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Original Article

A prospective-randomized placebo-controlled trial comparing the effects of nebulized dexmedetomidine v/s dexmedetomidine-lignocaine mixture on intraoperative hemodynamics and surgical field quality in patients undergoing endoscopic transnasal transsphenoidal pituitary tumor surgery

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ABSTRACT

Background: During transnasal transsphenoidal pituitary surgery (TNTSS), the primary objective is to maintain stable hemodynamics while ensuring ideal surgical conditions. This study aimed to investigate the effect of nebulized dexmedetomidine on hemodynamic parameters and the quality of the surgical field during TNTSS.

Methods: Seventy-five patients scheduled for TNTSS were randomized into three groups of 25 each and received preoperative nebulization with 5 mL of nebulizing fluid consisting of 1.5 μg/kg of dexmedetomidine with saline in dexmedetomidine (D) group; 1.5 μg/kg of dexmedetomidine with 2% lignocaine in dexmedetomidine-lignocaine (DL) group and normal saline in the control (S) group. Heart rate (HR), mean blood pressure, Formmers score, anesthetic requirement, and emergence were evaluated for each group.

Results: Group S had significantly higher HR and mean arterial pressure than the other two groups across various time points during surgery ($P < 0.01$). The total requirements for fentanyl, propofol, sevoflurane, and labetalol and the incidence of delayed emergence were significantly higher in the S group compared to the other two groups ($P < 0.01$). The D and DL groups exhibited significantly better surgical field conditions than the S group. In all the parameters assessed, patients in the D group outperformed those in the DL group.

Conclusion: The administration of nebulized dexmedetomidine, both alone and in combination with lignocaine, resulted in stable hemodynamics, favorable operative conditions, reduced anesthetic requirement, and facilitated prompt emergence during TNTSS. Nebulized dexmedetomidine proved superior to its combination with lignocaine across all evaluated parameters.

Keywords: Dexmedetomidine, Lignocaine, Nebulization, Pituitary surgery, Transnasal transsphenoidal surgery

INTRODUCTION

The anesthetic objective in transnasal transsphenoidal pituitary surgery (TNTSS) is to ensure stable hemodynamics in ideal surgical conditions, along with prompt and smooth recovery for early neurological evaluation.[12] A relatively bloodless surgical field enhances visibility and is conventionally achieved by applying adrenaline-soaked gauze to the nasal mucosa at the procedure's outset, often leading to tachycardia and hypertension. These hemodynamic disturbances manifest at various TNTSS stages, such as endoscope insertion, mucosal resection, sphenoid drilling, and sellar dissection.[12,33] Moreover, the use of exogenous catecholamines and resultant exaggerated hemodynamic responses could result in adverse cardiovascular events in the perioperative period, especially in patients with secretary pituitary tumors such as Cushing's disease and Acromegaly.[22] Furthermore, the standard anesthetic and analgesic concentrations are often inadequate to dampen these undesired hemodynamic responses, necessitating additional doses and resulting in delayed postoperative recovery.[4] In addition, these residual effects can precipitate respiratory distress in the postoperative period, especially in the setting wherein nasal packing is routinely done.[12] This is further compounded by the inability to provide continuous positive airway pressure ventilation as it is contraindicated in the immediate postoperative period in patients undergoing TNTSS due to the risk of tension pneumocephalus.[32]

Various adjuvants, such as lignocaine and dexmedetomidine, have been shown to enhance the surgical field and reduce anesthetic requirements in TNTSS.[12,17] Dexmedetomidine's selective α2A-receptor agonism induces sedation, analgesia, sympatholysis, and obtund stress responses during intubation and surgery.[3,18,21] Intravenous dexmedetomidine use in TNTSS provides hemodynamic stability, an optimal surgical field, and reduced anesthetic requirements.[12,31] Lignocaine, by topical and intravenous route, has been found to provide optimal surgical field and blunts hemodynamic responses to stress in nasal endoscopic procedures, in addition to reducing the inhalational anesthetic requirements during TNTSS.[5,17,28] Although nebulized dexmedetomidine and its mixture with lignocaine have effectively attenuated intubation responses in other surgical settings, its impact on the hemodynamic and perioperative surgical condition during TNTSS has not been explored.[14,27] Therefore, in this study, we aim to evaluate the efficacy of nebulized dexmedetomidine in providing optimal surgical conditions along with stable hemodynamics in patients presenting for TNTSS surgery.

MATERIALS AND METHODS

This prospective, double-blinded, and randomized controlled trial received approval from the Institutional Ethics Committee (SCT/IEC/1720/SEPTEMBER/2021) and was registered with the Clinical Trials Registry India (CTRI/2022/03/052460). The study included consenting patients aged 18–60 years presenting with pituitary tumors of any gender and classified as American Society of Anesthesiologist (ASA) physical status 1 or 2 and a Glasgow Coma Scale score (GCS) of 15 undergoing elective TNTSS. Exclusion criteria encompassed patients with GCS <15, elevated intracranial pressure, pregnancy, nursing mothers, pituitary apoplexy, and individuals with Cushing's and Acromegaly accompanied by cardiac abnormalities. In addition, the study did not include patients with severe concurrent medical conditions such as decompensated heart failure, advanced liver disease, renal failure, medication allergies, or a history of prior nasal surgery.

Using a computer-generated random number table, patients were allocated into three groups: the dexmedetomidine group, n = 25 (group D); the dexmedetomidine-lignocaine group, n = 25 (group DL); and the control group, n = 25 (group S) [Figure 1]. An anesthesia technician, who was not involved in the study, prepared the nebulization medication in the operating room from a sealed, opaque envelope containing the randomly assigned numbers. Group D patients received nebulization of dexmedetomidine at a dosage of 1.5 μg/kg mixed with saline, resulting in a total volume of 5 mL. Group DL patients received nebulization of dexmedetomidine at a dosage of 1.5 μg/kg combined with 2% lignocaine to a total volume of 5 mL. Meanwhile, Group S patients received nebulization with 5 mL of saline.

Anesthesia protocol

Standard ASA pre-induction monitors, such as a pulse oximeter, electrocardiogram, and non-invasive blood pressure (BP), were applied in the operating room. Radial artery cannulation was performed under local anesthesia. The patient received nebulization for 10 min, after which anesthesia was induced with injections of fentanyl (2 μg/kg) and propofol, titrated to achieve a loss of verbal response. Endotracheal intubation was facilitated using atracurium (0.5 mg/kg), and a throat pack was inserted following intubation. Anesthesia was maintained using a combination of oxygen and medical air (1:1), sevoflurane at a concentration of 0.8–1 minimum alveolar concentration (MAC), and continuous infusions of fentanyl (1–2 μg/kg/h) and atracurium (0.3 mg/kg/h) to maintain a bispectral index within the range of 40–60. All patients were ventilated to ensure normal carbon dioxide levels, and normothermia was maintained throughout the procedure.

The surgery was performed by an experienced neurosurgeon using a Mayfield 3-pin head clamp to facilitate neuronavigation. The infusions of fentanyl and atracurium were discontinued at the time of graft harvesting from

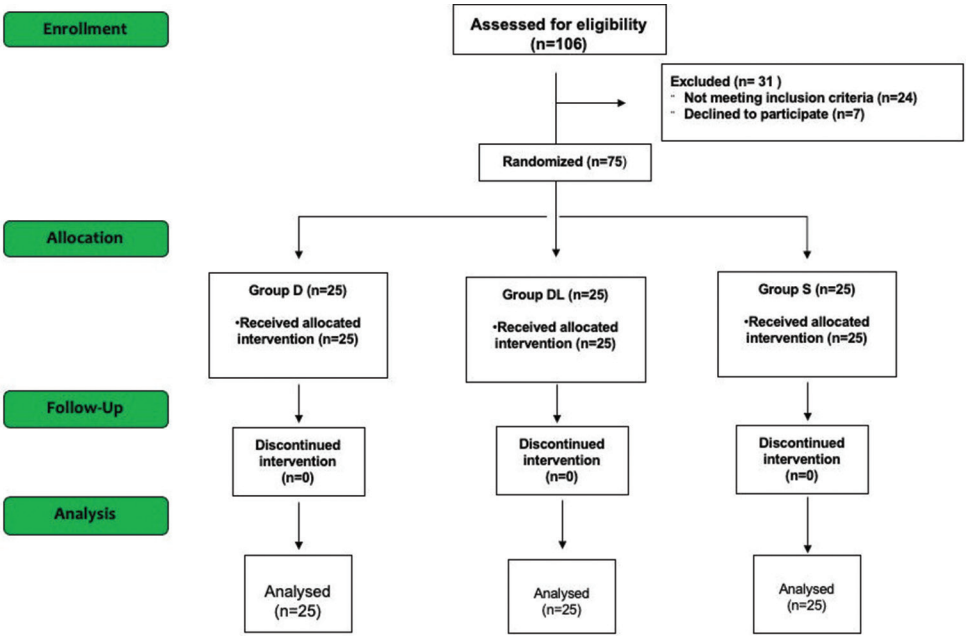

Figure 1: Consort flow chart describing the patient recruitment and randomization into groups, D: Dexmedetomidine, DL: Dexmedetomidine-Lignocaine and S: Control.

the thigh for packing the sphenoid defect. In addition, ondansetron (0.1 mg/kg) and paracetamol (15 mg/kg) were administered. Sevoflurane was discontinued at the end of the surgery following the final nasal packing. The Mayfield head pins were subsequently removed, and comprehensive oral suction was performed, including removing the throat pack. Patients were ventilated with 100% oxygen, and after the reversal of neuromuscular blockade, they were extubated once it was confirmed that they exhibited sufficient respiratory efforts and appropriate response to simple commands. Subsequently, patients were monitored in the intensive care unit for the following 24 hours.

Study protocol

Hemodynamic parameters, including heart rate (HR), systolic BP, diastolic BP, and mean BP (MBP), were monitored at various time points during anesthesia and surgery, denoted as follows: T0 (Baseline), T1 (post-nebulization), T2 (post-anesthesia induction), T3 (post-intubation), T4 (pre-nasal endoscope insertion), T5 (at endoscope insertion), T6 (before adrenaline pack placement), T7 (during adrenaline packing), T8 (during mucosal resection), T9 (during sphenoid drilling), T10 (during tumor resection), T11 (after discontinuing fentanyl infusion), T12 (after stopping inhalational agent), T13 (after extubation), and T14 (30 min post-extubation).

In the event of MBP or HR > 20% of the baseline, additional intravenous bolus doses of fentanyl (50 μg/bolus) were administered. If elevated BP or HR values persisted, additional intravenous boluses of propofol (30 mg/bolus) and labetalol (5 mg/bolus) were given, and the sevoflurane MAC was increased up to 1. These boluses were repeated to maintain optimal hemodynamics (HR and BP within 20% of baseline). Intravenous mephentermine boluses (3 mg/bolus) were administered when BP < 20% of baseline, and atropine (0.6 mg) was prepared for administration if HR dropped below 40 beats/min. Total doses of fentanyl and propofol (during intubation and head clamping), fentanyl infusion, and additional amounts of propofol and fentanyl at different time points were documented. The use of labetalol, mephentermine, and sevoflurane MAC at various time points was also recorded. Emergence and extubation times were noted, as well as postoperative nausea and vomiting (PONV), pain, and the need for supplementary analgesia during the 24-hour postoperative period. The surgical field quality during the procedure was evaluated by surgeons using Formmer's scores, with a score of one considered excellent, one and two as acceptable, and three and above as indicative of unacceptable surgical conditions.

Statistical analysis

We conducted the statistical analysis using SPSS Inc., Chicago, IL, version 26.0. Continuous variables were presented as mean ± standard deviation or median (interquartile range) for skewed data, while categorical data were described using frequency, ratio, and percentage (%). We employed one-way analysis of variance (ANOVA) and the Kruskal–Wallis test to compare continuous and categorical parameters between groups. ANOVA for repeated measures was used to compare continuous variables within the groups.

$P < 0.05$ was considered statistically significant for intergroup comparisons.

The sample size was determined based on the available literature, specifically regarding Formmer's score from a prior study. In this study, the proportion of outcomes with Formmer's scores >3 in the control group was 53%, whereas in the treatment group, it was 16%.[38] To detect this difference in outcomes with a significance level of 5% and a power of 80%, a sample size of 25 patients per group was calculated. Consequently, the total sample size for our study was 75 patients.

RESULTS

Overall, 106 patients were screened for eligibility; 24 did not meet the inclusion criteria, and seven declined participation. Other 75 patients who participated in the study were randomized into the S, D, and DL groups, comprising 25 patients in each group. All these patients completed the study [Figure 1]. There was no significant difference in patient demographics and baseline characteristics of the three groups [Table 1]. The S group exhibited a significantly higher HR than the D group at T4 to T 14-time points, and the DL group displayed an increased HR compared to the D group during various time frames of surgery [Table 2]. Nonetheless, these HR changes were not clinically significant, and none of the patients in any group experienced tachycardia or bradycardia [Table 2]. Although the baseline mean arterial pressure (MAP) and HR were comparable across all groups, the S group showed a significantly higher MAP than the D and DL groups during T5, T7, T8, T9, T12, and T13 time points [Table 2]. Moreover, a significant increase in MAP (>20% of baseline) was noted in the S group after adrenaline packing and mucosal resection, which was absent in the other two groups ($P < 0.01$) [Table 2].

The S group, compared to the D and DL groups, required additional doses of fentanyl to attenuate the stress responses during endoscope insertion (T5), adrenaline packing (T7), and mucosal resection (T8) [Table 3]. Median fentanyl use during these time frames was significantly higher in the S group ($P < 0.001$). Moreover, the DL group had a higher median fentanyl use at the T8 time point ($P < 0.01$) as compared to group D. Median propofol use was significantly higher in the S group compared to the D group ($P = 0.007$) [Table 3]. The median use of labetalol was significantly higher in the S group than in the D and DL groups at the T7 time point [Table 4]. In addition, the D group had a significantly lower median use of labetalol compared to the DL and S groups during the extubation time point ($P = 0.012$). Furthermore, the total dose of labetalol used throughout the surgery was significantly higher in the S group than in the D group ($P = 0.007$), although there was no significant difference in the use of mephentermine.

The S group required a significantly higher MAC to maintain optimal hemodynamics than the D group from endoscopic insertion until tumor resection (T5 to T10) ($P < 0.01$). Moreover, a higher MAC of sevoflurane was needed in the S group compared to the DL group during the T8 and T9 time frames. The DL group required a significantly higher MAC from T5 to T8 than the D group [Figure 2]. The total fentanyl used during the entire intraoperative period was found to be considerably lower in the D group as compared to the DL and S groups ($P < 0.01$). In addition, the total intraoperative use of propofol and the induction dose of propofol was significantly lower in the D and DL groups compared to the S group ($P = 0.000$) [Table 4].

In the D group, 16 patients (64%) achieved a grade one Formmer score, as compared to two patients (8%) in the DL group and none in the S group, which was statistically significant ($P = 0.000$). A combination of grade 1 and grade 2 Formmer scores considered an acceptable surgical field was observed in all patients (100%) in the D group versus 22 patients (88%) in the DL group versus 16 patients (64%) in the S group. Formmer scores of >3, indicating a

Table 1: Comparison of demographic data, patient characteristics, tumor characteristics, and surgery duration between the studied groups.

Patient demographics	Group S	Group D	Group DL	*P*-value
Age (years)	46.24 (±12.38)	46.08 (±12.07)	44.40 (±11.14)	0.832
Weight (kg)	65.80 (±11.31)	73.16 (±13.90)	70.76 (±12.23)	0.113
Sex (male/female)	12/13	11/14	11/14	0.948
ASA I/ASA II	16/9	16/9	12/13	0.420
Hypertension (yes/no)	6/19	7/18	8/17	0.82
Diabetes (yes/no)	5/20	3/22	7/18	0.368
Hypothyroidism (yes/no)	7/18	11/14	7/18	0.383
Hypocortisolism (yes/no)	6/19	6/19	7/18	0.932
Diagnosis (NFPT/acromegaly/cushings/prolactinoma)	20/1/1/3	17/2/3/3	16/1/1/7	0.537
Duration of surgery (min)	226.8 (±18.19)	229.2 (±17.78)	231.2 (±23.50)	0.739

Data expressed as mean (SD) or absolute numbers. D: Dexmedetomidine, DL: Dexmedetomidine-lignocaine, S: Control, ASA: American society of anesthesiologist, NFPT: Non-functional pituitary tumor, SD: Standard deviation

Table 2: The comparison of HR and mean blood pressure at different time frames among study groups.

Stages	HR in beats/min (mean±SD)				Mean arterial pressure in mm Hg (mean±SD)			
	Group S (*n*=25)	Group D (*n*=25)	Group DL (*n*=25)	*P*	Group S (*n*=25)	Group D (*n*=25)	Group DL (*n*=25)	*P*
T0 (Baseline)	76.08 (±4.88)	77.6 (±8.87)	76.28 (±8.34)	0.744	93.63±6.98	96.51±6.1	93.65±8.86	0.294
T1 (Post nebulization)	73.96 (±4.33)	71.64 (±8.39)	70.72± (7.27)	0.237	94.38±6.24	93.11±6.03	90.19±8.2	0.095
T2 (Anesthesia induction)	66.8 (±3.87)	68.76 (±7.17)	66.8± (6.91)	0.436	87.09±5.26	89.74±5.32	86.89±7.17	0.178
T3 (Intubation)	78.16 (±6.79)	72.92 (±7.2)$^{\Omega\Omega}$	74.44± (6.23)	0.023*	96.37±5.96	93.49±5.02	91.52±7.54$^{\Phi}$	0.027*
T4 (Pre endoscope insertion)	70.64 (±4.29)	70.52 (±6.92)	69.72± (4.61)	0.808	90.46±5.04	91.63±3.79	88.84±7.4	0.217
T5 (Endoscope insertion)	79.64 (±6.84)	77.56 (±7.29)	83.52 (±7.72)$^{\#\#}$	0.017*	106.69±6.63	98.96±4.32$^{\Omega}$	101.9±10.59$^{\Phi}$	0.003**
T6 (Pre adrenaline pack)	79.32 (±2.98)	76.2 (±6.26)$^{\Omega}$	78.96 (±5.79)	0.076	103.37±7.08	96.88±4.57$^{\Omega\Omega}$	97.56±9.5$^{\Phi\Phi}$	0.004**
T7 (Adrenaline pack)	90.88 (±4.65)	85.0 (±7.21)$^{\Omega\Omega}$	89.44 (±7.13)$^{\#}$	0.005**	116.4±5.15	107.58±6.32$^{\Omega}$	107.88±10.07$^{\Phi\Phi}$	0.000**
T8 (Mucosal resection)	89.4 (±4.57)	81.32 (±6.71)$^{\Omega\Omega}$	87.08 (±6.89)$^{\#\#}$	0.01*	115.87±5.94	103.72±5.66$^{\Omega}$	107.24±9.56$^{\Phi\Phi}$	0.000**
T9 (Sphenoid drilling)	80.6 (±3.8)	76.08 (±5.92)$^{\Omega\Omega}$	79.0 (±5.02)$^{\#}$	0.007**	105.21±5.88	97.68±4.37$^{\Omega}$	99.84±8.93$^{\Phi\Phi}$	0.001**
T10 (Tumour resection)	72.88 (±3.47)	70.76 (±5.48)	74.64 (±4.58)$^{\#\#}$	0.015*	95.34±5.45	92.92±4.31	92.68±7.73	0.229
T11 (Fentanyl infusion cessation)	75.72 (±5.04)	74.76 (±5.06)	78.28 (±4.58)$^{\#\#}$	0.037*	98.88±4.8	95.68±4.63	94.96±7.75	0.050
T12 (Sevoflurane cessation)	80.64 (±4.42)	77.72 (±5.18)$^{\Omega}$	81.8 (±5.13)$^{\#\#}$	0.014*	102.01±4.87	97.54±5.01$^{\Omega}$	97.24±7.72$^{\Phi\Phi}$	0.010*
T13 (Extubation)	85.4 (±4.28)	82.4 (±6.19)	86.64 (±5.35)$^{\#\#}$	0.019*	104.88±4.91	99.45±5.14$^{\Omega\Omega}$	100.2±7.54$^{\Phi}$	0.004**
T14 (1 h post extubation)	75.64 (±3.41)	72.64 (±5.1)$^{\Omega}$	75.96 (±4.5)$^{\#\#}$	0.017*	95.38±4.03	93.32±4.87	92.92±7.21	0.248

*P<0.05 b/w C, D and DL **P<0.01 b/w C, D and DL, $^{\Omega}P$<0.05 b/w C and D, $^{\Omega\Omega}P$<0.01 b/w C and D, $^{\Phi}P$<0.05 b/w C and DL, $^{\Phi\Phi}P$<0.01 b/w C and DL, $^{\#}P$<0.05 b/w D and DL, $^{\#\#}P$<0.01 b/w D and DL. D: Dexmedetomidine, DL: Dexmedetomidine-lignocaine, S: Control, HR: Heart rate, SD: Standard deviation

Table 3: Comparison of various additional intravenous medications used at different time frames among study groups.

Medications	Group S	Group D	Group DL	*P*-value
Additional fentanyl at T5 (μg)	50 (25–50)	0 (0–0)$^{\Omega\Omega}$	0 (0–50)$^{\Phi}$	<0.001**
Additional Fentanyl at T7 (μg)	75 (50–100)	50 (0–50)$^{\Omega\Omega}$	50 (50–50)$^{\Phi\Phi}$	<0.001**
Additional Fentanyl at T8 (μg)	50 (50–100)	0 (0–0)$^{\Omega\Omega}$	50 (50–50)$^{\Phi\#\#}$	<0.001**
Propofol (T7) (mg)	0 (0–30)	0 (0–0)$^{\Omega\Omega}$	0 (0–30)	0.007**
Propofol (T8) (mg)	0 (0–30)	0 (0–0)	0 (0–0)	0.065
Labetalol (T7) (mg)	5 (0–5)	0 (0–0)$^{\Omega\Omega}$	0 (0–0)$^{\Phi}$	0.002**
Labetalol (T8) (mg)	0 (0–5)	0 (0–0)	5 (0–5)	0.057
Total Labetalol (mg)	10 (5–15)	0 (0–10)$^{\Omega\Omega}$	10 (5–10)	0.007**
Labetalol (during extubation) (mg)	5 (5–10)	5 (0–5)$^{\Omega}$	5 (5–5)	0.012*
Total Mephentermine (mg)	3 (3–6)	3 (0–6)	3 (3–6)	0.229

Data expressed as median (IQR). *P<0.05 b/w C, D and DL, **P<0.01 b/w C, D and DL, $^{\Omega}P$<0.05 b/w C and D, $^{\Omega\Omega}P$<0.01 b/w C and D, $^{\Phi}P$<0.05 b/w C and DL, $^{\Phi\Phi}P$<0.01 b/w C and DL, $^{\#}P$<0.05 b/w D and DL, $^{\#\#}P$<0.01 b/w D and DL. D: Dexmedetomidine, DL: Dexmedetomidine-lignocaine, S: Control, IQR: Interquartile range

compromised surgical field, were found to be significantly higher in groups S and DL, with nine patients (32%) in the S group, three patients (12%) in the DL group, and none in the D group [Table 4]. Patients in the D group experienced

Table 4: Comparison of the surgical field, total intravenous anesthetics used, and recovery characteristics among study groups.

	Group S	Group D	Group DL	*P*-value
Formmer's surgical field score				
1 (Excellent surgical condition) (*n*)	0	$16^{\Omega\Omega}$	$2^{\#\#}$	0.000**
2 (Good surgical condition) (*n*)	16	9	$20^{\#\#}$	0.006**
>3 (Poor surgical condition) (*n*)	9	$0^{\Omega\Omega}$	3^{Φ}	0.002**
1 and 2 (Surgically accepted) (*n*)	16	$25^{\Omega\Omega}$	22^{Φ}	0.002**
Total intravenous anesthetic used				
Total fentanyl ((μg/kg)	10.41±1.49	$7.67\pm0.76^{\Omega\Omega}$	$9.01\pm0.6^{\Phi\#\#}$	0.000**
Total propofol (mg/kg)	2.21±0.28	$1.45\pm0.19^{\Omega\Omega}$	$1.57\pm0.37^{\Phi}$	0.000**
Propofol (during induction) (mg/kg)	1.8±0.17	$1.37\pm0.10^{\Omega\Omega}$	$1.28\pm0.21^{\Phi}$	0.000**
Recovery characteristics				
Emergence time	16.4±1.38	$11.24\pm1.39^{\Omega\Omega}$	$13.72\pm1.2^{\Phi\Phi\#\#}$	0.000**
Extubation time	17.8±1.32	$12.5\pm1.3^{\Omega\Omega}$	$14.88\pm1.33^{\Phi\Phi\#\#}$	0.000**
PONV (Yes/no)	10/15	5/20	6/19	0.249
Rescue analgesics (Yes/no)	4/21	3/22	3/22	0.891

Data expressed as absolute numbers or mean (SD). **P<0.01 b/w C, D and DL, $^{\Omega}P$<0.05 b/w C and D, $^{\Omega\Omega}P$<0.01 b/w C and D, $^{\Phi}P$<0.05 b/w C and DL, $^{\Phi\Phi}P$<0.01 b/w C and DL, $^{\#}P$<0.05 b/w D and DL, $^{\#\#}P$<0.01 b/w D and DL. PONV: Postoperative nausea and vomiting, D: Dexmedetomidine, DL: Dexmedetomidine-lignocaine, S: Control, SD: Standard deviation

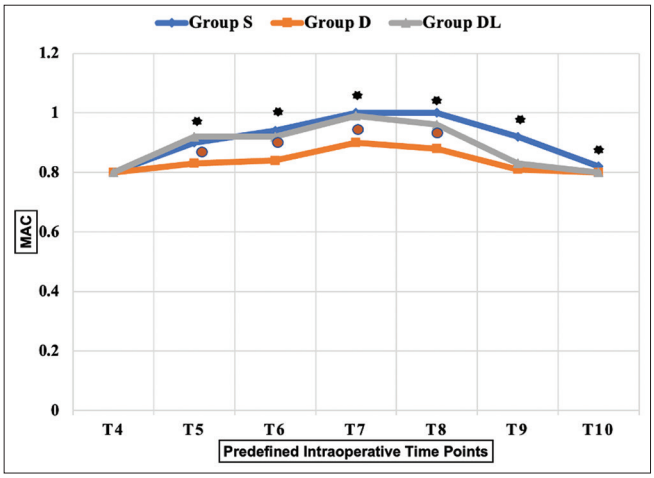

Figure 2: Comparison of minimum alveolar concentration (MAC) of sevoflurane at predefined intervals among groups. P < 0.01 between S and D group ----, P < 0.01 between D and DL group -----. D: Dexmedetomidine, DL: Dexmedetomidine-lignocaine, S: Control.

significant early emergence and extubation compared to the DL and S groups (P = 0.000). No significant differences were observed in the onset of PONV or the requirement for rescue analgesics among the three groups [Table 4].

DISCUSSION

Our study marks the first attempt to assess the impact of nebulized dexmedetomidine, either alone or in combination with lignocaine, on the surgical field, hemodynamic stability, and anesthetic requirements in TNTSS. We discovered that pre-anesthesia nebulization of dexmedetomidine or its combination with lignocaine in TNTSS patients resulted in several favorable outcomes compared to saline nebulization. These outcomes included optimal intraoperative hemodynamic parameters, improved surgical conditions, reduced anesthetic requirements, and facilitated early emergence and extubation.

One of the distinctive challenges in endoscopic TNTSS, compared to endoscopic nasal surgeries, is the need to maintain sufficient cerebral blood flow (CBF) and ensure early emergence for neurological assessment. Induced hypotension, often used to minimize bleeding in endoscopic nasal surgery, can jeopardize CBF in TNTSS.[12] The use of additional anesthetics to mitigate intraoperative hemodynamic disturbances can delay emergence and lead to residual effects, which can be problematic in the postoperative period. Various regional anesthetic techniques described for TNTSS to blunt stress responses are associated with complications.[32] While topical and intravenous lignocaine are known to provide an optimal surgical field and blunt hemodynamic stress responses, their impact on reducing anesthetic requirements is debatable.[17,26,28]

Dexmedetomidine has been safely used as an adjuvant in central neuraxial and peripheral nerve blocks, with substantial bioavailability when absorbed through the nasal and buccal mucosa.[6,8,9,16] Intravenous and intranasal cotton-soaked dexmedetomidine have been found to achieve optimal surgical fields and reduce anesthetic requirements in TNTSS.[12,15] Recently, nebulization has emerged as a novel route for dexmedetomidine administration, safely used for various purposes in different medical settings.[2,11,24,39] Furthermore, combinations of nebulized lignocaine and dexmedetomidine have been demonstrated as effective in procedures related to airway anesthesia.[13,14,23,34,37] Our study

demonstrates that nebulized dexmedetomidine (1.5 μg/kg) and its combination with lignocaine effectively mitigated the intubation response in TNTSS, similar to previous studies involving intravenous dexmedetomidine in TNTSS.[12,25,29]

The patients in the control group experienced a significant increase in MAP from the baseline during adrenaline packing and mucosal resection, necessitating higher sevoflurane MAC, additional doses of fentanyl, propofol, and labetalol to maintain stable hemodynamics. However, patients who received nebulized dexmedetomidine alone or in combination with lignocaine maintained stable hemodynamics throughout the surgery. In addition, the total requirement of fentanyl, propofol, and sevoflurane was significantly lower in these groups as compared to the control group. The sympatholytic properties of dexmedetomidine could have blunted the response to noxious stimuli during various surgical stages, resulting in a significantly reduced requirement for anesthetics.[12,20,35,36] Our findings align with the previous studies involving intravenous dexmedetomidine in TNTSS, leading to early emergence and extubation.[7,12]

In our study, patients in the dexmedetomidine groups had optimal surgical fields, with a substantial percentage of patients having excellent Formmers grades. In contrast, many patients in the control group experienced poor surgical conditions. Dexmedetomidine's ability to attenuate stress-induced hypertension also aided in minimizing surgical field bleeding, resulting in better operating conditions.[1,18,31,36] The use of intravenous dexmedetomidine in TNTSS has been associated with hypotension and bradycardia, necessitating the use of atropine in one study.[35] In addition, another study reported prolonged hypotension for up to 30 min following administering an intravenous dexmedetomidine loading dose before anesthesia induction.[7] This type of hypotensive response may not be well-tolerated, particularly in specific subsets of TNTSS patients, such as those with pre-existing cardiac conditions like Cushing's and Acromegaly, where cardiac compromise is a concern. In our study, the control group necessitated significantly higher doses of labetalol and anesthetics to achieve stable hemodynamics. Moreover, there was no significant difference regarding the need for vasopressor therapy between the dexmedetomidine and the control group, indicating the better hemodynamic profile offered by nebulized dexmedetomidine. Therefore, our study on nebulized dexmedetomidine, which achieves similar effects to intravenous dexmedetomidine but without hemodynamic perturbations, could offer a distinct advantage in this particular context.

Intravenous dexmedetomidine during TNTSS has been associated with a lower incidence of PONV and reduced need for postoperative rescue analgesics.[7,12] However, in our study, there were no differences in the incidence of PONV or the requirement for postoperative analgesics among the groups. The relatively prolonged duration of surgery and variations in bioavailability in the nebulized route compared to the intravenous route could account for our results.[6,16]

Our findings indicate that the D group outperformed the DL group in terms of stable hemodynamic profile, providing an excellent surgical field with reduced anesthetic requirement and emergence time. This difference may be attributed to the altered behavior of nebulized particles of the two compatible drug preparations, which may differ from the properties of individually nebulized drug preparation particles.[19,30] The particle size of the nebulized mixture of dexmedetomidine and lignocaine may vary when compared to nebulized dexmedetomidine particles alone, leading to differences in their deposition across the nasal and respiratory mucosa. The pH and pKa of the nebulized mixture of dexmedetomidine and lignocaine would be altered compared to nebulized dexmedetomidine particles alone, making it less favorable for absorption across the nasal mucosa.[10,30] Several other factors also influence the drug absorption across the nasal mucosa, including particle size (particles larger than ten μg tend to deposit in the nose, while those smaller than five mcg may reach the lungs), pH/pKa (each drug has a specific value for effective absorption), and molecular weight (inversely proportional to absorption).[10,19,30] In addition, the type of compressor used in the nebulizer is known to produce particles of varied sizes.[19,30] Consequently, we hypothesize that lignocaine, when mixed with dexmedetomidine for nebulization, could reduce the availability and absorption of dexmedetomidine across the nasal mucosa compared to dexmedetomidine alone, resulting in the superior performance of dexmedetomidine alone in nebulization.

Limitations

While most of the cases were operated on by the same surgeon, a small number were operated on by other surgeons with more than five years of experience in TNTSS. We included patients with a good ASA grade and normal cardiac function, and further studies including higher ASA grade patients with borderline cardiac function will help confirm the advantages described in our research over intravenous dexmedetomidine in TNTSS. In our study, lignocaine and dexmedetomidine were mixed and nebulized to save time. Nebulizing lignocaine and dexmedetomidine separately might yield different results when comparing the dexmedetomidine alone and combination groups.

CONCLUSION

Administering nebulized dexmedetomidine at a dose of 1.5 μg/kg, both alone and in combination with lignocaine, ensured stable hemodynamics and favorable surgical conditions during TNTSS surgery. In addition, it reduced the

need for anesthetics and promoted a prompt and seamless emergence from anesthesia in this group of patients. Notably, nebulized dexmedetomidine outperformed its combination with nebulized lignocaine in achieving excellent surgical conditions, reducing the need for anesthetics, and facilitating early post-anesthesia recovery.

Ethical approval

The author(s) declare that they have taken the ethical approval from IEC - SCT/IEC/1720/SEPTEMBER/ 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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