Original Research Article

Comparison of Dexmedetomidine Infusion with Nitroglycerine Infusion for Hypotensive Anaesthesia in Functional Endoscopic Sinus Surgery: A Prospective Randomized Clinical Trial

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Abstract

Background: Functional endoscopic sinus surgery (FESS) is a commonly performed procedure for patients with chronic rhinosinusitis. Ensuring a bloodless surgical field improves efficiency and safety during the procedure. **Aim:** To compare intravenous infusions of dexmedetomidine and nitroglycerine in FESS for quality of the surgical field, hemodynamics, time to first rescue analgesia, and recovery profile. **Patients and Methods:** This was a prospective, randomized double-blinded comparative study comprising 60 ASA PS I and II patients posted for functional endoscopic sinus surgery. Patients were randomized into two groups of 30 patients each. Group D (n=30) received dexmedetomidine infusion and group N (n=30) received nitroglycerine infusion after general anaesthesia. Both intravenous drug infusions were titrated to achieve the target blood pressure, i.e. Mean arterial pressure ≤ 20 % of baseline or between 55-65 mmHg. Surgical field quality, duration of postoperative analgesia, and sedation score were assessed. **Statistical Analysis:** The Student's independent t-test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever is appropriate, was applied for comparing categorical variables. **Results:** Patients of Group D had a better surgical field quality, duration of analgesia, better cardiovascular stability, higher sedation scores in the PACU, and an increase in mean awakening time as compared to the nitroglycerine group. **Conclusions:** Dexmedetomidine intravenous infusion provides better quality of the surgical field, longer duration of postoperative analgesia, and cardiovascular stability as compared to the nitroglycerine infusion in functional endoscopic sinus surgeries.

Keywords: Controlled Hypotension, Dexmedetomidine, Nitroglycerine, Functional Endoscopic Sinus Surgery.

Introduction

Functional endoscopic sinus surgery (FESS) is a commonly performed procedure for patients with medically refractory chronic rhinosinusitis[1]. The main obstacle to good visibility is excessive bleeding during surgery that can compromise the safety and efficiency of this surgical procedure[2]. It can lead to serious complications like orbital cellulitis, optic nerve injuries, meningitis, etc[3,4]. To ensure hemodynamic balance and patient safety it is mandatory to keep the surgical field free of blood, as much as possible, to improve the visibility of anatomical landmarks and structures. This can be achieved with the use of topical vasoconstrictors, local anaesthesia, or the use of controlled hypotension with general anaesthesia.

Controlled hypotension involves reducing arterial blood pressure 20% below its normal range or reducing mean arterial pressure (MAP) to 55-65 mmHg reversibly and maintaining it at that level throughout the surgery[5]. Several pharmacological agents have been used successfully to produce controlled hypotension for FESS surgeries, for example, inhalational anaesthetics, direct vasodilators(NTG, sodium nitroprusside), alpha-adrenergic agonists (clonidine, dexmedetomidine), beta-adrenergic antagonists (propranolol, esmolol), calcium channel blockers, lignocaine, magnesium sulfate, etc [2]. Nitroglycerine (NTG) is a nitric oxide releaser that dilates preferentially venous capacitance vessels leading to a decrease in venous return to the heart resulting in systemic hypotension[5]. Dexmedetomidine is a potent highly selective alpha2 adrenergic receptor agonist which has sedative, analgesic, and anaesthetic sparing effects along with sympatholytic properties. Its central and peripheral sympatholytic action is manifested by a dose-dependent decrease in arterial blood pressure, heart rate, cardiac output, and norepinephrine release[6,7]. Ideally, a hypotensive agent should be easy to administer, have a short onset time, have effects that disappear soon after discontinuation, metabolic clearance without harmful products, insignificant effects on vital organs, and predictable dose-dependent effects[8,9].

This study was conducted to compare intravenous infusions of dexmedetomidine and nitroglycerine in FESS for the quality of the surgical field, hemodynamics, time to first rescue analgesia, and recovery profile.

Materials and methods

After obtaining institutional ethics committee approval and registration at the clinical trials registry of India (CTRI/2021/05/033541, registered on 11/05/2021), this prospective randomized clinical study was conducted. After obtaining informed consent, 60 American Society of Anaesthesiologists Physical Status I

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and II patients, of either sex, in the age group of 18-65 years undergoing FESS under general anaesthesia were selected and consecutively enrolled into the study. Patients allergic to drugs to be used in this study, pregnant and lactating women, with a history of chronic hypertension, sinus bradycardia, a history of bleeding disorders, and a history of antiplatelet medications were excluded from the study. The regular pre-anaesthetic assessment was done along with baseline laboratory investigations (complete blood count, renal function tests, liver function tests, bleeding time, clotting time, prothrombin time, and partial thromboplastin time).

All patients fasted according to standard guidelines. Vital parameters i.e. Non-Invasive Blood pressure- MAP, Heart rate, End-tidal CO_2, and oxygen saturation was recorded at 5 minutes intervals till the end of surgery.

Patients were pre-medicated with, intravenous glycopyrrolate 0.004mg.kg^{-1}, midazolam 0.07 mg.kg^{-1}, fentanyl 2 µg.kg^{-1} and ondansetron 0.1mg.kg^{-1}. Propofol 2 mg.kg^{-1} was used for induction and Vecuronium 0.1 mg.kg^{-1} was used for endotracheal intubation. Anaesthesia was maintained with oxygen and nitrous oxide mixture (50: 50) and Sevoflurane (2% dial concentration) along with Vecuronium. Patients were placed in Reverse Trendelenburg position (15-degree head up) after induction and hypotensive drug infusion was started.

Using computer-generated random number tables all patients were randomized into two groups.

Group D: Patients in group D received Inj. Dexmedetomidine 1 µg.kg^{-1} i.v. as a bolus dose over 10 minutes then followed by infusion at the rate of 0.2 - 0.7 µg/kg/hour.

Group N: Patients in group N received Inj. Nitroglycerine as a continuous intravenous infusion at the rate of 0.5 – 5 µg/kg/minute.

Both drug infusions were titrated to achieve the target blood pressure, i.e. mean arterial pressure (MAP) ≤ 20 % of baseline or between 55-65 mmHg. After achieving and maintaining the MAP for 10 minutes surgical field grade was assessed by the surgeon using a predefined category scale adopted from the Fromme-Boezaart Scale (Average Category Scale) which is as follows[10].

Grade 0: No bleeding
Grade 1: Slight bleeding- no suctioning of blood required
Grade 2: Slight bleeding—occasional suctioning required
Grade 3: Slight bleeding—frequent suctioning required
Grade 4: Severe bleeding—frequent suctioning required, threatens the surgical field
Grade 5: Severe bleeding—constant suctioning required

The surgical field quality in terms of excellent, good and poor will be defined by Grades 0-1, 2-3 and 4-5 respectively. 45 minutes before planning reversal. Infusion of the hypotensive drug was stopped 5 minutes before the end of surgery. Injection neostigmine 50µg.kg^{-1}and glycopyrrolate 10µg.kg^{-1} was used for reversal and patients were extubated. The recovery profile was noted as per the Modified Aldrete score[11] (Table-1) in PACU till the patient reached a score of nine or more. The time to reach Aldrete's score of 9 was noted.

Table-1: Aldrete Score[11]

Parameter	Definition	Score
Activity	Able to move 4 extremities voluntarily or on command	2
	Able to move 2 extremities voluntarily or on command	1
	Able to move 0 extremities voluntarily or on command	0
Respiration	Able to take a deep breath and cough heavily	2
	Dyspnoea or limited breathing	1
	Apnoea	0
Circulation	Blood pressure ≤20% of preanesthetic level	2
	Blood pressure 20-50% of preanesthetic level	1
	Blood pressure >50% of preanesthetic level	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
O_2 Saturation	Maintains >92% on room air	2
	Needs O_2 inhalation to maintain O_2 saturation >90%	1
	Saturation <90% even with supplemental Oxygen	0

Duration of postoperative analgesia was noted using VAS score which was assessed hourly until four hours after surgery. If the VAS score was more than 4, the patient received diclofenac 1.5mg.kg^{-1} as an intravenous infusion. Time to first rescue analgesic demand was noted.

Postoperative sedation was monitored using Ramsay Sedation Score[12] from the time of extubation at 15 minutes intervals till 1 hour.

Table-2: Ramsay Sedation Score[12]

Definition	Score
Patient is anxious and agitated or restless, or both	1
Patient is cooperative, oriented and calm	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

Hypotension was defined as MAP < 50 mmHg and was treated by increment doses of ephedrine 6 mg i.v., bradycardia was defined as HR < 50 beats/ min and was treated by atropine 0.01 mg.kg^{-1}, and patients who displayed shivering were warmed with heated blankets.

Statistical Analysis

Statistical tests and analysis were done using Statistical Package for Social Sciences (SPSS, version 20; SPSS Inc., Chicago, Illinois, USA). Normally distributed continuous data were analyzed using the student t-test. Non- normally distributed continuous data and ordinal data were analysed using the Mann Whitney test. Categorical data were analyzed using Chi-square or Fischer Exact whichever is appropriate. A p-value <0.05 was considered to be significant.

Results

No significant difference was observed between the groups regarding gender, age, height, weight, ASA physical status, distribution of surgical diagnosis, and duration of the operation (Table 3). Ratio or

interval data are expressed as mean ± SD and ASA I or II and Gender are expressed as numbers. Both the groups were comparable in demographical characteristics, and duration of surgery (p>0.05). The details of the quality of the surgical field derived from the grades are shown in table 4.

Table 3: Patient's characteristics and clinical data		
Variable	**Group D (n=30)**	**Group N (n=30)**
ASA I/II (n)	23/7	24/6
Gender Male/Female	14/16	17/13
Polyp / Chronic sinusitis/Allergic fungal sinusitis	8/14/8	9/15/6
Age (years)	42.2 ± 10.4	43.00 ± 8.9
Weight(kg)	68 ± 5.40	66 ± 6.00
Height (m)	1.61± 0.06	1.59 ±0.04
BMI ($m^2.kg^{-1}$)	26.5 ± 2.48	26.1 ± 2.68
Duration of surgery (min)	104.8 ± 18.96	107.4 ± 15.65

Table 4: Distribution of Quality of Surgical field among the patients Frequency (Percentage)			
Group	**Group D (n=30)**	**Group N (n=30)**	**Fischer Exact p-value**
Excellent (0-1)	15 (50)	5 (16.7)	0.008
Good (2-3)	14 (46.7)	18(60)	
Poor(4-5)	1(3.3)	7(23.3)	

Dexmedetomidine group had more patients with the favourable quality of surgical field than the Nitroglycerine group and the difference in the distribution was statistically significant (p<0.05).

MAP changes of both groups were shown in Figure.1. Dexmedetomidine group had significantly lower MAP values at all time intervals during surgery and post-extubation than the Nitroglycerine group (p<0.05). Heart rate observations were given in Figure. 2. Mean Heart rate showed an increasing trend in the Nitroglycerine group and decreasing trend from the baseline in the Dexmedetomidine group and the differences were statistically significant(p<0.05).

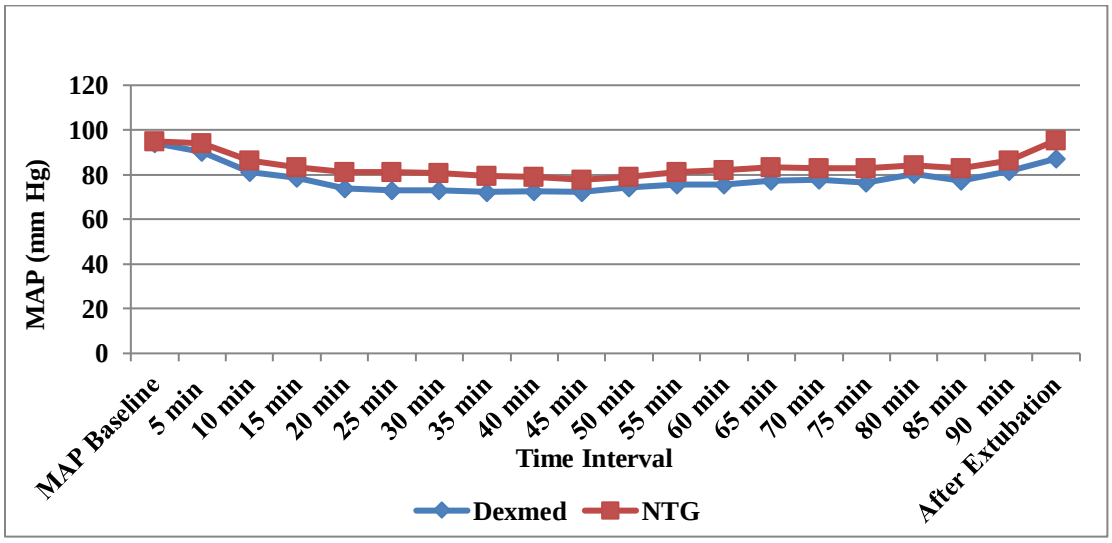

Fig 1:MAP Trend in both groups

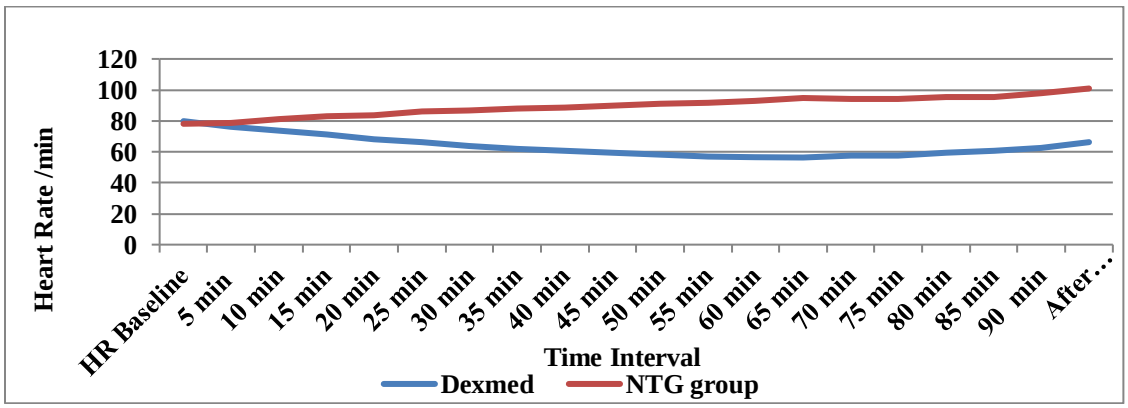

Fig 2:Heart rate changes

Ramsay sedation scores at 15min, 30 min, and 60 min intervals were given in table 5.
The sedation scores at all three-time intervals were higher in the dexmedetomidine group when compared to the Nitroglycerine group and the differences were statistically significant (p<0.05).

Table 5: Ramsay Sedation Score (mean ± std)			
Time interval	**Group D (n=30)**	**Group N (n=30)**	**p-value**
15 min	3.5±0.6	1.6±0.57	<0.001
30 min	3.1±0.55	1.7±0.52	<0.001
60 min	2.8±0.55	1.9±0.51	<0.001

The time taken to reach the Alderete score of 9 or more in the dexmedetomidine group was 88.8± 8.58 min and in the Nitroglycerine group was 32.3± 6.26 min (Table 6). This difference was statistically significant (p<0.05). Dexmedetomidine group had a statistically significant longer duration of postoperative analgesia as the time for the first analgesic request was longer, 294.5± 80.26 min when compared to the Nitroglycerine group, 83.3± 36.3 (p<0.05).

Table 6: Time to reach Alderete Score 9 or more and Time of First rescue analgesic requirement			
	Group D (n=30)	**Group N (n=30)**	**p-value**
Time to reach Alderete score of 9 or more (min)	88.8± 8.58	32.3± 6.26	< 0.001
First analgesic request (min)	294.5± 80.26	83.3± 36.3	< 0.001

The incidence of Side effects were shown in Table 7. Dexmedetomidine group had a higher incidence of MAP going below 55 mmHg and bradycardia (less than 50/min) than the Nitroglycerine group but the differences were not statistically significant (p>0.05). Nausea and Vomiting incidences were comparable in both groups (p>0.05).

Table 7: Side effects (n)			
Adverse event	**Group D (n=30)**	**Group N (n=30)**	**p-value**
MAP < 55 mmHg	3	1	>0.05
Bradycardia <50/min	3	Nil	>0.05
Nausea, vomiting	4	5	>0.05

Discussion

Functional endoscopic sinus surgery (FESS) plays an important role in the management of patients with medically refractory chronic rhinosinusitis[9]. It has the potential for re-establishing natural mucociliary clearance mechanism as well as drainage and aeration of sinuses, whilst maintaining the normal anatomy to the maximum. So, it has become popular worldwide due to its minimally invasive nature and preservation of mucosa. As even minimal bleeding could interfere with the surgical field visibility, it is preferable to maintain a bloodless surgical field. Various approaches have been used to secure a dry operating field like the use of topical vasoconstrictors, Fowler's position, alpha- and beta-adrenergic blockade, and preoperative steroids. All these methods are associated with significant side effects. Another approved approach to this problem is to combine total intravenous anaesthesia using propofol and remifentanil, together with esmolol (Drozdowski et al. 2011)[13]. Oral nifedipine was used as a premedication in the study done by Hassanien and Talaat for the hypotensive field in FESS[14].

The goal of controlled hypotension is to reduce bleeding during surgery and improve visibility within the surgical field. Also, it decreases the time taken for surgery and the duration of General Anaesthesia[8].

As vital organ perfusion is decided by mean Arterial Pressure (MAP), MAP is usually taken as the parameter to quantify hypotension. The target MAP in our study was between 55-65 mm of Hg and it was based on previous studies (by Newton et al). They investigated the hormonal and metabolic responses to induced hypotension and concluded that there was no risk of tissue ischemia in this range[15].

Our study compared the efficacy of dexmedetomidine and Nitroglycerine in achieving controlled hypotension during FESS in terms of quality and grades of the surgical field, sedation scores, recovery profile, hemodynamic changes, and postoperative analgesia.

Our primary outcome parameters were to assess the visibility of the surgical field with the use of the Average Category Scale (ACS) Score using reference from the study of Fromme et al[10]. In our study, it is evident that patients of Group D (dexmedetomidine)had a better surgical field quality and grade than the Nitroglycerine group, that may be attributed to the fact that it being a highly potent and selective alpha 2 agonists, with central and peripheral sympatholytic property causes reduced blood pressure, cardiac output and heart rate thereby decreasing blood loss at the surgical site and improving the quality of the surgical field[9]. Bayram et al. compared the efficacy of $MgSO_4$ and dexmedetomidine in producing hypotension in FESS surgeries and found that dexmedetomidine resulted in a higher surgeon satisfaction when compared to the $MgSO_4$ group[16]. Regarding the recovery profile, patients in Group D had higher sedation scores in the PACU and an increase in mean awakening time assessed by the time taken to reach Aldrete score more than 9 following administration of dexmedetomidine as compared to nitroglycerine. This is in concurrence with the findings of a study by Shams et al and Durmas et al[13-15] which reported higher postoperative sedation scores with the intra-operative use of dexmedetomidine. These results are consistent with Faranak et al. study, in which patients in the dexmedetomidine group had higher sedation scores in PACU, and the time to reach modified Aldrete score ≥ 9 was longer compared with those of the magnesium group[17]. In Erdem et al. study, the sedation score was higher when dexmedetomidine was administered to induce hypotension during FESS when compared with esmolol[18]. In a study conducted by Lee et al. which compared dexmedetomidine and remifentanil administration as a hypotensive agent during surgery, they observed that patients receiving dexmedetomidine had a higher sedation score and the time needed to reach modified Aldrete score ≥ 9 was longer than those of the patients that received remifentanil[19]. Similarly, Ozcan et al. compared dexmedetomidine and remifentanil during FESS and found that the dexmedetomidine group had a longer recovery than the remifentanil group[20]. Time for first rescue analgesia was prolonged in group D as compared to group N and this difference was statistically significant. The intraoperative use of dexmedetomidine has been shown to significantly reduce the perioperative analgesic requirerments[14,15].The sedative and analgesic sparing effects of dexmedetomidine are mediated through its action in the locus coeruleus and dorsal horn of the spinal cord respectively[21]. Postoperative sedation is often desirable, but may sometimes prolong the emergence time.In terms of hemodynamic profile, patients who received Dexmedetomidine infusion showed cardiovascular stability whereas there was raise in the heart rate in Group N which persisted throughout the surgical duration and this difference was statistically significant. Our results aligned with the study done by Jamaliya et al. and Vali et al who also observed that dexmedetomidine had better control over vital parameters e.g heart rate, mean arterial pressure, systolic blood pressure, and diastolic

blood pressure than nitroglycerine[22,23]. In a study conducted by Khalifa et al., a significant decrease in heart rate was seen in patients who received dexmedetomidine infusion, and a significant increase in heart rate was seen among Those who received nitroglycerine infusion during the period of observation, as we observed[2]. The heart rate was higher in group N due to reflex tachycardia associated with nitroglycerine infusion. Dexmedetomidine caused a lower heart rate due to its sympatholytic effect[23]. In Patel et al. study, dexmedetomidine was compared with nitro-glycerin to produce controlled hypotension; dexmedetomidine had the advantage of maintaining better cardiovascular stability as compared to nitroglycerine.Though the dexmedetomidine group had a higher incidence of patients having a MAP of less than 55 mmHg and heart rate less than 50 beats per minute as compared to the nitroglycerine group but this difference was not statistically significant. There was no difference between the groups in the incidence of nausea and vomiting. We conclude that both dexmedetomidine and nitroglycerine infusions successfully provided controlled hypotension but dexmedetomidine provided better surgical field and hemodynamic stability during FESS. Dexmedetomidine has an additional advantage of inherent analgesic and sedative effect and is thus better than nitroglycerine infusion for FESS.

Conclusion

Dexmedetomidine infusion provides better quality of surgical field, hemodynamic stability, intraoperative and postoperative analgesia and thus can be used as an effective agent for controlled hypotension during FESS with negligible side effects.

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