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Efficacy of Intraoperative Dexmedetomidine on Emergence from Anesthesia and on Recovery Characteristics after FESS (Functional Endoscopic Sinus Surgery)

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Abstract

Context: Emergence agitation is a post anesthetic phenomenon commonly associated with ENT surgeries. We studied the effects of maintenance infusion of Dexmedetomidine on prevention of Emergence agitation in adult patients undergoing FESS. *Aims:* To see the effects of intraoperative dexmedetomidine infusion on incidence of emergence agitation and recovery characteristics in terms of cough, pain and nausea vomiting scores. *Settings and Design:* A prospective, randomized, controlled, double blinded comparative study done at our institute. *Methods and Material:* One hundred patients undergoing FESS surgery were randomized into two groups. Group D (n=50) received dexmedetomidine infusion at a rate of 0.5 μg kg^{-1} hr^{-1} from induction of anesthesia until extubation, while group C (n=50) received volume-matched normal saline infusion. The incidence of agitation and recovery characteristics in terms of Cough score, Nausea vomiting score and Pain scores were evaluated in both groups. *Statistical analysis used:* Parametric data were analyzed using one-way ANOVA and the Student's paired t-test where appropriate. Non parametric data were analyzed using Chi-square test. A value of $p < 0.05$ was considered statistically significant. *Results:* The incidence of Emergence Agitation (Ricker sedation agitation score ≥ 5) was higher in group C compared to group D ($p < 0.001$). Recovery characteristics in terms of Cough score ($p = 0.118$) and Nausea vomiting score ($p = 0.589$) were similar in both groups, while Pain score was higher in Group C compared to Group D ($p < 0.001$). Increase in Heart rate and MAP at emergence was more in Group C compared to Group D. Conclusions: Dexmedetomidine as an adjuvant to general anesthesia for FESS is an excellent drug to reduce Emergence agitation, provide better postoperative pain relief and also maintains stable hemodynamics at emergence.

Keywords: Dexmedetomidine; Emergence agitation; Nasal surgery.

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Introduction

Emergence agitation is a post anesthetic phenomenon that develops in the early phase of general anesthesia recovery and is characterized by agitation, confusion, disorientation and possible violent behavior [1]. Though emergence agitation is observed more frequently in pediatric patients, its incidence in adults has been reported [2].

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Emergence agitation can lead to consequences such as self extubation or removal of catheters, which can cause serious complications such as hypoxia, aspiration pneumonia, bleeding and sometimes can cause severe injuries [3].

Previous studies have reported that ENT (ear, nose, and throat) surgical procedures have a higher incidence of emergence agitation which can be due to sense of suffocation during emergence from anesthesia caused by intranasal packing [3,4,5].

Dexmedetomidine is a selective α2-receptor agonist is known to reduce agitation from general anesthesia in children [6] and from ventilator weaning in ICU patients [7]. However, the data related to the effects of dexmedetomidine on reducing agitation from general anesthesia in adults is limited. Perioperative use of dexmedetomidine also decreases perioperative opioid consumption, post operative pain intensity and need of antiemetic therapy [8,9]. Therefore it is known to improve quality of recovery after surgery [10].

In this study, we hypothesized that intraoperative use of dexmedetomidine until extubation would reduce emergence agitation in adult patients undergoing Functional Endoscopic Sinus Surgery (FESS).

Materials and Methods

After obtaining the Institutional Ethics Committee approval, 100 patients belonging to the American Society of Anesthesiologists physical status Classes I and II, aged between 18–60 years, belonging to either sex, scheduled for elective FESS under general anesthesia were enrolled into the study.

Patients with uncontrolled Hypertension, Diabetes mellitus, coronary artery diseases and any other renal, respiratory, hepatic or cerebral insufficiency were excluded from the study. Patients who were allergic to drugs used in the study and those receiving β-blockers were excluded from the study. Patients with history of any psychiatric disorders or drug abuse were also excluded.

The study was conducted over a period of 8 months in the Operation theater complex, Department of Anesthesia in our Institute. Study design was prospective, randomized, controlled, double blinded trial.

Primary aim of the study was to see the effect of intraoperative dexmedetomidine infusion on incidence of emergence agitation from anesthesia recovery after Functional endoscopic sinus surgery. Secondary goals were to study the effect of intraoperative dexmedetomidine infusion on recovery characteristics from anesthesia by evaluating cough score at emergence, Pain score and Nausea vomiting score in post anesthesia care unit (PACU) and also study its effect on intraoperative hemodynamics.

The sample size calculation was based on previous study, which showed the incidence of emergence agitation after ENT surgery was 55.4%. [3] A sample size was calculated based on these findings, with a value of $\alpha = 0.05$ and power $(1-\beta)$ of 0.80. It was calculated that 48 patients were required per group. We included fifty patients in each group (total of 100 patients) for better validation of results. Data values are presented as mean (standard deviation), median (range), or number (percentage). Parametric data were analyzed using one-way ANOVA and the Student's paired t-test where appropriate. Non parametric data were analyzed using Chi-square test. A value of $p < 0.05$ was considered statistically significant. The statistical software Windostat Version 9.2 was used for the analysis of the data.

After obtaining informed consent, 100 patients who met inclusion criteria were allocated randomly using a closed envelope technique into one of the two groups. The consort flow diagram is given in Figure 1. Patients were allocated to Group D (n = 50) or Group C (n = 50) to receive intraoperative dexmedetomidine or Saline infusion respectively. Patient and the anesthetists conducting the case were unaware of drug dilution and group allocation.

All patients were kept nil by mouth for at least 6 hours prior to surgery. On arrival to operation theatre, an intravenous line was secured and all patients were started on maintenance intravenous fluid 0.9 percent sodium chloride/ringer lactate. All patients were monitored with non-invasive blood pressure (NIBP), ECG (lead II and V5), and pulse oximeter (SpO_2), End-tidal CO_2 ($ETCO_2$), end-tidal anesthetic agent (EtAA) and MAC (Minimum alveolar concentration) throughout intra operative period.

All the patients were pre medicated with injection Glycopyrrolate 0.2 mg intravenously (IV). After pre-oxygenating the patient, they were induced with injection Fentanyl 2 $\mu g.kg^{-1}$ IV and injection Propofol in titrated doses to around 1.5-2 $mg.kg^{-1}$ IV and intubation facilitated with injection Atracurium 0.5 $mg.kg^{-1}$ IV. After induction, trachea was intubated with cuffed oral endotracheal tube of appropriate size. Patients were ventilated with

volume control mode and minute ventilation adjusted to maintain $EtCO_2$ between 33 and 38 mmHg. Oro-pharyngeal packing was done and patients were positioned for surgery. For topical vasoconstriction and local anesthesia, epinephrine soaked cotton was placed in the nasal cavity for 5 min. Group D received Dexmedetomidine IV infusion at rate of 0.5 $\mu g.kg^{-1}.hr^{-1}$ after induction of anesthesia and was continued until extubation, while the control group (Group C) received volume-matched normal saline infusion. Anesthesia was maintained with 50 percent oxygen in air, isoflurane concentration to achieve MAC of 1. Additional muscle relaxant was given as needed. All patients were given Paracetmol 1 gm IV as routine analgesic intraoperatively. Inj Ondansetron 4 mg slow IV was given as emesis prophylaxis half hour before end of surgery. At the end of surgery reversal agents (Glycopyrrolate 0.004 $mg.kg^{-1}$ and Neostigmine 0.05 $mg.kg^{-1}$) was given and then oral suction was performed and throat pack was removed.

Following these steps, inhalation agent was turned off (defined as 'time zero' in the emergence process) in both groups, and mechanical ventilation was then converted to manual ventilation with 100% oxygen at 8 litres/min. The patients were not disturbed, except by continual verbal requests to open their eyes. All other stimuli were prevented. Extubation was performed when patients started to breathe spontaneously and were able to respond to verbal requests. After extubation, dexmedetomidine or saline infusion was stopped.

Emergence is defined as the time interval from 'time zero' to 2 min after extubation. During emergence, the level of agitation was evaluated using the Ricker sedation-agitation scale and each patient's maximum agitation score was recorded accordingly: [11].

1- Minimal or no response to noxious stimuli.

2- Arousal to physical stimuli but does not communicate.

3- Difficult to arouse but awakens to verbal stimuli or gentle shaking.

4- Calm and follows commands.

5- Anxious or physically agitated and calms to verbal instructions.

6- Requiring restraint and frequent verbal reminding of limits.

7- Pulling of tracheal tube, trying to remove catheters or striking at staff.

Emergence agitation was defined as any score on the sedation-agitation scale ≥5. Dangerous agitation was defined as a sedation-agitation scale score=7.

Other parameters observed were Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) at baseline, 10 min and 30 min after induction, at the end of surgery, at extubation, and at 2 min, 15 min and 60 min post extubation. Respiratory rate at extubation was observed in both groups.

Grade of cough during emergence was assessed using a four-point scale (0-no cough; 1-single cough; 2-persistent cough lasting less than 5 sec; and 3-persistent cough lasting ≥5 s or bucking).

In PACU, Pain score on numerical rating scale (NRS) for pain (0-no pain to 10-worst pain) was recorded and a Four point nausea and vomiting scale (0-no nausea; 1-mild nausea; 2-severe nausea requiring antiemetic; and 3- retching, vomiting, or both) was evaluated.

Desaturation (SpO_2 < 90%), laryngospasm and other complications if any were recorded during emergence and postoperative period. Heart rate less than 50 bpm was treated with 0.6 mg of IV Atropine. Mean arterial pressure (MAP) less than 60 mmHg was treated with IV Mephentramine 6 mg. Patients with pain score more than 4 were given Injection Tramadol 1 $mg.kg^{-1}$ as rescue analgesic and patients with Nausea vomiting score ≥2 were given Injection Dexamethasone 8 mg as rescue drug.

Results

The demographic data (Table 1) of the patients belonging to two groups were comparable and did not show any statistical significance.

Emergence Agitation was assessed in both the groups based on Ricker sedation agitation score (Table 2). It was observed that Emergence Agitation (score ≥ 5) was higher in patients belonging to Group C compared to patients belonging to group D which is statistically significant (p value <0.001). Similarly the incidence of Dangerous Agitation (score = 7) was observed in four patients in group C and in one patient belonging to group D. (Fig. 2).

Heart rate and MAP was compared between two groups at various intervals (Fig. 3). Their values at various intervals and P values between the two groups at those intervals are mentioned in Table 3. Their baseline values were comparable. The Heart rates and MAP values in group D were significantly lower compared to group C at various intervals from 10 min post induction to 15 min post extubation (p values in Table 3). However their

1 hour post extubation values were comparable and did not show significance.

Recovery characteristics were assessed in terms of Cough Score at emergence, Pain score and Nausea vomiting score in PACU between two groups (Table 4). We observed that there was no difference between Cough score (p= 0.118) and Nausea Vomiting score (p =0.589) between two groups, but the Pain score was more in group C compared to group D with a p value <0.001, which is statistically significant.

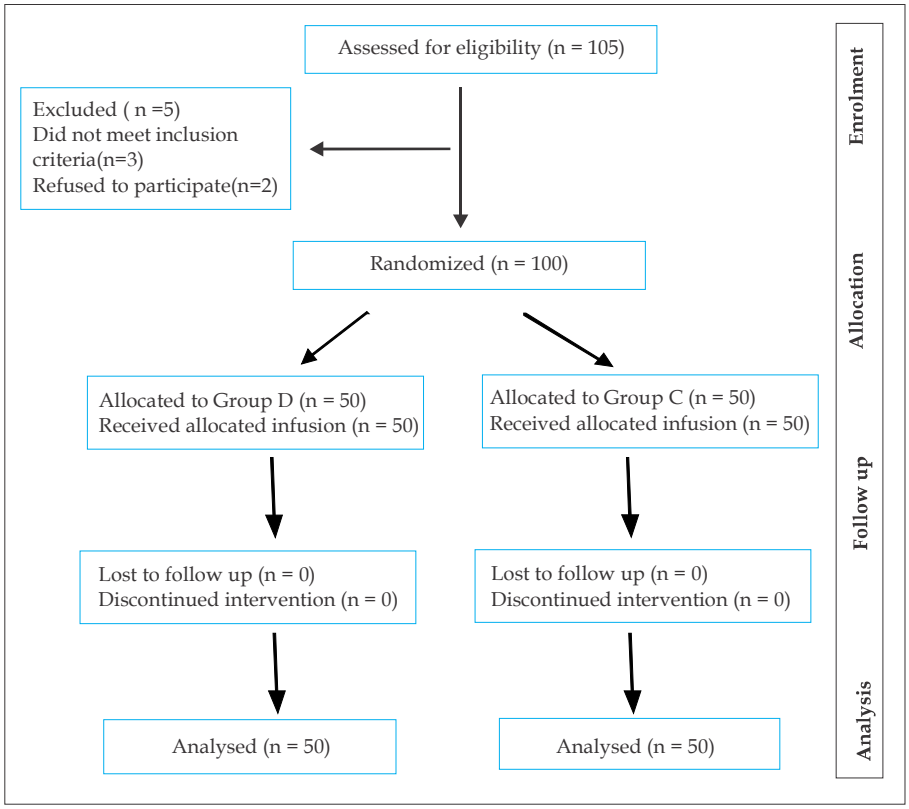

Fig. 1: Consort flow diagram of Randomization, group allocation and Number of patients analyzed

Table 1: Comparing patient demographics between two groups, (Std.Dev – Standard deviation)

Variable	Group D Mean	Std. Dev.	Group C Mean	Std. Dev.	p value
Age	32.160	± 10.082	32.240	9.584	± 0.968
Sex	1.360	± 0.485	1.340	0.479	± 0.836
Weight kg	68.000	± 10.467	69.240	10.344	± 0.553
ASA Grade	1.240	± 0.431	1.260	0.443	± 0.820

Table 2: Ricker Sedation Agitation score among two groups (n=Number)

Ricker Sedation-Agitation score(Grade 1-7)	Group D (n=50)		Group C (n=50)	
	Number	Percent	Number	Percent
1-minimal or no response to noxious stimuli	0	0	0	0
2-arouse to physical stimuli but does not communicate.	1	2	0	0
3-difficult to arouse but awakens to verbal stimuli or gentle shaking	15	30	4	8
4-calm and follows commands	21	42	13	26
5-anxious or physically agitated and calms to verbal instructions	9	18	25	50
6-requiring restraint and frequent verbal reminding of limits	3	6	4	8
7-pulling at tracheal tube, trying to remove catheters or striking at staff	1	2	4	8
Total	50	100	50	100

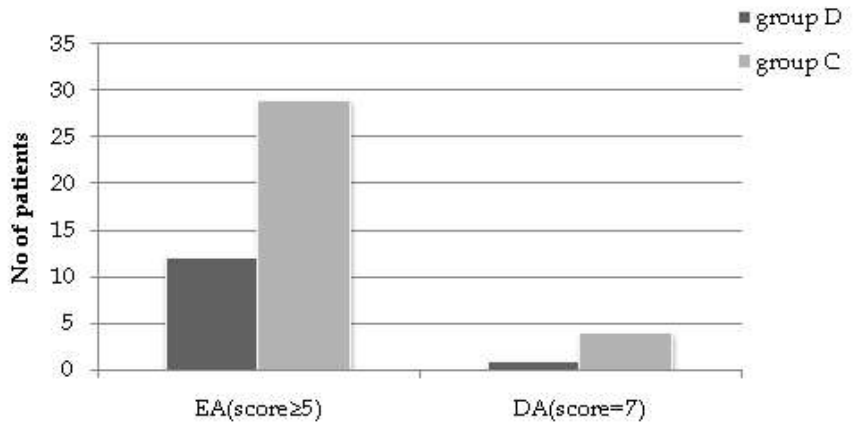

Fig. 2: Incidence of Emergence agitation and Dangerous agitation among two groups (EA –Emergence Agitation, DA- Dangerous Agitation)

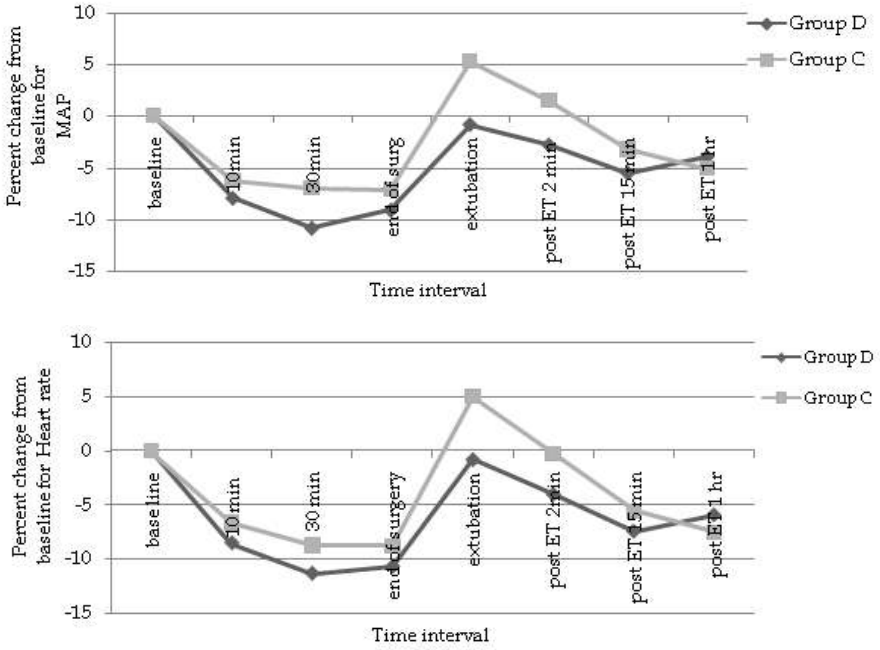

Fig. 3: Comparison of percentage change from baseline for Heart rate and MAP in two groups studied

Table 3: Comparing Mean Heart Rate (in beats/min) and Mean MAP (in mmHg) between two groups and P values

	HR Group D	HR Group C	HR P value	MAP Group D	MAP Group C	MAP p value
BaseLine	77.80 ± 6.57	78.46 ± 5.59	0.590	89.72 ± 5.70	90.2 ± 5.16	0.660
10 min	71.18 ± 4.85	73.20 ± 4.56	0.035	82.62 ± 4.92	84.58 ± 4.56	0.042
30 min	68.98 ± 4.07	71.56 ± 4.13	0.002	80.04 ± 4.34	82.920 ± 4.11	0.003
End of Surgery	69.48 ± 3.89	71.52 ± 4.09	0.012	81.58 ± 4.39	83.80 ± 4.92	0.019
Extubation	77.18 ± 5.36	82.34 ± 9.55	0.001	88.96 ± 5.15	94.96 ± 5.64	<0.001
Post ET 2 min	74.68 ± 5.06	78.22 ± 6.68	0.004	87.20 ± 4.73	91.52 ± 4.87	<0.001
Post ET 15 min	72.02 ± 4.80	74.02 ± 4.85	0.041	84.78 ± 3.64	87.28 ± 3.97	0.001
Post ET 1 hr	73.2 ± 4.50	72.48 ± 4.67	0.435	86.18 ± 4.03	85.60 ± 3.68	0.454
μ Groupi	73.06 ± 5.80	75.22 ± 6.83		85.135 ± 5.66	87.60 ± 6.18	

Table 4: Distribution of Cough score, Pain score and Nausea vomiting score among both groups

Variable	Group D	Std. Dev.	Group C	Std. Dev.	p value
Cough Score	0.600	± 0.728	0.840	± 0.792	0.118
Pain Score	2.140	± 0.756	2.820	± 0.873	<0.001
Nausea Vomiting Score	0.300	± 0.544	0.360	± 0.563	0.589

Discussion

Emergence agitation is characterized by agitation, confusion, disorientation, and possible violent behavior leading to various complications [1]. Male gender, type of surgery, inhalation anesthetics, presence of tracheal tube and presence of urinary catheter are risk factors for postoperative agitation in adults. Emergence agitation is especially common after ENT surgery, where 55.4% of patients experienced agitation [3].

In our study, we expected patients undergoing FESS to have a higher risk of emergence agitation because patients required general anesthesia and packing of both nostrils after surgery. Demographic data like age, sex, weight and ASA physical status was comparable between two groups. Inducing agents and maintenance agents for anesthesia also remained same in both the groups except for the study drug. Urinary catheter was not used in any of the patients. Bilateral nasal packing was placed in all patients after surgery.

Dexmedetomidine, a selective α2-receptor agonist with sympatholytic, analgesic, and sedative properties is known to reduce emergence agitation without causing respiratory depression [12]. In previous studies involving use of dexmedetomidine for preventing emergence agitation, the protocols used for administration were diverse (one study used loading dose of 1 µg.kg-1 in 15 min followed by maintenance infusion of 0.7 µg.kg-1.hr-1 [6] and other study used only bolus dose of 1 µg.kg-1 [13]). It is known that hypotension and bradycardia are common after administration of the loading dose of dexmedetomidine [14]. In the present study, only continuous infusion of dexmedetomidine at 0.5 µg.kg-1.hr-1 was administered without loading dose to prevent complications associated with it.

Present study showed that the incidence of Emergence Agitation (Ricker sedation agitation score ≥ 5) was higher in patients belonging to group C compared to that of group D which is statistically significant (p value <0.001). These findings were similar to a study which concluded that use of dexmedetomidine as intraoperative infusion in nasal surgeries resulted in smooth emergence with better hemodynamic stability [15]. The incidence of Dangerous Agitation (scale =7) was seen in 1 patient belonging to group D and in 4 patients belonging to group C.

Our study showed that, intraoperative administration of dexmedetomidine reduced emergence agitation by 40% in group D. These results were comparable to study, which showed dexmedetomidine was effective in reducing emergence agitation by around 30% in adults [15].

Recovery characteristics in terms of Cough score at emergence, Pain score and Nausea vomiting score in PACU was observed in our study. We found that, Cough score at emergence was similar in both groups (p=0.118) and Nausea and vomiting score in PACU was similar in both groups (p=0.589). We observed in our study, that patients belonging to group D had less pain scores in PACU than those in group C which is statistically significant (p<0.001). This can be attributed to the analgesic property of dexmedetomidine [12]. Our findings were consistent with other studies, which showed that intraoperative infusion of dexmedetomidine, reduces perioperative analgesic requirements and post operative pain intensity [8,9].

It was observed that increase in Heart rate and MAP at extubation and 2 min post extubation was more in patients belonging to group C compared to group D. It was also observed that mean Heart rate and MAP at different intervals after induction up to one hour post extubation was always below baseline in group D which is desirable in nasal surgeries. This can be explained by the fact that dexmedetomidine has better hemodynamic stability due to its α_2-agonistic action. Our findings were comparable to other studies, which observed that the increase in heart rate and MAP was much less and in turn more stable hemodynamics was achieved in group receiving dexmedetomidine [16,17].

As dexmedetomidine does not depress respiratory drive inspite of its sedative property and hence does not interfere with criteria for extubation. So, maintaining its infusion until extubation is considered safe [12]. It was observed that mean respiratory rates at extubation was similar in both groups (p value=0.463). There were no complications, including desaturation or laryngospasm, during emergence or while in PACU. Only two patients

in group D had significant bradycardia in the intraoperative period, though they did not have an episode of hypotension associated with the bradycardia. Both patients responded to single dose Injection of Atropine 0.6 mg IV.

Limitations of the study were that dose reduction effect of anesthetic agents when Dexmedetomidine was used could not be studied because we did not have a depth of anesthesia monitor. Our study population consisted of American Society of Anesthesiologists physical status Classes I and II. The organ protective effects of perioperative dexmedetomidine infusion would potentially be more pronounced in higher risk patients.

Further Scope of Study: Larger randomized studies need to be conducted to test the effect of intraoperative maintenance dose of dexmedetomidine infusion on emergence from anesthesia in adult patients. The use of depth of anesthesia monitors such as Bispectral Index or Entropy monitoring along with the use of dexmedetomidine intraoperatively could potentially reduce the anesthetic and analgesic requirements and their consequent side-effects.

Conclusion

Our results allow us to conclude that the use of Dexmedetomidine as an adjuvant to general anesthesia for Functional Endoscopic Sinus Surgery is an excellent drug to reduce Emergence agitation and provide better recovery in terms of reduced postoperative pain and also maintains stable hemodynamics at emergence.

Key Message

Prevention of Emergence agitation in patients undergoing nasal surgeries is very essential to avoid various complications associated with it. Maintainance dose of dexmedetomidine alone as an adjuvant to other general anesthetics is sufficient to prevent it along with other benefits of reducing post operative pain and also maintaining stable hemodyanmics at emergence.

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