

To Evaluate the Effect of Intraoperative Dexmedetomidine on Emergence Agitation in Patient Undergoing Nasal and Pharyngeal Surgery

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ABSTRACT

Background: “Emergence agitation” is a transient but potentially dangerous state that might result in bleeding, hypoxia, pneumonia, or the need for additional treatment. This study aimed to determine the effect of intraoperative dexmedetomidine on emerging agitation in adult patients undergoing pharyngeal & nasal surgery.

Methods: One hundred patients undergoing pharyngeal & nasal operations under general anaesthesia participated in the study; 50 subjects were assigned to the dexmedetomidine group and 50 to the control group. While patients in the control group got a placebo of normal saline infusion, those in the study group received dexmedetomidine at a rate of 0.4 $\mu\text{g kg}^{-1} \text{h}^{-1}$ after induction of anesthesia till extubation and completion of surgery. Numerous indicators were tracked in the study, such as end-tidal CO_2 levels, non-invasive blood pressure, pulse, oxygen saturation, & ECG. Agitation levels were measured using the RICKER sedation-agitation scale. After their transfer, the patients were observed for any issues in the post-anesthetic care unit.

Results: The proportion of participants with emerging agitation with a Ricker sedation agitation score of 5 to 7 was decreased in Group D (8%) than in Group C (26%). In all cases, agitation was reduced after 5 minutes of extubation. One patient (2%) in Group D experienced post-operative nausea & vomiting, while three patients (6%) in Group C did. Furthermore, Group D has a continuously lower mean heart rate & blood pressure than Group C at all periods. $p < 0.05$ indicates a statistically significant difference ($p < 0.05$).

Conclusion: The present study showed that intraoperative continuous dexmedetomidine infusion reduced the incidence of emerging agitation after nasal & pharyngeal surgery while not delaying extubation or worsening other problems.

Key-words: Dexmedetomidine, Emergence Agitation, Nasal surgery, Pharyngeal Surgery, RICKER sedation-agitation scale

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INTRODUCTION

“Emergence agitation” (EA) occurs in the early recovery stage after general anesthesia and is determined by restlessness, excitement, confusion, non-purposeful movement, inconsolability, thrashing, & incoherence. The range of EA incidence is roughly 0.25 to 90.5% [1]. It can turn dangerous at any time, with potentially dangerous outcomes for the patient, including bleeding, self-extubation, self-harm, increased post-operative

pain, & catheter removal necessitating physical or medication restriction. Moreover, EA worries recovery room workers & anesthesiologists, increasing hospital expenses [2]. Self-extubation or catheter removal due to emergent agitation following general anesthesia may result in major problems such as hypoxia, aspiration pneumonia, hemorrhage, or the need for reoperation [2]. Emergence agitation is more common following ear, nose, & throat (ENT) surgery [3]. Due to blood contamination of the airway & surgical pack obstruction of the nasal airway during nasal surgery, conscious extubation is recommended [4]. Extubation when awake, however, might exacerbate emerging agitation. Usually, EA has a brief lifespan & ends on its own. Managing emerging agitation mostly involves removing things that cause it, such as pain, worry, or the presence of intrusive equipment. Preferred therapeutic pharmacological therapies for emerging agitation, according to several research are sedatives (like propofol & midazolam) and opioids (like fentanyl & morphine) [1].

“Dexmedetomidine” is a highly selective α_2 agonist that reduces sympathetic central nervous system activity to cause sedation & anxiolysis. Its association with low respiratory depression is one of its main advantages over other sedatives [5]. Dexmedetomidine used during surgery reduces the number of opioids used after surgery, the severity of pain, & the need for antiemetic medication [6-9]. Furthermore, it has been demonstrated that intra-operative dex infusion improves the recovery quality following major spine surgery by reducing stress response [10]. There is little information on adult patients' emerging agitation; most research on this topic has been done on pediatric patients. We conducted this trial to determine the impact of intra-operative dexmedetomidine on emerging agitation in adult patients following pharyngeal & nasal surgery.

MATERIALS AND METHODS

This prospective, randomized, double-blind study was undertaken at Nobel Medical College Teaching Hospital, Biratnagar, from February 05, 2023, to December 05, 2023. The study involved 100 patients. These patients were assigned to two groups based on computer-generated random numbers. The dexmedetomidine group (Group D; n=50) received $0.4 \mu\text{g kg}^{-1} \text{h}^{-1}$ from anesthesia induction to extubation, while the control

group (Group C; n=50) received volume-matched normal saline infusion as a placebo.

Inclusion criteria- The study included ASA class 1-2 patients (aged 20-60 yrs) undergoing nasal and pharyngeal surgery and surgery not lasting more than two hours.

Exclusion criteria- The trial excluded patients who were unwilling to participate, allergic to the study drug, had coagulopathies, or were classified as ASA-III or above.

Methodology- Routine preanaesthetic check-up and counselling were done a day before the surgery. Patients were kept nil per oral for at least 8 hours before surgery. All patients were crystalloid-preloaded & given intravenous Midazolam 0.04 mg/kg 30 min after intravenous access with 18G cannula before anesthesia was administered. Routine monitors were employed & monitored at 5-minute intervals, including the ECG, non-invasive blood pressure, pulse, oxygen saturation (SpO_2), & end-tidal CO_2 ($\text{E}'\text{CO}_2$). Fentanyl (1 mg kg^{-1}) and propofol 1.5 mg kg^{-1} were used to induce general anesthesia following the loading of 4 ml kg^{-1} of crystalloid solution. Before orotracheal intubation, rocuronium bromide (0.8 mg/kg) was administered intravenously and then a 7-7.5 mm tube was inserted for females and males, respectively. The ETCO_2 was maintained between 30-40 mm hg in 50% oxygen/air by adjusting the ventilation frequency and setting the mechanical ventilation to 6 ml/kg tidal volume. Isoflurane was utilized to keep the anesthetic at 1-1.5 volume % for maintenance of anaesthesia. Reversal medications were administered after surgery to restore neuromuscular function (glycopyrrolate 0.004 mg/kg & neostigmine 0.02 mg/kg). After that, manual ventilation using 100% oxygen at an 8 L/min rate was substituted for mechanical ventilation. Group D patients received dexmedetomidine until they were extubated. Other than being repeatedly asked to open their eyes verbally, the patients were not disturbed. We avoided any other stimuli.

We measured each patient's degree of agitation using the RICKER sedation-agitation scale [11], with the highest possible agitation score noted. 1: little or no reaction to unpleasant stimuli; 2: arousal to physical stimuli but lack of communication; 3: difficult arousal but awakening to

verbal stimuli or light shaking; 4: composure & obedience to commands; 5: anxiety or physical agitation & calming to spoken instructions; 6: necessity for restraint & frequent verbal reminders of boundaries; & 7: pulling at tracheal tube, trying to remove catheters, or hitting staff. A score of 5 or higher on the sedation-agitation scale indicated emergent agitation. Dangerous agitation was defined as a score of 7 on the sedation-agitation scale [2,11]. After that, the patients were taken to the post-anesthesia care unit (PACU), where they were observed for any complications such as increased salivation, nausea, vomiting, desaturation, & laryngospasm. Heart rate & blood pressure were periodically checked.

RESULTS

The study included a total of 100 participants having pharyngeal & nasal surgery. Of these, 50 were assigned to the study group, the Dexmedetomidine group. Fifty people were distributed to the control group, the non-dexmedetomidine group (normal saline). The two groups' demographic profiles & surgical characteristics,

Statistical Analysis- Data was collected & recorded as per working proforma. Observed data was entered in MS Excel sheet & analysis was done using two-sample t-tests in SPSS software version 23. P value <0.05 was defined as statistically significant.

Ethics approval and consent to participate- The above study was approved by the Human Ethical Committee (Ethics Committee approval number: IRC-NMCTH/741/2023 dated February 01 2023) of the Department of Anaesthesiology, Nobel Medical College Teaching Hospital, Biratnagar, Nepal and informed consent was obtained from the patients before the study.

including age, gender, BMI, length of surgery, study drug infusion time, & intraoperative fluid volume, were compared using the t-test (Table 1). The p-values for BMI, infusion duration of study drug & amount of intraoperative fluid were p<0.05, which showed a significant difference.

Table 1: Demographic profile & operation details of patients.

| | Group C (n=50) | Group D (n=50) | p-value |
|---------------------------------------|----------------|----------------|---------|
| Age (Years) | 37.5±13.15 | 37.2±11.04 | 0.44 |
| Sex (Male/Female) | 35±15 | 37±13 | 0.48 |
| Body Mass Index (Kg/m ²) | 23.12±1.32 | 22.05±1.20 | 0.0001 |
| Duration of Surgery (min) | 56±23 | 50±20 | 0.17 |
| Infusion Duration of Study Drug (min) | 58±25 | 62±20 | 0.005 |
| Amount of Intraoperative Fluid (ml) | 500±210 | 450±223 | 0.0005 |

Values are mean ±SD. D=Dexmedetomidine; C=Control (normal saline)

As shown in Fig. 1, there were fewer EA patients in Group D (n = 4; 8%) than in Group C (n = 13; 26%) with a Ricker sedative agitation score of 5 to 7. Five minutes after extubation, all patients' agitation subsided. Three (6%) subjects in group C & one (2%) subjects in group D suffered adverse effects such as post-operative nausea & vomiting. Neither group experienced additional side effects, including bradycardia, desaturation, hypersalivation, hypotension, or laryngospasm (Fig. 2).

Table 2 shows the differences in heart rate & blood pressure between the study & control groups. Group D has a continuously lower mean heart rate than Group C at all periods. Similarly, the mean blood pressure in Group D is continuously lower than Group C's at all time intervals. Mean heart rate & blood pressure had p<0.05 across all time intervals, indicating a significant difference.

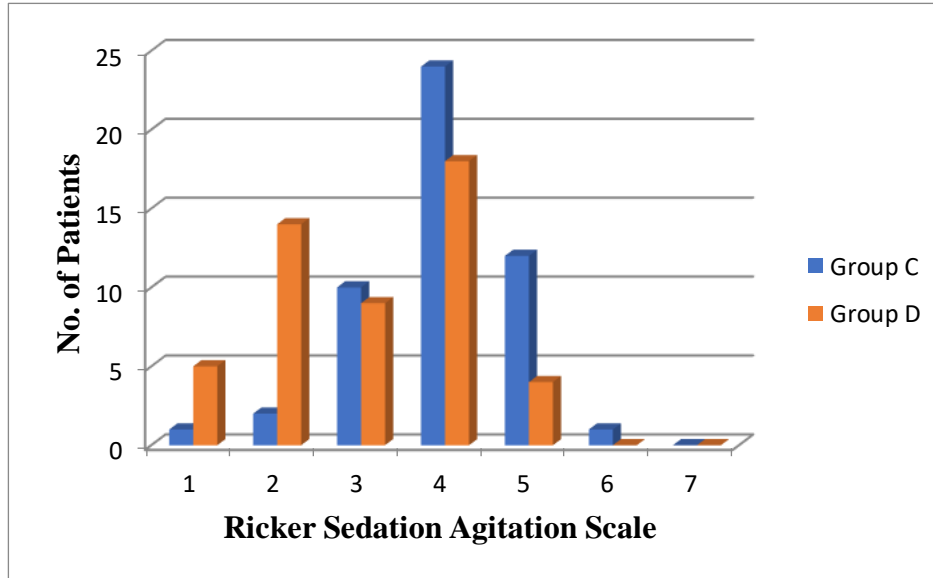


Fig. 1: Distribution of Ricker sedation agitation scale among study participants.

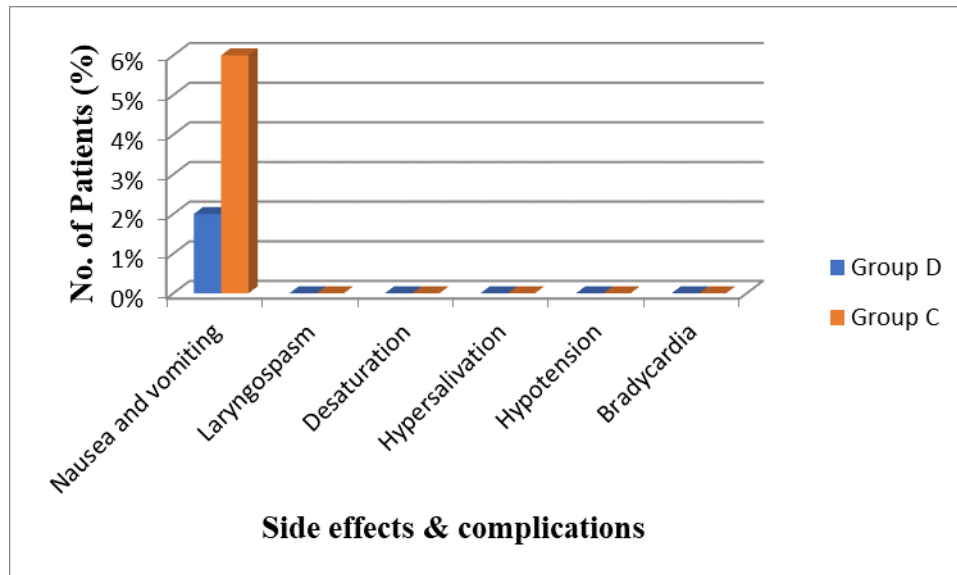


Fig. 2: Post-operative side effects & complications in patients.

Table 2: Comparison of heart rate & blood pressure between the study & control groups.

| Time Intervals (Min) | Mean Heart Rate | | p-value | Mean Blood Pressure | | p-value |
|----------------------|-----------------|----------------|---------|---------------------|----------------|---------|
| | Group C (n=50) | Group D (n=50) | | Group C (n=50) | Group D (n=50) | |
| 5 | 82.3±9.8 | 67.2±6.3 | 0.0001 | 85.7±7.4 | 67.4±6.1 | <0.001 |
| 10 | 81.1±9 | 66.1±5.9 | <0.001 | 83.4±7.2 | 65±5.4 | |
| 15 | 78.1±7.5 | 66.1±6 | <0.0001 | 83.1±7.9 | 64.9±4.9 | |
| 30 | 77.9±7.1 | 65.5±5.7 | <0.001 | 82.9±7.5 | 65.5±5 | |
| 60 | 77.5±6.9 | 64.8±5.1 | <0.001 | 79.6±6.4 | 65.3±4.7 | |
| 90 | 76.4±6.4 | 67±5.5 | 0.06 | 81.3±6.2 | 65±4.6 | |
| 120 | 79.5±6 | 64.4±4.8 | <0.001 | 81.8±6 | 65.2±4.6 | |

Data is presented as mean±SD. D=Dexmedetomidine; C=Control (normal saline)

DISCUSSION

“Dexmedetomidine” induces sleepiness & analgesia without impairing the respiratory system [12]. As a result, it has been used to avoid emerging agitation. In comparison to control groups, intraoperative dexmedetomidine therapy reduced emergent agitation in children by 57-70% [13-16]. Dexmedetomidine can also produce hemodynamic abnormalities such as hypotension (30%), hypertension (12%), & bradycardia (9%) [17]. Earlier studies of emerging agitation used a variety of dexmedetomidine administration regimens (e.g., only loading of 0.5 mg kg⁻¹, only infusion of 0.2 mg kg⁻¹ h⁻¹, or loading of 2 mg kg⁻¹ followed by infusion of 0.7 mg kg⁻¹ h⁻¹) [13-16].

After general surgery, up to 20% of adult patients have been reported to experience emergent agitation [2,3]. It is notably common following ENT surgery, with 55.4% of subjects reporting agitation [3]. There have been few studies on the relationship between intraoperative dexmedetomidine infusion & emerging agitation in adults. Only a few such trials have been conducted; one discovered that dexmedetomidine reduced emergent agitation from 52% to 28% in people after nose surgery (n=50 per group) [18]. The other study compared a dexmedetomidine infusion group to two other groups (epidural & control, each with 30 participants) after a gastrectomy & discovered that dexmedetomidine reduced emergence agitation compared to the control (7% vs 27%) [19]. Our findings support an earlier study, suggesting that continuous dexmedetomidine infusion (0.4 µg kg⁻¹ h⁻¹) during nasal & pharyngeal surgery minimizes emerging agitation without delaying extubation or worsening complications. In contrast to the current study, Kim *et al.* [18], Khurshid *et al.* [20] found a slightly different incidence of emerging agitation, at 28% & 26%, respectively. Furthermore, the incidence & severity of EA were higher in Abdellatif and Ali *et al.* [21] than in our study. The difference could be a single dosage of 0.3 µg/kg dexmedetomidine administered 5 minutes before the completion of surgery.

Adverse events such as post-operative nausea & vomiting were reported in one (2%) patient in group D & three (6%) in group C. Neither group had negative effects, such as laryngospasm, desaturation, hypersalivation, hypotension, or bradycardia. In a comparable trial, Kwon *et al.* [22] found nausea & vomiting in 4 (17%) & 1 (3%), respectively. This could be

because the medications were administered at the same doses.

In the current study, we also found that the study group had lower heart rate & blood pressure than the control group. Although this difference was statistically significant, it was not clinically meaningful & did not necessitate any intervention. The lower heart rate & blood pressure seen in Group D could be attributed to Dex-induced decreased sympathetic output & circulating catecholamine levels. Unlike this discovery, Kim *et al.* [18], Khurshid *et al.* [20], Reddy *et al.* [23], & Deepak *et al.* [24] did not notice statistically significant alterations in heart rate & mean arterial pressure during the procedure with dexmedetomidine (0.4 µg/kg) infusion.

In our investigation, maintaining dexmedetomidine until extubation resulted in more stable hemodynamic alterations after emergence. A previous study demonstrated that sustaining a dexmedetomidine infusion of 0.2 µg kg⁻¹ h⁻¹ during extubation did not impact mean arterial pressure (MAP) or heart rate (HR) in both the dexmedetomidine & control groups [14]. The outcome discrepancies may be attributable to patient age (adults vs children) or infusion concentration (0.4 µg kg⁻¹ h⁻¹ vs 0.2 µg kg⁻¹ h⁻¹).

CONCLUSIONS

Emergence agitation can have serious consequences for patients, including self-injury, increased post-operative pain, hemorrhage, self-extubation, and removal of catheters. The study concluded that intraoperative dexmedetomidine infusion can effectively reduce emergence agitation in patients undergoing nasal and pharyngeal surgery without causing additional complications. Dexmedetomidine infusion until extubation provided more stable hemodynamic changes during emergence.

However, further research is needed to explore the impact of different factors on the efficacy of dexmedetomidine infusion and assess its long-term effects beyond 2 hours post-operatively. Additional studies could focus on comparing the effectiveness of dexmedetomidine with other sedatives and opioids in managing emergence agitation.

LIMITATIONS

The study only included ASA class 1-2 patients aged between 20-60 years undergoing nasal & pharyngeal

surgery, so the findings may not apply to patients with higher ASA classifications or different age groups. The study did not assess the long-term outcomes or complications associated with dexmedetomidine use beyond the immediate post-operative period. Also, the study did not compare dexmedetomidine with other sedatives or opioids commonly used for emergence agitation management, so the relative efficacy & safety of dexmedetomidine compared to other pharmacological treatments could not be determined.

CONTRIBUTION OF AUTHORS

Research concept- Dr. Bandana Paudel

Research design- Dr. Bandana Paudel

Supervision-Dr. Sanjay Gautam

Materials- Dr. Sumitra Paudel

Data collection- Dr. Dinesh Bhandari, Dr. Sumitra Paudel

Data analysis and Interpretation- Dr. Bandana Paudel and Dr. Sanjay Gautam

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Article editing- Dr. Bandana Paudel and Dr. Sumitra

Final approval- Dr. Bandana Paudel

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