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Dexmedetomidine versus propofol for prevention of emergence delirium in pediatric cataract surgery: Double blinded randomized study

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ABSTRACT

Background: Emergence delirium (ED) is a common complication after general anesthesia in pediatrics, as reported by pediatric anesthesiologists. Multiple drugs have been suggested to prevent the incidence of this problem. Herein, we compared dexmedetomidine and propofol in the prevention of ED in pediatric patients undergoing cataract surgery under general anesthesia.

Patients and methods: This prospective study included 80 children who were randomly allocated into two groups; the Dex group, which received dexmedetomidine, and the Pro group, which received propofol. All operations were performed under general anesthesia, and both drugs were administered 20 minutes before the end of surgery. Our primary outcome was to compare between the incidence of ED in both groups, while secondary outcomes included hemodynamic changes, pain scores, and other complications.

Results: Age, gender, and the duration of PACU stay showed no significant difference between the two groups. ED was encountered in 5% and 27.5% of patients in the Dex and Pro groups, respectively, with a significant decline in association with dexmedetomidine. Delirium and pain scores were significantly decreased in the Dex group throughout all times of measurement. The same group expressed a significant decrease in most heart rate and arterial pressure measurements. Hypotension was encountered in 15% of patients in the Dex group versus no cases in the Pro group.

Conclusion: Dexmedetomidine is superior to propofol in the prevention of ED in pediatrics. It is also associated with better post-operative pain scores.

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1. Introduction

Emergence delirium (ED) is a common postoperative neurological complication that could be encountered in up to 80% of pediatrics after general anesthesia. It is defined as involuntary agitation associated with crying, shouting, kicking, uncooperability, inconsolability, lack of awareness of the surroundings, and absent eye contact with parents or healthcare staff [1,2]. The etiology of this problem is multifactorial, as multiple patients, anesthetic, surgical, and medication-related factors play a role in its development [3,4].

ED constitutes a major problem for both parents and healthcare staff, as the child may injure himself, harm the surgical wound, remove the drain, urinary catheter, or any attached devices. ED is a major source of dissatisfaction for both parents and caregivers [5,6]. Therefore, the prevention of such a problem is crucial in pediatric anesthesiology practice [7].

Adjunctive drug administration to decrease the incidence of ED is common among pediatric anesthesiologists. These drugs could be commenced as premedication or a part of the anesthetic technique itself [6]. These drugs could include propofol, benzodiazepines, opioids, gabapentin, ketamine, or dexmedetomidine [6,8–10].

Propofol is an intravenous anesthetic drug, which could be administered for induction or procedural sedation [11]. It was reported to be an effective intervention to decrease ED in pediatrics [12]. It is commonly used for the prevention and treatment of ED, especially among German anesthesiologists [13].

Dexmedetomidine is a selective alpha-2 receptor agonist, which has more potency compared to clonidine [14]. It has some characteristics making it preferable for the pediatric population. It activates these receptors in the pons and locus coeruleus, leading to anxiolysis and sedation. In addition, it has a potent analgesic effect through its action on the same receptors located at the dorsal horn of the spinal cord leading to substance P release [15].

We conducted the present study to compare dexmedetomidine and propofol in the prevention of ED in pediatric patients undergoing cataract surgery under general anesthesia.

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2. Patients and methods

The current prospective randomized, double-blinded study was conducted at Mansoura University Hospitals after gaining approval from the local scientific committee and Institutional Review Board (IRB) of our medical school (IRB Number: R.21.05.1326.R1-2021/05/23)

The study was designed for pediatric patients scheduled for cataract surgery under general anesthesia at the Ophthalmology Center of our university. It was conducted during the period between July and December 2021.

Sample size calculation: G power analysis program was used to estimate sample size with an effective size of 0.8, an 80% power, and a 0.05 alpha error. A total sample size of 80 patients was required to achieve the previous requests (40 patients in each group).

We included pediatric patients whose ages were between two and 10 years, from either gender, diagnosed with cataract and scheduled for surgery under general anesthesia. Contrarily, we excluded patients with neurological disease or known sensitivity to any of the study medications.

All patients received standard preoperative care, including history taking, clinical examination and required investigations. The 80 patients were divided into two groups (40 patients in each) according to the drug commenced for ED prevention; the Dex group included patients who received dexmedetomidine, and the Pro group included patients who received propofol. Randomization was done via the sealed envelope method. Informed written consent was obtained from the guardians of all patients after a complete explanation of the benefits and possible side effects of each approach.

Patients in both groups were kept fasting for 6–8 hours before the operation. After arrival to the operative room, routine hemodynamic monitoring was established before anesthetic induction. This included pulse, blood pressure and O2 saturation. General anesthesia was induced by sevoflurane 5% in 100% oxygen via a face mask, a wide bore cannula was inserted into a suitable peripheral vein. A suitable size endotracheal tube was inserted after muscle relaxation (which was performed by atracurium 0.5 mg/kg. All patients received paracetamol suppositories (15 mg/kg) after intubation. Maintenance of anesthesia was done by sevoflurane 2–3%, and its dose was adjusted according to the measured pulse and mean arterial pressure (MAP), which was kept within 20% of their basal values. ETCO2 was monitored and maintained around 35 mmHg. No propofol or opioid medications were commenced during the operation.

Fluid balance during the operation was maintained by ringer lactate solution (7 ml/kg/hr) for replacement of deficit in addition to maintenance. Before the end of the operation, by 20 minutes, patients received either of the study drugs according to group allocation. The Dex group received an IV infusion of dexmedetomidine (0.2 µgm/kg) diluted in normal saline 0.9% (20 ml) over 10 minutes, and this was followed by IV administration of 5 ml 0.9% normal saline. In the Pro group, patients were commenced on IV infusion of normal saline 0.9% (20 ml) over 10 minutes, followed by IV propofol 1 mg/kg. We ensured that all syringes were completely covered with foil as our study was blinded in nature.

After finishing the surgical procedure, sevoflurane was discontinued, and the neuromuscular block was reversed via neostigmine (0.4 mg/kg)and atropine (0.2 mg/kg). The patient was extubated when he was fully awake, expressing eye-opening and purposeful movement, in addition to maintaining good tidal volume. Then, the patients were transferred to the PACU, where they received O2 via a face mask to maintain oxygen saturation above 95%.

During their stay at PACU, delirium was assessed at 5, 10, 15, 20, 25, and 30 minutes following extubation via the Pediatric Anesthesia Emergence Delirium scale-(PAED)(Table 1) [16] and ED was established when the child had a score of 10 or more. If the child has a score of 16 or more, rescue sedation was done via propofol 1 mg/kg.

The postoperative pain was assessed via the Face, Legs, Activity, Cry, and Consolability (FLACC) scale 0 = Relaxed and comfortable,1–3 = Mild discomfort, 4–6 = Moderate pain, 7–10 = Severe discomfort/pain [17]. IV fentanyl 1 µgm/kg was administered if the child expressed a score of 3 or more.

Both pulse and MAP were recorded at PACU on arrival, then at 5 and 10 minutes, then every 10 minutes until the patient was discharged to the internal ward. Any post-operative complications including bradycardia, hypotension or hypersensitivity reaction were recorded. Both bradycardia and hypotension were established when they decreased by 20% or more of their baseline value [18]. They were managed by atropine 0.02 mg/kg. The incidence of postoperative vomiting, together with the duration of stay in PACU, was recorded.

Our primary outcome was the incidence of ED, while secondary outcomes included hemodynamic changes, pain scores, and other complications.

3. Statistical analysis

Data collection, tabulation and analysis were conducted by using statistical package of social science (SPSS, IBM, Inc, Chicago; USA) version 26 for windows. Quantitative data were tested for normality using Kolmogorov-Smirnov test and expressed as mean ± SD or median and interquartile range. Categorical data were expressed percentage and frequency.

Table 1. Pediatric Anesthesia Emergence Delirium Scale [16].

Behaviour	Not at all	Just a little	Quite a bit	Very much	extremely
Makes eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surroundings	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

Independent sample T and Mann Whitney tests were used for intergroup comparison of parametric and non-parametric continuous data respectively. Chi square test or Fisher's exact test was used for comparing two or more groups of categorical data Probability ($P < 0.05$) was considered to be statistically significant.

4. Results

The included participants had mean ages of 5.73 and 6.1 years in the Dex and Pro groups, respectively. Regarding gender distribution, boys represented 60% and 50% of participants in the same two groups, respectively. Both of the previous two variables were statistically comparable between the two groups.

The incidence of delirium was significantly increased in the Pro group, as it was detected in 27.5% of its cases, compared to only 5% of Dex group participants ($p = 0.006$). Nevertheless, both groups showed no difference regarding the duration of PACU stay ($p = 0.071$).

When it comes to post-operative complications, no cases of hypersensitivity were encountered in the two groups. Post-operative vomiting was encountered in 2.5% and 10% of patients in the Dex and Pro groups, respectively, which was statistically comparable between the two groups. However, the incidence of hypotension showed a significant increase in association with the Dex group (15% vs 0% in the Pro group – $p = 0.011$). Table 2 summarizes the previous data.

The PAED scale showed a significant decrease in the Dex group compared to the Pro group throughout all times of measurement ($p < 0.05$). This implied that dexmedetomidine had a protective role against post-operative delirium (Table 3).

Patients in the Dex group expressed significantly lower pain scales compared to the Pro group ($p < 0.05$), as shown in Table 4.

During their stay at PACU, patients in the Dex group expressed a significant decrease in their heart rates compared to the Pro group ($p < 0.05$), apart from the 50-minute reading, which was statistically comparable between the two groups ($p = 0.323$). Table 5 shows these data.

As illustrated in Table 6, the Dex group showed a significant decrease in their MAP during their PACU stay compared to the Pro group ($p < 0.05$). This was evident during the PACU stay except for the last reading, which showed no significant difference between our two groups ($p = 0.513$).

5. Discussion

Prevention of ED is mainly dependent on reduction of preoperative anxiety, better control of postoperative pain, and sedative and/or analgesic agent administration. Many research focused on pharmacological measures against ED, and numerous agents were proven to be effective in preventing this problem [19].

Our findings showed that ED was encountered in 27.5% and 5% of patients in the Dex and Pro groups, respectively, with a significant decrease in association with dexmedetomidine administration ($p = 0.006$). Moreover, the PAED score had significantly lower values in the Dex group compared to the other one throughout all times of measurement.

The superiority of dexmedetomidine could be attributed to its sedative and analgesic effects. On the other hand, although propofol has a sedative effect, it lacks the analgesic one [20] Others attributed the inferiority of propofol to its shorter half-life, which makes its serum concentrations below the therapeutic level on arrival to PACU [19].

Previous studies have confirmed the superiority of dexmedetomidine compared to propofol in the prevention of ED. Makkar and his colleagues reported that ED was encountered in 9.4% and 13.9% of children in the Dex and Pro groups, respectively. Statistical analysis showed a significant difference between the two groups ($p = 0.043$). PAED score had lower values in the Dex group compared to the Pro group during the early 20 minutes after surgery [4].

Table 2. Demographic data, the incidence of delirium, and postoperative recovery profile in the two groups.

		Dex group (n = 40)	Pro group (n = 40)	95% CI/ Odds ratio	P
Age (years)		5.73 ± 2.592	6.10 ± 2.285	−1.5, 0.7	0.494
Gender	Female	40.0% (16)	50.0% (20)	-	0.369
	Male	60.0% (24)	50.0% (20)		
Incidence of delirium		5.0% (2)	27.5% (11)	7.21	0.006
PACU stay (minutes)		38.00 ± 5.862	40.63 ± 6.905	−5.5, 0.2	0.071
Complications	Vomiting	2.5% (1)	10.0% (4	4.33	0.166
	Hypotension	15.0% (6)	0.0% (0)	0.46	0.011
	Hypersensitivity	0% (0)	0% (0)	-	1

Table 3. PAED score followup of the two groups.

PAED	Dex group (n = 40)	Pro group (n = 40)	95% CI	P
5 minutes	5.00 ± 2.970	7.18 ± 4.206	−3.8, −0.6	0.009
10 minutes	4.10 ± 3.144	6.78 ± 4.221	−4.3, −1.0	0.002
15 minutes	3.15 ± 2.957	6.23 ± 4.306	−4.7, −1.4	< 0.001
20 minutes	2.35 ± 2.806	5.80 ± 4.214	−5.0, −1.9	< 0.001
25 minutes	1.90 ± 2.489	5.28 ± 4.126	−4.9, −1.9	< 0.001
30 minutes	1.55 ± 2.195	4.70 ± 3.988	−4.6, −1.7	< 0.001

Table 4. FLACC score follow-up of the two groups.

FLACC	Dex group (n = 40)	Pro group (n = 40)	95% CI	P
5 minutes	1.90 ± 1.355	3.08 ± 2.336	−2.0, −0.3	0.007
10 minutes	1.68 ± 1.526	2.85 ± 2.214	−2.0, −0.3	0.007
15 minutes	1.33 ± 1.492	2.25 ± 1.808	−1.7, −0.2	0.015
20 minutes	1.08 ± 1.248	2.55 ± 2.264	−2.3, −0.7	0.001
25 minutes	0.83 ± 1.130	2.20 ± 1.924	−2.1, −0.7	< 0.001
30 minutes	0.73 ± 1.109	1.75 ± 1.958	−1.7, −0.3	0.005

Table 5. Heart rate follow-up of the two groups.

Heart rate	Dex group (n = 40)	Pro group (n = 40)	95% CI	P
Admission	95.10 ± 10.876	119.80 ± 8.856	−29.1, −20.3	< 0.001
5 minutes	97.10 ± 10.994	119.78 ± 9.183	−27.2, −18.2	< 0.001
10 minutes	99.30 ± 10.859	119.58 ± 9.524	−24.8, −15.7	< 0.001
20 minutes	100.85 ± 11.452	120.03 ± 9.051	−23.8, −14.6	< 0.001
30 minutes	102.50 ± 11.453	119.90 ± 9.097	−22.0, −12.8	< 0.001
40 minutes	102.70 ± 11.703	122.00 ± 8.357	−25.1, −13.5	< 0.001
50 minutes	114.50 ± 14.849	123.00 ± 8.246	−27.8, 10.8	0.323

Table 6. MAP follow-up of the two groups.

MAP	Dex group (n = 40)	Pro group (n = 40)	95% CI	P
Admission	71.65 ± 13.055	92.90 ± 10.303	−26.5, −16.0	< 0.001
5 minutes	70.85 ± 13.049	93.20 ± 10.663	−27.7, −17.0	< 0.001
10 minutes	70.80 ± 12.972	92.75 ± 11.254	−27.4, −16.5	< 0.001
20 minutes	70.88 ± 13.663	92.73 ± 11.500	−27.5, −16.2	< 0.001
30 minutes	71.45 ± 14.066	92.85 ± 11.709	−27.2, −15.6	< 0.001
40 minutes	71.35 ± 15.212	93.73 ± 11.460	−30.1, −14.7	< 0.001
50 minutes	83.50 ± 21.920	92.50 ± 14.363	−40.7, 22.7	0.513

Ali and Abdellatif reported a significant increase in the incidence of emergence agitation (a wide term including ED, pain, and several other factors) in the propofol group compared to the dexmedetomidine one during the early 15 minutes in PACU. It was encountered in 12.5% and 32.5% on arrival, in 5% and 22.5% after five minutes, and in 2.5% and 10% of children after 15 minutes in the Dex and Pro groups respectively ($p < 0.05$). Additionally, the PAED scale showed significantly lower values in association with dexmedetomidine administration during the same time points ($p < 0.05$) [20].

On the other hand, Bong and his associates negated any significant benefit of either dexmedetomidine or propofol on the incidence of the same problem after general anesthesia for MRI studies. These authors administered the tested drugs at the time of anesthetic induction, and the procedure itself lasted for about 70 minutes [21]. As dexmedetomidine reaches its maximum action after 15 minutes, and propofol has a short half-life, it was reasonable to detect no significant impact of both drugs on the incidence of such a problem in the previous study.

In our study, the Dex group expressed significantly lower pain scales compared to the Pro group ($p < 0.05$). This was evident through the early 30 minutes in PACU. Dexmedetomidine could achieve analgesia via multiple mechanisms. It inhibits nociceptive C-fibers and Aα-fibers in a dose-dependent manner. It also acts on alpha-2 receptors in the locus ceruleus area leading to inhibition of nociceptive signal transmission through the posterior spinal horn. Furthermore, it inhibits norepinephrine release from the presynaptic neurons leading to its hyperpolarization and decreasing pain transmission to the brain [22]. The better control of pain in the Dex group had a beneficial impact on both PAED scores and incidence of ED, as post-operative pain is one of the major factors attributing to this problem [7,23].

Another study also confirmed our findings regarding better pain management with dexmedetomidine administration. During the early five minutes in PACU, the Dex group expressed lower pain scores compared to the Pro group ($p < 0.05$). Although the remaining pain scores were statistically comparable between the two drugs, children in the Dex group still expressed lower values [20].

Our findings showed that the Dex group expressed a significant decrease in most heart rate and arterial pressure measurements. Hypotension was encountered in 15% of patients in the Dex group versus no cases in the Pro group.

Multiple studies reported that dexmedetomidine is associated with a dose-dependent decline in both blood pressure and heart rate [18,24]. This is mediated by the central sympatholytic effects induced by a small dexmedetomidine dose [19].

Hasanin and Sira also reported that dexmedetomidine administration in the pediatric population was associated with a significant decrease in heart rates compared to the propofol group. However, the same authors failed to detect any significant difference between the two groups regarding MAP [25]. These differences could be explained by different doses and times of administration.

The current study has some limitations; the small sample size that was collected from a single center is the main one. Also, we should have included a control group to assess if propofol itself had a beneficial impact on ED. The upcoming studies should cover these drawbacks.

6. Conclusion

Dexmedetomidine is superior to propofol in the prevention of ED in paediatrics undergoing cataract surgery. It is also associated with better post-operative pain scores. Although the incidence of hypotension

was significantly higher with dexmedetomidine administration, it was successfully managed with medications without further consequences.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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