable and incidence of adverse events was minimal.

Conclusion: Addition of Dexmedetomidine to scalp block provided better perioperative haemodynamic stability and significantly prolonged analgesia.

KEYWORDS

Scalp block, Dexmedetomidine, haemodynamics, analgesia

Introduction:

Development in neurosurgery and improvement in patient care has been provided by advances in neurophysiology, neuropharmacology, and advances in modern diagnostic and monitoring tools. This in turn has widened the scope of neuroanaesthesia [1]. Still, basic principles of neuroanaesthesia remain unchanged; the provision of optimal operative conditions, control of intracranial pressure (ICP), maintenance of cerebral perfusion pressure (CPP), and cerebral oxygenation [2]. Maintenance of normal haemodynamic is essential for control of CPP and ICP, specially during important events of intense stimulation. Besides endotracheal intubation, noxious stimuli such as insertion of cranial pins and scalp incision can alter haemodynamic during neurosurgical procedures. These stimuli can lead to sympathetic stimulation leading to increase in heart rate and blood pressure which in turn raises the intracranial pressure and cause oedema or bleeding in the operating field. Various methods and pharmacologic agents have been employed to prevent these undesired alterations in haemodynamic parameters in response to pin insertion and scalp incision. Scalp block is one of these methods used mainly in supratentorial craniotomy procedures [3]. But it has a disadvantage of short duration. Dexmedetomidine, a new versatile alpha 2 agonist is known to provide excellent haemodynamic conditions when used by intravenous for major surgical procedures. It is also used routinely to prolong the duration of analgesia in peripheral nerve blockade as well as central neuraxial blockade [4,5]. In this prospective randomised double blinded study, on supratentorial craniotomy procedures we have combined these two modalities of analgesia by adding Dexmedetomidine as an adjuvant to Bupivacaine for scalp block.

Materials and Methods:

This study was a randomised double blind controlled study. Institutional ethical committee approval was obtained. Only the patients posted for elective supratentorial craniotomy under general anaesthesia were included in this study after obtaining valid informed written consent from them. Total sixty patients of age from 18 to 60 years with normal neurological status posted for supratentorial craniotomy were included in the study. Patient with any motor or sensory deficit or behavioural or higher functions were excluded from study. Patients with co-morbidities like hypertension, diabetes mellitus, ischemic heart disease and patient receiving analgesics were also excluded form study.

Patients were divided into two groups of 30 patients each, by means of computer-generated randomisation:

- **Group B:** These patients received scalp block with injected bupivacaine 0.25% 19 ml plus normal saline 1 ml. (control group)
- **Group BD:** Patients received scalp block using 0.25% inj. Bupivacaine to which 1 µg/kg of Dexmedetomidine diluted to 1 ml (for blinding purpose) was added.

Patients were shifted to operation table after confirming adequate nil by mouth status, written informed consent. Electrocardiograph (ECG), Pulse oximeter and Non-invasive blood pressure (NIBP) were attached to patient and baseline reading of vital parameters were recorded. intravenous access was secured and inj. Midazolam 1mg and inj. Fentanyl 2µg/kg were given as a premedication. Induction was done using inj. Propofol 2mg/kg and inj. Rocuronium 1mg/kg. Endotracheal intubation was performed using a proper sized endotracheal tube. Anaesthesia was maintained by inhalational agent Sevoflurane, Oxygen 50% with Nitrous oxide 50% and with infusion of inj. rocuronium.

The Modern scalp block technique [6] was used to block the supratrochlear and supraorbital branches of the trigeminal nerve, the auriculotemporal nerve, zygomaticotemporal nerve and the greater and lesser occipital nerves on both sides, using 20 ml of solution (approximately 2 ml at each site). Pin Insertion was done 15 minutes after completion of scalp block while incision was planned and 5 minutes after pin insertion. Vital parameters were recorded every 5 mins, immediately after each noxious stimulus and every 15 mins intraoperatively and in postoperative period.

Hypotension was treated with intravenous fluids and bolus inj. Mephentermine if needed.

Hypertension was treated with increase in Sevoflurane or with bolus of inj. Propofol 20mg i.v. or Inj. Fentanyl 1µg/kg as per need if persistent. At the end of surgery, neuromuscular blockade was reversed using neostigmine 0.05 mg/kg and glycopyrrolate (0.008 mg/kg), and the patient was extubated. Monitoring was continued by a trained staff nurse in postoperative care room.

All the data was recorded in pretexted proforma, tabulated and analysed using students t test, Annova test and chi square test wherever appropriate. A p value of < 0.05 was deemed statistically significant.

Results:

Demographic profile (age, weight and gender distribution) of study groups were comparable. The mean age of patients in groups B and group BD was (38.73 + 12.35 yrs) and (40.00 + 11.18 yrs) respectively. Mean weight of patients in groups B and BD was (53.37 + 11.09 kg) and (55.27 + 8.89) kg respectively.

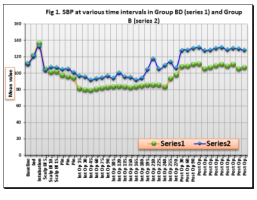
Mean duration of surgery in group BD and B was also comparable (4.12 + 0.28 and 4.22 + 0.70 hours) respectively. (Unpaired t-test, p>0.05).

Systolic Blood pressure (SBP):

Table 1: Comparison of Systolic Blood pressure (SBP) between the two groups

SBP mmHg	GROUP B			Group B				
	Mean	S..D.	Median	Mean	S.D.	IQR	Unpaired T test	P Value
Baseline	111.80	8.36	111.00	110.97	8.14	12.00	0.562	0.698
Ind SBP	121.73	11.55	123.00	120.50	10.83	17.00	0.427	0.671
Intubation SBP	135.90	11.32	140.00	132.23	9.82	16.00	1.340	0.185
Scalp Bl SBP 5 min	105.07	10.76	105.00	103.80	22.29	16.00	0.280	0.780
Scalp Bl SBP 15 min	101.33	10.17	103.00	106.50	11.44	10.00	-1.849	0.070
Pin Insertion SBP 5 min	97.23	8.21	96.00	104.83	10.39	16.00	-3.143	0.003
Pin Insertion SBP 15 min	93.77	5.72	94.50	100.73	10.65	15.00	-3.156	0.003
Int Op SBP 15 min	81.23	8.93	78.00	96.63	6.97	9.00	-7.447	0.000
30 min	79.63	8.02	77.50	95.50	8.16	10.00	-7.593	0.000
45 min	78.73	6.64	78.00	91.70	7.48	11.00	-7.102	0.000
75 min	81.40	8.46	80.00	94.53	7.44	13.00	-6.383	0.000
Int Op SBP 90 min	82.73	8.16	83.00	96.43	7.04	9.00	-6.962	0.000
105 min	83.33	8.87	83.00	93.90	9.76	12.00	-4.390	0.000
135 min	83.47	9.34	84.00	95.47	7.15	12.00	-5.587	0.000
150 min	82.00	9.25	81.00	94.77	5.96	9.00	-6.357	0.000
180 min	84.27	5.75	84.50	94.17	9.21	12.00	-4.995	0.000
225 min	85.47	6.12	87.00	105.27	9.49	14.00	-4.755	0.000
240 min	83.00	6.96	83.50	109.27	6.21	7.00	-9.547	0.000
255 min	93.20	8.41	93.00	113.50	11.09	16.00	-1.591	0.156
Int Op SBP 270 min	97.67	9.45	101.00	106.00	5.66	8.00	0.218	0.842
Post Op SBP 30 min	107.73	5.65	109.00	127.73	5.65	6.00	-13.709	0.000
60 min	108.13	4.98	108.00	128.13	4.98	8.00	-15.551	0.000
90 min	110.47	6.36	110.00	130.47	6.36	8.00	-12.177	0.000
Post Op SBP 120 min	111.20	6.16	110.00	131.20	6.16	10.00	-12.572	0.000
180 min	106.60	5.36	108.00	128.13	4.98	8.00	-16.119	0.000
240 min	110.40	5.18	110.00	131.20	6.16	10.00	-14.150	0.000
300 min	110.47	6.36	110.00	130.27	5.48	6.00	-12.920	0.000
Post Op SBP 360 min	106.60	5.36	108.00	128.10	8.16	8.00	-12.067	0.000

The baseline systolic blood pressure was comparable in both the groups, group BD (111.80 +/- 8.36 mmHg) and in group B (110.97 +/- 8.14 mmHg). After intubation also SBP was comparable, (135.90 +/- 11.32 mmHg) in group BD and (132.23 +/- 9.82) in group B. SBP did not vary significantly at the time of pin insertion or after scalp incision in both the groups. As evident from table 1, SBP remained fairly stable up to 5 after pin insertion. Bothe the groups exhibited a steady drop in SBP thereafter. 30 minutes after scalp block there was further decrease in SBP in group BD to mean (79.63 +/- 8.02 mmHg) and also in group B SBP to (mean 95.50 +/- 8.16 mmHg) which was statistically significant.



As evident by fig.1, his drop I SBP was more in group BD than in group B and persisted till 270 mins after scalp block and remained on lower side throughout postoperative period too. Diastolic blood pressure followed similar trends as in SBP.

Mean Arterial Pressure (MAP):

Baseline MAP in group BD was comparable with (85.50 + 6.21mmHg) group B (83.97 +7.17 mmHg) and remained so during intubation and upto 15 mins after scalp block. MAP at 15 minutes after scalp block in group BD was 79.17 +/- 7.32 and in group B was 81.33 +/- 9.02. This difference was not significant (p>0.05).

However, MAP in group B increased significantly 5 minutes after pin insertion (p<0.05) compared to group BD. MAP at 10th minute after pin insertion in group BD was 70.27 +/- 6.27 and in group B was 78.23 +/- 11.55. In 15th minute MAP in group BD was 69.40 +/- 4.49 and in group B was 75.30 +/- 8.96. This difference in MAP remained significant (p<0.05) after scalp incision and was less than in group B in the entire intraoperative period. Post operatively the differences were

Mean Arterial Pressure (MAP)	GROUP BD		Group B		Unpaired T test	P Value
	Mean	S..D.	Mean	S.D.		
Baseline	85.50	6.21	83.97	7.17	0.468	0.381
Ind MAP	91.70	10.21	91.10	8.54	0.247	0.806
Intubation MAP	103.23	8.25	98.73	7.58	2.200	0.032
Scalp Bl MBP 5 min	79.73	8.79	81.83	8.15	-0.960	0.341
Scalp Bl MBP 15 min	79.17	7.32	81.33	9.02	-1.021	0.311
Pin Insertion MBP 5 min	71.47	7.01	77.57	9.89	-2.755	0.008
Pin Insertion MBP 10 min	70.27	6.27	78.23	11.55	-3.321	0.002
Pin Insertion MBP 15 min	69.40	4.49	75.30	8.96	-3.225	0.002
Int Op MAP 15 min	66.74	6.24	78.90	7.02	-7.087	0.000
Int Op MAP 45 min	65.09	4.77	74.94	5.11	-7.719	0.000
Int Op MAP 60 min	66.23	4.07	75.84	5.01	-8.155	0.000
Int Op MAP 90 min	68.44	6.80	79.01	5.18	-6.771	0.000
Int Op MAP 120 min	69.13	6.62	80.96	6.46	-6.999	0.000
Int Op MAP 150 min	68.62	5.80	77.46	5.91	-5.847	0.000
Int Op MAP 180 min	70.27	4.76	75.83	5.15	-4.351	0.000
Int Op MAP 210 min	71.22	5.17	79.01	5.84	-5.468	0.000
Int Op MAP 240 min	68.98	5.29	79.29	5.48	-7.414	0.000
Int Op MAP 270 min	74.67	4.93	77.50	12.02	-0.387	0.725
Post Op MAP 30 min	84.17	6.18	97.73	7.61	-7.579	0.000
Post Op MAP 90 min	83.97	7.17	95.80	5.31	-7.266	0.000
Post Op MAP 150 min	93.27	4.77	97.93	5.92	-3.363	0.001
Post Op MAP 180 min	95.57	3.87	97.73	7.61	-1.390	0.170
Post Op MAP 210 min	96.70	4.33	95.87	5.73	0.636	0.528
Post Op MAP 270 min	91.57	4.50	97.17	6.12	-4.038	0.000
Post Op MAP 330 min	93.63	3.93	95.87	5.73	-1.760	0.084
Post Op MAP 360 min	91.57	4.50	95.80	5.31	-3.332	0.002

significant statistically and clinically upto 150th minute. [Table 2].

Table 2: Comparison of mean arterial pressure in two groups:

Heart rate (HR):

Baseline mean heart rate in group BD was 72.87 +/- 4.62 and in group B was 71.17 +/- 5.94. This difference was statistically not significant (p>0.05) even after induction and intubation (p>0.05). Heart rate in both the groups was stable clinically on pin insertion and scalp incision. However, HR at 15th minute of pin insertion in group BD was 68.80 +/- 5.80 and in group B was 75.27 +/- 9.05 while HR on scalp incision in group BD was 62.57 +/- 7.05 and in group B was (70.17 +/- 9.97 per min). this difference was statistically significant and persisted intraoperatively, during skin closure, pin removal and till 150th minute in postoperative period. (Fig. 2)

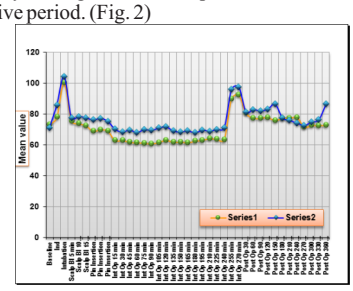


Figure 2: Comparison of Pulse rate between both the groups. (Series 1: group BD and series 2: group B)

Sedation score:

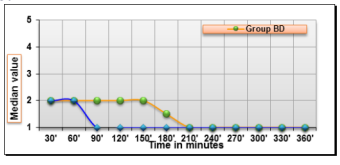


Figure 3: Sedation score in both the groups in the postoperative period

Level of sedation was monitored postoperatively using Modified Ramsay Sedation scoring system as shown in figure 3. According to Modified Ramsay sedation score patients in group BD had score 2 till 150 minutes. Whereas, in group B sedation score was 2 till 60 minutes post operatively. At 180 minutes in group BD 15 patients had score 2 and rest 15 had score 1. Whereas, in group B, 60 minutes onwards patients had score 1.

Pain scores:

Perception of pain was monitored postoperatively using Verbal pain scale for 360 minutes (6 hours). As evident from fig 4. at 120 minutes grade 1 pain was complained by only one patient in group B and none of the patients in group BD. At **210 minutes** 18 patients in group B had grade 2 pain requiring analgesic supplementation while grade 3 pain was observed in 4 patients. While none of the patients complained of pain in group BD. At 300th minute in group BD 14 patients had grade 1 pain and 16 had grade 2 pain. This difference was highly significant. (Fig. 4) Additional analgesic was supplemented in group BD patients and good response to the analgesic was seen in group B. At 360th minute in group BD 16 patients had grade 3 pain while 14 patients had grade 2 pain requiring analgesic supplementation. Whereas, in group B most of the patients had already received rescue analgesic. (p< 0.05, statistically significant).

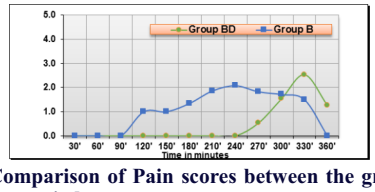


Figure 4: Comparison of Pain scores between the groups in the postoperative period.

Additional drugs:

Inj. Fentanyl 50 µg was supplemented intra-operatively in 3 patients in group BD. While, in group B 13 patients required inj. Fentanyl 50µg intra operatively. Inj.Propofol 20mg additionally was required in 14 patients in group B. While only 1 patient in group BD required inj. Propofol 20mg.

Requirement of Sevoflurane in both the groups was noted as displayed in gas usage in the anaesthesia machine which showed a significant difference. Sevoflurane requirement was mean 15.30 +/- 1.90 in group BD and 25.10 +/- 1.86 in group BD (p<0.05).

DISCUSSION:

Blocking noxious input to the abundant sensory nerve supply of the scalp can prevent the haemodynamic response to noxious stimuli like head pin insertion and incision. Thus, the idea of combining regional anaesthesia with general anaesthesia offers an advantage and helps to maintain haemodynamic stability.

Afonso et al [7] found that after intravenous administration (IV) in healthy adult volunteers, Dexmedetomidine has an onset of action after approximately 15 minutes. Haemodynamic alteration due to absorption of dexmedetomidine from scalp site into circulation will surely take more time than this. Therefore, we assume that haemodynamic stability during pin insertion seen in both the groups was due to local anaesthetic action of Bupivacaine. However, the density of block was augmented by Dexmedetomidine in group BD. Uyar et al [8] tested Dexmedetomidine 1 µg/kg intravenously in neurosurgery. They concluded that Dexmedetomidine before induction of anaesthesia attenuated the haemodynamic and neuroendocrinal responses to skull-pin insertion in patients undergoing craniotomy.

30 minutes after scalp incision systolic blood pressure in group BD was 80.57 +/- 6.48 and in group B was 93.40 +/- 9.33. This decrease in SBP was treated with intravenous fluid administration SBP remained in this range with better haemodynamics in the entire intra operative period. At 240 minutes in group BD SBP was 83.00 +/- 6.96 while it increased to 109.27 +/- 6.21 in group B and remained on higher side thereafter. This increase in SBP 240 minutes onwards in group B was mostly due to noxious stimuli associated with scalp closure and extubation which occurred during this period. Similar events occurred in group BD also 240 minutes onwards but less haemodynamic alterations were seen. Lower MAP in group BD probably would be due to central sympatholytic action of drug leading to decrease in systemic vascular resistance as mentioned by Panzer et al [9] in their study.

Shrikant et al in 2016 also found that α2 agonist inj. Clonidine 2µg/kg used in scalp blocks combined with general anaesthesia reduced pin insertion and scalp incision response, along with providing stable perioperative haemodynamics and analgesia. We found no change in heart rate in both the groups on pin insertion and scalp incision. Lower heart rate in group BD as compared to group B could be due to systemic absorption of Dexmedetomidine. This significant difference in heart rate between two groups persisted throughout the intraoperative period (p<0.05). Lowest heart rate in group BD was 61/minute at 135th minute. But none of the patients required inj. Atropine or inj. Glycopyrrolate as a treatment of bradycardia.

These findings were in accordance with the findings of Oak et al [10] who also used an α2 agonist inj. Clonidine 2 µg/kg with inj. Bupivacaine 0.25% in scalp block. Better perioperative haemodynamic stability and significantly prolonged analgesia post operatively were observed.

Similar results were obtained by Dash et al. [11] They used inj. Clonidine 2 µg /kg an α2 agonists with inj. Bupivacaine 0.25% in scalp block and inj. Clonidine 2 µg /kg intravenously. They found Clonidine intravenously or in scalp block offers better haemodynamic stability intraoperatively and blunts haemodynamic response to surgical stimulus in the form of pin insertion, scalp incision. Clonidine in scalp block also had better postoperative outcomes with prolonged analgesic time.

Over all, group BD showed better haemodynamic stability compared to group B in the intraoperative and postoperative period. Blood pressure and heart rate in group BD remained on lower side with minimum fluctuations. This can be explained by two mechanisms. Firstly, potentiation of scalp block as well as prolongation of action of inj. Bupivacaine probably blunted the noxious stimuli during various intra operative events like pin insertion, scalp incision and closure. This minimised the fluctuations in heart rate and blood pressure during these extremely painful procedures. Prolongation of analgesia due to Dexmedetomidine also provided better haemodynamics in post-operative period. While, group B patients exhibited greater increase in

heart rate, SBP, MAP, DBP during scalp closure and in post-operative period.

This was probably due to early termination of action of Bupivacaine in scalp block compared to group BD. α-2 agonist as an adjuvant increases duration and potency of scalp block. This was the finding also obtained by Oak et al [10] who used inj. Clonidine as an adjuvant in scalp block. They found that addition of Clonidine 2 µg/kg in the infiltrative block potentiated the block action with analgesia lasting 960 ± 120 minutes

Secondly, systemic absorption of Dexmedetomidine from scalp infiltration site can also be a major contributing factor towards better haemodynamic stability in group BD. This probably mimicked haemodynamic action of α2 agonists injected by intravenous route.

α-2 agonists act by inhibition of central sympathetic outflow. Also, stimulation of presynaptic α-2 receptors by Dexmedetomidine decreases Norepinephrine release, which may explain a decrease in blood pressure and heart rate and better haemodynamic stability in the group BD throughout the intra operative period. The dose dependent bradycardia by Dexmedetomidine is primarily mediated by the decrease in sympathetic tone and partly by baroreceptor reflex and enhanced vagal activity. This explains our finding that heart rate and blood pressure remained on lower side in group BD throughout the surgery.

Pain score: There are many articles depicting the efficacy of post-operative pain relief with scalp block in craniotomy surgeries [10,11,12,13,14,15]. Abdallah et al [15] in 2013 showed that Dexmedetomidine prolonged duration of peripheral nerve blocks. Duration of action in brachial plexus block with Dexmedetomidine as an adjuvant in four trials was prolonged by 268 minutes (95% CI: 15.47, 520.06, P=0.04wed) or 87%, and an increase in time to first analgesic request by 345 min (95% CI: 102.68, 587.23, P=0.005) or 70% compared with LAs alone. Bajwa et al [16] in their review article on Dexmedetomidine as an adjuvant concluded that in peripheral nerve blocks also Dexmedetomidine has shown its efficacy in prolonging the duration of sensory block as well as prolongation of post-operative analgesia when used along with local anaesthetic. Bajwa et al [16] in 2013 in their review article on Dexmedetomidine as an adjuvant concluded that in peripheral nerve blocks also Dexmedetomidine has shown its efficacy in prolonging the duration of sensory block as well as prolongation of post-operative analgesia when used along with local anaesthetic.

Requirement of Sevoflurane in both the groups was noted as displayed in gas usage in the anaesthesia machine which showed a significant difference. Sevoflurane requirement was mean 15.30 +/- 1.90 in group BD and 25.10 +/- 1.86 in group BD ($p<0.05$). Lower requirement of Sevoflurane in group BD can be explained by excellent haemodynamic stability provided by Dexmedetomidine. Harsoor et al [17] in their study on abdominal surgeries also found that bolus IV Dexmedetomidine 1 µg/ kg combined with infusion of 0.5 µg/kg/hr resulted in 39% reduction in Sevoflurane requirements during 1st hour of anaesthesia. Harsoor et al [17] in their study on abdominal surgeries also found that bolus IV Dexmedetomidine 1 µg/ kg combined with infusion of 0.5 µg/kg/hr resulted in 39% reduction in Sevoflurane requirements during 1st hour of anaesthesia.

Adverse effects: Patients in group BD showed intra operative haemodynamic stability. Whereas, dexmedetomidine is known to cause bradycardia and hypotension as the most common side effects in the intra operative and postoperative period [16]. These side effects were not seen using inj. Dexmedetomidine in scalp block.

Dash et al [11] in 2010 also observed no adverse effects of scalp block in their study with 60 patients undergoing supratentorial craniotomy Guilfoyle et al [14] found no adverse effects of scalp block in their meta-analysis of craniotomies using scalp block with inj. Bupivacaine and inj. Clonidine as an adjuvant.

Conclusion: Thus, it can be concluded from above findings that Dexmedetomidine as an adjuvant in scalp block also improved quality of intraoperative and postoperative analgesia, provides excellent haemodynamic stability analgesia, without any significant adverse effects. That makes it a useful weapon in armamentarium of an anaesthetist.

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