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Research Article

EFFECT OF DEXMEDETOMIDINE ON ANAESTHESIA AND ANALGESIA REQUIREMENT DURING BISPECTRAL INDEX GUIDED ANAESTHESIA FOR NEUROSURGERY-A RANDOMISED CLINICAL TRIAL

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A B S T R A C T

Background- Anaesthesia for neurosurgery aims to bestow good operating conditions and to ensure stable cerebral haemodynamics without sudden increase in the acute brain swelling or intracranial pressure. Recently developed monitors for depth of anaesthesia such as Bispectral Index (BIS, Aspect Medical System, Newton, NA, USA) and Spectral Entropy (GE healthcare, Helsinki, Finland) uses the dimensionless monotonic index for the measure of depth of anaesthesia Dexmedetomidine, is the pharmacologically active of isomer of the medetomidine, and is a highly specific and selective α-2 adrenoceptor agonist. This drug provides haemodynamic stability intraoperatively when used as an adjuvant with standard general anaesthesia drugs. This is attributed to its central sympatholytic action. It has good analgesic and also anaesthetic sparing properties. **Aim-** To study the effect of dexmedetomidine on anaesthesia and analgesia requirement during Bispectral index Guided anaesthesia for neurosurgery. **Methods-** This was a Prospective, Randomised Clinical trial (Clinical trial registry of India number CTRI/2021/10/037597). After obtaining the Institutional Ethics Committee clearance and written informed consent from each patient, 60 adult patients of either sex of American Society of Anaesthesiologists (ASA) Grade I and II aged 20–60 years undergoing neurosurgery under general anaesthesia were included in this study. Group D(n=30) received dexmedetomidine as an adjuvant anaesthetic agent in premedication. Group F(n=30) received anaesthetic agents as per standard general anaesthesia protocol. The following parameters were considered during the study like Haemodynamic changes in Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure(DBP) and Mean Arterial Pressure (MAP) from baseline, after induction and after application of dexemeditomidine at different time intervals in both the groups and also the Depth of anaesthesia using bispectral index monitoring, To calculate and compare the volume of inhalational agents used, Haemodynamic parameters Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure(DBP) and Mean Arterial Pressure (MAP) in post op period and adverse effects, if any. P value <0.05 was considered to be statistically significant.
Results and Conclusion- Haemodynamic changes in Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure in the patients who were administered dexemeditomidine (0.5ug/kg given over 10mins) were in more stable lower range intraoperatively. The volume of inhalational agents used after giving dexmedetomidine was significantly lower. Haemodynamic parameters Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure in post op period was also noted to be on stable lower range as compared to baseline in the group who received dexmedetomidine.

INTRODUCTION

Anaesthesia for neurosurgery aims to bestow good operating conditions and to ensure stable cerebral haemodynamics without sudden increase in the acute brain swelling or intracranial pressure. Also, immediate post operative neurological evaluation is essential mandating rapid recovery from anaesthesia is also essential.[1]

Anaesthesia in these cases is specially defined as the equilibirium between the amount of anaesthetic drug administered and the state of arousal at the end of surgery. Inadequate depth of anaesthesia can be assessed by patient movement in response to noxious stimulation, however its reliability is questionable due to concurrent use of muscle relaxants. Tachycardia, hypertension, lacrimation and diaphoresis are subjective clinical signs of Depth of anaesthesia.

Depth of anaesthesia is a concept of hypnosis, antinociception, amnesia and reflex suppression. Minimum alveolar concentration (MAC) of inhaled anaesthetic agents guides us to achieve adequate depth of anaesthesia.

Recently developed monitors for depth of anaesthesia such as Bispectral Index (BIS, Aspect Medical System, Newton, NA, USA) and Spectral Entropy (GE healthcare, Helsinki, Finland) uses the dimensionless monotonic index for the measure of depth of anaesthesia.[2]

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Dexmedetomidine, is the pharmacologically active of isomer of the medetomidine, and is a highly specific and selective α-2 adrenoceptor agonist.

This drug provides haemodynamic stability intraoperatively when used as an adjuvant with standard general anaesthesia drugs. This is attributed to its central sympatholytic action. It has good analgesic and also anaesthetic sparing properties.[3] However the recovery profile of use of intra operatively continuous infusion of dexmedetomidine is not yet established. This study is designed to ascertain the efficacy of the dexmedetomidine as an adjuvant in anaesthesia management during neurosurgery under bispectral index guided anaesthesia.

METHODOLOGY

After obtaining the Institutional Ethics Committee clearance and written informed consent from each patient, 60 adult patients of either sex of American Society of Anaesthesiologists (ASA) Grade I and II aged 20‑60 years undergoing neurosurgery under general anaesthesia were included in this study. Patients not willing to be a part of the study, on pain perception modifying drugs, with cardiac co-morbidities were excluded from the study. This was a Prospective, Randomised Clinical trial (Clinical trial registry of India number CTRI/2021/10/037597).

By keeping the significance level of 0.05, power of study 80% the sample size was calculated by Winpepi statistical software (version 11.65). The calculation of sample size was based on a recent clinical trial by Chakrabarti *et al*[4] in 2019.Entering mean and standard deviation values of this study in the WINPEPI software the calculated sample size was 56 (28 in each group). But, considering dropout rate and for effective study, we have chosen sample size as 30 per group, making total sample size as 60.

They were given their respective drug according to a computer generated random number allocation. The drug preparation was done by an anaesthesiologist who was not involved in administration of anaesthesia and patient care. Data collection and analysis was done by separate anaesthetist who was not involved in drug administration.

Group D(n=30) received dexmedetomidine as an adjuvant anaesthetic agent in premedication. Group F(n=30) received anaesthetic agents as per standard general anaesthesia protocol. The following parameters were considered during the study like Haemodynamic changes in Heart Rate (HR), Systolic Blood Pressure (SBP) , Diastolic Blood Pressure(DBP) and Mean Arterial Pressure (MAP) from baseline, after induction and after application of dexemeditomidine at different time intervals in both the groups and also the Depth of anaesthesia using bispectral index monitoring, To calculate and compare the volume of inhalational agents used, Haemodynamic parameters Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure(DBP) and Mean Arterial Pressure (MAP) in post op period and adverse effects, if any.

In the operation theatre, all monitors such as pulse oximeter, non invasive blood pressure (NIBP), ECG were attached and baseline SBP, DBP, MAP, HR, SPO2 and EtCO2 were recorded.
IV line was secured with 20 G intra cath, IV fluids RL started.
BIS monitoring Strip was attached on patient's forehead or on temporal area based on available area as per the surgery. Baseline BIS monitor value was noted.

Then patients were pre-medicated with Inj Glycopyrolate 0.2mg and Inj. Midazolam 1mg I.V., Inj Fentanyl 2mcg/kg given slowly three mins prior to the induction.

Inj. Dexmedetomidine 0.5ug/kg given over 10mins as an adjuvant in the Group D after premedication.

Induction was done with standard care of general anaesthesia without use of any adjuvant drug in the Group F.

Preoxygenation was done with 100% oxygen for 3 mins before induction in both groups. All patients were induced with Propofol 2 mg/kg IV, followed by Inj. Vecuonium bromide 0.1mg/kg IV given after confirming whether patient is able to get ventilated. After an interval of 3mins, when neuromuscular block is achieved, laryngoscopy and intubation was performed by an experienced anaesthesiologist using an appropriate Macintosh blade and endotracheal tube. Inj. Vecuonium then given as top ups as when required.

All hemodynamic measurements HR, SBP, DBP, MAP and BIS value was noted at baseline, after premedication and after induction at 3 mins, 5 mins, 10 mins, 15 mins, 1 hour and 2 hours interval. Further the patient was maintained on O_2 /Air / Sevoflurane and Vecuronium top ups as and when required, and patients vitals were monitored continuously intra operatively.

Sevoflurane concentration was adjusted to maintain BIS in the range of 40-60. Duration of surgery noted. EtCO2 was maintained between 30-40mmHg At the end of surgery, volume of inhalational agent(sevoflurane) used was calculated by:-

Ehrenworth and Eisenkraft formula-
3 x Fresh Gas flow(FGF) (L/min) x volume% = mL liquid used per hour In the event that SBP fell below 90 mm Hg, or 30% from the baseline, 3 mg of mephentermine was administered IV as a rescue measure.

At end of the surgery, after the return of spontaneous efforts of respiration, suctioning was done, patient is reversed with Inj.Glycopyrrolate 0.4mg I.V , Inj.Neostigmine 2.5mg I.V.

Patient was extubated and shifted to recovery room for observation after recording the postoperative vitals.

Patient was followed up in PACU for monitoring of post operative vitals (HR, SBP, DBP and MAP at 15 and 30 mins interval) and any adverse reaction.

Statistical Data Analysis

All the cases were completed in stipulated time. Data was collected, compiled and tabulated. Data of different parameters was summarised using arithmetic mean and standard deviation. The comparison of quantitative data was done using test of significance based on student 'T'-test. Unpaired T-test for intergroup & paired T-test for within the group comparisons. Qualitative parameters were analysed by chi-square test.

The P value of 0.05 was considered significant.

The statistical analysis was done using SPSS Version 20.0

RESULTS

The demographic parameters between both the groups showed comparable characteristics with P value of non significant difference. (Table 1) The baseline values of PR, SBP, DBP,

MAP and BIS values among two groups showed non significant difference (P value>0.05).

We found that there was a significant difference in PR, SBP, DBP and MAP after induction and at all time intervals thereafter when the values were found to be lower in the Group D and the difference in value from Group F was statistically significant (p <0.05).(Figure 1-4) Sevoflurane concentration was adjusted to maintain the BIS value between 40-60. The value of BIS at baseline and after premedication showed non significant difference between both the groups (P value>0.05). Statistically significant difference was found in BIS value after induction and thereafter when the values were lower in Group D (p<0.05). (Figure5)

There was significant difference in the volume of inhalational agent used in both the group with P value of <0.001 and less volume was used in Group D. The mean volume used in study group was 37.8 ml and in control group was 80.9 ml. (Figure 6) There was significant difference at 15mins interval in post operative vitals, with values lower in Group D and P value was <0.05. (Figure 7). There was no difference in the value of PR and SBP post operatively at 30 mins. There was significant difference in DBP and MAP at 30 mins interval, with values lower in Group D.

On comparing post operative vitals with baseline in Group D, post operative vitals were on lower and stable side as compared to baseline in the Group D. (Table 2)

In Group F, there was no significant difference in PR at 15 mins interval. At 30 mins, there was significant difference in PR with value lower at baseline. There was no difference in the value of DBP and MAP at 15min and 30 mins interval post operatively with P value of 0.679, 0.327, 0.452 and 0.351 respectively. All values were almost equal to baseline value. (Table 3)

Table 1 Demographic characteristics comparison of the Group D and Group F

Demographic characteristics	Group D		Group F		P value	Interference
	n	%	n	%		
Mean (SD) age	40.3	12.57	40.96	12.79	0.8363	Non significant difference
Male	17	56.7	19	63.3	0.792	Non significant difference
Female	13	43.3	11	36.7		
Weight	57.60	7.295	54.27	5.477	0.062	Non significant difference
Height	155.08	4.17	155.06	4.00	0.98	Non significant difference
Duration of surgery	122.10	33.51	124.00	39.62	0.8418	Non significant difference

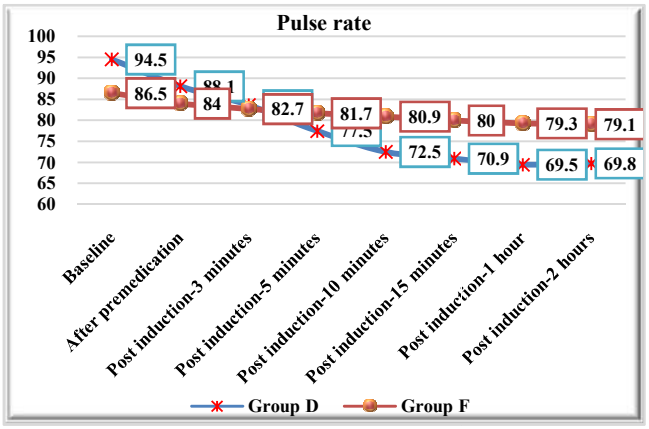

Figure 1 Line diagram showing comparison of pulse rate between two groups

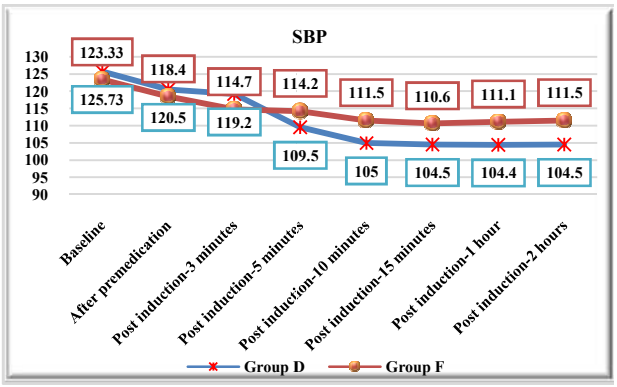

Figure 2 Line diagram showing comparison of SBP between two groups

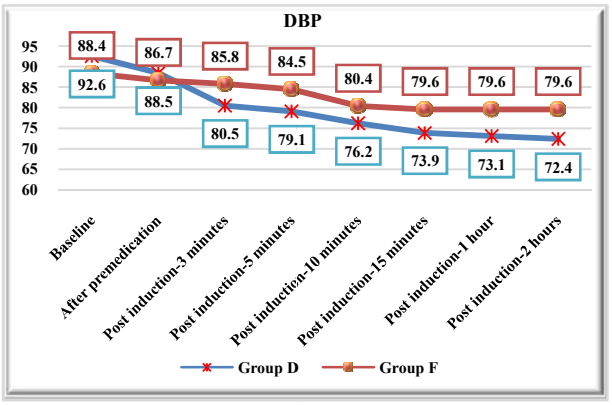

Figure 3 Line diagram showing comparison of DBP between two groups

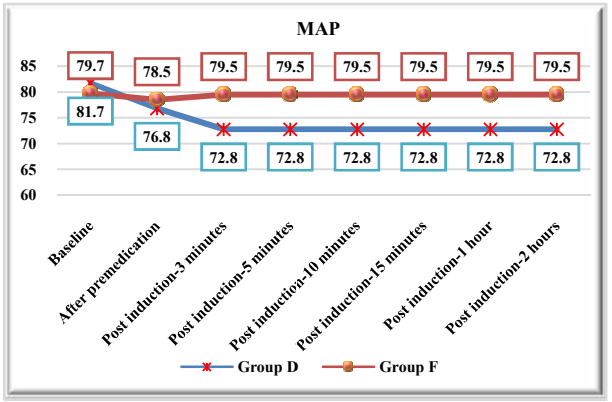

Figure 4 Line diagram showing comparison of MAP between two groups

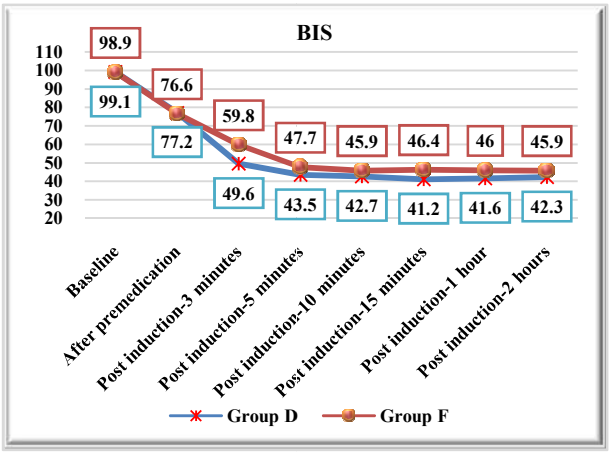

Figure 5 Line diagram showing intra operative BIS values in both the groups

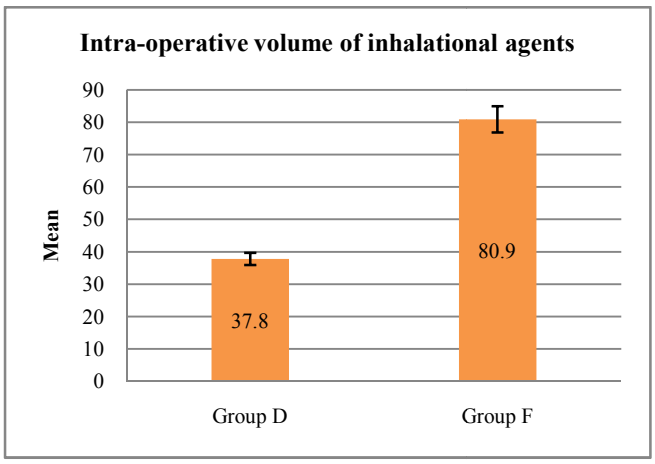

Figure 6 Bar diagram comparing volume of inhalational agents used intraoperatively in Group D and Group F.

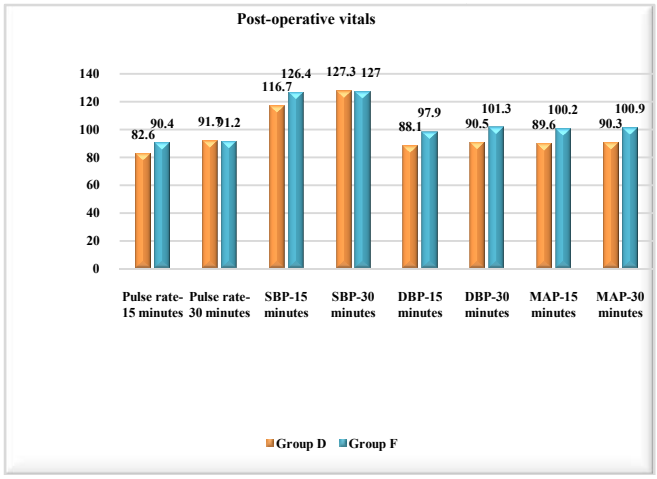

Figure 7 Bar diagram comparing the post operative vitals (PR, SBP, DBP, MAP) in Group D and Group F

Table 2 Comparison of post-operative vitals with baseline in the Group D

Parameter	Baseline		15 minutes		30 minutes		Baseline vs 15 mins	Baseline vs 30 mins
	Mean	SD	Mean	SD	Mean	SD	P value	P value
Pulse rate	94.5	19.3	88.6	19.2	90.7	24.7	<0.001	0.02
SBP	129.7	14.1	116.7	24	120.3	12.7	0.002	0.004
DBP	94.7	7.1	80.2	15.4	84.9	15.6	0.003	0.004
MAP	110.6	16.5	97.9	14.3	102.3	16.1	0.028	0.003

Table 3 Comparison of post-operative vitals with baseline in the Group F

Parameter	Baseline		15 minutes		30 minutes		Baseline vs 15 mins	Baseline vs 30 mins
	Mean	SD	Mean	SD	Mean	SD	P value	P value
Pulse rate	86.5	18.6	87.4	14.7	91.2	15.4	0.439	<0.001
SBP	119.7	9.6	124.4	8	127	8.9	<0.001	<0.001
DBP	84.7	12.6	88.1	10.8	90.5	11.3	0.679	0.327
MAP	103.1	126.5	89.6	11.1	90.3	11.2	0.452	0.351

DISCUSSION

Maintenance of adequate depth of anaesthesia throughout the intraoperative period is vital to prevent intraoperative awareness, to maintain haemodynamic stability and to reduce intraoperative stress response during neurosurgery.

Dexmedetomidine, a novel alpha-2 agonist with multifaceted beneficial actions such as sedative analgesic and anxiolytic properties, has been found to reduce anaesthetic drug requirements in the intraoperative period.[5] Its sympatholytic effect had shown to decrease MAP and HR by reducing norepinephrine release. They had also shown to decrease BIS value in the intraoperative period when used as an adjuvant with other drugs.[6]

Few of recently done studies have found definite role of dexmedetomidine in reducing dose requirement of other drugs for maintaining stable hamodynamics and for maintenance of anaesthesia.

Cattleya Thongrong *et al*,[7] also observed that after giving the infusion of dexmedetomidiene there was a progressive decrease in HR, but intraoperative HR remained within 20% of baseline.

Sukhminder Jit Singh Bajwa *et al*,[8] stated that cause of lower heart rate with dexmedetomidine is due to its sympatholytic properties.

Fatemeh Javaherforooshzadeh *et al*,[9] used dexmedetomidine infusion in dose of 0.3 - 0.7 µg/kg/hour and found that from the first to 60th minute, heart rate, MAP, SBP, and DBP gradually decreased and then increased after extubation.

Tarek Shams *et al*,[10] in 2013 studied Induced hypotension for functional endoscopic sinus surgery for comapring dexmedetomidine versus esmolol. In their study they state that if dexmedetomidine infusion has been started 10 mins prior to surgery in dose of 1mcg/kg/hr there is significant decrease in MAP and mean heart rate throughtout the surgery.

Ramila H Jamaliya *et al*,[11] found that when dexmedetomidine was used, MAP decreased from baseline values, and remain low throughout the surgery and at the time of extubation it increased.

The lower values of Bispectral index in the study group can be due to sedation effect of the dexmedetomidine and also better control haemodynamics and analgesia.

Reshma B. Muniyappa *et al*,[12] had similar findings as our study and they found that preanesthetic single loading dose of dexmedetomidine will reduce the dose of inhalational anesthetics to achieve BIS between the range of 45–60.

Hye Won Shin *et al*,[13] also had similar findings as our study and stated that preanesthetic dexmedetomidine given as 1 µg/kg single infusion can be a simple, easy, and also economical adjuvant for general anesthesia. They found that end-tidal concentration and total cumulative consumption of sevoflurane were lower when dexmedetomidne was used.

During the period of recovery from anesthesia, patient often complains of pain, elevating catecholamine concentrations. Also during this time there can be compromised breathing because of residual effects of anesthesia. Alpha 2-adrenoceptor agonists have proven to be beneficial during the postoperative period because of their sympatholytic and analgesic effects but do not cause any respiratory depression. Also all effects of dexmedetomidine can be antagonized by administering the alpha 2-adrenoceptor antagonist called as atipamezole [14]

Awakening and recovery time were similar in both the groups. We did not observe any significant side effects in the form of bradycardia, hypotension, nausea or vomiting.

Limitations of the Study

Cost-effective analysis of the study was not conducted. Our findings cannot be extrapolated in patients with hypertension, Ischaemic heart disease or any other cardiac disease.

CONCLUSION

Effect of dexmedetomidine on anaesthesia and analgesia requirement during bispectral index guided anaesthesia for neurosurgery is very favourable. Haemodynamic changes in Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure in the patients who were administered dexemeditomidine (0.5ug/kg given over 10mins) were in more stable lower range intraoperatively.

The volume of inhalational agents used after giving dexmedetomidine was significantly lower.

Haemodynamic parameters Heart Rate, Systolic Blood Pressure , Diastolic Blood Pressure and Mean Arterial Pressure in post op period was also noted to be on stable lower range as compared to baseline in the group who received dexmedetomidine.

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