Comparison Between Two Different Regimens of Dexmedetomidine in Functional Endoscopic Sinus Surgery: A Prospective, Randomized Double Blind Study

Saurav A. Das[1],MBBS, Anjuri Goyal[1],MD, Udita Naithani[1],MD, Siddharth Khatri[1],MBBS, Ansika Yadav[1],MBBS, Monika Gupta[1*],MD

Abstract

Background: Dexmedetomidine is a useful adjunct to anesthesia to provide controlled hypotension and minimize bleeding during functional endoscopic sinus surgery (FESS). This study was aimed to compare efficacy of two different regimens of dexmedetomidine to induce hypotension and improvement in surgical field visualization in FESS.

Methods: Sixty patients aged 18-65 years undergoing FESS in general anesthesia were randomized into two groups destined to receive preinduction i.v. dexmedetomidine 1mcg/kg over 10 min bolus dose alone (group B) or bolus followed by infusion at 0.5mcg/kg/hr (group BI). Target MAP (65-75mmHg) was achieved by increasing isoflurane. Hemodynamic parameters, isoflurane inspired volume%, Frommes' bleeding score, Alderte score and side effects were recorded.

Results: Mean Frommes' bleeding score was significantly less in Group BI (1.97±0.72) as compared to Group B (2.47±0.68), ($p=0.01$) showing significantly better surgical field conditions in group BI. Isoflurane requirement and mean heart rate were significantly less in Group BI as compared to Group B, ($p<0.05$). Mean time to achieve Aldrete score ≥9 was significantly longer in group BI (15.60±1.45 min) than in group B (13.20±1.35 min) though the difference of 3 min did not make any clinical significance.

Conclusion: Administration of dexmedetomidine as pre-induction bolus dose 1mcg/kg intravenously followed by continuous infusion 0.5mcg/kg/hr was found to be superior regimen as compared to only bolus dose during FESS, as it provided controlled hypotension in a more effective manner with reduced need of isoflurane and improved visualization of surgical field without delaying the recovery or producing any significant side effects.

Keywords: Dexmedetomidine, FESS, controlled hypotension, isoflurane requirement

---

[1] Department of Anesthesia, RNT Medical college, Udaipur, India

***Mailing address of the corresponding author**

Monika Gupta, MD, Assistant professor, Department of Anesthesia, RNT Medical college, Udaipur, Rajasthan, India. Mailing address: 17/717, chopasani housing board, Jodhpur, Rajasthan, India, Pin-342008. Telephone number: +918949510998, Email address: moniks111@gmail.com

Introduction

Functional endoscopic sinus surgery (FESS) is a minimally invasive technique in which manipulation of nasal and parasanal sinuses is done using an endoscope to restore sinus ventilation and function. Good visibility during FESS is of paramount importance because of rich blood supply in sinuses, and endoscopic manipulation can result in excessive bleeding compromising clarity of surgical field.[1]

Induced hypotensive anesthesthetic technique is advantageous in FESS as it reduces bleeding during surgery, improves surgical field visualization, leading to reduction in blood transfusion rates, duration of surgery and complications. For achieving controlled hypotension several agents have been tried such as nitroglycerine,[2] beta blockers,[2,3] magnesium sulfate,[4] and high dose of inhaled anesthetics[5] with variable outcome.

Dexmedetomidine a potent and highly selective alpha2 adrenergic agonist with a differential affinity for the alpha2:alpha1 receptors in a ratio 1620:1 is increasingly being used as an adjunct to anesthesia. By specifically activating alpha2 adreno receptors, dexmedetomidine causes decrease in sympathetic tone, reducing peripheral arterial resistance, lowering the blood pressure and heart rate effectively. By producing sedation and analgesia, it has anesthetic sparing effect also.[6]

Dexmedetomidine has been found effective in FESS for providing induced hypotension and bloodless surgical field when either administered as bolus dose alone[7] or bolus followed by infusion.[3,4,8] But to compare the efficacy of these two regimens of dexmedetomidine, there are not enough clinical studies available.[9]

Therefore, the aim of the present study is to compare dexmedetomidine administration as a single bolus dose (1mcg/kg over 10min) or bolus followed by infusion (0.5mcg/kg/hr) for controlled hypotension during FESS under general anesthesia to determine the effect on quality of surgical field as primary objective; secondary objectives of the study were changes in hemodynamic parameters, anesthetic requirement, recovery profile and side effects.

Material and methods

This study was approved by the institutional ethics committee (No.RNT/Stat./IEC/2019/830) andwritten informed consent forms were obtained from all patients prior to participation in the study. This randomized, prospective, double blind, comparative clinical study was carried out in the Department of Anesthesia in ENT operation theatre at a tertiary care centre from 1st January 2019 to 31st March 2020 and was registered under Clinical Trials Registry- India (CTRI/2019/12/022375). Sample size was calculated on the basis of previous study by Rahman A et al (2014)[9] in which Frommes' bleeding score was 2.4±0.4 in group Dex-P (dexmedetomidine 1mcg/kg bolus over 10 min before induction followed by saline infusion) and 1.4±0.3 in group Dex-0.8 (dexmedetomidine 1mcg/kg bolus over 10 min before induction followed by 0.8mcg/kg/hr infusion). Based on the above study and to detect similar reduction in bleeding score with power of 90% with an alpha error of 0.05, 5 patients were needed in each group. Since this sample size is very small for a biomedical study and based on central lim-

it theorem, we decided to include 30 patients in each group.

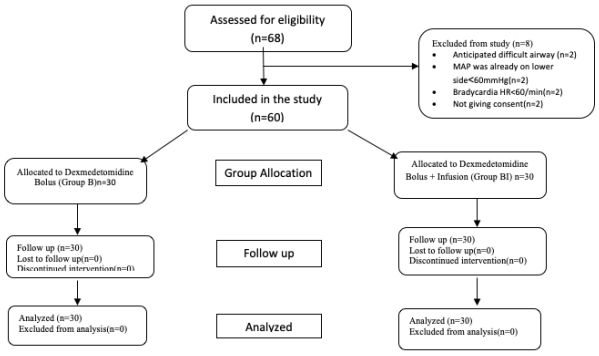
Sixty patients aged 18-65 years, ASA I/II, undergoing FESS under general anesthesia were included in the study. Patients with ASA III and higher, history of cardiovascular disease, hypertension, heart block, pregnancy, body mass index >35kg/m^2, chronic obstructive pulmonary disease, hepatobiliary diseases, renal diseases, endocrine diseases, cerebrovascular diseases, coagulopathies, drug addiction, allergy to study drug, patient refusalwere excluded from the study.

Selected patients were randomized into two groups of 30 each using computer generated random number table and sealed envelope technique as Group B(Bolus only) and Group BI(Bolus+Infusion) depending on dexmedetomidine regimens.

Dexmedetomidine used in the study was Inj-Dextomid* 1 ml ampoule containing dexmedetomidine hydrochloride 100 mcg/ml, Neon Laboratories, India. Bolus dose of dexmedetomidine was given in both groups as 1mcg/kg over 10 min before induction using a syringe pump. For maintenance, patients in Group BI patients received dexmedetomidine infusion at 0.5mcg/kg/hr while patients in Group B received normal saline infusion at 0.1 ml/kg/hr. To ensure double blindness, drugs were prepared by one anesthesiologist as per group allocation who was not involved further in the study. A secondanesthesiologist who administered the drugs and recorded datawas unaware of groups allocation. The patients and surgeons were also unaware of group allocation. Consort flow chart (phases of progress of the clinical trial) is shown in Figure 1.

After fasting for 8 hours, patients were taken

Figure 1. Consort flow chart



into the operation theatre (OT) and two peripherali.v. cannula 20G were insertedin the upper limbs (one for injection of the study drug and another for i.v. fluids) and preloading with injection Ringer lactate 500ml was done. A multiparameter monitor including noninvasive blood pressure (NIBP), pulse oximetry (SpO_2), electrocardiogram (ECG), end tidal carbondioxide (ETCO2) and bispectral index (BIS) and neuromuscular (NMT) monitoring was attached to all patients and baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2) were recorded. Bolus doses of dexmedetomidine (1mcg/kg) were given by syringe pumps in patients in both groups. Then patients were premedicated with injective glycopyrrolate 0.2mg, ondansetron 4mg, midazolam 1mg and fentanyl 2mcg/kg intravenously and induced using injective propofol (2mg/kg) and vecuronium 0.1mg/kg intravenously. After ventilating the patient with 100% O_2 for 3min, patients were intubated with Portex cuffed endotracheal tube of appropriate size when (TOF) count showed disappearance of T1 (0/4). Intra-operative anesthesia was maintained with intermittent doses of 1mg

vecuroniumevery 20-30min guided with TOF count aiming to keep it as 1/4, inspired isoflurane 0.2-1.5 volume%, 60%N_2O in 40% O_2 and intermittent positive pressure ventilation using closed circuit targeting $EtCO_2$ of 30-35 mm Hg. Maintenance infusion was started at 0.1ml/kg/hr as per group allocation and continued till 15min before anticipated closure. Inspired Isoflurane volume% was varied in order to achieve bi-spectral index (BIS) of 40-60 and further increasedif required to achieve a target mean arterial pressure (MAP) of 65-75 mm Hg and was tapered gradually till closure. Intraoperative fluid and blood were given as needed. Reversal of residual neuromuscular blockade was done using injective neostigmine 0.05mg/kg and injective glycopyrrolate 0.4mg intravenously when the TOF count is 2/4. Patients were extubated whenconscious, following verbal command, with adequate tidal volume and muscle powerand then were shifted to postanesthetic care unit (PACU). Surgery was carried out by same surgical team using standard protocol and after the end of surgery, the surgeon was asked regarding Frommes' Bleeding Score[10] (0-5) to assess surgical field condition as: 0= No bleeding, 1= Very mild bleeding that may be considered dry, 2=Mild bleeding with occasional suctioning that does not threaten the surgical field, 3= Moderate bleeding requiring frequent suctioning that affects the surgical field, 4= Excessive bleeding which destroys the surgical field directly after suctioning but can be controlled, 5= Severe bleeding that cannot be controlled which affects the surgical field such that surgery is not possible.

Hemodynamic variables (systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, heart rate, and arterial oxygen saturation (SpO_2) were recorded upon arriving to operation theatre (Baseline), at 5min and 10min, during bolus injection of study drug, after premedication (before induction), at 0min, 5min, 10min, 15min after intubation, then every 15min till extubation. Isoflurane requirement was noted by inspired isoflurane volume%, immediately after intubation then at every 5 min till 15 min, thereafter every 15 min till end of surgery. Any intra-operative and post-operative complications that occurred were noted and treated accordingly. Hypotension was defined as fall in MAP >25% from baseline or MAP <60mmHg and was treated by stopping dexmedetomidine infusion, giving fluid and injective mephentermine 6mg. Bradycardia was defined as fall in HR >25% from baseline or HR<55 per min and was treated by stopping dexmedetomidine infusion and injective atropine 0.6mg. Duration of surgery and duration of anesthesia were also noted.

After extubation, sedation was assessed using Ricker Sedation Agitation Score (SAS)[11] 1-7 as : **7 =** Dangerous Agitation: Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side-to-side, 6=Very Agitated: Requiring restraint and frequent verbal reminding of limits, biting ETT, 5= Agitated: Anxious or physically agitated, calms to verbal instructions, 4= Calm and Cooperative: Calm, easily arousable, follows commands, 3= Sedated: Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again, 2= Very Sedated: Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously, 1=Unarousable: Minimal or no

response to noxious stimuli, does not communicate or follow commands. After extubation when Ricker SAS was 3 or more, patients were shifted to PACU from OT.
In PACU, Aldrete[12]score (0-10) was recorded every 15 min and time to achieve 9 or more was noted which was the criteria to shift patient from PACU to the ward, and study was declared completed.

Statistical analysis

Data were entered and analyzed using MS (Microsoft) Excel and SPSS (Statistical Package of Social Sciences) version 16. Initially the uniform distribution of data was investigated using Skewness and Kurtosis test. Categorical (qualitative) data were presented as number (percentage) and compared using chi-square test. Continuous variables (quantitative) were presented as Mean±SD and compared using student't'test. Ordinal data were presented as Median (Interquartile Range) and compared with Mann Whitney U test. $p<0.05$ was considered as statistically significant.

Results

Bothgroups were statistically comparable regarding age, weight,gender distribution and mean duration of anesthesia. However, mean duration of surgery was significantly shorter in group BIas compared to group B(Table1).

Table 1. Demographic data and duration of surgery and anesthesia

Variables	Group B (n=30)	Group BI (n=30)	p-value
Age (years)	33.5±13.6	34.0±11.1	0.88
Weight (kg)	68.4±8.93	64.5±10.0	0.12
Gender (Male/ Female)	22/8	20/10	0.57
Duration of surgery (min)	128.80±4.04 (95% CI: 127.29 – 130.3)	125.50±5.38 (95% CI: 123.49-127.51)	0.005
Duration of anesthesia (min)	146.13±4.35 (95% CI 144.50-147.75)	144.23±4.82 (95% CI 142.42-146.03)	0.11

Data is presented as Mean ±SD or number/proportion as appropriate

The systolic, diastolic and mean arterial blood pressures were comparable between the two groups at all time intervals during the study and target MAP of 65-75 mm Hg was well maintained for con-

Figure 2. Comparison of changes in mean arterial blood pressure

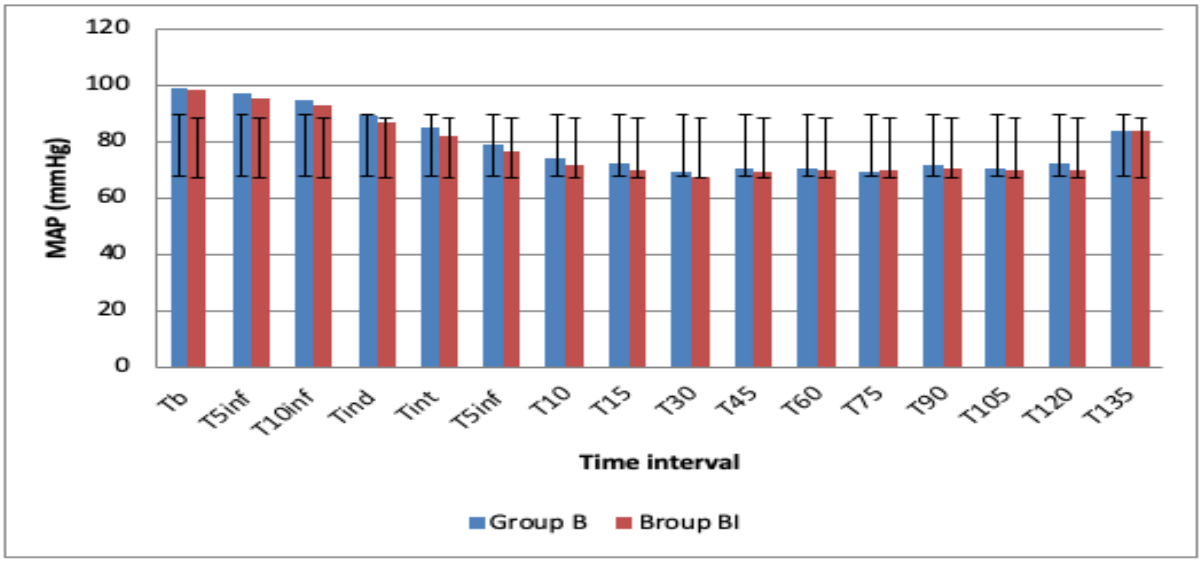


Figure 3. Comparison of Changes in Heart Rate

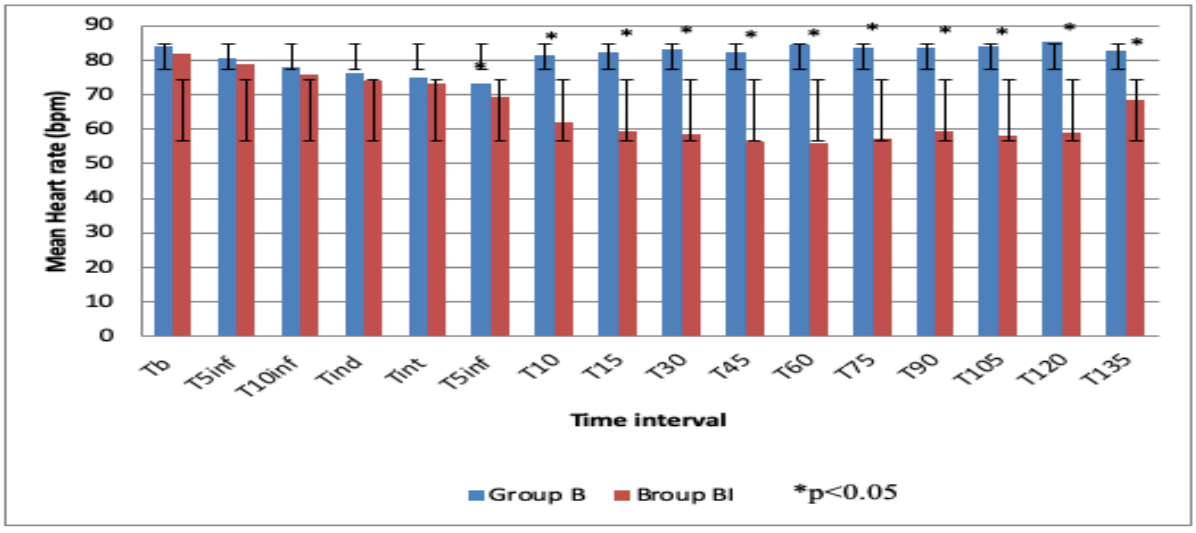
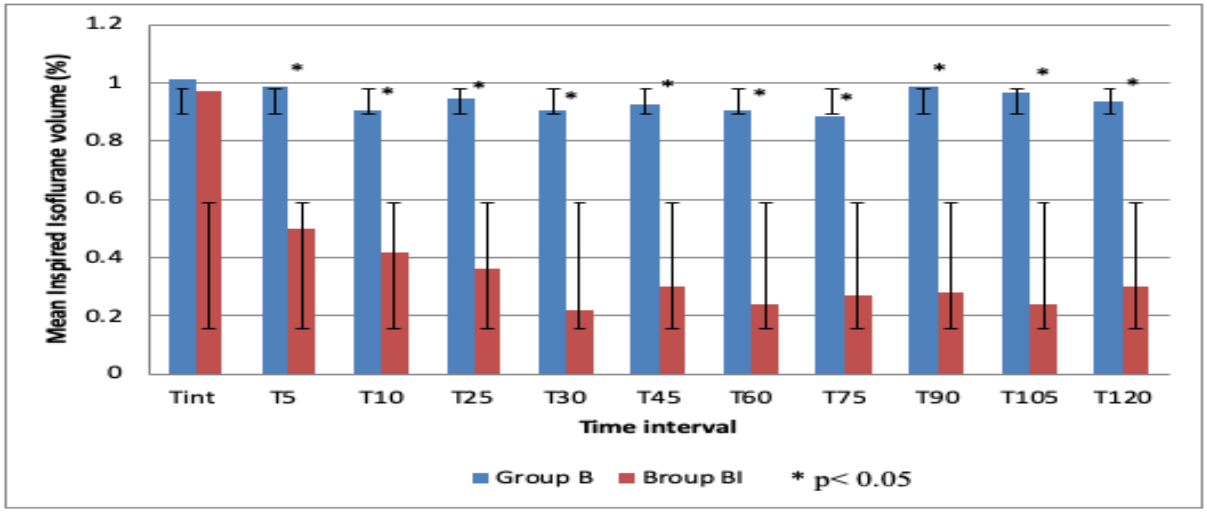


Figure 4.Comparison of changes in inspired isoflurane volume%



trolled hypotension during FESS(Fig 2).

There were no significant differences in mean heart rates from baseline till intubation in two groups (Fig. 3). Administration of dexmedetomidine bolus dose before induction was effective in attenuating the intubation pressor response in both groups as heart rates and blood pressures did not increase after laryngoscopy and intubation and remained lower than baseline upto 5 min after intubation (Fig 2 and 3).

Mean HR becomes significantly lower in group BI as compared to group B at 5min after intubation and remained significantly lower thereafter at all time intervals till the end of surgery(Fig 3).

Inspired isoflurane volume % was significantly lower in Group BI as compared to Group B at all time intervals from 5 min after intubation till the end of anesthesia, $p<0.05$ (Fig 4). Overall Inspired Isoflurane volume% was also significantly lower in Group BI [0.38 (95% CI 0.290- 0.469)] as compared to Group B [0.93(95% CI 0.594- 1.266)] indicating a 59% reduction in isoflurane requirement in group BI than in group B (Table 2).

Table 2. Comparison of Isoflurane requirement, Bleeding score, and Recovery profile in both groups

Variable	Group B (n=30)	Group BI (n=30)	p-value
Inspired isoflurane vol (%)	0.93±0.90	0.38±0.24	0.00
Frommes' bleeding score	2.47±0.68	1.97±0.72	0.01
Ricker's sedation agitation score	4.1±0.55	3.3±0.47	0.00
Time to Aldrete 9 or more(min)	13.20±1.35	15.60±1.45	0.00

Mean Frommes' bleeding score (FBS) was significantly lower in Group BI [1.97 (95% CI 1.70- 2.24)] as compared to Group B [2.47 (95% CI 2.22- 2.72) reflecting better surgical field conditions in group BI. In group B, FBS was 1 in 3 (10%), 2 in 10 (33.33%) and 3 in 17 (56.66%) of patients while in Group BI, FBS was 1 in 8 (26.66%), 2 in 15 (50%) and 3 in 7 (23.33%) of patients. Scores of 4, 5 signifying unacceptable bleeding scoreswere not found in any patient of bothgroups. None of the patients needed blood transfusion throughout the study.

Mean Rikers Sedation Agitation Score at extubation was significantly lower in group BI [3.3 (95% CI 3.12- 3.48)] as compared to group B [4.1(95% CI 3.89- 4.30)]. Scores 1,2 implicating unacceptable sedation and scores of 6, 7 implicating unacceptable agitation were not observed in any patient of both groups.

Mean time to achieve Aldrete score of 9 or more was significantly longer in Group BI [15.60 (95% CI 15.06- 16.14 min)] than in group B [13.20 (95% CI 12.69- 13.70 min)]. However, the difference was around 3min, which did not make any clinical significance in terms of recovery time to allow shifting of patient from PACU to ward (Table 2).

Only one patient (3.33%) of Group BI had bradycardia (HR<55) around 30 min after intubation for which dexmedetomidine infusion was stopped andheart rate increased back to greater than 60/min after half an hour. Dexmedetomidine infusion was started again and continued without any further bradycardia. No other side effects were observed in the study.

Discussion

In the present study, we compared two regimens of dexmedetomidine as pre induction bolus (1mcg/kg) alone in group B and bolus followed by infusion (0.5mcg/kg/hr) in group BI to provide controlled hypotension and blood less surgical field during FESS. Our target MAP was 65-75mm Hg in order to achieve desired surgical field condition without the risk of tissue hypoperfusion[13]. As we administered dexmedetomidine in fixed dose regimens in two groups, we achieved target MAP by increasing isoflurane concentrations if needed. Therefore SBP, DBP, and MAP were comparable in the two groups at all time intervals in our study showing that controlled hypotension was successfully provided in both groups. However, it was observed that there was a 59% reduction in inspired isoflurane concentration when bolus was followed by infusion. It is evidence of both hypotensive and anaesthetic sparing effect of Dexmedetomidine which is dose dependent and more pronounced when bolus dose is followed by infusion. Similar to our study Rahman et al[9] compared dexmedetomidine bolus(1mcg/kg) followed by infusion of dexmedetomidine at 0.8mcg/kg/hr(Group Dex 0.8) or placebo saline infusion(Group Dex P) in FESS. They achieved target MAP of 55-65 mmHg by Nitroglycerine infusion. They reported that all patients in Group Dex P needed Nitroglycerine as compared to none in Group Dex 0.8 showing hypotensive effect of dexmedetomidine.

The hypotensive effect of dexmedetomidine is mediated by stimulation of central alpha 2 receptors decreasing the sympathetic outflow and accentuating the cardiac vagal activity, thus resulting in reduction in HR and cardiac output contributing to hypotension.[14] In our and Rahman study[9] also, mean HR was significantly less in dexmedetomidine infusion group than in bolus group.

Sympatolytic effect of dexemedtomidine was also proven by other authors like Chiruvella et al[15] and Somayaji et al[16] who found that mean arterial pressure and heart rate were significantly lower in dexmedetomidine group as compared to control group during FESS.

Primary outcome of our study was effect of two regimens on surgical field condition as assessed by Frommes Bleeding Score(FBS). Best operative field quality in FESS surgeries by using FBS is reported as 2-3 points[17,18] which was achieved in our study in both groups but it was significantly less in group BI[median 2(1-2); mean 1.97±0.72] as compared to group B [median 3(2-3); mean 2.47±0.68], p=0.01, indicating significantly superior surgical field visualisation in Group BI. These findings were in coherence with Rahman et al[9] who also reported significantly lower FBS in Dex 0.8 infusion group (1.4±0.3) than in bolus alone group Dex-P(2.4±0.4).Lower bleeding scores have been reported in FESS with use of dexemedetomidine bolus alone (Das et al[7]) or bolus followed by infusion (Parvizi et al[8] and Somayaji

et al[16]) as compared to control group.

Dexmedetomidine produces clearer surgical field owing to its effect by decreasing MAP and heart rate. In our study and Rahman study[9] target MAP were comparable in both groups, but mean HR was significantly less in bolus with infusion groups as compared to bolus alone group. The positive effects of a decrease in heart rate on bleeding are known.[19]Significantly lower HR might have contributed to significantly less bleeding scores in infusion group and that's why duration of surgery was also significantly less in infusion groups than bolus alone groups in our study as well as in Rahman study.

The anaesthetic sparing effect of dexmedetomidine that was observed in present study as well as by others[4,20,21] is attributed to inhibition of adenylate cyclase in pontine locus ceruleus which contains high density of alpha 2 receptors resulting in changes in transmembrane ion conductance and hyperpolarization of excitable neural cells.[22]

In our study mean Mean Rikers Sedation Agitation Score at extubation was significantly less implicating more sedation in group BI as compared to group B. However, all patients had Rickers SAS of 3 or more at extubation fulfilling the criteria to shift to PACU. In our study mean time to achieve Aldrete score of 9 or more was significantly longer in group BI though the difference was around 3 min, which did not make any clinical significance in terms of recovery time to allow shifting of patient from PACU to ward.

Similarly, Rahman et al[9] observed that Ramsay sedation scores measured in the PACU were significantly higher in both infusion groups (Dex-0.8 and Dex 0.4) as compared to bolus alone(Dex-P) at all time intervals.

The sedative effects of dexmedetomidine are mediated through its action in the locus coeruleus.[23] The postoperative sedation is often desirable but may sometimes prolong the emergence time.[24] Hypotension and bradycardia are known side effects of dexmedetomidine due to its sympatholytic effect and are dose dependent.[14,22] In our study, the dose of dexmedetomidine was not very high. That could be the reason that no significant adverse effects were observed in the study.

Our study has certain limitations. We measured quality of surgical field with Frommes' bleeding score which being a subjective method may be erroneous sometimes. Also, we have not assessed amount of bleeding or change in hemoglobin levels postoperatively which could have added more value to the study.

Conclusion

We conclude that administration of dexmedetomidine as pre-induction bolus dose 1mcg/kg intravenously followed by continuous infusion 0.5mcg/kg/hr was found to be superior regimen as compared to only bolus dose during FESS as it provided controlled hypotension in a more effective manner with reduced need of isoflurane and improved visualization of surgical field without delaying the recovery or producing any significant side effects.

Conflict of Interest: None.

Funding: None.

References

1. Jacobi K, Rickauer AJ. Prophylactic analgesia in functional endoscopic sinus surgery. Hemodynamics, surgical conditions, stress response. AnasthesiolIntensivmedNotfallmedSchmerzther1999;34:278-87.
2. Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A. Controlled hypotension for functional endoscopic sinus surgery: Comparison of esmolol and nitroglycerine. Indian J Otolaryngol Head Neck Surg 2013; 65 (Suppl 2):440-4.

3. Eghbal A, Modir H, Moshiri E, Khalili M, Barsari FZ, Mohammadbeigi A. Hypotensive effect of labetalol and dexmedetomidine blood loss and surgical conditions in functional endoscopic sinus surgery: A double-blind randomized clinical trial. Formos J Surg 2018;51:98-104.
4. Chhabra A, Saini P, Sharma K, Chaudhary N, Singh A, Gupta S. Controlled hypotension for FESS: A randomised double-blinded comparison of magnesium sulphate and dexmedetomidine; Indian J Anaesth 2020;64(1): 24-30.
5. Dal D, Celiker V, Ozer E, Basgul E, Salman MA, Aypar U. Induced hypotension for tympanoplasty: A comparison of desflurane, isoflurane and sevoflurane. Eur J Anaesthesiol 2004; 21:902-6.
6. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (BaylUniv Med Cent) 2001;14(1): 13–21
7. Das A, Mukherjee A, Chhaule S, Chattopadhyay S, Halder PS, Mitra T, Basunia SR et al. Induced hypotension in ambulatory functional endoscopic sinus surgery: A comparison between dexmedetomidine and clonidine as premedication. A prospective, double-blind, and randomized study. Saudi J Anaesth 2016;10:74-80.
8. Parvizi A, Haddadi S, Habibi AF, Nemati S, Akhtar N, Ramezan H. Dexmedetomidine efficacy in quality of surgical field during endoscopic sinus surgery. Iran J Otorhinolaryngol 2019;31(5): 281-8.
9. Rahman NIA, Eman A, Fouad EA, Ahmed A, Youness AR, Wahib M. Efficacy of different dexmedetomidine regimens in producing controlled hypotensive anesthesia during functional endoscopic sinus surgery, Egypt J Anaesth 2014; 30(4):339-345, DOI: 10.1016/j.egja.2014.04.001.
10. Fromme GA, MacKenzie RA, Gould AB Jr, Lund BA, Offord KP. Controlled hypotension for orthognatic surgery. AnesthAnalg 1986; 65(6):683-6.
11. Khan BA, Guzman O, Campbell NL, Walroth T, Tricker J, Hui SL, et al. Comparison and agreement between the Richmond Agitation-Sedation Scale and the Riker Sedation-Agitation Scale in evaluating patients' eligibility for delirium assessment in the ICU. Chest 2012;142(1):48-54.
12. Aldrete JA, Kroulik D. A postanesthetic recovery score. AnaesthAnalg 1970; 49(6): 924-34.
13. Eghbal A, Modir H, Moshiri E, Khalili M, Barsari FZ, Mohammadbeigi A. Hypotensive effect of labetalol and dexmedetomidine blood loss and surgical conditions in functional endoscopic sinus surgery: A double-blind randomized clinical trial. Formos J Surg 2018;51:98-104
14. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmakokinet 2017;56(8):893-913.
15. Chiruvella S, Donthu B, Siva V, Babu D. Controlled hypotensive anesthesia with dexmedetomidine for functional endoscopic sinus surgery: A prospective randomized double blind study. Journal of Evolution of Medical and Dental Sciences 2014; 3(37):9556-63.
16. Somayaji A, Raveendra US. Effect of dexmedetomidine on blood loss and quality of surgical field in functional endoscopic sinus surgery: A double blinded prospective controlled study. Karnataka Anaesth J 2016;2:90-8.
17. Boezaart AP, Merwe J, Coetzee A. Comparison of sodium nitroprusside and esmolol induced controlled hypotension for functional endoscopic sinus surgery. Can J Anaesth 1995;42:373–6.
18. Jacobi KE, Bohm BE, Rickauer AJ, Jacobi C, Hemmerling TM. Moderate controlled hypotension with sodium nitroprusside does not improve surgical conditions or decrease blood loss in endoscopic sinus surgery. J Clin Anesth 2000;12:202–7.
19. Milonski J, Zielinska-Blizniewska H, Golusinski W, et al. Effects of three different types of anesthesia on perioperative bleeding control in functional endoscopic sinus surgery. Eur Arch Otorhinolaryngol. 2013;270:2045-50.
20. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers.1: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth 1999; 83: 372–80.
21. Gupta P, Choudhary R, Ojha T, Jethava D. To study the efficacy of dexmedetomidine in providing hypotensive anesthesia so as to minimize bleeding during endoscopic sinus surgery in a randomized double blind control study. IOSR Journal of Dental and Medical Sciences 2016; 15(8) :143-6.
22. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. CurrOpin Crit Care 2001;7:221-6.
23. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology 1996;84:873-81.
24. Richa F, Yazigi A, Sleilaty G, Yazbeck P. Comparison between dexmedetomidine and remifentanil for controlled hypotension during tympanoplasty. Eur J Anaesthesiol 2008;25:369-74.