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RESEARCH ARTICLE

COMPARISON OF DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN SCALP BLOCK FOR SUPRATENTORIAL CRANIOTOMY SURGERY - A PROSPECTIVE, RANDOMISED INDIAN STUDY

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Abstract

Background: Current era of minimally invasive surgery and awake craniotomy has created revived attention towards scalp blocks and its benefits. Present study was conducted to evaluate and compare effects of dexmedetomidine and clonidine as an adjuvant to bupivacaine in scalp block for supratentorial craniotomy surgery.

Methods: The prospective, comparative, randomized study was conducted by Department of Anaesthesia at J.J. Hospital and Grant Medical College, Mumbai, India. Data was collected between September 2018 to August 2020. Adult subjects between 18 years and 60 years (both inclusive) of either gender with ASA-I, Glasgow Coma Scale (GCS) of 15, and indicated to undergo supratentorial craniotomy surgeries were enrolled. One study group received 1 mcg/kg Clonidine, while other 1 mcg/kg Dexmedetomidine, both diluted with normal saline. Hemodynamic parameters, analgesic requirement and Ramsay Sedation score (RSS) were assessed.

Results: 60 patients (30 in each group) were enrolled. Mean age, baseline weight, gender distribution and duration of surgery were statistically comparable between study groups (P>0.05). Mean blood pressure, mean arterial pressure and heart rate were significantly higher in the clonidine group at the time of pin insertion, incision and during most of the intraoperative period (p<0.05). RSS was comparable between study groups at all time-points (p>0.05). Analgesic requirement was overall higher in clonidine group, indicating better analgesia with Dexmedetomidine.

Conclusion: Dexmedetomidine led to lesser vascular parameters changes, with lower analgesic requirement versus clonidine; however, sedation scores were comparable.

Introduction:-

Craniotomies are painful procedures which are being conducted by surgeons since decades. Cerebrovascular alterations during craniotomies can lead to raised intracranial pressure (ICP), reduction

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in cerebral perfusion pressure, more evident in patients having disordered autoregulation as well as compromised cerebral compliance.[1] These events can cause abrupt escalations in blood pressure (BP)and heart rate (HR), which can lead to possible morbidity because of greater surges in intra-cranial pressure (ICP) in patients suffering from intracranial pathology, and a superior risk for rupture in patients diagnosed with intravascular aneurysms.

Local anesthetic infiltration prior to craniotomy incision is a recognized routine by neurosurgeons, but the effect is brief. A ‘‘scalp block’’ means administering regional anesthesia to the nerves which innervate the scalp, delivering analgesia for a substantial period of time with the possibility for postoperative effect.The current era of minimally invasive surgery as well as awake craniotomy has created revived attention towards this technique and its benefits for patients.[2]

In brain, activation of pre-synaptic α2-receptors leads to inhibition of nor-epinephrine release. Stimulation of α2-adrenoceptors situated post-synaptic in the dorsal horn and on vascular smooth muscle prevents nociceptive signal transmission leading to vasoconstriction.[3] Clonidine is utilized primarily for its α2 receptor facilitated antihypertensive properties. Stimulation of α2 receptors by clonidine in the central nervous system has been related with sedation for which clonidine is extensively utilized as an adjunctive agent to anesthesia as well as pain medicine.[4] Clonidine reduces sympathetic tone as well as the nor-epinephrine release from nerve terminals.[5] Thus, the usage of clonidine during surgery has been projected as a mode of improving perioperative hemodynamics, reducing both intracranial pressure and anesthetic requirements.

Dexmedetomidine has developed into a frequently used α2 agonist agent in anesthetic armamentariumbecause of its hemodynamic, anxiolytic, sedative, neuroprotective analgesic, and anesthetic-sparing effects. α-1 to α-2 ratio of 1:1600 makes it an extremely selective α-2 agonist in comparison to clonidine, thus decreasing the unsolicited side effects which involve α-1 receptors. Because of its central sympatholytic effect, dexmedetomidine is beneficial in dampening hemodynamic responses in perioperative period.[6]

Though the usage of clonidine and dexmedetomidine has been assessed individually in various studies with success in adjuvant to bupivacaine for different kinds of blocks, comparative studies in scalp block are lacking, especially in Indian setting. Hence, present study was conducted to evaluate and compare effects of dexmedetomidine and clonidine as an adjuvant to bupivacaine in scalp block for supratentorial craniotomy surgery, in a tertiary care Indian teaching hospital.

Methods:-

The prospective, comparative, randomized study was conducted by Department of Anaesthesia at J.J. Hospital and Grant Medical College, Mumbai, India. Data was collected between the period of September 2018 to August 2020.Study was initiated after institutional ethics committee permission. Details of procedure was explained to patient and a written informed consent was obtained.The study population was composed of subjects between the age of 18 years and 60 years (both inclusive) of either gender with ASA-I, Glasgow Coma Scale (GCS) of 15, and indicated to undergo supratentorial craniotomy surgeries. Exclusion criteria was as follows: allergy to study drugs, hepatic/respiratory/cardiac/endocrine, or metabolic impairment, emergency surgery requirement, presence of vascular lesions like aneurysm, pregnant females, or refusal to sign informed consent form. On day of surgery, patients were shifted to operation table after confirming adequate nil by mouth status, written informed consent and preparation of general anaesthesia.

Operation theatre protocol and study drug administration

Enrolled patient was kept in supine position.An intravenous access was secured using an 18 G IV cannula.Patient was pre-medicated using inj. Glycopyrrolate 0.2 mg, inj. Ondansetron 4 mg, inj.

Midazolam 1 mg and inj. Fentanyl 2 mcg/kg. Pre-oxygenation was started, followed by induction using inj. Propofol 2 mg/kg, and inj. Rocuronium 1 mg/kg. After achievingneuromuscular blockade, endotracheal intubation was performed,and vital parameters were recorded. Immediately after this scalp block was performed.

Drug used for scalp block was 19 ml of 0.50% inj. Bupivacaine to which either of the following study drugs were added:

Clonidine Group: 1 mcg/kg Clonidine diluted with normal saline so as to make total volume 1 ml for blinding purpose.

Dexmedetomidine Group: 1 mcg/kg Dexmedetomidine diluted with normal saline so as to make total volume 1 ml for blinding purpose.

Final volume of local anaesthetic solution was 20 ml. Both, the observer and the interpreter were blinded with regards to additive used in any case.

Anaesthesia was maintained using nitrous-oxygen on circle absorber system and inj. Rocuronium top ups. Sevoflurane was started 10 minutes after scalp block and its concentration was changed as per the need. 15 minutes after completion of scalp block patient was given surgical position and the head pins were inserted as per surgeon's requirement. Incision was planned 15 minutes after pin insertion. Sevoflurane was stopped immediately after skin closure. N2O was stopped after head pin removal and patients could recover from anesthesia. Neuromuscular blockade was reversed and extubation was performed only after Train-of-four ratio of 90% was achieved. Patient was monitored in operation room for 30 minutes and shifted to recovery room.

Variables assessed

1. Hemodynamic Parameters:

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- HR
- MAP

Pre-operatively, hemodynamic parameters were measured at baseline, pre-medication, and induction, and then every 5 minutes during intubation and scalp block period, and during pin insertion and incision. The parameters wererecorded immediately after incision and every 5 minutes after that for 30 minutes. Thereafter, vital parameters were recorded every 10 minutes till Dura closure, and then every 5 minutes after Dura closure till extubation.

Analgesia requirement

Calculated every 15 minutes in recovery ward for 2 hours and then every 30 minutes till first analgesic demand by patient in recovery room or ward.

Degree of sedation by Ramsay Sedation Score

Ramsay Sedation Scale (RSS) is a standardized tool to precisely evaluate the level of consciousness during titration of sedative medications in the ICU. Use of a sedation scale is an integral component of most patient-focused management algorithms. RSS has been known to have excellent inter-rater reliability and validity, and is one the most frequently used sedation scale system.[7] The level of sedation is graded by RSS in the form of 6-point score:

Table 1:- Ramsay Sedation Score.

Ramsay Sedation Scale	
Score	Definition
1	Anxious and agitated or restless or both
2	Cooperative, oriented, and tranquil
3	Responds to commands only
4	Brisk response to a light glabellar tap or loud auditory stimulus
5	Sluggish response to a light glabellar tap or loud auditory stimulus
6	No response to a light glabellar tap or loud auditory stimulus

Statistical Analysis

Data entry was done in Microsoft Excel. Data analysis was done with statistical software Graphpad InStat.v3.0. Quantitative data was presented as Mean and Standard deviation. Comparison of continuous data (hemodynamic parameters, pain scores, sedation scores) was done between the two study groups using unpaired student's t test. Qualitative data (requirement of analgesics) were noted down descriptively and compared using chi-square analysis between study groups. P value <0.05 was considered statistically significant.

Results:-

Demographic and baseline details of enrolled patients

60 patients, (30 in each study group) were enrolled in study. Mean age, mean baseline weight, gender distribution and mean duration of surgery were statistically comparable between study groups (P>0.05)(Table 2).

Table 2:- Demographic details of enrolled patients in study.

Parameter assessed	Dexmedetomidine group (n=30)	Clonidine group (n=30)	P value
Mean age (years)	38.43 + 10.89	38.53 + 9.87	0.81*
Median age with range (years)	37.5 (18-58)	37.5 (24-58)	-
Number of males	22	19	0.58$
Number of females	8	11	
Mean weight (kg)	62.67 + 6.59	62.23 + 7.01	0.86*
Median weight with range (kg)	62 (45-75)	62.5 (48-75)	-
Mean surgery duration (hours)	4.45 + 0.37	4.51 + 0.22	0.25*

P value calculated by *Unpaired t test or $Chi-square test, p>0.05 considered not significant

Diagnosis of enrolled cases

In dexmedetomidine study group, majority patients were diagnosed with glioma and meningioma. 5 patients had parietal glioma, 3 patients had frontal glioma, while 3 patients had temporal glioma. On the other hand, 3 patients had frontal meningioma while 3 other patients had falcine meningioma. 2 cases each presented with parietal glioblastoma, temporal meningioma and temporal space occupying lesion (SOL). Single patient had fronto-parietal astrocytoma, parafalcine meningioma, parasagittal meningioma, tuberculoma, pituitary adenoma, temporal epidermoid tumour and thalamic tumour.

In the Clonidine study group, as seen in Dexmedetomidine group, majority patients were diagnosed with glioma and meningioma. 2 patients each had frontal meningioma, temporal glioma, parietal glioma, parietal meningioma or temporoparietal glioma. 2 other patients suffered from frontal SOL and craniopharyngioma. 1 patient each were diagnosed with basal ganglia astrocytoma, caudate epidermoid, cerebral SOL, fronto-parietal meningioma, frontal glioma, optic glioma, parietal AVM, pituitary adenoma, temporal ependyoma or glioma or meningioma or SOL each.

Hemodynamic variables

- SBP and DBP:

No statistically significant difference was found in mean SBP and DBP between two study groups at baseline, during pre-medication and induction phase, and during intubation and scalp block phase ($p>0.05$). However, at the time of pin insertion and incision, and during intraoperative period at all measured time-points (except at 270 minutes), SBPand DBP in the clonidine group was significantly higher ($p<0.05$).Mean SBP and DBP were statistically comparable between the study groups at all time-points post-operatively, except at 30 minutes, when DBP was significantly higher in Clonidine group ($p<0.05$). (Figure 1, Figure 2)

- HR:

Like noted for BP, no statistically significant difference was found in mean HR between the two study groups at baseline, during pre-medication and induction phase, and during intubation and scalp block phase ($p>0.05$).However, at the time of pin insertion and incision, mean HR in the clonidine group was significantly higher ($p<0.05$).During the intra-operative assessment, the mean HR was found to be significantly higher in the clonidine group till 150 minutes of intraoperative assessment ($p<0.05$).During the post-operative period at all time-points, the mean HR was found to be comparable between study groups ($p>0.05$). (Figure 3)

- MAP:

Pre-operatively, the mean MAP was found to be statistically comparable between study groups at all time-points except at time of incision during scalp block, when the MAP in the clonidine group was significantly higher ($p<0.05$). Intraoperatively, mean MAP was significantly higher in clonidine group till 135 minutes ($p<0.05$), after which it was statistically comparable ($p>0.05$). Post-operatively, at time of extubation, the mean MAP was significantly higher in the clonidine group ($p<0.05$). (Figure 4)

Post-operative sedation score

At none of the time points postoperatively was there a significant difference noted between the mean sedation scores of the dexmedetomidine group and the clonidine group ($p>0.05$). (Table 3)

Table 3:- Sedation score assessment at various post-operative time points.

Time of assessment	Dexmedetomidine group (n=30)	Clonidine group (n=30)	P value
Post—operative time points			
15 minutes	2 + 0	2 + 0	1

30 minutes	2 + 0	2 + 0	1
45 minutes	2 + 0	2 + 0	1
60 minutes	2 + 0	2 + 0	1
75 minutes	1.97 + 0.18	2 + 0	0.67
90 minutes	1.97 + 0.18	1.97 + 0.18	1
105 minutes	1.97 + 0.18	2 + 0	0.67
120 minutes	2 + 0	2 + 0	1
150 minutes	2 + 0	2 + 0	1
180 minutes	2 + 0	2 + 0	1
210 minutes	2 + 0	1.97 + 0.18	0.67
240 minutes	1.93 + 0.25	1.77 + 0.43	0.35
270 minutes	1.8 + 0.41	1.67 + 0.4	0.17
300 minutes	1.7 + 0.47	1.9 + 0.31	0.3
330 minutes	1.5 + 0.45	1.97 + 0.18	0.23
360 minutes	1.2 + 0.1	2 + 0	0.13

P value <0.05 considered significant by unpaired t test

Additional analgesic requirement

No analgesic requirement was noted in either of the study groups post-operatively till 210 minutes. At 240 minutes and 300 minutes post-operatively, significantly higher number of patients in the clonidine group required analgesia (n=7 vs 1). At 330 minutes, 3 patients in the dexmedetomidine group required analgesia, while none of the patients in clonidine group required analgesia, though this was not a significant finding (p>0.05). Overall, there were 9 instances of analgesia requirement in dexmedetomidine group while 20 instances of analgesia were noted in the clonidine group, and this was significant finding (p<0.05).

Discussion:-

Present study comparedeffects of dexmedetomidine and clonidine as adjuncts to bupivacaine in cases undergoing supratentorial craniotomy surgeries. The baseline data of age and gender distribution were like other identical studies (table 4).

Table 4:- Demographic details of similar studies.

Study Assessed	Evaluated parameter	
Mean age (in years)		
	Dexmedetomidine group	Clonidine group
This study	38.43 + 10.89	38.53 + 9.87
Swami et al. (2012)[8]	33.83 + 16.78	33.73 + 12.09
Wajekar et al. (2016)[9]	-	39 + 14
Tripathi et al. (2016)[10]	38.03 + 11.25	37.83 + 11.28
Kumar et al. (2017)[11]	37.12 + 11.39	-
Vellapu et al (2018)[12]	42.2 + 14.3	-
Chowdhary et al. (2019)[13]	-	39 + 6.66
Lalwani et al. (2019)[14]	31.87 + 8.02	-
Gender distribution		
	Dexmedetomidine group	Clonidine group
This study	M: 73.33%, F: 26.67%	M: 63.33%, F: 36.67%
Swami et al. (2012)[8]	M: 63.33%, F: 36.67%	M: 73.33%, F: 26.67%
Wajekar et al. (2016)[9]	-	M: 60%, F: 40%
Tripathi et al. (2016)[10]	M: 56%, F: 44%	-
Kumar et al. (2017)[11]	M: 54%, F: 46%	-
Vellapu et al (2018)[12]		M: 63.64%, F: 36.36%

Chowdhary et al. (2019)[1]	M: 69%, F: 31%	-

The blood pressure was noted to be significantly higher in the clonidine group at most time-points of intraoperative period. The MAP and HR values were also similarly higher in the clonidine group at same time-points.It has been mentioned in scientific literature that noxious stimuli like head pinning can lead to acute hypertension which can cause rise intracranial pressure, increased risk of herniation and also pulmonary edema.[13,14] In the study by Kumar et al., dexmedetomidine-bupivacaine group showed the maximum attenuation of hemodynamic responses to skull pin placement, which has been similarly found in our study.[11]Proposed mechanisms include central analgesia, vasoconstriction, and anti-inflammatory effects.[15]Another study by Vallapu et al., none of the patients administered dexmedetomidine with bupivacaine developed any kind of hemodynamic abnormality.[12] In the comparative study by Ganesh et al.,[16] mean HR was significantly higher in clonidine group at 5 minutes, 10 minutes and 15 minutes. The blood pressure, though numerically lower in dexmedetomidine group like seen in our study, was statistically comparable ($p>0.05$) with clonidine group.

Thehemodynamic findings in study 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 minimized the fluctuation in heart rate and blood pressure during these extremely painful procedures. Prolongation of analgesia due to Dexmedetomidine provided better hemodynamics in post-operative period. On the other hand, patients in clonidine group 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 Dexmedetomidine group. α-2 agonist as an adjuvant increases duration and potency of scalp block. This was the finding also obtained by Shrikant et al in 2014 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. [17]Secondly, systemic absorption of Dexmedetomidine from scalp infiltration site can also be a major contributing factor towards better hemodynamic stability. This probably mimicked hemodynamic action of α2 agonists injected by intravenous route. Panzer et al in 2009 found that Dexmedetomidine is also absorbed systemically through the transdermal, oral, or intramuscular routes, with a mean bioavailability from the latter two routes of 82 and 104%, respectively.[18]

On sedation score comparison, at none of the time points was there a significant difference noted between study groups ($p>0.05$).Scientific literature has shown that stimulation of α2receptors in CNS has role on sedation which act on locus ceruleus in brainstem centre for wakefulness. Activation of these receptor suppresses signal in locus ceruleus.[4] Hence, addition of such agents to anesthetic drugs can help tackle sedation which can occur post-operatively in neurosurgery. In the study by Vallapu et al., the sedation scores were found to be lower than 3 for all patients given dexmedetomidine, indicating arousable on verbal stimulus.[12] In the study by Swami et al., 80% patients in dexmedetomidine group had grade IV block (no supplementary sedation or analgesia) versus 40% in clonidine group. This indicated that probably dexmedetomidine may have better effect on sedation during surgery.[8]

Analgesic requirement was overall higher in the clonidine group in our study, indicating better analgesia with Dexmedetomidine. The study by Swami et al. found that the duration of analgesia was significantly higher in the dexmedetomidine group ($p<0.05$) indicating better analgesia versus clonidine group.[8] Another study by Tripathi et al. also found that duration of analgesia was significantly higher in the dexmedetomidine group ($p<0.05$) versus clonidine.[10] In the study by Kumar et al., 16% of patients in the bupivacaine-only group required rescue analgesia while none of patients in the dexmedetomidine + bupivacaine group needed rescue analgesia.[11]In the study by Ganesh et al., the maximum time to rescue was noted in dexmedetomidine group versus clonidine group, and this was again a significant finding.[16]

These findings in other studies show that dexmedetomidine has better post-operative analgesic effect in comparison to clonidine.

There were a few limitations in present study. The sample size in the study was limited and it was conducted in only one study center. Future studies done with a larger sample size and done at multiple centers may help in validating our findings. Another limitation was that we did not compare the duration of motor blockade or sensory regression features of study groups. These parameters may be explored in future similar studies.

Conclusion:-

Dexmedetomidine was found to lead to lesserelevation in vascular parameters in patients undergoing scalp block in supratentorial craniotomy procedures, in comparison to clonidine. The sedation scores were comparable between dexmedetomidine and clonidine groups, but overall additional analgesia requirement was higher with clonidine.

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