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Effect of single dose versus continuous infusion of dexmedetomidine for reduction in incidence of emergence agitation in adults following nasal surgeries: A randomized double-blind study

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Abstract

Introduction: Emergence agitation is a serious post-anaesthetic event occurring in the early phase of recovery from general anesthesia. If untreated, this may result in significant morbidity.

Aim: To compare the effect of single dose versus continuous infusion of dexmedetomidine for reduction in incidence of emergence agitation in adults following nasal surgeries.

Methods: This study was conducted on 62 patients of 20-60 years, randomly divided into two groups (31 in each group), with ASA physical status I, II who were scheduled for elective nasal surgeries under general anaesthesia. Group S received iv dexmedetomidine 1µg/kg in 10 ml of saline, over 10 min before induction of anaesthesia, while group C received iv dexmedetomidine 0.5µg/kg in 20 ml of saline as continuous infusion from the induction of anaesthesia up to the time of extubation. Incidence of emergence agitation was recorded as primary outcome along with severity of emergence agitation, sedation score, adverse effects and hemodynamic parameters as secondary outcomes.

Results: Incidence and severity of emergence agitation was lower in group C, 8 (25.80% and 6.45%) as compared to group S, 15 (48.38% and 19.35%), ($p>0.05$). Haemodynamic variables, mean sedation score and side effects and complications were comparable between the two groups.

Conclusion: Dexmedetomidine as continuous infusion is more effective in reducing the incidence and severity of emergence agitation in adults following nasal surgeries compared to single dose of dexmedetomidine.

Keywords: Emergence agitation, dexmedetomidine, nasal surgery

Introduction

Emergence agitation (EA) involves restlessness, disorientation, excitation, non-purposeful movement, inconsolability, thrashing, and incoherence during early recovery from general anesthesia. Incidence of EA varies from approximately 0.25% to 90.5% [24]. The clinical consequences of EA are similarly varied. It ranges from increased risk of bleeding, falling, removal of catheters and self extubation, which may lead to further complications like hypoxia and aspiration. Thus, increasing the need for continuous monitoring, medication and physical restraint. An agitated patient has the potential for self-injury and furthermore, very agitated patients can pose an immediate danger to operating room staff.

Occurrence of emergence agitation from general anaesthesia is common after nasal surgeries in which intranasal packing is used and varies up to 22% [4]. Many patients complain of difficulty in breathing due to intranasal packing. EA is typically short lived and resolves spontaneously. The elimination of causative factors such as pain, anxiety, presence of invasive devices is the mainstay of emergence agitation management. Some studies revealed that sedatives (eg. propofol and midazolam) and opioids (eg. fentanyl and morphine)²⁴ are preferred therapeutic pharmacological treatments for emergence agitation.

Dexmedetomidine is a highly selective α_2 agonist which produces sedation and anxiolysis through reduction in sympathetic central nervous system activity. It has a major advantage over other sedatives, it is associated with minimal respiratory depression [22]. Dexmedetomidine infusion reduces agitation on emergence from GA in pediatric patients. Most research regarding emergence agitation has been conducted on pediatric patients, and data regarding adult patients is limited.

Thus we performed this study to evaluate the efficacy of pre operative as well as intraoperative infusion of dexmedetomidine in reducing emergence agitation in adults undergoing nasal surgeries.

Methodology

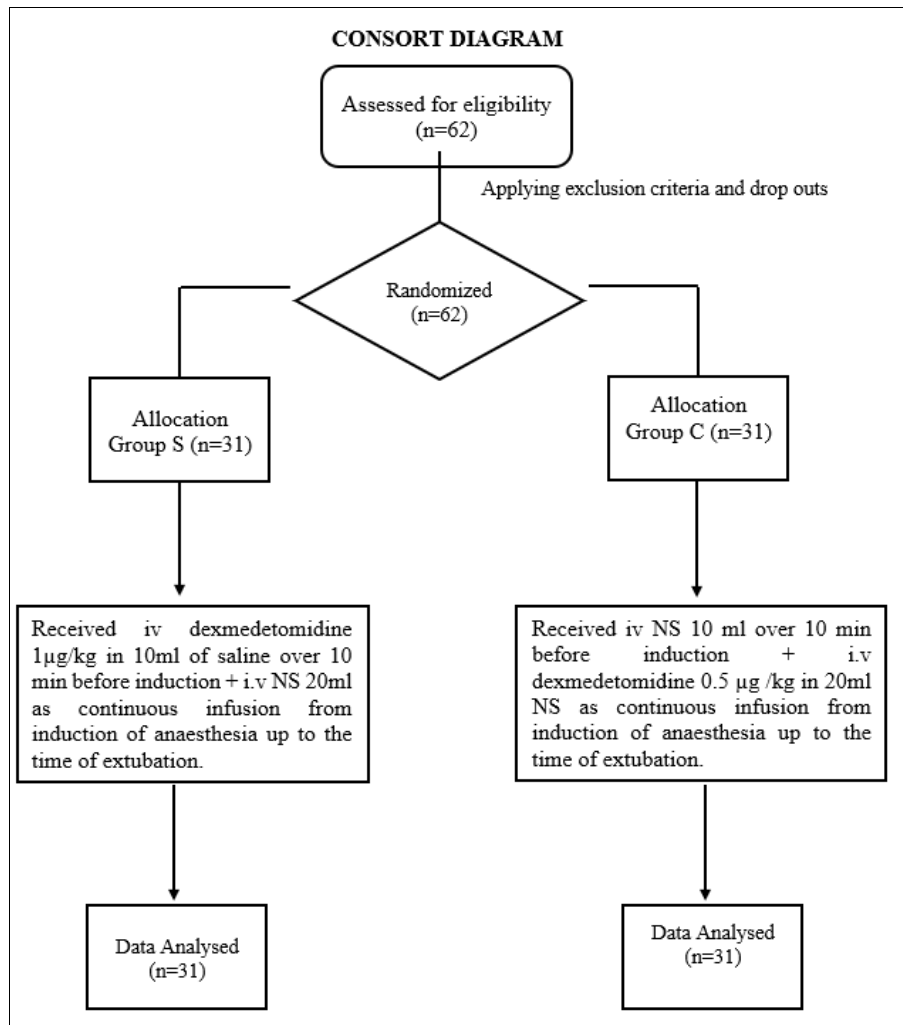
This prospective, randomized double blind study was from August 2021 to September 2022 in tertiary center of Chhattisgarh, after approval from Institutional Scientific & Ethics Committee. 62 patients of age 20-60, ASA I-II grade, BMI <30 and undergoing elective nasal surgeries under general anaesthesia of <2 hr duration in which nasal packing on each side was used postoperatively were included in the study. Patients with cognitive dysfunction or psychiatric problems, neurological or cardiac disease, uncontrolled hypertension or COPD, use of antipsychotics, MAO inhibitors or adrenergic blocking agents, renal insufficiency or liver dysfunction, addiction to nicotine, substance abuse and pregnant woman were excluded. The sample size has been derived by taking reference from the study conducted by Khurshid *et al.* [15] in which they found 26% incidence of emergence agitation in dexmedetomidine group and 50% incidence in control group. A sample of total 62 were required at 95% confidence and 80% power.

All the patients were informed about the anaesthesia technique following which written informed consent was taken. Patients were randomly assigned to two groups by sealed envelope technique, Group S and Group C with 31 patients in each group. Patients in group S received iv dexmedetomidine 1µg/kg in 10 ml of saline, over 10 min before induction of anaesthesia, while the other group received 10 ml of saline (without dexmedetomidine) over 10 minutes. Patients in group C received iv dexmedetomidine 0.5µg/kg/h in 20 ml of saline as continuous infusion from the induction of anaesthesia up to the time of extubation and the other group simultaneously received 20 ml of saline (without dexmedetomidine). All the study medications were prepared and administered by a single researcher, who was not involved in any other part of this study.

As per the protocol of our institute, all patients were fasted for 8 hours prior to operation. On arrival to the operation theatre, patient was positioned in supine position, routine monitors were attached and baseline HR, NIBP, SpO₂ and ECG were recorded. Patients were educated that they might feel discomfort postoperatively due to the nasal packing. Iv

glycopyrrolate 0.1 mg/kg, iv fentanyl 2 µg/kg and iv midazolam 2 mg was given as premedication along with study drug as per the group. After pre-oxygenation with 100% oxygen for 3 mins, induction was carried out with iv propofol 2mg/kg in titrating dose till the loss of verbal response. Iv succinyl choline 2mg/kg was given to facilitate tracheal intubation. Anaesthesia was maintained with sevoflurane 1-2% MAC along with oxygen and air in a 1:1 ratio and iv atracurium 0.6mg/kg. At the end of the procedure, the inhalational anaesthetic was stopped and 100% oxygen was administered. The reversal agent iv neostigmine 0.05mg/kg with 0.01 mg/kg glycopyrrolate was given after return of neuromuscular function, and patients were extubated when they breathe spontaneously and responded to verbal commands. After that, dexmedetomidine or saline infusion was stopped. Vital parameters like blood pressure (systolic blood pressure, diastolic blood pressure and mean arterial pressure), pulse rate, oxygen saturation and EtCO₂ were recorded initially before intubation and measured at 15 min interval from the time of intervention till the end of surgery. MAP<55 mm Hg was considered as hypotension and managed by decreasing the concentration of sevoflurane and rapid iv fluids (250-500 ml), followed by incremental doses of intravenous ephedrine. Sinus bradycardia i.e., HR<50 beats/min, was treated with iv atropine (0.02 mg/kg).

Post extubation, level of agitation and sedation was assessed at 5 min intervals until 30 minutes. Level of agitation was measured with the help of Aono's four-point scale and the highest agitation score for each patient was recorded: 1=Calm; 2=Not calm but could be easily consoled; 3=Moderately agitated or restless and not easily calmed; 4=Combative, excited, or disoriented, thrashing around. Score of 2 was considered as emergence agitation and >3 as severe agitation. Level of sedation was measured using Ramsay sedation scale: 1=Anxious or agitated or restless; 2=Cooperative, oriented, and tranquil; 3=Drowsy but responds to commands; 4=Asleep, brisk response to light glabellar tap or loud auditory stimulus; 5=Asleep, sluggish response to light glabellar tap or loud auditory stimulus; 6=Asleep and unarousable. Patient was then transferred to the post-anaesthetic care unit (PACU) and observed for any complications like nausea, vomiting, desaturation, laryngospasm, hyper salivation.



Results

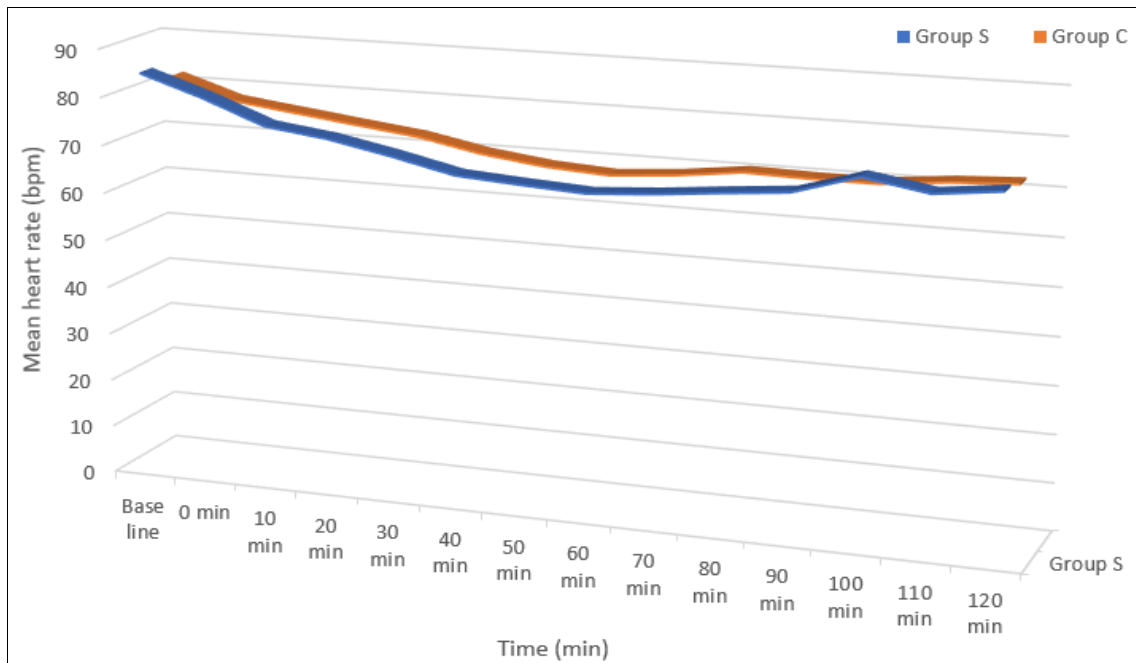
The demographic profile i.e. mean age, sex, BMI and duration of surgery were comparable in both the groups. (Table 1).

The incidence of emergence agitation was lower in group C, 8 (25.80%) compared to group S, 15 (48.38%) ($p>0.05$). Maximum incidence of EA was observed at 5 minutes in both the groups. At 10 min emergence agitation in group S was 3 (9.68%) and none in group C. None of the patients had emergence agitation in either groups at 20 min, 25 min and 30 min. (Table 2). 6 (19.35%) and 2 (6.45%) patients suffered severe emergence agitation in group S and C respectively ($p>0.05$). Maximum number of patients suffered severe emergence agitation at 5

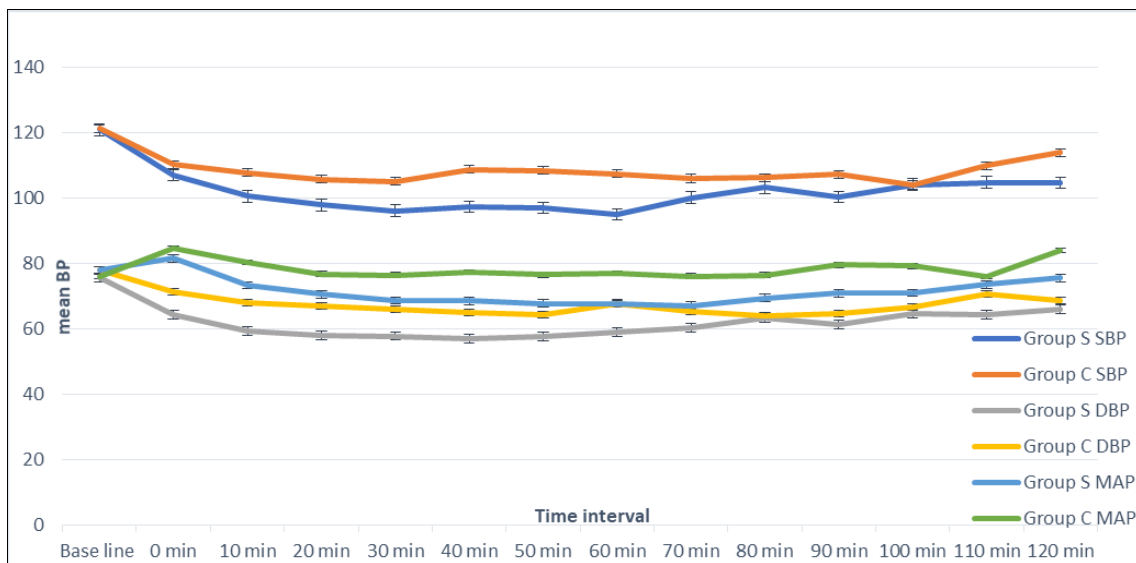
minutes 3 (9.68%) and 2 (6.45%) in group S and group C respectively. At 20 minutes, 3 (9.68%) in group S suffered severe emergence agitation. and the difference was statistically not significant ($p>0.05$). (Table 3). The incidence of adverse events such as postoperative nausea and vomiting was seen in 1 (3.3%) patient in group S and 1 (3.3%) in group C. None of the patients had any other side effects like laryngospasm, desaturation, hypersalivation, hypotension, bradycardia in either group. Mean heart rate graph no 1, mean systolic, diastolic blood pressure, mean blood pressure graph no 2 and mean sedation score graph no 3 were comparable at various time interval throughout the study period.

Table 1: Demographic Profile, Duration of Surgery

Parameters	Group S (Mean ± SD)	Group C (Mean ± SD)	p value	
Demographic Profile				
1	Age	38.2±12.18	38.9±10.04	0.78
	Sex (M: F)	20:11	19:12	0.7
	BMI	22.17±1.62	22.59±1.24	0.18
2	Duration of surgery	63.83±18.79	62.67±23.77	0.79



Graph 1: Mean heart rate



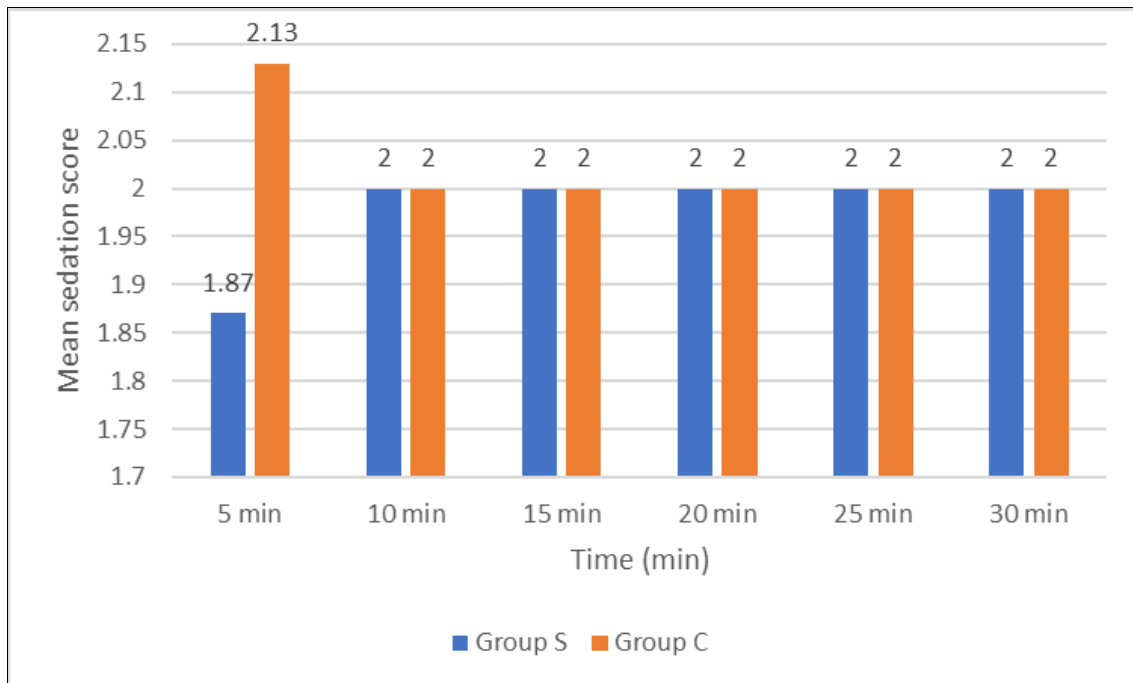
Graph 2: Mean blood pressure

Table 2: Incidence of emergence agitation

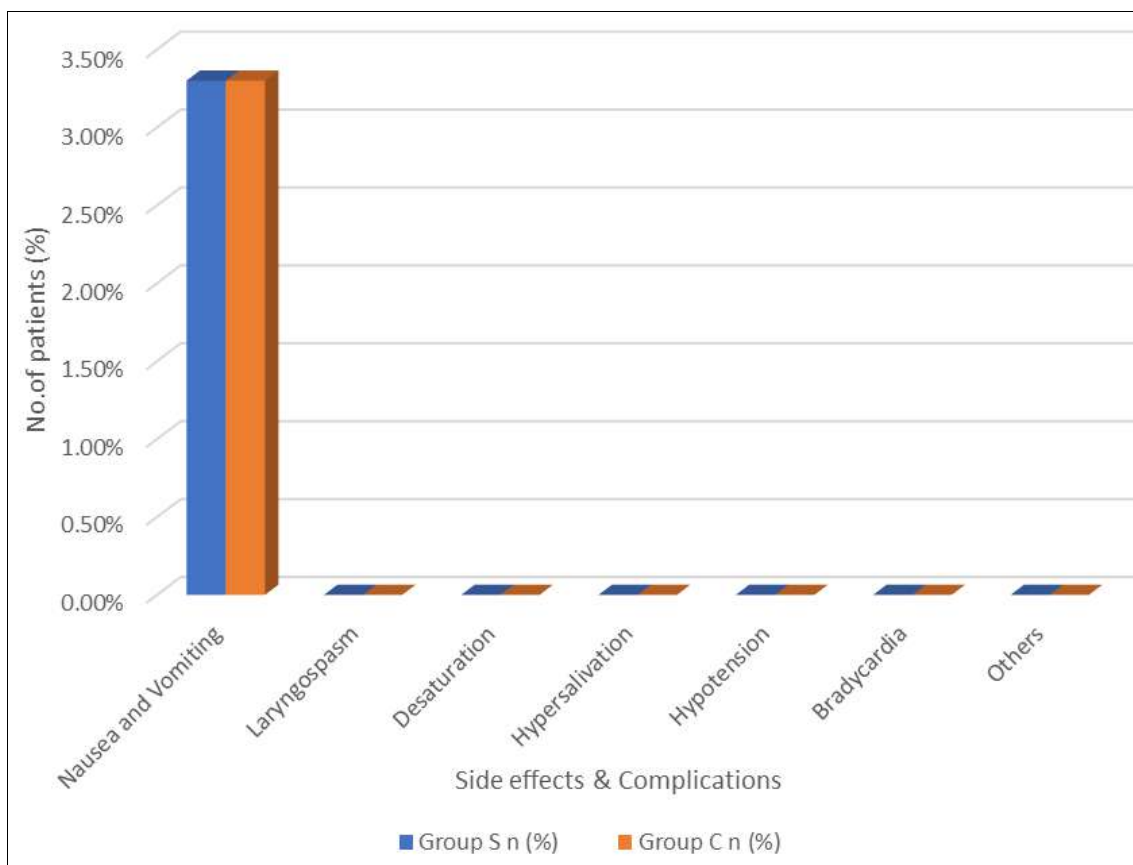
Time	Aono's score								Total p value
	1		2		3		4		
	Group S n (%)	Group C n (%)	Group S n (%)	Group C n (%)	Group S n (%)	Group C n (%)	Group S n (%)	Group C n (%)	
5 min	19(61.29)	23(74.19)	9(29.03)	6(19.35)	3(9.68)	2(6.45)	0(0)	0(0)	0.55
10 min	28(90)	31(50)	0(0)	0(0)	3(9.68)	0(0)	0(0)	0(0)	
20 min	31(50)	31(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
25 min	31(50)	31(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
30 min	31(50)	31(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	

Table 3: Severity of emergence agitation

Time	Group S n (%)	Group C n (%)	p value
5 min	3(9.68%)	2(6.45%)	0.55
10 min	3(9.68%)	0	-
20 min	0	0	-
25 min	0	0	-
30 min	0	0	-



Graph 3: Sedation score



Graph 4: Incidence of side effects & complications

Discussion

Rapid recovery from anaesthesia has been associated with development of EA. It is also referred as emergence delirium or emergence excitement, it may lead to a dissociative state with altered cognitive perception, excitation, and agitation during recovery from anaesthesia. Incidence varies with age, assessment tool used, definitions, anesthetic techniques, type of surgery, emergency operation, method of anaesthesia (inhalation anaesthesia), duration of

surgery or anaesthesia, pre-existing mental health problems, anticholinergics, doxapram, premedication with benzodiazepines, voiding urgency, postoperative pain and the presence of invasive devices (e.g. urine catheter, chest tube, or tracheal tube) [24] and time of EA assessment during recovery. The incidence of emergence agitation was lower in group C, 8 (25.80%) compared to group S, 15 (48.38%) ($p > 0.05$). Maximum emergence agitation was observed at 5 minutes in both the groups. Severe emergence agitation was

observed in 6 (19.35%) and 2 (6.45%) patients suffered in group S and C respectively ($p>0.05$). The incidence of adverse events such as postoperative nausea and vomiting was seen in 1 (3.3%) patient in group S and 1 (3.3%) in group C. None of the patients had any other side effects like laryngospasm, desaturation, hypersalivation, hypotension, bradycardia in either group.

Kim S Y *et al.* [15] and Khurshid H *et al.* [12] observed similar incidence of emergence agitation i.e. 28% and 26%. The reason for slight difference might be the dose of dexmedetomidine 0.4mcg/kg/hr as continuous infusion and fentanyl 1 mcg/kg in their study compared to 0.5mcg/kg/hr as continuous infusion and 2 mcg/kg fentanyl in our study. 28% (n=28) and 26% (n=55) incidence of EA in dexmedetomidine group by Deepak B K *et al.* [5] and Krishna Reddy G V *et al.* [8] is comparable with group C 25.80% (n=31) of our study. The minor difference might be due to dexmedetomidine 0.4mcg/kg/hr as continuous infusion and fentanyl 1 mcg/kg in their study compared to 0.5mcg/kg/hr as continuous infusion and fentanyl 2 mcg/kg in our study.

Incidence and severity of EA was higher in the study of Monaz Ali *et al.* [1] compared to our study. The difference might be use of single dose of 0.3 mcg/kg dexmedetomidine given 5 min before the end of surgery, iv dexamethasone 1 mg/kg and iv paracetamol 15 mg/kg, mean duration of surgery was 36.7 ± 10.8 min and inclusion of children for adenotonsillectomy. Similar to our study Khurshid H *et al.* [12] and Krishna Reddy G V *et al.* [8] did not show statistically significant difference in the incidence of dangerous agitation between the two groups. Kavalci G *et al.* (2013) [14], Kim S Y *et al.* (2013) [15], Khurshid H *et al.* (2015) [12], Krishna Reddy G V *et al.* (2017) [8], Deepak B K *et al.* (2018) [5], Kurhekar P *et al.* (2018) [20], Ossama H *et al.* (2022) [28] did not observe statistically significant variations in heart rate and mean arterial pressure throughout the procedure with dexmedetomidine (0.4 mcg/kg) infusion. In the current study we observed that mean heart rate remained slightly lower from the baseline value in both the groups. The HR in both the groups was statistically comparable at various time intervals throughout the surgery. Variations in the mean sedation score by Kim S Y *et al.* [15], Krishna Reddy G V *et al.* [8] and Garg *et al.* from our result might be because we noted score in immediate postoperative period whereas they observed the score after shifting of patients in postoperative care unit. Kwon SY *et al.* (2015) [21] and Kai Xu *et al.* (2016) [13] reported nausea and vomiting in 4(17%, n=30) patients and 1(3%) and 5(17%) and 1(3%) patients respectively which is comparable to our study. This might be due to the same dosages of drugs used.

The limitations of our study are possible effects of pain and preoperative anxiety on emergence agitation could not be ruled out as we did not assess preoperative anxiety and postoperative pain. With the help of our study further studies will be conducted to know the potential benefits.

Conclusion

From the observations & results, it can be concluded that dexmedetomidine as a single dose & continuous infusion reduces the incidence and severity of emergence agitation to a similar extent, provides comparable hemodynamic stability with minimal sedation & side effects.

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Conflict of interest: Nil

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