Original Article

Effect of dexmedetomidine on emergence agitation using desflurane in pediatric cataract surgery

ABSTRACT

Background: In this study, we compared effectiveness of two doses of dexmedetomidine (0.15 μg/kg and 0.3 μg/kg) in preventing desflurane-induced emergence agitation (EA) in pediatric patients undergoing elective cataract surgery.

Methods: It is a prospective double-blinded randomized study conducted on 65 American Society of Anesthesiologists 1 children (2–10 years) who underwent elective cataract surgery at our institute. They were randomized into two equal groups, who received either dexmedetomidine 0.15 μg/kg (Group $D_{0.15}$) or dexmedetomidine 0.30 μg/kg (Group $D_{0.3}$) intravenously after induction of anesthesia. An observer blinded to groups recorded heart rate (HR), arterial blood pressure, oxygen saturation, end-tidal carbon dioxide, and respiratory rate (RR) at regular intervals and evaluated preoperative anxiety, state of agitation, and postoperative pain using validated scores.

Results: Both groups (Group $D_{0.15}$, $n = 27$ vs. Group $D_{0.3}$, $n = 26$) were demographically identical. In intraoperative period, the difference in HRs was significantly lower in Group $D_{0.3}$ from 5 min till 15 min of the surgery ($P < 0.05$), but thereafter, from 20 min till end of surgery, the rates were comparable in both the groups, whereas RR and blood pressure fluctuations were comparable throughout. Postoperative pain scores and postoperative agitation score were significantly lower in Group $D_{0.3}$ than $D_{0.15}$ at all time intervals ($P < 0.05$).

Conclusions: In our study, 0.3 μg/kg intravenous dexmedetomidine was found to be superior to 0.15 μg/kg group in effectively reducing EA and postoperative pain, without producing adverse effects such as hypotension or bradycardia.

Key words: Desflurane; dexmedetomidine; emergence agitation

Introduction

Desflurane, a day-care anesthetic agent, causes rapid emergence and recovery from general anesthesia. However, its beneficial effects are nullified by a high incidence of emergence agitation (EA), especially in pediatric population.[1,2] EA may cause physical harms to patient such as bleeding from site of surgery, psychological trauma, and delayed discharge from postanesthesia care unit (PACU).[3] Recently, dexmedetomidine is known to decrease EA in pediatric and day-care surgery following sevoflurane.[4] However, its role in preventing postdesflurane EA is yet to be elucidated. In this study, we compared the effectiveness of intravenous (IV) dexmedetomidine (0.15 μg/kg vs. 0.3 μg/kg) in preventing desflurane EA in children aged 2–10 years, undergoing elective cataract surgery.

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Materials and Methods

This prospective randomized study was approved by the Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh (NK/841/MD/3332–33) and was registered with Clinical Trial Registry of India (CTRI) CTRI/2014/06/004694. Written informed consent was obtained from the parents of the children. Children, aged 2–10 years, with ASA I status, undergoing elective cataract surgery were included in our study. Sixty-five children were assessed for eligibility, and 59 met inclusion criteria of which six were excluded because of parent's consent refusal. Hence, 53 patients were randomized into two groups using computer-generated permuted block randomization and kept in opaque-sealed envelopes. Group $D_{0.15}$ ($n_1 = 27$) received 0.15 μg/kg IV and Group $D_{0.3}$ ($n_2 = 26$) received 0.30 μg/kg IV dexmedetomidine [Figure 1]. The anesthesiologist not involved in the study opened envelope and prepared the drug. Children with airway abnormalities precluding the use of laryngeal mask airway (LMA), tumor or infection of orbit, raised intraocular pressure, known adverse effects to dexmedetomidine, or psychiatric illness associated with agitation were excluded from the study. No premedication was given. Parental presence was facilitated during induction of anesthesia. An observer blinded to groups evaluated modified Yale preoperative anxiety scale (m-YPAS)[5] preoperatively. Anesthesia was induced with 8% sevoflurane in 40%:60% mixture of oxygen (O_2)/nitrous oxide (N_2O) using a face mask and appropriate-sized LMA was inserted. Anesthesia was maintained with N_2O:O_2 (60%:40%) and desflurane (4%–6%) with cumulative minimum alveolar concentration of 1–1.2 with spontaneous respiration. If required (when $EtCO_2$ >45 mmHg), ventilation was assisted to maintain $EtCO_2$ between 35 and 45 mmHg. The study drug (diluted in 10 ml syringe) was administered over 5 min slowly. A sub-Tenon block with 0.08–0.1 ml/kg of 0.5% bupivacaine and 15 mg/kg IV acetaminophen was administered for pain relief. No opioid was administered preoperatively or intraoperatively. HR, arterial blood pressure, oxygen saturation (SO_2), end-tidal carbon dioxide, and respiratory rate (RR) were recorded after induction (baseline), after LMA insertion, at sub-Tenon injection, at surgical incision, and then at 5-min intervals until the end of surgery or more frequently when complications such as oculocardiac reflex occurred. When HR decreased abruptly by 20% or more,[6] the surgeon was asked to discontinue muscle traction and atropine 0.02 mg/kg IV was administered. Mean arterial pressure or HR increase of more than 20% above baseline, if present, was treated by administering rescue analgesic 0.5 μg/kg IV bolus of fentanyl. At the end of surgery, N_2O was switched off, 100% O_2 was administered, and LMA was removed in deeper plane. Desflurane was turned off after LMA removal. Complications related to airway, sub-Tenon block, or surgery were documented. Then, the child was shifted to PACU and SO_2, electrocardiography, pain score,[7] and noninvasive pressure were recorded every 15 min and monitored for an hour.

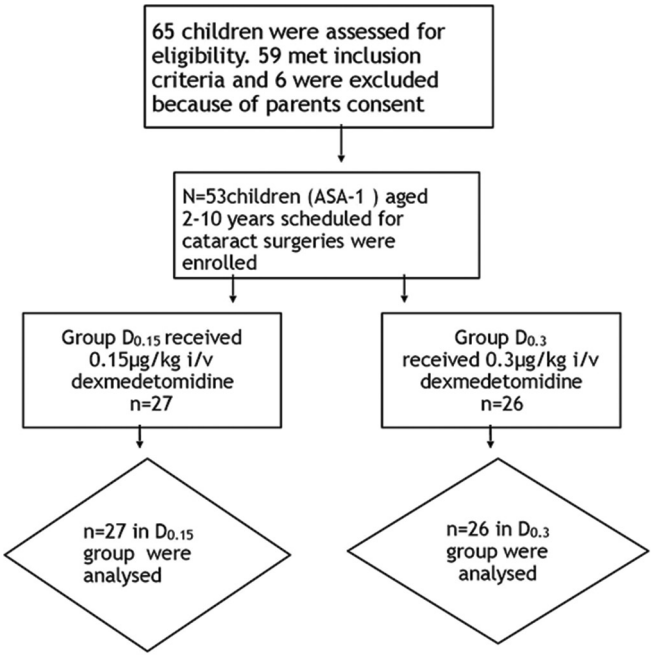

Figure 1: Consort diagram of participants

The state of agitation was assessed in the postoperative period using Pediatric Anesthesia Emergence Delirium (PAED)[8] scale and postoperative pain using face, legs, activity, cry, and consolability (FLACC) pain[7] scale every 10 min and monitored for an hour. Adverse effects (postoperative nausea and vomiting, excessive secretions, breath holding, laryngospasm, and coughing) need for rescue medication and time to discharge from PACU were also noted. Children were discharged when they were calm, had no pain, and a modified Aldrete score >9.[9] A total PAED score >12 at any time was considered postanesthetic EA. For patients with PAED score >12 or FLACC >4, parental contact was facilitated and if failed, rescue medication in the form of IV fentanyl 0.5 μg/kg was administered and repeated after 10 min if agitation continued.

Statistical analysis

Sample size was calculated based on the results of Ibacache *et al*.[10] They calculated sample size to detect a 75% reduction in incidence of EA from 37% in control group with a power of 80% and $\alpha = 0.05$. Based on these assumptions, the sample size is estimated to be 26 per group. For all quantitative variables mean and median and for measures of dispersion standard

deviation or standard error were calculated. Normality of data was checked by measures of Kolmogorov–Smirnov tests of normality. For normally distributed data, mean of two groups was compared using *t*-test and for skewed data Mann–Whitney test was used. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever is applicable. For comparison of time-related variables, repeated measures ANOVA followed by one-way ANOVA was applied. All statistical tests were two-sided and were performed at a significance level of $P = 0.05$.

Results

Both groups were comparable in terms of age, sex, body weight, duration of surgery [Table 1], and preoperative anxiety score at parental separation and induction of anesthesia [Table 2].

Mean baseline HR, systolic blood pressure (SBP, 91.56 ± 11.504, vs. 97.15 ± 13.818 mmHg), diastolic blood pressure (DBP, 50.30 ± 8.009 vs. 56.19 ± 12.983 mmHg), mean blood pressure (MBP, 69.82 ± 6.0, 61.71 ± 7.88 vs. 68.65 ± 6.61 mmHg), RR (RR, 32.81 ± 6.691 vs. 30.77 ± 6.953), and end-tidal carbon dioxide ($ETCO_2$, 38.81 ± 4.884 vs. 38.50 ± 5.982) were comparable between both groups throughout the surgery. However, HRs were significantly lower in Group $D_{0.3}$ when compared to Group $D_{0.15}$ at 5, 10, and 15 min [Figure 2].

Within groups, no difference in postoperative baseline HR was recorded. However, Group $D_{0.3}$ had statistically significantly lower HRs in comparison to Group $D_{0.15}$ in immediate postoperative period and throughout up to 45 min postoperatively. Thereafter, HRs were comparable. Whereas, postoperative SBP and DBP were comparable at all time intervals [Figure 3].

Pain scores were significantly lower in Group $D_{0.3}$ compared to Group $D_{0.15}$ at all time intervals postoperatively. Three children in Group $D_{0.15}$ were found to have FLACC >4, whereas no child was found to have FLACC >4 in Group $D_{0.3}$ [Table 3 and Figure 4].

Using PAED[8] score >12 criteria to define EA, no EA was found in either of groups. When compared to baseline score, PAED score reduced significantly in each group after 10 min. However, when compared between groups, PAED scores were statistically significantly reduced in Group $D_{0.3}$ as compared to Group $D_{0.15}$ with $P < 0.05$ at all time intervals throughout surgery [Table 4 and Figure 5].

Table 1: Comparison of the demographic variables* *t*-test

Parameter assesed	Mean±SD		*P*
	Group $D_{0.15}$ (*n*=27)	Group $D_{0.3}$ (*n*=26)	
Age (years)	4.56±2.375	5.04±2.457	0.470*
Gender (%)			
Females	9 (33.3)	10 (38.5)	0.697#
Males	18 (66.7)	16 (61.5)	
Weight (kg)	15.778±4.8543	15.862±5.9547	0.955*
Duration of surgery	24.44ion of	23.46ion of	0.491*

#Chi-square-test. SD: Standard deviation

Table 2: Preoperative anxiety score (modified Yale Preoperative Anxiety Scale) at parental separation and induction

m-YPAS	Median (IQR)		*P*#
	Group $D_{0.15}$ (*n*=27)	Group $D_{0.3}$ (*n*=26)	
At parental separation	7 (5-10)	12 (9-14)	0.249
At mask induction	7 (5-8.25)	9.50 (6.50-12)	0.097

#Mann-Whitney *t*-test. m-YPAS: Modified Yale Preoperative Anxiety Scale; IQR: Interquartile range

Table 3: Comparison of postoperative pain assessment by face, legs, activity, cry and consolability score

Postoperative duration (min)	FLACC score, median (IQR)		*P*#
	Group $D_{0.15}$ (*n*=27)	Group $D_{0.3}$ (*n*=26)	
0	3 (1-4)	0 (0-2)	0.001
10	2 (0-3)	0 (0-1)	0.001
20	1 (0-3)	0 (0-0.25)	0.001
30	1 (0-3)	0 (0-0)	0.001
40	1 (0-2)	0 (0-0)	0.001
50	1 (0-2)	0 (0-0)	0.001
60	1 (0-2)	0 (0-0)	0.001

#One-way ANOVA test. FLACC: Face, legs, activity, cry and consolability; IQR: Interquartile range

Rescue medication was given when PAED score was ≥12 and/or FLACC was >4 in postoperative period. No child in Group $D_{0.3}$ required rescue medication. In Group $D_{0.15,}$ 3 children (11%) required rescue medication with FLACC >4.

The time to discharge was 31.48 ± 18.7 min in Group $D_{0.15}$ and 20.96 ± 10.96 min in $D_{0.3}$ groups using modified Aldrete Score[9](9/10). The groups were comparable with time to discharge ($P = 0.071$).

One child in each group had vomiting, which responded to a single dose of IV ondansetron. No episode of desaturation or laryngospasm was noted in either of groups.

Discussion

The results of our study suggest that 0.3 μg/kg IV dexmedetomidine effectively reduce postdesflurane EA

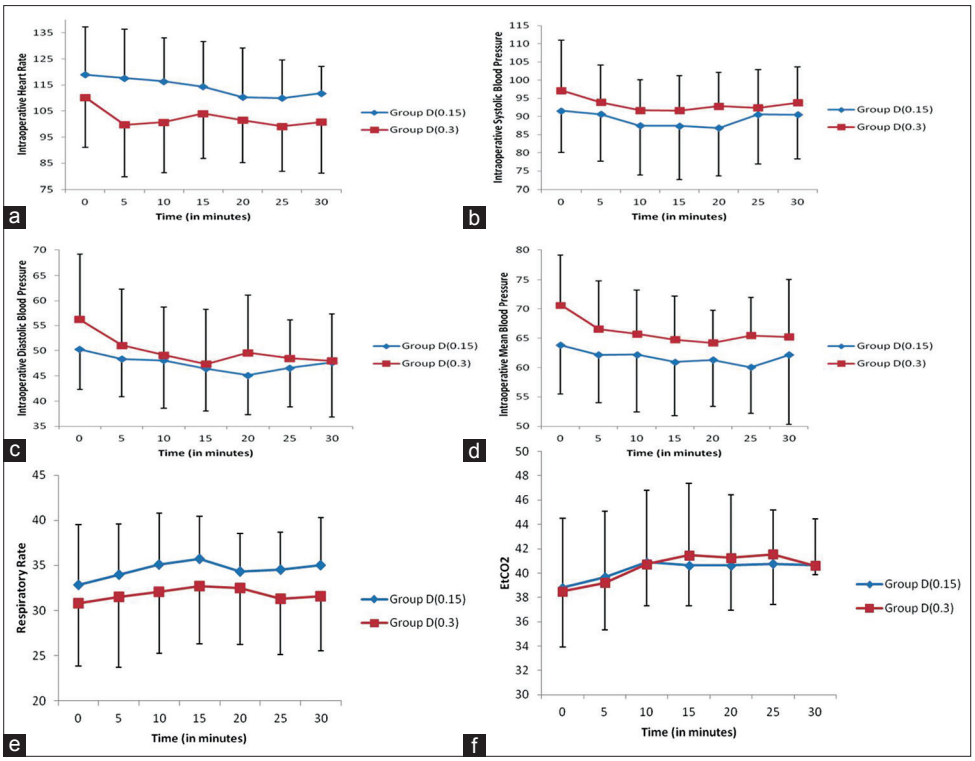

Figure 2: Comparison of fluctuations in (a) intraoperative heart rate, (b) systolic blood pressure, (c) diastolic blood pressure, (d) mean blood pressure, (e) respiratory rate, (f) end-tidal carbon dioxide

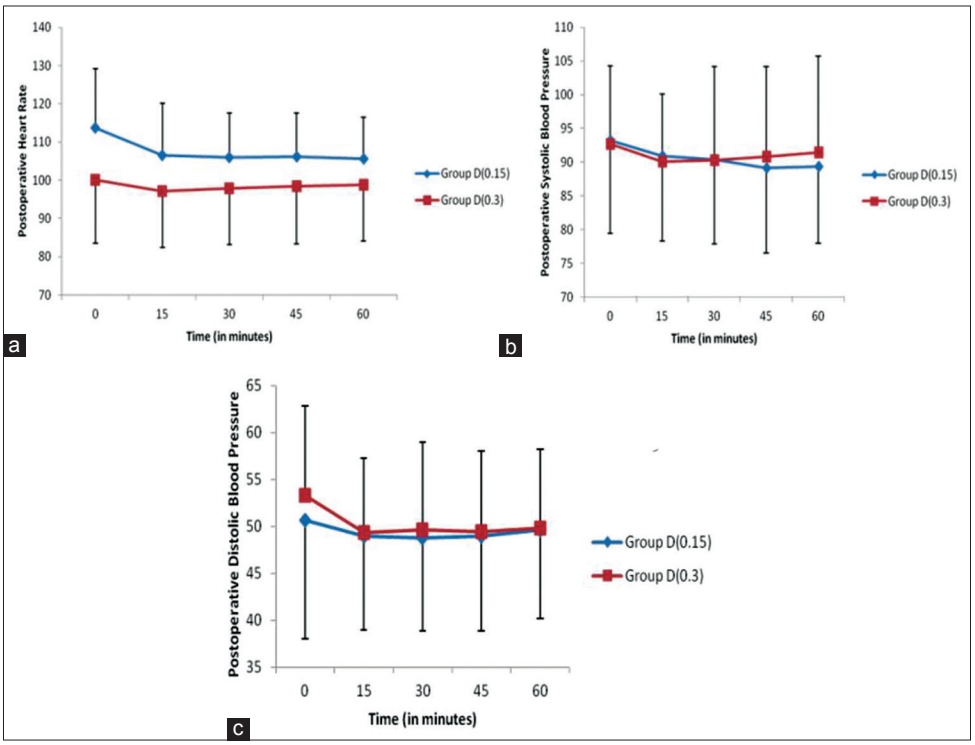

Figure 3: Comparison of fluctuations in postoperative heart rate (a), systolic blood pressure (b), and diastolic blood pressure (c)

with sub-Tenon block without producing adverse effects such as hypotension or bradycardia. Significant reduction in EA was also found in 0.15 μg/kg IV dexmedetomidine. However, this dose did not completely eliminate EA (11%) and was associated with higher PAED scores when compared to 0.3 μg/kg (0%). Hence, 0.3 μg/kg IV dexmedetomidine

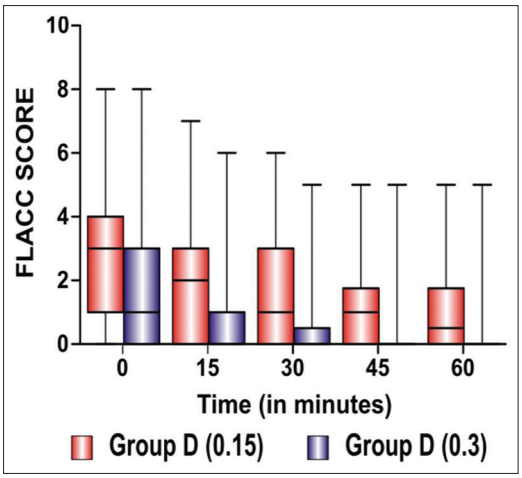

Figure 4: Postoperative pain score– face, legs, activity, cry, and consolability score in relation to time in both groups

Table 4: Pediatric Anesthesia Emergence Delirium score of both groups

Postoperative duration (min)	PAEDS score, median (IQR)		*P*#
	Group $D_{0.15}$ (n=27)	Group $D_{0.3}$ (n=26)	
0	6 (4-8)	1.50 (0-3.25)	<0.001
10	4 (2-7)	0.50 (0-2)	<0.001
20	4 (2-6)	0 (0-1)	<0.001
30	4 (2-6)	0 (0-0)	<0.001
40	3 (1-5)	0 (001	<0.001
50	2 (1-4)	0 (0-0)	<0.001
60	2 (1-4)	0 (0-0)	<0.001

#One-way ANOVA test. PAEDS: Pediatric Anesthesia Emergence Delirium Scale; IQR: Interquartile range

was found to be superior to 0.15 μg/kg group in effectively reducing EA and analgesia with lower PAED and FLACC scores, respectively.

EA is not clearly defined and has been used interchangeably with emergence delirium. Sikich and Lerman[11] defined EA as "a disturbance in child's awareness and attention to his/her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behavior in immediate postanesthesia period". This cognitive disturbance is overlapped by various confounding factors such as preoperative anxiety, pain, and other factors contributing to the restlessness of child in immediate postoperative period.

In our study, we tried to eliminate these confounding factors. We facilitated parental presence reducing anxiety as measured by m-YPAS at parental separation and mask induction with decreased and comparable scores ($P > 0.05$).[5] Pain is also a confounding variable associated with EA. We attempted to eliminate pain as a confounding variable in both groups through effective sub-Tenon block (0.08 ml/kg

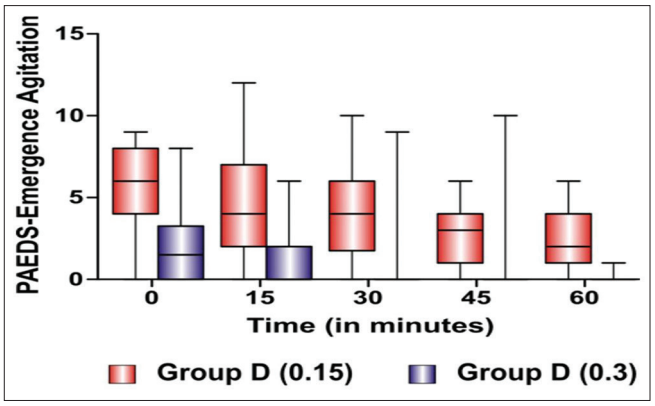

Figure 5: Pediatric anesthesia emergence delirium scale with relation to time in both groups

of bupivacaine 0.5%)[12] and IV paracetamol (15 mg/kg). We also found lower pain scores in both groups with significant lower FLACC scores in 0.3 μg/kg group than 0.15 μg/kg. This can be explained by the analgesic and opioid sparing effect of increased dose of 0.3 μg/kg dexmedetomidine with comparable postoperative complications such as nausea and respiratory depression.[13]

Various studies have used variable doses of dexmedetomidine in preventing EA.

Jeongmim *et al*.[14] studied the effects of continuous perioperative infusion of 0.2 μg/kg/h dexmedetomidine in 96 children aged 1–5 years undergoing strabismus surgery following desflurane anesthesia. They found that the severity of EA and frequency of rescue analgesia was significantly lower in dexmedetomidine group (12.8% vs. 74.5%, $P < 0.001$). They concluded that intraoperative low-dose infusion of dexmedetomidine effectively reduces EA in children undergoing strabismus surgery following anesthesia with desflurane.

Zhu *et al*.[15] conducted a meta-analysis including 20 prospective randomized controlled trials to compare the impact of dexmedetomidine with fentanyl, midazolam, and placebo on EA and recovery profiles following sevoflurane anesthesia in in PACU. They found that when compared to placebo, dexmedetomidine decreased incidence of EA (risk ratio [RR] 0.37; 95% confidence interval [CI] 0.30 t0 0.46), incidence of nausea, vomiting (RR 0.57; 95% CI 0.38–0.85), and number of patients requiring rescue analgesic (RR 0.43; 95% CI 0.31–0.59). However, as compared to fentanyl and midazolam, dexmedetomidine had no significant difference on EA.

Ghai *et al*.[16] conducted a randomized trial in sixty-three children, 1–6 years of age, to assess efficacy of low-dose

dexmedetomidine (0.15 μg/kg and 0.3 μg/kg) on postsevoflurane EA in children undergoing cataract surgery. They found that EA was significantly decreased with incidence of 10% in 0.15 μg/kg group, none in 0.3 μg/kg, and 35% in normal saline group.

Ibacache *et al*.[10] used dexmedetomidine 0.3 μg/kg and 0.15 μg/kg compared to placebo for prevention of EA in 90 unpremedicated children (1–10 years) undergoing lower abdominal and genital surgery under sevoflurane anesthesia and caudal analgesia using a 4-point scale. They observed a reduction in agitation from 37% in placebo group to 17% and 10%, respectively, in dexmedetomidine 0.15 ug/kg and 0.3 ug/kg groups. No side effects such as bradycardia or hypotension were noted suggesting safety of these doses.

However, unlike many previous studies, we used validated scales such as m-YPAS[5] for preoperative anxiety assessment, PAED scale[8] for assessment of postoperative agitation, and FLACC score[7] for postoperatively pain assessment. The incidence of EA in our study using desflurane anesthesia was 11% in 0.15 μg/kg group and 0% in 0.3 μg/kg group. Furthermore, we have chosen pediatric cataract surgery with highest incidence of EA using similar doses of dexmedetomidine as age group (2–10 years) and ophthalmic surgery have much higher incidence of EA (28%) compared to lower abdominal and genital surgery (12%).[10]

Although in our study, a drop in HR was observed intraoperatively in both the groups after administration of dexmedetomidine with a greater drop in 0.3 μg/kg group at 5, 10, and 15 min ($P < 0.05$) with comparable rates; thereafter, no bradycardia was reported. Other parameters – mean BP, RR, and $EtCO_2$ – were comparable and not statistically significant ($P > 0.05$).

Postoperative complications were also decreased in both the groups. Three patients in Group $D_{0.15}$ required rescue medication postoperatively and were observed to have PAEDS >12 and FLACC >4. Although we have used validated scales in our study, there is considerable overlapping between these pain and EA measuring tools. It is therefore difficult to distinguish between pain and EA.

Two patients, one from each group, developed vomiting in postoperative period which responded to a single dose of IV ondansetron. One child in Group $D_{0.15}$ was found to have an episode of breath holding which responded to jaw lift and administration of 100% O_2. Two children in Group $D_{0.15}$ had excessive secretions and three had coughing. In Group $D_{0.3}$, one child developed excessive secretions and one developed coughing. No child was reported to have an episode of laryngospasm, hypotension, or bradycardia. It was observed that there was no delay in recovery of any children.

However, our study has following limitations. First, in our study, the children were induced with sevoflurane followed by the maintenance with desflurane. Hence, initial exposure to sevoflurane could be a confounding factor. Second, the incidence of EA was assessed using PAED Scale at every 15 min. However, the 5 min interval would have led to reduced intraobserver variability

Conclusions

The results of our study suggest that 0.3 μg/kg IV dexmedetomidine effectively reduced postdesflurane emergence agitation in children undergoing cataract surgery with sub-Tenon block without producing adverse effects such as hypotension or bradycardia.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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