Attenuation of Haemodynamic Response to Placement of Mayfield Skull Pin Head Holder - Comparison of Dexmedetomidine Versus Propofol Infusion - A Randomized Interventional Trial Done in a Tertiary Centre in Central Kerala

Sruthy Unni[1], Ranju Sebastian[2], Elizabeth Joseph[3], Remani Kelan Kamalakshi[4], Jamsheena Muthira Parambath[5]

[1, 2, 3, 4, 5] Department of Anaesthesiology, Government Medical College, Thrissur, Kerala, India.

ABSTRACT

BACKGROUND

Anaesthesia for neurosurgery requires special considerations. The brain is enclosed in a rigid cranium, so the rise in intracranial pressure (ICP) which impairs cerebral perfusion pressure (CPP), results in irrepairable damage to various vital areas in the brain. Stable head position is required in long neurosurgical procedures. This is obtained with the use of clamps which fix the head rigidly. This is done usually under general anaesthesia because it produces intense painful stimuli leading to stimulation of sympathetic nervous system which in turn causes release of vasoconstrictive agents. This can impair perfusion in all organ systems. The increase in blood pressure due to sympathetic nervous system causes increase in blood flow. This causes increases in intracranial pressure which result in reduction in cerebral perfusion pressure once the auto regulatory limits are exceeded. We compared the effects of dexmedetomidine 1 µgm/kg and propofol 100 µgm/kg given as infusion over a period of 10 minutes before the induction of anaesthesia and continued till 5 minutes after pinning to attenuate the stress response while cranial pinning. In this study, we wanted to compare the effects of dexmedetomidine and propofol as infusion to attenuate the stress response while cranial pinning in patients undergoing neurosurgical procedures.

METHODS

This is a randomized interventional trial. Patients were divided into 2 groups of 20 each. Group 1 receiving dexmedetomidine and group 2 receiving propofol, both drugs given as infusion. Haemodynamic variables were monitored before and after cranial pinning. Data was analysed using IBM statistical package for social sciences (SPSS) statistics. The parameters recorded were analysed with the help of a statistician.

RESULTS

The two groups were comparable in demographic data. Incidence of tachycardia between group 1 and 2 showed that tachycardia to pinning was better controlled with propofol than dexmedetomidine ($P < 0.05$) which is statistically significant. There is no statistically significant difference in blood pressure values between group 1 and 2 after pinning.

CONCLUSIONS

From our study, we came to a conclusion that propofol was superior to dexmedetomidine in attenuating the heart rate response to cranial pinning. The effect of propofol and dexmedetomidine was comparable in attenuating the blood pressure response to cranial pinning.

KEYWORDS

Cranial Pinning, Dexmedetomidine, Propofol

Corresponding Author:
Dr. Ranju Sebastian,
Assistant Professor,
Department of Anaesthesiology,
Government Medical College,
Thrissur, Kerala, India.
E-mail: drranjusebastian@gmail.com

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BACKGROUND

During neurosurgery, anaesthesiologist must maintain adequate anaesthetic depth and haemodynamic stability. Physiologic effects controlled by anaesthesiologists have profound effect on surgical outcome in neurosurgery. Even anxiety in vulnerable patients result in sympathetic stimulation which may lead to adverse cardiac events in the perioperative period. Rigid head fixation during neurosurgical procedure is attained with the use of Mayfield skull pin head holder/clamp. The application of cranial pins produces an intense painful stimulus which leads to severe haemodynamic responses.

The stress responses to surgical stimulus should be attenuated to obtain good post-operative recovery. Stress is the disturbance in the physiological and psychological homeostasis which is mediated by hypothalamopituitaryaxis (HPA) leading to secretion of various hormones from adrenal cortex and medulla. Adrenal cortex release corticosteroids and adrenal medulla release catecholamines.

HPA axis stimulation also result in norepinephrine secretion from presynaptic nerve terminals. Maximum concentration of corticosteroid receptors in the brain is in the hippocampus and so the stress has effects on learning and memory process. Although the monitoring of heart rate and blood pressure is not specific as a measure of autonomic activity, we usually use these parameters for assessing sympathetic activity.

The increase in mean arterial pressure (MAP) increases the cerebral blood flow and cerebeal blood volume which results in increase in intracranial pressure. The increase in intracranial pressure leads to reduction in cerebral perfusion pressure which is deleterious to the patients undergoing neurosurgical procedures who have poor intracranial compliance. So, the maintenance of haemodynamics is essential during pinning to prevent further deterioration of the clinical condition. The attenuation of sympathetic nervous system activity is important in neurosurgical patients.

Different techniques can be used for attaining stable haemodynamic conditions during neuroanesthesia. This can be achieved with various methods, use of α-2 agonists such as clonidine and dexmedetomidine, local anaesthetic infiltration at pin site, scalp blocks, opioids, beta blockers, sub-anaesthetic dose of ketamine and deepening of general anaesthesia.

Aim

To determine which one among the two drugs (dexmedetomidine and propofol) is more effective in attenuating heart rate and blood pressure response while cranial pinning.

Objective

To compare the effects of dexmedetomidine and propofol as infusion to attenuate the stress response while cranial pinning in patients undergoing neurosurgical procedures.

METHODS

This study was conducted as a randomized interventional trial in the Department of Anaesthesiology, Government Medical College, Thrissur after obtaining approval from hospital ethics committee and written informed consent from patients. The study was conducted from January 2016 to December 2016. Study subjects were patients belonging to American Society of Anaesthesiologists (ASA) physical status I and II in the age group of 18 – 65 years scheduled for elective procedures with Glasgow coma scale 15/15 who need cranial pinning. Patients were allocated into two groups - Group 1 and Group 2 of 20 each by random sequence generation using hospital inpatient numbers. Group 1 received dexmedetomidine and group 2 propofol as infusion. Exclusion criteria includes patient refusal, heart block, allergy to dexmedetomidine or propofol, pre-operative heart rate less than 50 beats per minutes, patients on beta blockers, coronary artery disease, hypertension, LV dysfunction, intracranial aneurysm and pregnancy. All patients in the study group had their pre-anaesthetic check up and a written informed consent was taken from all patients in their local language. All patients were kept nil per oral 8 hours prior to surgery. Tab alprazolam 0.25 mg was given the night before surgery. On arrival in the operating room, electrocardiogram (ECG), non-invasive blood pressure (NIBP), pulse oximeter were attached and basic parameters like heart rate, NIBP and SPO2 were noted. An 18-gauge intravenous cannula was inserted in the forearm and 0.9 % normal saline was started. Dexmeditomidine 1 µgm/kg and propofol 100 µgm/kg were given as infusion over a period of 10 minutes before the induction of anaesthesia and it is continued till 5 minutes after pinning in group 1 and 2 respectively. All received inj midazolam 0.02 mg/kg, inj glycopyrrolate 0.01 mg/kg, inj fentanyl 1 µgm/kg and inj ondansetron 0.08 mg/kg. Preoxygenated with 100 % oxygen for 3 minutes. Thiopentone sodium 5 mg/kg was used as induction agent. 3 minutes after giving vecuronium 0.1 mg/kg intubated with appropriately sized cuffed oral endotracheal tube. Mintainance of anaesthesia was done with nitrous oxide and oxygen 2 : 1 and isoflurane as inhalational agent. End tidal CO2 was monitored during the entire procedure. Scalp pins were applied after intubation. Heart rate and blood pressure were monitored continuously with multipara monitor. Parameters recorded were heart rate and blood pressure. Baseline values before induction of anaesthesia, before intubation, 3 minutes after intubation, before pinning, 0, 1, 2, 3, 4, 5, 6 minutes after pinning. The variations in parameters were monitored and compared between group 1 and 2. The muscle relaxation is maintained with inj vecuronium 0.04 mg/kg with neuromuscular monitoring. After surgery, patients were electively ventilated and reversed after full recovery from muscle relaxants as evidenced by neuromuscular monitoring in post anaesthesia care unit. The patients were monitored 24 hours in the post anaesthesia care unit. The parameters recorded were analysed with the help of a statistician. *t* test and chi square test were used to analyse the data.

Statistical Analysis

Normally distributed data were analysed using *t* test and categorical data was analysed using chi square test. Continuous data are presented as mean and standard deviation, where as categorical data are presented as number of patients. P < 0.05 was considered statistically significant.

RESULTS

The results obtained from both the groups of patients (1 and 2) were recorded and entered in Excel. Normally distributed data were analysed using *t* test and categorical data were analysed using chi square test. Continuous data are presented as mean and standard deviation, where as categorical data are presented as number of patients. P < 0.05 was considered statistically significant.

Groups	Age (Years)	Weight (Kilogram)	Sex (M / F)
Dexmedetomidine	51.85	59.3 + 11	10 / 10
Propofol	49.40	62.7 + 11.14	11 / 9
P - value	0.681		

Table 1. Distribution of Age, Weight and Sex between the Groups

The age, mean weight and sex of the patients were comparable between the 2 groups.

Heart Rate	Group 1	Group 2	P Value
Baseline	90.45	91.32	0.901
1 minute before intubation	78.5	74.45	0.825
3 minutes after intubation	78.45	75.85	0.807
Before pinning	78.05	72.60	0.028
After pinning P0	79	71.15	0.021
P1	76.65	70.35	0.056
P2	77.42	70.25	0.088
P3	75.50	70.05	0.184
P4	73.80	69.20	0.029
P5	73.45	68.90	0.069
P6	69.17	70.80	0.899

Table 2. Changes in Heart Rates between Group 1 and 2

Changes in heart rate between group 1 and 2 were comparable. As evidenced by the above table, heart rate response was better controlled with propofol than dexmedetomidine.

	Group 1		Group 2		
Time	Mean	S. D	Mean	S. D	P value
Baseline	103.07	9.772	107.68	11.068	0.847
1 min before intubation	74.90	11.841	75.70	8.073	0.279
3 min after intubation	88.45	9.825	88.10	7.376	0.314
Before pinning	83.57	8.216	86.32	7.459	0.447
After pinning P0	85.28	7.363	84.35	6.867	0.311
P1	85.88	7.555	83.17	6.720	0.406
P2	85.13	8.303	82.90	7.399	0.185
P3	84.6	5.958	81.75	5.865	0.761
P4	84.48	8.192	81.92	4.734	0.319
P5	84.12	5.05	82.48	5.245	0.911
P6	74.95	26.44	78.62	19.205	0.288

Table 3. Changes in Blood Pressure between Group 1 and 2

The baseline mean arterial pressure was 103.07 in group 1 and 107.68 in group 2. There was 27.33 % decrease in baseline MAP in group 1 and 29.26 % in group 2 prior to intubation. Intubation produced modest increase in MAP in both groups. After pinning MAP values were comparable between both groups (P > 0.05).

DISCUSSION

Microneurosurgery involves working with small incision and vital structures. So, the head should be fixed in the desired position. Usually the Mayfield pin head holder is used. The Mayfield frame has three pins to be inserted. Fixing the head in neurosurgery allow the surgeon to do their work with comfort. Skull pins are inserted up to the outer table of the cranium from skin. Cranial pinning is associated with intense painful stimulus which leads to adverse haemodynamic effects. The stimulus is so intense to produce severe hypertension and tachycardia which may even result in rupture of untreated cerebral aneurysm. Usually this painful stimulus produces tachycardia but sometimes the increase in ICP causes mechanical distortion of vagal nerve resulting in bradycardia. The increase in ICP leads to cerebral herniation in patient with abnormal intracranial compliance. These haemodynamic effects also precipitate acute cardiovascular events. So, the attenuation of haemodynamic response is essential during skull pin fixation. The depth of anaesthesia and analgesia should be supplemented during pinning without much haemodynamic effects.[1,2,3,4]

Dexmedetomidine an alpha 2 receptor agonist has greater alpha 2 : alpha 1 receptor affinity. It has no direct action on gamma amino-butyric acid (GABA) receptors. Alpha 2 receptors are located in supraspinal and spinal sites. These receptors are placed pre and post synaptically. Dexmeditomidine is a highly protein bound drug with high volume of distribution. It is metabolised in liver by glucuronidation and cytochrome P450 mediated metabolism. So, the dose should be adjusted in patients with hepatic insufficiency.

Dexmeditomidine has significant analgesic qualities in addition to its sedative and anxiolytic effect and has the added advantage of lack of respiratory depression. Sedation and anxiolysis by its action on alpha 2 receptors in the locus coeruleus. Inhibition of ascending norepinephrine pathways also contribute to sedation. Analgesic action by its effect on presynaptic alpha 2 receptors which inhibit the release of norepinephrine and thus the propagation of pain signals are terminated. Peripheral alpha2 adrenoreceptors also have the ability to mediate antinociception. It blunts the stress response and establish more natural sleep like state.[5] It preserve arousability. Post synaptic activation of alpha 2 adrenoceptors in the central nervous system inhibits sympathetic activity and thus can decrease blood pressure and heart rate. Activation of alpha2 receptors in the CNS attenuate the neuroendocrine and haemodynamic response to noxious stimuli. Activation of alpha2 receptors causes reduction in cyclic AMP by inhibiting adenylate cyclase which in turn result in hyperpolarisation due to efflux of potassium, thus neuronal firing is suppressed. It also supresses the calcium entry in to nerve terminal, thus release of neurotransmitters is also inhibited. In this way, both firing and propagation of signals are inhibited. As an analgesic, it has a unique advantage in neurosurgery because it helps in reduction of opioid use, the respiratory depression caused by opioids result in raise in ICP which is of detrimental effect in patients with poor intracranial compliance.

Along with direct analgesic effect, it potentiates the analgesic effect of opioids. The hypnotic effect of dexmedetomidine is mediated by the hyperpolarisation of the noradrenergic neurons in the locus coeruleus. Global and focal cerebral ischaemic events can be attenuated by the use of alpha 2 adrenoceptor agonists. Catecholamines can exacerbate neuronal injury by increase in the sensitivity to neurotransmitter such as glutamate. Increased neuronal activity leads to expression of catabolic enzymes and possibly cell death due to excessive excitation. Increased catecholamine metabolism could increase free radical formation. Increased sympathetic activity may reduce perfusion in the ischaemic penumbra.[6,7,8]

The alpha 2 receptors in the cerebral blood vessels when stimulated can decrease cerebral blood volume by vasoconstriction and thus result in reduction in ICP. The decrease in blood pressure is due to sympatholytic activity and the reduction in heart rate by augmenting cardiac vagal activity. Attractive features of dexmedetomidine are the short terminal half life of 2 hour and absence of respiratory depression.

Rapid infusion of dexmedetomidine causes hypertension due to the direct stimulation of alpha2 receptors in the peripheral vasculature. The central sympatholytic effect is partially antagonised by this effect so help in maintaining haemodynamic stability. It also produces sinus arrest in young individuals with high vagal tone. Because of these effects the bolus dose should be given slowly as infusion in 10 minutes. The effect on electrophysiological properties is modest. The haemodynamic control obtained with dexmedetomidine helps in reducing the use of antihypertensive drugs used intra-operatively. Compared to propofol there is minimal amnesia and more analgesia but the duration of sedation is more with dexmedetomidine on stopping the infusion.

The hypnotic effect of propofol is potentiated by dexmedetomidine reducing the dose of propofol used up to 50 %. The emergence delirium in children after the sevoflurane anaesthesia and the delirium in elderly patients after benzodiazepine use are better eliminated with the use of dexmedetomidine. Hypothalamopituitaryadrenal axis hyper responsiveness is attributed to post-operative delirium which is produced in response to acute stress. Perioperative use of dexmedetomidine cause reduction in the level of serum cortisol. So, it can decrease the occurrence and it also delay the onset of delirium. In intensive care unit (ICU) patients, it shortened the duration of delirium. In neonates with intracranial haemorrhage and cerebral ischaemia, dexmedetomidine is found to have neuroprotective effects. But further researches are needed to prove its perioperative neuroprotective effects. The intra-operative haemodynamic stability attained with dexmedetomidine can be extended to post-operative period. The heart rate and blood pressure in the post-operative period influence the outcome in high risk patients undergoing major neurosurgical procedures. Prolonged use can result in withdrawal symptoms which include nausea, vomiting and hypertension. In our study dexmedetomidine attenuated the haemodynamic response to skull pin insertion similar to the study by Ankita Batra, Reetu Verma and Shashi Bhushan.[9,10]

Propofol is included in group of alkylphenol with hypnotic effects. It has rapid onset due to high lipophilicity and rapid redistribution into the central nervous system and short duration of action. Propofol is found to have anti-oxidative and neuroprotective effects. The neuroprotective effect by decreasing cerebral metabolic rate.[11] Propofol has immumomodulating effect there by decreasing the systemic inflammatory response which is attributed to organ disfunction. Propofol has an analgesic effect and blunt response to painful stimuli if given in sufficient amount.[12] There is well documented effect of propofol on sympathoadrenal system. The surgical stress induced elevation of cortisol is not prevented by induction dose of propofol. The analgesic action is through mechanisms linked to both central hypnotic effects and direct peripheral analgesic action.[13,14,15]

Effects to anticipate after propofol administration include a decrease in heart rate and blood pressure. Direct effect on smooth muscle is lacking. So, hypotension produced by its sympatholytic effect is not antagonized. The mechanism of action is not clear but propofol seems to stimulate GABA receptors, block N-methyl-D-aspartate (NMDA) receptors and diminish Ca^{2+} influx via slow Na^{+} channel.[16] Anxiolytic dose of propofol is much smaller than the dose needed for sedation. Propofol reduces cerebral blood flow and cerebral metabolic rate. It has the added advantage on the preservation of autoregulation and vascular reactivity.

In experimental studies, propofol is shown to protect brain from ischemic injury due to its antioxidant, anti-inflammatory properties and its ICP reducing effect. Ethylene diamine tetraacetic acid (EDTA) in the propofol formulation is a chelator of bivalent ions like calcium, magnesium and zinc. EDTA has been reported to exert neuroprotective effect by chelating excess intracerebral zinc in ischemic model. The effects to anticipate after propofol administration include a reduction in heart rate and blood pressure. Due to its short context sensitive half life the action is terminated within 10 minutes of stopping the infusion. So, the neurological examination can be done immediately after surgery after the use of propofol.[16]

Propofol infusion seems to have better attenuation of heart rate response to pin insertion. The MAP variations were comparable between group 1 and group 2.

CONCLUSIONS

We compared the effects of propofol and dexmedetomidine infusion while cranial pinning in attenuating stress response. We came to a conclusion that propofol is superior to dexmedetomidine in attenuating the heart rate response and the effects of two drugs were comparable in attenuating the blood pressure response to cranial pinning.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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