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EFFECT OF DEXMEDETOMIDINE ON BLEEDING DURING ENDOSCOPIC NASAL SURGERY: A DOUBLE BLIND, RANDOMIZED, CLINICAL STUDY

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ABSTRACT

Background and Aims: In Functional Endoscopic Sinus Surgery (FESS), hypotensive anaesthesia is becoming increasingly popular now a days. This study evaluated the effect of Dexmedetomidine in minimising surgical blood loss, on intraoperative haemodynamics as well as its effect on reducing isoflurane requirement during FESS. **Material and Methods:** in this study 48 patients undergoing FESS were divided into two groups. Group C / Control Group (n=24) received bolus of 100 ml normal saline over 10 mins followed by placebo infusion @ 0.2 mcg/kg/hr whereas Group D / Dexmedetomidine Group (n=24) received dexmedetomidine as a loading dose of 1mcg/kg over 10 min followed by maintenance infusion of 0.2 mcg/kg/hr. The Primary outcome measure was to see the efficacy of dexmedetomidine in providing bloodless surgical field in terms of bleeding score whereas secondary outcome measures were its effect on haemodynamic variables as well as reduction in dose requirements of isoflurane. The qualitative data was presented as number (Proportion) and compared with Chi square test. Quantitative variables were expressed as mean +/- standard deviation and were compared using students 'f' test. The statistical analysis of data was performed with MS Excel, SPSS 16.0. **Results:** The mean bleeding score was significantly lower in dexmedetomidine group as compared to control group(0.47 +/- 0.5 v/s 1.02 +/- 0.51 , $P < 0.05$). The MAP were statistically comparable intraoperatively in both the groups whereas heart rate decreased significantly in group D ($p < 0.05$) from 30 to 120 mins intraoperatively. The mean overall requirement of isoflurane concentration (vol %) was significantly lower in Group D as compared to Group C (0.43 +/ - 0.19 v/s 0.92 +/- 0.23, P= 0.004). **Conclusion:** Controlled hypotension with Dexmedetomidine provided a bloodless surgical field for Endoscopic Sinus Surgeries as well as provide optimal intraoperative hemodynamics. It also reduced the requirement of isoflurane to produce controlled hypotension resulting in lesser sedation, faster recovery and discharge from post anaesthesia care unit.

KEYWORDS: Endoscopic Sinus Surgery, Dexmedetomidine, Controlled Hypotension, Bleeding Score.

INTRODUCTION

Hypotensive anaesthesia is gaining popularity nowadays. This carries even more significance in endoscopic sinus surgeries (ESS), which are performed in tiny surgical fields.[1] Even minor bleeding often interferes with the optimal visualization of the tiny intranasal field, which not only hinders the operation but also increases the incidence of complications.[2,3]

Controlled (deliberate/induced) hypotension is a technique wherein the arterial blood pressure is lowered in a deliberate but controllable manner to minimize surgical blood loss and enhance the operative field visibility.[4,5,19] However, deliberate hypotension is not without potential complications, including delayed awakening, cerebral thrombosis, brain ischemia, permanent cerebral damage and death.

Various drugs have been used successfully to produce deliberate hypotension, including volatile anaesthetics, direct acting vasodilators, autonomic ganglion-blockers, β-adrenergic receptor blockers, combined α- and β-adrenergic receptor blockers, calcium channel-blocking drugs and prostaglandin E_1.[6] But majority of these drugs have some drawbacks, which limit their application.

Ideally, hypotensive agents should be easy to administer, have rapid onset, have effects that disappear quickly when administration is discontinued, have negligible effects on vital organs and have predictable and dose dependent effects.[7]

Dexmedetomidine is a potent, highly selective α_2-adrenoceptor agonist with a α_2:α_1 activity ratio of 1620:1. Activation of CNS postsynaptic α_2- receptors leads to inhibition of sympathetic activity, which decreases blood

pressure and heart rate.[8,9] Dexmedetomidine has additional properties like anxiolysis, sedation, hemodynamic stability, anti-shivering effects and decreased nausea & vomiting.

Moreover dexmedetomidine not only reduces anesthetic requirements, it also induces anaesthesia by itself.[10,11]

Hence we undertook this study to evaluate role of dexmedetomidine in controlled hypotension, its effect on bleeding as well as reducing the anesthetic requirement of isoflurane in endoscopic nasal surgeries.

MATERIAL AND METHODS

A prospective, randomized, double blind study was undertaken after approval from institutional ethics committee. Informed consent was taken from all the 48 patients included in the study. Inclusion criteria considered were patient with ASA grade I-II, 18-60 years of age and scheduled for elective endoscopic nasal surgery. The Exclusion criteria included patients with uncontrolled hypertension, coronary artery disease, heavy smokers, major hepatic or renal disease, bleeding disorders and patient on antiarrhythmic or anticoagulation therapy.

Subjects were randomized using computer generated random numbers into two groups. Control group/Group C (n= 24) received a bolus of 100 ml saline (Placebo) over 10 mins followed by placebo infusion @ rate of 0.2 µg/kg/hr. While Dexmedetomidine group/group D (n=24) received 200µg (2 ml) dexmedetomidine, diluted with 100 ml normal saline to a final concentration of 2µg/ml and received an infusion of 1 µg/kg as loading dose over 10 min followed by maintenance infusion of 0.2 µg/kg/hr. The drugs were prepared by a separate anesthesiologist who was blinded to the patient's group assignment and the study data was recorded by another blinded anesthesiologist. Surgeons and patients were also blinded to the hypotensive agents used.

The night before the surgery tab alprazolam 0.5 mg was given to the patients. Half an hour before surgery nasal packing was done by the surgeon with cotton pledgets soaked with 30 ml of 4% lignocaine and 3 ampoules of adrenaline. Patient's vitals monitoring included pulse oximetry, ECG and NIBP. The patients were premedicated with intravenous midazolam 0.02 mg kg^{-1}, Glycopyrolate 0.01 mg kg^{-1}, Ondansetron 0.01 mg kg^{-1}. Anaesthesia was induced with injection thiopentone 5 mg kg^{-1}, fentanyl 2 µg kg^{-1} & succinylcholine 1.5 mg kg^{-1} & intubated with cuffed oral endotracheal tube of appropriate size. The patients were ventilated with 50% O2:N2O mixture and isoflurane 1% to maintain ETCO2 within normal range of 30-35 mm of Hg. Intravenous atracurium was used for maintenance of muscle relaxation. Deliberate hypotension was maintained by titration of isoflurane up to 1.5% to maintain mean arterial pressure (MAP) up to target limit (65-75 mm Hg).[12] Concentration of isoflurane was recorded in volume % every 10 minutes. Where the target MAP was not achieved after 10 mins of maximum isoflurane concentration (1.5%), titrated nitroglycerine was administered to a maximum of 1 µg/kg/min and the amount of nitroglycerine administered was noted. Study drug/placebo infusion was continued in both groups at rate of 0.2 µg/kg/hr.

A local vasoconstrictor was not used to control the bleeding any time during the surgery. Infusion of the study drugs was stopped 5 minutes before the anticipated end of surgery and isoflurane was discontinued on nasal packing. At the end of the surgery neuromuscular blockade was reversed with neostigmine 0.05 mg kg^{-1} and glycopyrrolate 0.008 mg kg^{-1}.

Patients who developed severe hypotension (MAP<60 mmHg) were managed by discontinuation of the hypotensive agent and reducing the concentration of isoflurane. If the MAP did not improve, 6 mg bolus of inj. mephentermine was given & these patients were excluded from the study. Patients developing bradycardia (<50bpm) were managed with intravenous atropine and were then excluded from the study.

Bleeding during surgery was assessed every 10 minutes by the surgeon on a four point scale [Intraoperative Bleeding Score]. Bleeding score 0 denote no bleeding (excellent surgical conditions). While 1 is for minimum bleeding (sporadic suction), 2 for diffuse bleeding (repeated suction) and 3 for considerable bleeding (continuous suction). Score of 0 to 1 was considered acceptable for good surgical conditions whereas Score of 2 to 3 was considered unacceptable.
The statistical analysis of data was performed with MS Excel, SPSS 16.0. Qualitative or categorical data was presented as number (proportion) and compared with chi square test. Quantitative or continuous variables was expressed as mean±SD and compared using student 't' test. P<0.05 was considered as statistically significant.

RESULTS

In our study both study and control groups were comparable demographically and there was no significant difference in terms of age, sex & body weight (Table 1).

Both the groups had comparable preoperative hemodynamics as well as the duration of surgery in both groups was statistically comparable.

Mean arterial pressure in group C was 74.83±5.88 as compared to 73.67±6.74 in group D. Changes in mean arterial pressure in both groups were also statistically comparable (P>0.05) at different time intervals intraoperatively (Fig. 1).

Intraoperative changes in heart rate were comparable for both the groups during initial 20 mins of surgery although heart rate decreased significantly in group D

(P<0.05) as compared to Group S from 30 min to 120 mins. Maximum fall in HR in group D was 19.43% from baseline (Fig. 2).

In dexmedetomidine group mean bleeding score was 0.47±0.5, which was lower than control group (1.02±0.57). Mean bleeding score in dexmedetomidine group were significantly lower (P<0.05) for the first 80 min of surgery as compared to group C (Fig. 3). Although bleeding score remained lower in dexmedetomidine group even after 80 mins but it could not reach statistical significance (P>0.05).

There was a significantly lower requirement of isoflurane (vol%) from 20 mins to 90 mins time interval in group D as compared to group S (P<0.05). Also, the mean overall requirement of isoflurane concentration (vol%) was significantly higher in group S(0.92±0.23) as compared to group D(0.43±0.19), (P=0.004). (Fig. 4).

Table 1: ***Demographic Profile***

Criteria	Group C	Group D	P Value
Mean Age	35.08±12.26	40.38±11.52	0.130
Sex Ratio (M:F)	12:12	14:10	0.297
Mean weight (Kg)	62.79±7.18	65.33±7.88	0.249

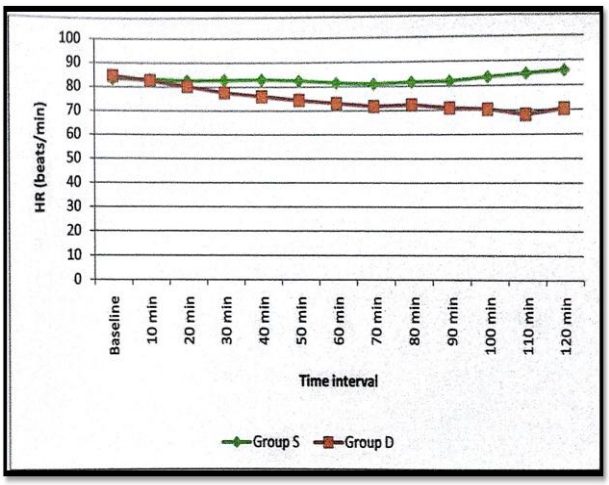

Figure 1: ***Comparison of Mean Arterial Pressure (MAP) during intraoperative period (mmHg)***

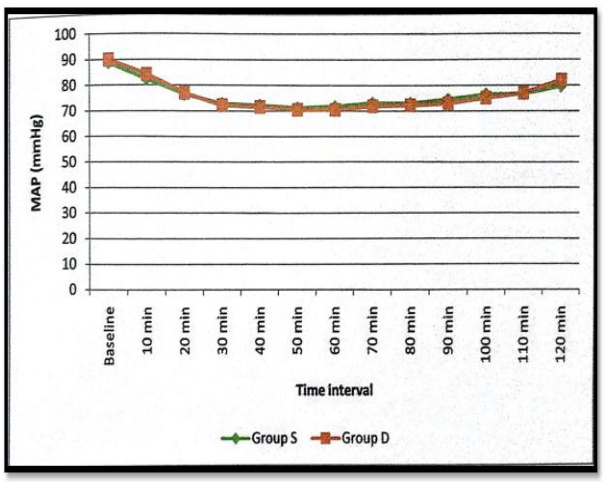

Figure 2: ***Comparison of Heart Rate (HR) during intraoperative period (beats/min)***

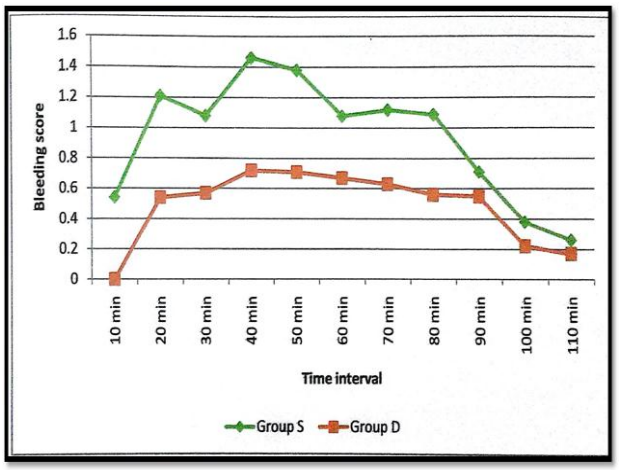

Figure 3: ***Comparison of Mean Bleeding Score during intraoperative period (0-3)***

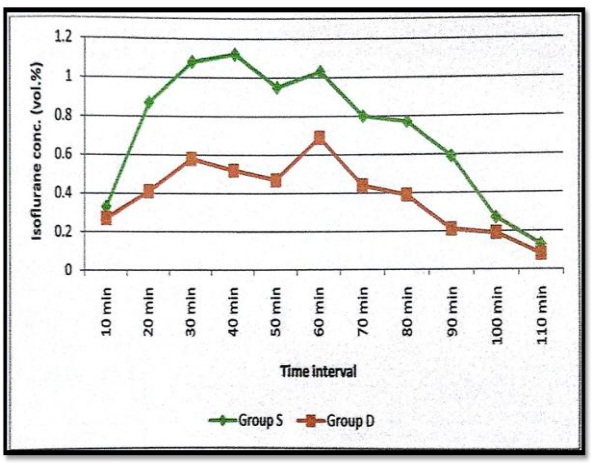

Figure 4: ***Comparison of Isoflurane Concentration used during intraoperative period (Vol %)***

DISCUSSION

FESS can be performed both under local anaesthesia or general anaesthesia. General anaesthesia is often preferred over topical anaesthesia because of discomfort

and incomplete block associated with the later.[13] Controlled hypotensive general anaesthesia is preferred to minimize blood loss and improve visualization of surgical field.

The Primary outcome measured in the study was to see efficacy of dexmedetomidine in providing bloodless surgical field in terms of bleeding score whereas secondary outcome measured were to see effect on hemodynamic variables like mean arterial pressure and heart rate as well as reduction in dose requirements of isoflurane in maintaining adequate depth of anesthesia.

This study demonstrated that mean intraoperative bleeding scores were significantly lower in the group D as compared to the group C ($P<0.05$) for the first 80 min of surgery. The mean bleeding score was less in group D even for the remainder of the intraoperative period but the difference could not reach statistical significance($P>0.05$). The authors observed that Dexmedetomidine intraoperatively reduces bleeding, gives better operative field and increased surgeon's satisfaction probably in relation to haemodynamic stability. Durmus et al(2007)[15] also showed that perioperative administration of dexmedetomidine provided significant lower intraoperative bleeding scores($P<0.001$) throughout the study period.

The target MAP was achieved in both the groups throughout the intraoperative period with isoflurane only and none of the patients required nitroglycerine intravenously. At all time intervals there was no statistically significant difference in intraoperative MAP between the two groups. A study done by Dikmen et al (2010)[14] also found similar results although time taken to achieve target MAP was higher in saline(30 min) as compared to dexmedetomidine group(5 min).

The mean HR in group D was significantly lower than group S after 30 mins of surgery and remained so for the rest of the surgery. The overall mean value of HR intraoperatively was 74.17±4.61 in group D which was significantly lower compared to 82.43±4.84 in group S($P<0.05$).

Durmus et al(2007)[19] while comparing dexmedetomidine (loading dose of 1 µg kg^{-1} over 10 min followed by maintenance infusion of 0.5µg $kg^{-1}hr^{-1}$) with placebo on bleeding during tympanpoplasty in their study also found that HR was significantly lower in the dexmedetomidine group as compared to saline group throughout the study period.

In the present study, it was demonstrated that isoflurane concentration(vol%) to achieve the target MAP(65-75 mmHg) was significantly lower($P<0.05$) for most of the intraoperative period in group D as compared to group S. Also, the mean overall isoflurane concentration(vol%) was significantly higher in group S(0.92±0.23) as compared to group D(0.43±0.19), ($P=0.004$) resulting in faster recovery and early discharge from post anesthesia care unit.

Aantaa et al(1997)[15] studied effect of dexmedetomidine (loading dose of 1 µg kg^{-1} over 10 min followed by maintenance infusion of 0.2-0.7µg $kg^{-1}hr^{-1}$) on minimum alveolar concentration of isoflurane during anaesthesia. They observed that clinically relevant doses of dexmedetomidine induced a dose dependent and significant reduction of isoflurane MAC in persons having gynecological surgery ($P<0.05$).

Dexmedetomidine, an imidazole compound, is the most selective central α-2 adrenoceptor agonist available clinically. It causes a dose dependent decrease in blood pressure and heart rate associated with decreased concentration of plasma norepinephrine.[16,17] Because dexmedetomidine was found to reduce HR and MAP, it was thought that it could be a beneficial agent for controlled hypotension. It was useful because it did not cause reflex tachycardia and it blocked the sympathetic system.[18]

In this study only (8.33%) patients developed hypotension (MAP <65 mm Hg) in group D as compared to none in group S, but the finding did not reach statistical significance. Single dose (6mg) ephedrine was enough to treat the hypotensive episode.

The present study was carried out in patients who were normotensive, not having hypertension or coronary artery disease. Hence our findings cannot be extrapolated in patients with hypertension and coronary artery disease.

The other limitations of our study was the lack of availability of neuromuscular and Bispecteral Index (BIS) monitoring in our institute. Hence we had to rely on hemodynamic parameters to ensure adequate depth of anaesthesia.

CONCLUSION

Controlled hypotension with dexmedetomidine provided a better bloodless surgical field for endoscopic sinus surgeries and enhanced operative field visibility thus improving surgeon's satisfaction compared to control group as it had lower bleeding scores as well as optimal hemodynamics.

Dexmedetomidine also reduced requirement of isoflurane to produce controlled hypotension hence resulting in lesser postoperative sedation, faster recovery and quicker discharge from postanaesthesia care unit.

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