



## Original Research Article

## Role of dexmedetomidine infusion on post operative emergence agitation and quality of recovery after nasal surgery: A prospective randomized double blind controlled trial

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## ARTICLE INFO

## Article history:

Received 09-01-2020

Accepted 22-02-2020

Available online 08-09-2020

## Keywords:

Emergence agitation

Nasal surgery

Quality of recovery

## ABSTRACT

**Aims:** Study aims to reduce the emergence agitation post operatively and improve the quality of recovery after nasal surgery which in-turn reduce the hospital stay and in-hospital mortality.

**Settings and Design:** Prospective, randomized, double blind study

**Material and Methods:** After institutional review board approval and informed written consent from patients, seventy patients undergoing nasal surgery were selected & randomized into two groups. The dexmedetomidine group (Group D, n=35) received dexmedetomidine infusion @ rate of 0.4 µg/kg/hr from induction of anaesthesia until extubation, while the control group (Group C, n=35) received volume-matched normal saline infusion as placebo. Induction of anaesthesia was done using Propofol (2 mg/kg) and fentanyl (1 µg/kg). Maintenance of anaesthesia was done using inhalational sevoflurane & inj.vecuronium. The incidence of agitation, haemodynamic parameters, and recovery characteristics were evaluated during emergence. Patients were assessed for quality of recovery using a 15-item quality-of-recovery questionnaire (QoR-15) 24 hr after surgery.

**Statistical Analysis:** Data were analysed by using unpaired t-test, Chi-square test.

**Results:** The incidence of agitation was lower in group D than group C (22.8% vs 51%). HR and MAP were comparable in group D & group C. Extubation time & grade of cough during emergence were similar between the groups. QoR-15 score was significantly more in group D compare to group C at 24 hour after surgery.

**Conclusions:** Intraoperative infusion of dexmedetomidine decreased incidence of agitation & improved quality of recovery after nasal surgery.

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### 1. Introduction

Emergence agitation is a common complication after general anaesthesia in the postanesthesia care unit (PACU), and its incidence is said to be around 3%.<sup>1</sup> Emergence agitation is a transient confusional state that is mostly associated with the early stage of emergence from general anaesthesia and is interchangeably described in the literature as post anaesthetic excitement and delirium.<sup>2</sup> Several risk factors identified for emergence agitation in adults include the use of etomidate, inadequate

postoperative analgesia, Otolaryngological surgery, breast surgery, abdominal surgery, prolonged surgical duration and presence of endo-tracheal tube, ryle's tubes or urinary catheter.<sup>3-5</sup> ENT surgery and oral surgery is associated with a higher incidence of emergence agitation, where 55.4% of patients experienced agitation.

Postoperative emergence agitation is associated with cognitive deficit, and increased physical dependence, duration of hospital stay and in-hospital mortality.<sup>6</sup> Prophylactic measures for reduction of post operative agitation include reduction of preoperative anxiety, the effective treatment of post operative pain, and the cultivation of a stress free recovery environment. Medications useful

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in the prophylaxis and treatment of emergence excitement include midazolam, clonidine, dexmedetomidine, fentanyl, ketorolac, and physostigmine.<sup>7</sup>

Dexmedetomidine, a selective  $\alpha_2$  receptor agonist and has analgesic, sympatholytic and sedative properties.<sup>8</sup> Decreased opioid requirements and stress response to surgery ensuring a stable hemodynamic state, antiemesis are beneficial property of the agent<sup>9–11</sup> One significant advantage is that in clinical dose range there is no respiratory depression.<sup>12,13</sup>

In this randomized double blind controlled study, we studied the effect of dexmedetomidine infusion until extubation would reduce emergence agitation in adult patients undergoing nasal surgery. We also evaluated the effects of dexmedetomidine on quality of recovery after nasal surgery.

## 2. Materials and Methods

After approval from the Institutional Review Board and informed written consent from all the patients, this prospective, randomized, double blind study was carried out. we enrolled 70 patients, 20–58 years of either sex and ASA physical status I/II, who were posted for nasal surgery under general anaesthesia in which intranasal packing was done and kept for 24 hours after surgery. Patients were explained the procedure & written informed consent was taken. Following patients were excluded from the study: (I) Known or suspected allergy to  $\alpha_2$ -adrenergic agonist or NSAIDs (II) Use of MAO inhibitors or adrenergic blocking drugs (III) History of uncontrolled HT (IV) Second or third degree heart block (V) Impaired cognition (VI) chronic use of antipsychotic medications (VII) Renal failure (VIII) Liver disease (IX) BMI  $\geq 30$  kg/m<sup>2</sup>. The patients were randomized using computer generated random number sequence method into 2 groups of 35 patients each.

Group D: Inj. Dexmedetomidine 2  $\mu$ g/ml @ rate of 0.4  $\mu$ g/kg/hr was started after induction of anaesthesia & stopped after extubation. Normal saline was used to dilute dexmedetomidine to a concentration of 2  $\mu$ g/ml in 50 ml.

Group C: Inj. NS 50 ml normal saline @ rate of 0.4  $\mu$ g/kg/hr (volume matched) as placebo. Patients were assessed before the procedure in pre-anaesthetic check-up (PAC) visit and thorough history was taken and proper examination was done.

Standard preoperative investigations (Hb, TLC, platelet count, RBS, RFT with s.electrolytes, chest Xray, ECG) prescribed to all patients. On the day of surgery, after shifting the patient to the pre anaesthetic check-up room, standard monitoring for heart rate (ECG), systolic and diastolic blood pressure (NIBP), peripheral oxygen saturation (pulse oximeter) was established and baseline vital parameters were recorded. IV access was secured using 20 G venous catheter in non dominant hand. Premedications were given which include Inj. Ondansetron 0.08mg/kg,

Inj. Glycopyrolate 0.004mg/kg, Inj. Midazolam 0.02mg/kg intravenously. Patient was shifted to operation theatre. Monitoring was done by ECG, pulse oximeter, end tidal CO<sub>2</sub> and MAP before induction of anaesthesia, 10 minutes after start of the surgery, 30 minutes after start of the surgery, at the end of the surgery and after extubation. General anaesthesia was induced by using Inj. Fentanyl 1  $\mu$ g/kg, Inj. Propofol 1.5–2 mg/kg and Inj. Succinyl choline 2mg/kg. Trachea was intubated using appropriate size cuffed portex endotracheal tube. Infusion Inj. Dexmedetomidine 0.4  $\mu$ g/kg/hr (group-D) or Inj. Normal Saline (group-C) was started after endotracheal intubation and stopped after the extubation. Anaesthesia was maintained using oxygen, nitrous oxide, intermittent positive pressure ventilation, Inj. Vecuronium and sevoflurane. At the end of surgery, intranasal packing was done. Inj. Diclofenac sodium 75 mg was given 15 minutes before the end of surgery. Inhalational sevoflurane was stopped (defined as ‘time zero’) at the end of the surgery. The patient was stimulated to open eyes using verbal communication. No other stimuli was used. After thorough oropharyngeal suction, anaesthesia was reversed using Inj. Glycopyrolate 0.008 mg/kg and Inj. Neostigmine 0.05 mg/kg after confirming return of neuromuscular function. Extubation was done when spontaneous breathing efforts of patient were adequate & was completely awake to respond to verbal commands. After extubation, infusion of Inj. Dexmedetomidine or NS was stopped. Emergence is the time interval from ‘time zero’ to 2 minutes after extubation. During emergence, evaluation was done for agitation using the Ricker sedation-agitation scale & maximum score was noted (Table 2) and monitoring for pain (Table 3 11-point NRS) and nausea-vomiting (Table 4 Four point nausea vomiting scale) was done at 5, 10, 15, 30, 60, 90, 120 minutes. Riker sedation agitation scale : 1 = minimal or no response to noxious stimuli; 2 = arouse to physical stimuli but dosen’t communicate; 3 = difficult to arouse but awakens to verbal stimuli or gentle shaking; 4 = calm and follows verbal commands; 5 = anxious or physically agitated and calms to verbal instructions; 6 = requiring restraint and frequent verbal reminding of limits; and 7 = pulling at tracheal tube, trying to remove catheters or striking at staff. Emergence agitation was defined as any score on the sedation-agitation scale  $\geq 5$ . Dangerous agitation was defined as a sedation-agitation scale score = 7. Grade of cough was evaluated during emergence using a four-point scale (0 = no cough; 1 = single cough; 2 = persistent cough lasting 5 s; and 3 = persistent cough lasting  $\geq 5$  s or bucking). Extubation time was recorded (time duration between ‘time zero’ to extubation). Patients were shifted to PACU, with supplemental oxygen & was discontinued if the patient would sustain a SpO<sub>2</sub>  $> 95\%$  for 5 minutes on room air.

An 11-point numerical rating scale (NRS) for pain (0 = no pain and 10 = worst pain imaginable), and four-

point nausea and vomiting scale (0 = no nausea; 1 = mild nausea; 2 = severe nausea requiring antiemetics; and 3 = retching, vomiting or both) were assessed in PACU. QoR-15 (15-item quality-of-recovery questionnaire) was used to evaluate quality of recovery 24 hour after surgery. Emergence agitation is defined as any score on the sedation-agitation scale  $\geq 5$ . Dangerous agitation is defined as a sedation-agitation scale score = 7.

### 2.1. Statistical analysis

The data entry was done in Microsoft Excel 2010 and the data analysis was done in GraphPad InStat. Frequencies and percentages were calculated and p-value was established to find a statistical difference between the variables. Unpaired t test was used to evaluate haemodynamic data & Chi-square test was applied for analysis of categorical data.. A P value  $< 0.05$  was considered statistically significant.

## 3. Observation and Results

Patient characteristics in terms of age, gender, weight and height were comparable among both the groups ( $p > 0.05$ ). (Table 1). Incidence of agitation was significantly less in group D compared to group C (51.4% vs 22.8%) (P value  $< 0.05$ ) (Table 2). Riker sedation agitation scale was found significantly low in group D compared to group C at 5 minutes, 10 minutes, 15 minutes, and 30 minutes after extubation (P value  $< 0.05$ ). The scale was found comparable between group D & group C at 1 hour, 1.5 hour and 2 hour after extubation. (P value  $> 0.05$ ). Extubation time was comparable but more in group D compare to group C (D:  $7.05 \pm 1.73$ , C:  $5.80 \pm 1.61$ ) (P value  $> 0.05$ ) (Table 3). Grade of cough was comparable between group D & group C (P value  $> 0.05$ ). In present study, 11 point numerical rating pain scale was comparable in group D & group C upto 2 hour after extubation. (P value  $> 0.05$ ) (Table 4). Haemodynamics (MAP and HR) were comparable but lower in Group D compared with Group C. (Figures 1 and 2) Quality of recovery questionirre - 15 score after 24 hours of surgery was significantly more in group D compare to group C. (D:  $122.31 \pm 6.87$ , C:  $106.69 \pm 10.73$ ) (P value  $< 0.05$ ). Total 4 patients (17.14%) from group C while only 1 patient (2.85%) from group D required antiemetic postoperatively.

## 4. Discussion

When emergence agitation occurs in an adult patient, it is usually aggressive and uncontrollable, causing a greater possibility of injury, such as increased pain, bleeding, self extubation, removal of catheters, hypoxia or even aspiration.<sup>3</sup> It is costly in several senses: in terms of morbidity, in human resources and on a financial level. Physical & chemical restrain may require to avoid the serious consequences to the patient & attending medical staff. Marked effort may be required by the entire medical

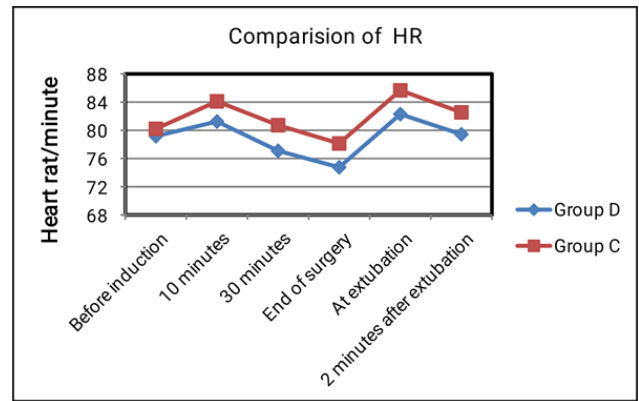


Fig. 1: Comparison of haemodynamics

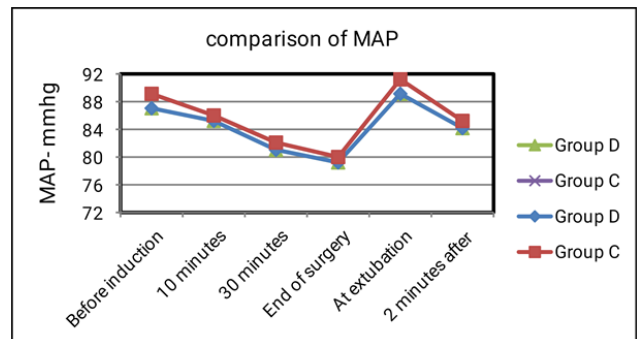


Fig. 2: Comparison of MAP

team for safety of patient & hospital staff.<sup>14</sup> Various studies<sup>3,15,16</sup> have reported that ENT surgical procedures particular nasal surgeries in which intranasal packing is used, have a higher incidence of emergence agitation in both adults and children. This reported higher incidence may be attributed to a sense of suffocation due to intranasal packing.<sup>17</sup>

In present study, Incidence of agitation less in group D (22.8%) as compared to group C (51.4%) (P value  $> 0.05$ ) (Table 1). In previous studies dexmedetomidine has been used as premedication  $1 \mu\text{g}/\text{kg}$  intranasal 45 minutes before induction,<sup>18</sup> loading dose  $2 \mu\text{g}/\text{kg}$  followed by maintenance dose  $0.7 \mu\text{g}/\text{kg}/\text{hr}$ ,<sup>12</sup> and at a dose of  $0.3 \mu\text{g}/\text{kg}$  i.v. 10 minutes before discontinuation of anaesthetics.<sup>19</sup> The results of all these studies showed decrease in emergence agitation. Decrease in incidence of agitation may be due to centrally acting, highly selective  $\alpha_2$  adrenoreceptor agonistic action which provides sedation, hypnosis, anxiolysis and analgesia.<sup>17</sup> In present study, similar to previous study<sup>20</sup> extubation time was comparable in group D & group C (P value  $> 0.05$ ) (Table 2). Sedative effect of dexmedetomidine should delay extubation, but comparable result in present study may be because we used optimum dose of dexmedetomidine ( $0.4 \mu\text{g}/\text{kg}/\text{hr}$ ) infusion & short half life of dexmedetomidine.

**Table 1:** Patient characteristics

Patient characteristics	Group – D Mean ± SD	Group - C Mean ± SD	P Value
Age (years)	33.14 ± 12.56	33.25 ± 10.89	0.967
Gender (M/F)	23/12	24/11	>0.05
Weight (Kg)	56.65 ± 11.31	57.58 ± 0 7.37	0.727
Height	158.5 ± 7.63	159.38 ± 8.78	0.714

**Table 2:** Incidence of emergence agitation

	No. of patients		P Value
	Group D (n=35)	Group C (n=35)	
Incidence of emergence agitation	8 (22.8%)	18 (51.4%)	<0.05

**Table 3:** Comparison of extubation time between both groups

	Group D Mean ± SD	Group C Mean ± SD	P Value
Extubation time	7.05 ± 1.73	5.80 ± 1.61	0.093

**Table 4:** Comparison of 11-point numerical rating pain scale (NRS)

Time after Extubation	Group- D Mean±SD	Group-C Mean±SD	P Value
5 minutes	2.40 ± 1.31	2.97 ± 1.72	0.123
10 minutes	2.40 ± 1.31	3.08 ± 1.65	0.058
15 minutes	2.48 ± 1.22	3.08 ± 1.59	0.082
30 minutes	2.42 ± 1.17	3.02 ± 1.56	0.073
1 hour	2.34 ± 0.16	2.91 ± 1.42	0.058
1.5 hour	2.22 ± 1.11	2.85 ± 1.35	0.037
2 hour	2.14 ± 1.11	2.85 ± 1.45	0.024

In present study, grade of cough was comparable between group D & group C (P value >0.05) which is similar to a previously done study.<sup>20</sup> Another study using dexmedetomidine 1 µg/kg concluded that dexmedetomidine decreases post-extubation cough.<sup>21</sup> Patients in group C also felt less pain similar to patients in group D (P value > 0.05) (Table 4) which may be due to use of inj. fentanyl as premedication and inj. diclofenac at the end of surgery. In present study, 4 patients in group C while 1 patient in group D required antiemetics postoperatively within 2 hours. Antiemetic effect of dexmedetomidine may be explained by its α<sub>2</sub> agonistic action or due to decrease in catecholamine. Haemodynamics (MAP and HR) were comparable in Group D & Group C which was similar to the previous study done using dexmedetomidine infusion @ 0.4 µg/kg/hr.<sup>20</sup> Because hypertension is common after administration of the loading dose of dexmedetomidine,<sup>22</sup> we administered a continuous infusion of 0.4 µg/kg/hr without a loading dose, which was also effective in reducing agitation after nasal surgery & weaning from mechanical ventilation in critically ill patient. In present study, quality of recovery questionnaire - 15 score after 24 hours of surgery was significantly more in group D compare to group C. This improved quality of recovery may be due to reduction in levels of stress markers associated with sickness behavior.

## 5. Conclusion

Intraoperative dexmedetomidine infusion reduced the incidence of emergence agitation in immediate post operative period in adult patients undergoing nasal surgery without delay in extubation and provided smooth emergence. Furthermore, it improved quality of recovery 24 hour after surgery.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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**Cite this article:** Marviya JR, Trivedi LH, Parmar SH. Role of dexmedetomidine infusion on post operative emergence agitation and quality of recovery after nasal surgery: A prospective randomized double blind controlled trial. *Indian J Clin Anaesth* 2020;7(3):533-537.