

Intranasal Dexmedetomidine as Adjuvant to Local Anaesthetic in Preparation of Nasal Passage for Functional Endoscopic Sinus Surgery: Randomized Controlled Trial

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ABSTRACT

Background: Intraoperative stress response and ongoing bleeding at surgical site especially in areas like head and neck can cause serious adverse reactions and affect the postoperative outcome. This study compared the effect of intranasally administered dexmedetomidine (dexmed) in combination with local anesthesia (LA) and local anesthetic alone on quality of surgical field, surgical bleeding and haemodynamic parameters during functional endoscopic sinus surgery (FESS).

Methods: Roller gauge strips dipped in dexmedetomidine were used for nasal packing. Sixty patients undergoing FESS were randomly allocated to receive either intranasal Dexmedetomidine with LA (D group) or intranasal LA alone (L group) via nasal packing 15 min before surgery. The primary objective was to study the quality view of surgical field through the endoscope and the blood loss that occurred while raising the nasal mucosal flap. The secondary objective was to study the intraoperative hemodynamic profile and anesthetic and analgesic requirement during surgery.

Results: Surgical field quality, Blood loss, hemodynamic profile and satisfaction scores of patients and surgeons were significantly better ($P < 0.05$) in dexmed group.

Conclusion: Patients receiving intranasal dexmed with LA for FESS had better surgical field, surgeon's satisfaction and minimal hemodynamic fluctuations with lesser blood loss as well as better postoperative comfort and analgesia.

Introduction

Functional endoscopic sinus surgery (FESS) is a commonly used technique in the field of nasal surgery, and has gained upper hand in the treatment of sinusitis [1]. Nasal cavity itself being a highly vascular area with further increase in vascularity due to inflammation in the sinuses, is more susceptible to bleed during FESS [2]. Therefore, in order to ensure the smooth surgical procedure of FESS, it is essential that despite of administering general anaesthesia there should be minimal haemodynamic fluctuations, clear surgical field with minimal bleeding to aid visualization through endoscope during surgery [3-4].

During FESS there are wide variations in hemodynamic parameters, particularly, hypertension and tachycardia that is attributed to the routine application of adrenaline-soaked nasal packing and the severe noxious stimulus during nasal speculum insertion and raising of mucosal flap. These fluctuations are not effectively blunted by any of the anaesthetic agents, thus resulting in a need for increased doses of anesthetic or vasoactive agents [5-6].

In this study we utilized the vasoconstrictive effect of dexmedetomidine by administering it intranasally and recorded the effect of topical dexmedetomidine on local bleeding while raising of the mucosal flap and the intraoperative hemodynamics after infiltration of the mucosa with adrenaline in patients undergoing FESS.

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This aspect of dexmedetomidine has not been explored earlier.

The primary objective of the study was to compare surgical field visualization (Former's Score) [7] and onsite bleeding while the secondary objectives were to compare hemodynamic profile of patients and post-operative recovery in terms of sedation and analgesic requirement.

Methods

We conducted this study after obtaining institutional ethical committee approval (SKNMC/ethics/App/2021/818) and in complete accordance with guidelines of Helsinki. Patients of both sexes in the age group of 18-65 years who had complaints of acute or chronic, unilateral or bilateral maxillary sinusitis requiring functional endoscopic sinus surgery were include in the study. All the patients underwent a thorough pre anesthetic examination and written, informed consent was taken. Patients who were pregnant or lactating had decreased levels of consciousness, raised, cardiac pathology, previous nasal surgery, or history of allergy to any of the study drugs were excluded from the study. The primary outcome parameters studied were the quality of surgical field visualization through the endoscope (Former's Score) and the amount of bleeding that occurred while raising the nasal mucosal flap. The secondary outcome parameters assessed were the hemodynamic profile and post-operative recovery in terms of sedation and analgesic requirement.

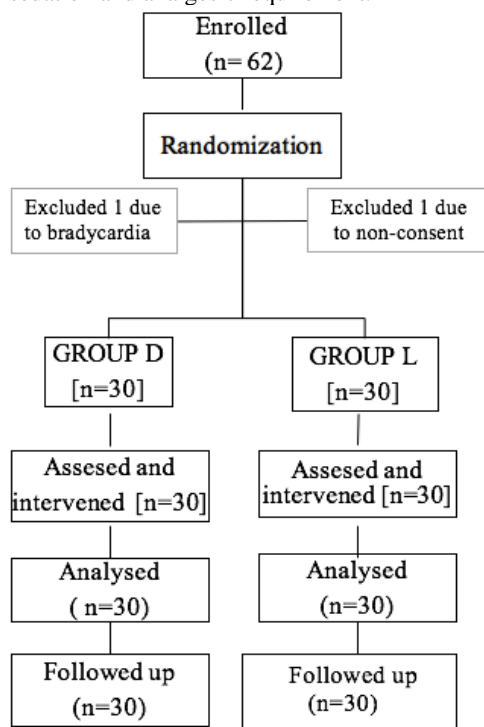


Figure 1- Consort flow chart of the study

Wide bore venous access was secured with 18/20 gauge intravenous catheter. Standard pre-induction monitoring consisted of electrocardiography (ECG), oxygen saturation (SpO₂), and non-invasive blood pressure. All the patients were premeditated with Inj.Glycopyrrolate 0.2 mg IV, Inj.Ondansetron 4 mg IV, Inj.Fentanyl 2 ug/kg IV and Inj.Midazolam 0.02 mg/kg IV. Standard anaesthetic induction was done with injections Inj. propofol 2 mg/kg, and vecuronium 0.1 mg/kg. Patients were intubated with appropriate size endotracheal tubes. After intubation, the posterior pharynx was packed with moist cotton gauze to prevent the entry of surgical bleed into the esophagus and stomach. Nasal preparation was performed by the surgeon using cotton strips soaked in either dexmed mixed with LA or only LA. The surgeon who was packing was blinded to the solution used for packing. Cotton strips were imbibed with the solution; the excess was carefully removed until the cotton strip was saturated but not dripping upon compression. The entire dose 2 ug/kg of dexmedetomidine was taken that will be adequate to soak the six cotton strips, which is required for the study. Each strip approximately absorbed approximately 1 to 2 mL. Each nasal cavity was packed with three packs. One placed on the floor of the nasal cavity, the other was placed over it to encroach into the middle meatus and the last one was placed over the second one to anaesthetize the frontal recess area. The nasal packs were left in situ for 10 minutes. Anaesthesia was maintained using a combination of oxygen: air (50:50) and sevoflurane (MAC 0.8 – 1). Hemodynamic parameters that included the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MAP) were measured at seven time points T0 (baseline), T1(10 min after packing), T2(at local infiltration), T3 (30 mins in between surgery), T4(at the end of surgery). Quality of intraoperative surgical field during endoscopic surgery was evaluated by the surgeons using the Former's score which is defined as

- 1- Mild bleeding without any surgical nuisance;
- 2- Moderate bleeding, without any interference to surgery;
- 3- Moderate bleeding that moderately compromised surgical field;
- 4- Bleeding, heavy but controllable, that significantly interfered the surgery;
- 5- Massive uncontrollable bleeding.

At the end of the surgery reversal of the residual neuromuscular block was done by 0.05 mg/kg Neostigmine and 0.04mg /kg Glycopyrrolate intravenously.

Postoperative Sedation score was assessed by Ramsay sedation score [8] which is defined as-

1. Anxious and agitated or restless or both
2. Co-operative, oriented, and tranquil
3. Responds to commands only
4. Brisk response to a light glabellar tap or loud auditory stimulus

5. Sluggish response to a light from glabellar or loud auditory stimulus

6. No response to a light glabellar tap or loud auditory stimulus

Statistical Analysis

A minimum of 28 patients were required in each group to achieve a significance level of 95% and power of 80% with type 1 (α) error of 0.05. Hence, we included 30 patients in each group to consider any dropouts. A total of 60 patients were enrolled for the study. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 15.0 (USA). Descriptive statistics was done for all data. The categorical variables in the two groups were analyzed using Chi-square test or Student 't' test unpaired test as appropriate. For the analysis of hemodynamic responses to intubation including heart rate, systolic, diastolic and mean arterial pressures, a repeated measure analysis of variance (ANOVA) was used. A two-tailed probability of less than 0.005 was considered statistically significant.

Results

Sixty patients were enrolled in our study. Demographically both the groups were comparable in terms of age, sex, weight and ASA grading and there was no statistically significant difference among them (Table 1).

The hemodynamic parameters when compared among the two groups were statistically different with high level of significance. the readings were recorded on a timeline

with time intervals like T0 (baseline), T1 (10 min after packing), T2 (at local infiltration), T3 (30 mins in between surgery), T4 (at the end of surgery). The heart rate recorded at these time intervals was significantly lower in D group than L group except for the baseline readings. There was a statistically significant difference among the two groups in terms of heart rate ($p < 0.001$) (Table 2).

The systolic, diastolic and mean arterial pressure (MAP) were also significantly lower in D group than L group except the baseline readings. This difference was statistically significant and p value < 0.001 (Table 3). shows the readings of MAP on the time line.

Former's score (Table 4), which was significantly lower in D group with mean values of 1.17 ± 0.461 versus 1.90 ± 0.548 which was statistically significant with $p < 0.001$.

Intraoperative inhalational requirement was significantly less in patients who were packed using dexmed with LA. The mean requirement in both the groups were 0.70 ± 0.535 in D group versus 1.60 ± 0.498 in L group. The calculated p value was < 0.001 which denotes high level of significance.

Blood loss was significantly lesser in D group than L group with p value < 0.001

Sedation score as assessed by Ramsay sedation score was lower in L group than D group which was statistically significant ($p < 0.001$) but was not clinically significant as to affect the patient's recovery.

The incidence of PONV was comparable among the two groups and was not statistically significant ($p < 0.094$) (Table 4).

Table 1- Comparison of demographic characters in two groups

Variables	Group D	Group L	P value#
Age (years)	37.77 \pm 11.557	36.23 \pm 11.239	*0.604; NS
Weight (Kg)	60.50 (8.83)	60.67 (7.48)	*0.93
Gender (Male/Female)	9/21	11/19	#0.784
ASA grade I/II	25/5	23/7	#0.748

*Student 't' test unpaired; * $p < 0.05$: Significant

Chi square test $p < 0.05$: significant

Table 2- Comparison of HR in two groups

Time	Group D		Group L		P value#
	Mean	\pm SD	Mean	\pm SD	
T0 Baseline	75.87	7.895	78.27	6.565	0.604; NS
T1 10 min after nasal packing	75.70	11.105	91.60	2.541	$< 0.001^{**}$
T2 At local infiltration	86.03	6.926	101.40	4.368	$< 0.001^{**}$
T3 30 min in surgery	87.00	7.830	99.40	4.461	$< 0.001^{**}$
T4 At the end of surgery.	82.47	6.157	98.40	1.773	$< 0.001^{**}$

#Student 't' test unpaired; NS: $p > 0.05$; Not significant; * $p < 0.05$: Significant; ** $p < 0.001$; Highly significant

Table 3- Comparison of MAP in two groups

Time	Group D		Group L		P value#
	Mean	\pm SD	Mean	\pm SD	
T 0 Baseline	90.13	4.191	87.62	4.370	0.028*
T1 10 min after nasal packing	93.17	2.793	91.62	3.821	0.081; NS

T2 At local infiltration	86.80	5.255	105.172	6.756	<0.001**
T3 30 min in surgery	88.57	1.591	103.03	8.131	<0.001**
T4 At the end of surgery.	88.17	3.769	104.21	5.608	<0.001**

Student's t' test unpaired; NS: p>0.05; Not significant; *p<0.05; Significant; **p<0.001; Highly significant

Table 4- Comparison of Former's Score, intraoperative inhalational requirement, estimated blood loss, Sedation, PONV and post op agitation in two groups.

Time	Group D			Group L			P value#
	Mean	± SD	Median	Mean	± SD	Median	
Former's score	1.17	0.461	1	1.90	0.548	2	<0.001**
Intraoperative inhalational requirement	0.70	0.535	1	1.60	0.498	2	<0.001**
Blood loss (ml)	135.06	36.88	123	337.45	125.78	340	<0.001**
Sedation (RSS)	2.17	0.461	2	1.70	0.548	1	<0.001**
PONV	0.20	0.407	0	0.40	0.498	0	0.094 NS

Discussion

In the present study we could derive a conclusion that addition of dexmedetomidine as per 1mcgm kg-1 dose to the nasal packing solution of 2% xylocaine with adrenaline definitely provides superior operating field as compared to conventional 2% xylocaine adrenaline used alone in cases of FESS.

There is very limited data exploring this route (topical absorption) of administration of dexmedetomidine and to the best of our knowledge this is the second only research, highlighting the use of dexmedetomidine along with LA via topical route while reporting its extent and effects of mucosal absorption.

The most important purpose to prepare the nasal mucosa during FESS is to reduce the intraoperative blood pressure and keep the surgical field relatively clean and help the surgeons to have better visualisation facilitating surgery. [9] The conventional practice of packing the nose with 2% lignocaine with adrenaline (1:10,000–1:20,000) with further infiltration of the nasal mucosa using lignocaine with adrenaline (1: 50,000–1: 200,000) often causes hypertension and tachycardia. Major changes in blood pressure and heart rate often lead to excessive blood loss, poor visibility, prolonged surgical duration, iatrogenic trauma which in turn may lead to surgeon's stress and disturb the operating room harmony. All these factors contribute to delayed patient's recovery.

Various new methods have evolved over a period of time to optimize the surgical conditions for FESS [10-11]. Amongst them Induced hypotension has been followed widely to control bleeding during FESS [12-13]. In our prospective randomized study we compared addition of dexmedetomidine to conventional 2% lignocaine-adrenaline solution with that of only 2% lignocaine adrenaline solution used for nasal packing during FESS and studied the quality of surgical field from surgeon's prospective.

Dexmedetomidine an alpha 2 agonist has been a highly recommended drug for induced hypotension during the last decade. All the effects of dexmedetomidine have been reported via intravenous route or onsite infiltration [14]. The vasoconstrictive effects of dexmedetomidine on peripheral blood vessels has been studied [15-16]. Locally administered dexmed causes its effect via the peripheral α 2A-adrenoceptor subtype leading to peripheral vasoconstriction without causing a direct effect on the cardiovascular system.

Providing a bloodless field to the surgeon not only prevents blood loss but also decreases the major complications and manipulations and decreases the duration of surgery [17].

Gu et al conducted a study using intravenous infusion of Dexmedetomidine preoperatively in patients undergoing FESS and reported that preoperative administration of dexmedetomidine not only alleviates anxiety but also reduces intubation stress response [18]. But unlike our study they studied the intravenous route of administration and its effect on anxiety and stress response to intubation. Though the route of administration was different we could achieve similar results in terms of hemodynamics and better field visualization using noninvasive administration.

Parvizi A et al conducted a study in patients undergoing FESS and administered dexmed at a rate of 1mcg/kg infusion over 10 minutes followed by maintenance of 0.4-0.8mcg/kg/hr. They concluded that patients receiving dexmedetomidine had better field visualization and hemodynamic control [19]. Their results were similar to those of ours. They also reported better surgeon's satisfaction score like ours.

Güven et al used dexmedetomidine for conscious sedation for FESS and reported similar results in terms of hemodynamic stability and improved surgical field quality [20].

Hrishi et al in their study report that preoperative nasal preparation with dexmedetomidine provide good surgical field with minimal haemodynamic fluctuations. They

conducted the study in patients undergoing trans nasal, trans sphenoidal approach for pituitary tumors [7]. Like our study they studied the mucosal absorption and surgical field quality and had similar results.

Mohammad Nassef et al administered 20micrograms of dexmedetomidine with local anaesthetic mixture to patients undergoing external dacryocystorhinostomy and their results suggest that this is a good mixture to achieve adequate sensory block, relieve anxiety and provides perioperative sedation [21]. In this study the mucosal absorption was not studied unlike our study.

Major challenge for endoscopic nasal surgery is rich vascularity. It is important to achieve vasoconstriction in this area with the combination of 1% lignocaine-adrenaline (1:200000) soaked in cotton pladget or injecting into the mucosa. Major complications seen with this technique are tachycardia, hypertension and arrhythmias. In order to prevent these effects, the alpha agonist action of dexmedetomidine plays a vital role. In our study we could get results which suggest favorable effect of dexmedetomidine.

Dexmedetomidine has sedative and opioid sparing effects via central actions in the locus coeruleus and in the dorsal horn of the spinal cord, respectively [3].

Richa et al in their study reported that extubation time was significantly slower in patients receiving dexmedetomidine compared with those receiving rami fentanyl for controlled hypotension ($P < 0.001$) [22]. In our study we do not report any such finding which may be due to the low dose or minimal systemic effects via mucosal route. The patients receiving dexmedetomidine were calm and less agitated inspite of nasal packing and dressing as compared to the control group patients.

Protection from aspiration of bleeding and secretions from surgical site via nasopharynx demands the intact airway reflexes of the patient. Dexmedetomidine allies the need to use more of analgesics in the form of opioids or non opioids by modifying the response to pain and stress thus maintains stable hemodynamics [23]. An additional advantage and favorable property of dexmed is its ability to preserve the upper airway reflexes whilst alleviating perioperative anxiety and causing mild sedation [24].

Yang et al emphasised the need of deep general anesthesia for hypotension which could be balanced with rapid intravenous infusion of solutions before infiltration in order to maintain hemodynamic stability. Use of lignocaine adrenaline solution for nasal mucosa infiltration is a primitive technique which though causes vasoconstriction but at the same time causes transient hypertension and tachycardia [25]. In our study also we compared the nasal mucosa prepared with lignocaine adrenaline with that prepared with lignocaine adrenaline along with dexmedetomidine to achieve bloodless surgical field and hemodynamic stability and report that addition of dexmedetomidine provides better surgical

field (as per former's score) while maintaining stable haemodynamics.

Limitations

We authors accept certain limitations for the study. Dexmedetomidine being a costly drug its availability in all cases of FESS becomes difficult and thus under utilization of this novel drug.

Secondly, further studies with larger sample size needs to be conducted to validate the efficacy of dexmed administered via this route.

We did not compare different time intervals between packing and surgical incision to evaluate the optimum time needed to get the maximum effect of dexmed via mucosal absorption.

Different doses of dexmed also need to be compared to derive a minimum effective dose

Conclusion

To conclude dexmedetomidine in a dose of 1mcg/kg when added to 2% xylocaine adrenaline solution for nasal passage preparation prior to FESS provides a superior field of vision during surgery with minimal intraoperative bleeding and enhancing surgeon's satisfaction and postoperative outcome.

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