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EFFECT OF DEXMEDETOMIDINE ON EMERGENCE FORM NEUROANAESTHESIA IN PATIENTS UNDERGOING SUPRATENTORIAL CRANIOTOMY

ANAESTHESIOLOGY

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ABSTRACT

Background: The dexmedetomidine is a highly selective α-2 adrenoreceptor agonist and frequently used as an adjuvant to anesthesia for perioperative hemodynamic stability. We have contemplated to study haemodynamic stability and the emergence response at the time of extubating in patients undergoing supratentorial tumour surgery.

Methods: Fifty ASA grades I/II patients, aged 14-65 years scheduled for elective surgery were divided randomly into two equal groups (n=50). In the study group dexmedetomidine was infused at the rate of 0.5 µg/kg/hr and control group received normal saline during the study period. The study period was from the start of dural closure to the closure of skin incision. The hemodynamic changes, emergence characteristics and complications during the study period were recorded.

Results: Heart rate and mean arterial pressure were significantly lower in dexmedetomidin group as compared to control group ($p<0.05$) at the time extubation and up to 10 minutes after extubation. Blunting of tachycardia response and the hypertensive response to extubation were observed in these patients. Statistically significant ($p< 0.05$) difference is found in emergence agitation, bucking, coughing and shivering in between the two groups. The time to eye opening and time for extubation were less in study group compared to control group but not statistically significant.

Conclusions: Dexmedetomidine attenuates stress responses to various noxious stimuli at the time of extubation, maintains haemodynamic stability, and blunts tachycardia and hypertensive response. At the same time it also reduces the emergence reactions to extutbation in patients undergoing supratentorial craniotomy

KEYWORDS

Dexmedetomidine, Supratentorial tumour, Haemodynamics , Emergence reactions

INTRODUCTION

The patients undergoing supratentorial craniotomy with different pathological conditions usually will have raised intracranial pressure (ICP).Any further increase in ICP may be detrimental to the patient and it is very difficult decide clinically which patient has impaired autoregulation and compromised cerebral compliance. The haemodynamic stability is not only important in the intraoperative period but also at the time of emergence of anaesthesia. Any abrupt changes in systemic arterial pressure and cerebral blood flow (CBF) will alter the ICP. It is particularly important at the time of emergence, because the patient will be in lighter planes of anaesthesia and at the same time patient may buck and cough which are likely to increase systemic arterial pressure, CBP, and the ICP.

Many drugs are used to control emergence reactions like opioids, anaesthetics, local anaesthetics, antihypertensives and α2-adrenoreceptor agonist like Clonidine to blunt hypertensive and emergence responses in cranial surgeries at the time of extubation [1].
Although various drugs have been evaluated, management of emergence hypertension in patients undergoing cranial surgeries continues to be a challenge. In the present study we compared the effect of continuous IV infusion of dexmedetomidine on controlling emergence reactions.Dexmedetomidine is a relatively new, a highly selective central α2-adrenoreceptor agonist, is increasingly being used for its sedative, analgesic, anxiolytic, sympatholytic and haemodynamic stabilizing properties. It also provides "conscious sedation", and analgesia without respiratory depression. [2-4]
Dexmedetomidine has been shown to provide good perioperative haemodynamic stability with decreased intraoperative opioid requirements. Dexmedetomidine can inhibit the stress responses thereby improving the outcomes of tracheal intubation.[5] It may also have neural protective effects.[6] A few studies have shown that dexmedetomidine has reduced shivering and requirement of anti-emetics in the postoperative period. Thus it can be a suitable anaesthetic adjuvant to neurosurgical anaesthesia. [7]

Though, the dexmedetomidine is used widely as an adjuvant, in the perioperative period in doses ranging from 2-7 µg/kg/hr. we designed a study with 5 µg/kg/hr dose of dexmedetomidine to observe haemodynamic stability and the emergence responses at the time of extubating in patients undergoing supratentorial tumour surgery.

MATERIALAND METHODS

The study was a prospective, randomized, double blind, parallel group comparative study. The study was conducted at Nizam's institute of Medical Sciences, Hyderabad in compliance with all applicable regulations and good clinical practice guidelines. The study was approved by Institutional Ethics Committee. Written inform consents were obtained from the patients before the enrollment.

Study population:

Patients scheduled for elective supratentorial tumour surgery, with age between 14-65 years, of either gender, with American Society of Anesthesiologists (ASA) status I or II, Glasgow coma scale score of 14 to15 and with Mallampati classification of I or II were included in the study.

The patients with morbid obesity, pregnant or lactating women, preoperative heart rate of <45 beats/ min, having second or third degree AV block, history of lung, liver or kidney diseases, having hypersensitivity to dexmedetomidine, history of drug or alcohol abuse, taking anti-hypertensive medication like α-methyldopa, clonidine or other α2- adrenergic agonist, participated in other drug study during the preceding one month were excluded from the study.

Randomization procedure:

Using computer based simple randomization method patients were allocated equally to two different groups. Control group patients receive continuous intravenous infusion of normal saline at the rate of 14ml/hr while in study group dexmedetomidine was infused with dexmedetomidine 0.5 µg/kg/hr as a continuous intravenous infusion at the rate of 14ml/hr at start of dural closure until the closure of skin incision. The case conducting anesthesiologist and recording anaesthesiologist was unaware of the concentration of the drug being infused as the drug dose syringe for the infusion was filled by another anaesthesiologist after randomization.

Study procedure:

All the patients were kept fasting overnight and were premedicated with tablet ranitidine 150mg orally 12 hours prior to surgery and on the day of the surgery. In the operation theatre after connecting the patients to standard monitoring, intravenous access was secured with minimum of two large bore cannula for drug and continuous fluid administration.

Arterial switch cannula was used for invasive blood pressure monitoring. Central venous pressure was also monitored. Baseline values for heart rate and mean arterial pressure were recorded before induction.

All patients were premedicated with intravenous fentanyl 2 µg/kg and intravenous glycoprrolate 0.1 mg prior to induction. Induction of anaesthesia was done with intravenous thiopentone sodium 5-6 mg/kg titrated to the loss of eye lash reflex. Following induction, patients were ventilated with (50:50) oxygen in air mixture. Endotracheal intubation was done after administering intravenous atracurium 0.6 mg/kg. Anaesthesia was maintained with air in oxygen (60:40%) along with isoflurane 0.4 MAC (Monitored on Datex Ohmeda workstation) and neuromuscular blockade was maintained by intravenous atracurium infusion 5µg/kg/min.

Scalp block was administered to all patients with mixture of lignocaine (1%) and bupivacaine (0.25%), total volume of 20cc.

The study drug was started at of dural closure and stopped the infusion at the colure of skin incision. At the end of surgery, after eye opening or response to verbal command, the residual neuromuscular blockade was antagonized with intravenous neostigmine 0.05 mg/kg and intravenous glycopyrolate 0.01 mg/kg. The tracheal extubation was performed in all patients after meeting the regular extubation criteria. The emergence characteristics like emergence agitation, time of eye opening, time for extubation, bucking, coughing, vomiting, shivering and requirement of nitroglycerin (NTG) to control the hypertensive response were noted.

Standard monitoring was done with ECG and pulse oximeter throughout the study period. Entropy leads were applied to forehead for monitoring of depth of anaesthesia intra-operatively and was kept at 40-60.. Primary outcome was to assess the hemodymanic responses to Dexmedetomidine. The changes in mean arterial pressure (MAP) and heart rate (HR) were recorded at the start of dural closure as basal then at 2,4,6,8,10,12,14,16,18,20,22,24, and 26 minutes and after the extubation at 0,2,4,6,8,10 minutes. Secondary outcomes included the assessment of emergence characteristics and assessment of complications if occurred.

Statistical Analysis:

Using PASS software [8] the group sample sizes of 20 and 20 each total of 40 patients were to be selected to achieve 95% power (1- β) to detect a difference of 5.00 in a design with 20 repeated measurements having a compound symmetry covariance structure when the standard deviation is 5.00, the correlation between observations on the same subject is 0.70, and the alpha (α) level is 0.05. However considering the drop outs of cases during the study which can be due to haemodynamic incidents and other incidents total of 50 patients 25 in each group were studied.

Normal distribution of the data was ascertained using Shapiro-Wilk test and homogeneity of variance is tested by modified Levene equal variance test. Continuous data like hemodynamic variables was expressed as Mean with standard deviation, categorical data as frequency & percentages. Haemodynamic variables were analyzed with repeated measures of analysis of variance (repeated measures of ANOVA) followed by post hoc analysis with Tukey-kramer multiple comparison test. Chi-Square test was used for categorical data. P value of < 0.05 was considered as statistically significant. Statistical analysis was carried out using NCSS 10 software. [9]

Results:

All patients were comparable with respect to age, weight and gender ratio (p>0.05). (Table 1) Distributions of patients with supratentorial tumour were similar in both the groups. Most common tumour in all the patients was glioma 24 (48%) followed by meningioma 18 (36%), pituitary adenoma 4 (8%), neurocytoma 2(4%), and cranioph aryngioma 2(4%).

Hemodynamic parameters:

Baseline HR, and MAP measurements were comparable between the groups. HR, and MAP measurements were significantly (p <0.05) different between both the group particularly at the time of extubation and the period of the study after extubation. (Figs.1 - 2) (Tables 2-3).

Emergence characteristics: The emergence agitation was observed in 2 (8%) patients in control group and nil in study group. The bucking was reported in 5 patients (20%) of control group; and nil in patients of study group (p value =0.0003). Coughing observed in 8 patients (32%) of control group and 2(8%) patients in study group (p value =0.007).

Table 1: Demographic profile of patients.

Variable	Control	Study	p Value
Age (Yrs)	41.44 ±10.75	39.76 ±14.58	0.64
Weight (Kg)	58.04 ±10.50	56.68 ±8.90	0.62
Sex (M/F)	11/14	5/20	0.13

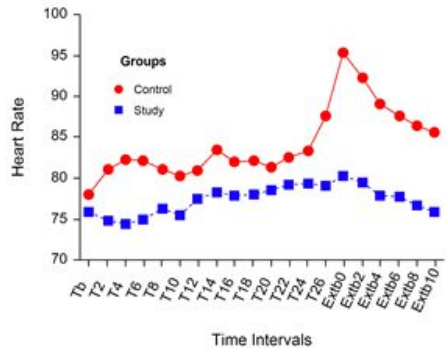

Figure 1: Means values of Heart rate at different time intervals.

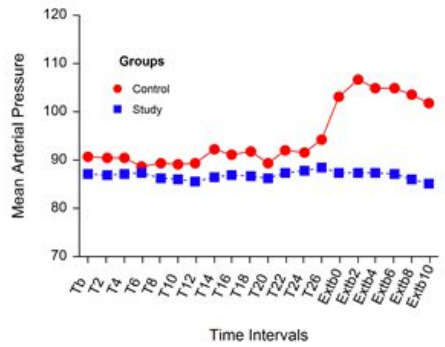

Figure 2: Means values of MAP at different time intervals.

Shivering occurred in 3 (12 %/) patients in control group and nil in study group. The NTG requirement was high in control group (56%) compared to study group (36%).Statistically significant (p <0.05) difference is found in emergence agitation, bucking, coughing, shivering in between the two groups. The time to eye opening and time for extubation were less in study group compared to control group but not statistically significant. (Table.4)

Table2: Comparison of heart rate at different time intervals.

Heart rate/min	Control	Study	p Value
Basal (Tb)	**78.36±10.03**	**75.60±11.03**	**0.99**
T2	81.48±12.37	74.52±9.44	0.054
T4	83.04±12.53	74.00±11.54	0.003
T6	82.64.±12.41	74.20±12.85	0.003
T8	82.00±14.00	73.93±11.11	0.525
T10	81.24±12.11	74.64±13.47	0.510
T12	81.96±13.32	76.52±15.07	0.974
T14	83.76±14.71	77.36±15.03	0.331
T16	82.96±13.09	77.12±15.61	0.866
T18	83.20±12.77	77.16±15.88	0.856
T20	82.28±11.57	77.68±14.59	0.992
T22	83.72±10.84	78..20±14.46	0.982
T24	84.06±10.66	78.40±15.54	0.887
T26	85.12±12.15	78.28±14.01	0.000
Extb0	91.24± 13.53	79.48±13.43	0.000
Extb2	90.88±12.93	78.56±13.25	0.000
Extb4	89.96±11.47	77.04±13.05	0.000

Extb6	88.92±11.16	76.72±13.10	0.000
Extb8	87.60±11.09	75.84±12.49	0.000
Extb10	86.88±10.00	75.04±12.91	0.000

DISCUSSION

The haemodynamic stability is very important in the patients undergoing supratentorial craniotomies, at the time of intubation and extubation. We have studied the haemodynamic response particularly the end of the

Table3: Comparison of MAP at different time intervals.

MAP	Control	Study	p Value
Basal (Tb)	90.64±6.61	87.04±9.35	0.974
T2	90.48±7.91	86.92±8.15	0.977
T4	90.78±9.64	87..08±9.92	0.985
T6	88.64.±8.50	87.24±9.76	0.983
T8	89.44±9.86	86.16±10.17	0.988
T10	89.08±8.58	85.96±9.90	0.991
T12	89.32±9.32	85.64±10.13	0.967
T14	92.24±11.70	86.36±10.41	0.146
T16	91.00±10.80	86.84±11.08	0.875
T18	91.68±9.77	86.72±12.08	0.520
T20	89.36±8.34	86.32±13.59	0.991
T22	91.96±9.74	87.32±14.46	0.683
T24	91.64±7.65	87.68±13.18	0.925
T26	94.28±8.90	88.36±11.53	0.136
Extb0	103.12± 11.77	87.36±10.91	0.00
Extb2	106.64±13.64	87.28±9.76	0.00
Extb4	104.92±12.10	87.04±9.86	0.00
Extb6	104.80±11.05	87.12±11.12	0.00
Extb8	103.48±11.70	85.96±10.61	0.00
Extb10	101.80±11.23	85.16±10.49	0.00

surgery as patients will be in lighter planes of anaesthesia and also at the time of extubation where the sympathetic response will be very high because of airway manipulation for suctioning and removal of endotracheal tube.

The emergence characteristics of anaesthesia namely the emergence agitation, time for eye opening, time for extubation and the untoward effects like bucking, coughing, shivering and vomiting were also studied.

Table 4: Comparison of emergence characteristics.

Variable	Control	Study	pValue
Time to eye opening (min) Mean ± SD	14.64 ±6.22	13.84±0.94	0.36
Time to extubation (min) Mean ± SD	19.40 ±1.12	17.84± 0.69	0.104
Bucking (Positive)	5 (20%)	Nil	0.0003
Coughing (Positive)	8 (32%)	2 (8%)	0.0071
Shivering (Positive)	3 (12%)	Nil	0.0003
NTG (Used)	14 (56%)	9 (36%)	0.715
Emergence Agitation (Positive)	2 (8%)	Nil	0.042
Vomiting	Nil	Nil	---

The dose of continuous intravenous infusion of dexmedetomidine used was ranging from 0.2-0.8 µg/kg/hr in different studies [10, 11, 12, 13, 14] However a few studies reported that the doses of 0.4 µg/kg/hr to 0.5 µg/kg/hr.[15,16] Considering these studies we have infused 0.5 µg/kg/hr.

The dexmedetomidine group showed significant hemodynamic stability compared to control group at various time intervals, particularly at the time of extubation and for a period of 10 minutes after extubation. Our results corroborated with the findings of other authors: Patel CR et al, concluded that dexmedetomidine given by infusion of 0.2–0.8 µg/kg attenuated the hemodynamic response in perioperative period.[17] Similarly, other studies concluded that dexmedetomidine by continuous infusion (0.2 and 0.4 µg/kg/hr) [18], (0.4 µg/kg/hr)[1], (0.2 and 0.4 µg/kg/hr) [6], (0.4-0.5 µg/kg/hr)[7], (0.25-0.7 µg/kg/hr) [19] improves haemodynamic stability with higher doses being more effective than the lower dose, but chances of bradycardia and hypotension will increase with higher doses.

In present study, the attenuation of haemodynamic responses to the emergence from anaesthesia at extubation and 10 minutes following extubation, were statistically significant in dexmedetomidine group compared to control group. This shows that the centrally mediated sympatholytic effect of dexmedetomidine has continued well into the postextubation period. Other studies have also shown similar blunting action. [15,20,21]

Most of the studies it is found that the time for eye opening and time for extubation was statistically less where dexmedetomidine is used, but in our study the time taken for eye opening and extubation are less in dexmedetomidine group but not statistically significant. The incidence of other emergence characteristics like emergence agitation, bucking, coughing and shivering were significantly low in study group compared to control group, which is similar to many studies published. This is possibly the centrally mediated sympatholytic effect of dexmedetomidine has blunted the emergence reactions.

CONCLUSION

Dexmedetomidine attenuates stress responses to various noxious stimuli at the time of extubation, maintains haemodynamic stability, and blunts tachycardia and hypertensive response. At the same time it also reduces the emergence reactions to extubation in patients undergoing supratentorial craniotomy.

Conflict of interest: Nil

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