Original Article

Impact of Caudal Dexmedetomidine Versus Midazolam on Preventing Emergence Delirium after Sevoflurane Anesthesia in Pediatric Patients: A Prospective Randomized Trial

Amin M. Alansary[1*], Rasha Mahmoud Hassan[1], Mohamed Mourad Ali[1]

Abstract

Background: Postoperative emergence delirium (ED) is common in pediatric patients anesthetized with sevoflurane. ED carries many complications, such as disorientation and perceptual changes, including motor hyperactivity and hypersensitivity to stimuli. ED usually appears in the early 30 min after awakening from general anesthesia. We assessed the effect of caudal dexmedetomidine versus midazolam added to bupivacaine in reducing the incidence and severity of ED.

Materials and Methods: Seventy-five children of either sex underwent lower abdominal or perineal surgeries. Patients were divided into three equal groups; BD (received caudal bupivacaine dexmedetomidine), BM (received caudal bupivacaine midazolam), and B(received caudal bupivacaine only). All patients were monitored intra and post-operatively regarding their hemodynamics. The post-operative pediatric anesthesia emergence delirium scale (PAED) and the post-operative face, legs, activity, cry, and controllability (FLACC) pain scale was used to assess ED and pain.

Results: Regarding the ED, group BD showed the least PAED score, followed by BM and then the B group, with the statistically significant difference found at 0 and 15 min in PACU ($P<0.05$). Assessment of the FLACC score and time of emergence revealed no statistically significant difference. At the same time, the number of patients who received IV dexmedetomidine and PACU stay was significant in group B ($P<0.05$). The intra-operative hemodynamics (NIBP, HR) showed no statistically significant difference between the three groups. In contrast, post-operative systolic blood pressure and heart rate showed a statistically significant difference at 0 and 15 minutes with higher values in group B, BM then the lowest values were recorded in group BD ($P<0.05$). Regarding the peri-operative complications, no patients experienced hypotension or bradycardia in the three groups.

Conclusion: Caudal dexmedetomidine and caudal midazolam are safe and efficient in decreasing the incidence and severity of ED. Furthermore, dexmedetomidine was more efficient, with the least PAED score. Dexmedetomidine is recommended to be used as an adjuvant to bupivacaine in the pediatric caudal block.

Keywords: Bupivacaine, Caudal block, Dexmedetomidine, Emergence delirium, FLACC score Midazolam, Sevoflurane

1. Department of Anesthesiology, Intensive care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Corresponding Author: Amin Mohamed Alansary, MD. Department of Anesthesiology, Intensive care, and Pain Management, Faculty of Medicine, Ain-Shams University, Abbassia, Postal code: 11591 Cairo, Egypt; Tel: (+20)-1007962192.
Email: Aminalansary@yahoo.com

Please cite this article as: Alansary AM, Hassan RM, Ali MM. Impact of Caudal Dexmedetomidine Versus Midazolam on Preventing Emergence Delirium after Sevoflurane Anesthesia in Pediatric Patients: A Prospective Randomized Trial. J Cell Mol Anesth. 2023;8(1):12-21. DOI: https://doi.org/10.22037/jcma.v8i1.38788

Introduction

Postoperative emergence delirium (ED) is often encountered in pediatric patients anesthetized with sevoflurane, with a prevalence of almost 10-80% (1, 2). Sevoflurane is commonly used for the induction and maintenance of anesthesia in pediatric patients (3).

ED refers to excessive motor activity, mental disturbances such as hallucinations, and marked irritation (4). Different factors contribute to the etiology of ED, such as pain, hypoxemia, lack of sedation before induction of anesthesia, waking up in a non-familiar environment, and noise. Pediatric patients younger than six years are the most commonly at risk of exhibiting ED in the early postanesthetic period (5, 6).

Complications associated with ED may include: Hemorrhage from surgical wounds, psychological trauma to parents, unexpected prolonged stay in the post-anesthesia care unit (PACU) with a subsequent prolonged hospital stay, and increased overall cost to the hospital (7, 8).

Calm emergence after general anesthesia would undoubtedly decrease the child's self-harming actions and improve parent/guardian and doctor satisfaction (8, 9).

Alpha$_2$ agonists such as clonidine and dexmedetomidine have been administered intravenously (IV) to prevent ED (10, 11). The affinity of dexmedetomidine to alpha$_2$ adrenoreceptors is approximately eight times greater than clonidine. Being more selective on alpha$_2$a adrenoreceptors accounts for this drug's sedative, sympatholytic, and analgesic effects (12).

Intravenous midazolam and dexmedetomidine have been used to reduce the incidence of ED and were found effective in minimizing the incidence and degree of ED without significantly prolonging recovery time (13, 14). However, some authors reported that IV dexmedetomidine increased the time to PACU discharge (15). Also, others have reported that IV midazolam increased the time to emergence (16, 17).

This study aimed to assess and compare the effect of caudal dexmedetomidine versus midazolam added to bupivacaine in reducing the incidence and severity of ED following sevoflurane-based anesthesia in pediatric patients.

Methods

This prospective, randomized, controlled, double-blinded study was conducted following ethical research committee approval (FMASU R64/2019) at Ain Shams University hospitals and obtaining parental/guardian written informed consent. This study was registered at the Pan African Clinical Trial Registry (PACTR202203663979478).

Seventy-five pediatric patients of either sex, aged 2-6 years, American Society of Anesthesiologists (ASA) physical status I-II, undergoing lower abdominal or perineal surgeries under sevoflurane-based anesthesia, were enrolled in the study. The study was conducted from January 1, 2020, to December 31, 2020.

Pediatric patients with neurological, neuromuscular, or spinal diseases were excluded. Other exclusion criteria were mental retardation, signs of infection at the caudal injection site, coagulopathies, history of allergy, hypersensitivity, or contraindications to the studied drugs.

Patients were allocated randomly (using computer-generated number lists and opaque sealed envelopes) into three equal groups to receive a single-shot caudal epidural block after induction of general anesthesia. Group BD (n=25, dexmedetomidine study group): received 0.25% bupivacaine (1 ml/Kg) with 1.5 µg/Kg dexmedetomidine in normal saline up to 1 ml. Group BM (n=25, midazolam study group): received 0.25% bupivacaine (1 ml/Kg) with 30 µg/Kg midazolam was mixed with normal saline up to 1 ml. Group B (n = 25, control group): received 0.25% bupivacaine (1 ml/Kg) in normal saline.

The drug mixtures were prepared by an anesthetist who did not participate in the study. The block was performed by an anesthesiologist blinded to the studied drugs. The surgeon and observer were also blinded, and the master code was kept with one person who did not participate in the study.

Parents were instructed to keep their children fasting according to the NPO guidelines. Patients were then transferred to the OR where basic monitors were applied, including electrocardiogram, pulse oximetry, and non-invasive blood pressure. Baseline values of heart rate, blood pressure, and arterial oxygen saturation (SaO_2) were noted. General anesthesia was

induced with 100% oxygen and 8% sevoflurane. Induction Score was noted and recorded for all patients as follows: 1- exceptionally good; cooperative; accepting the face mask, 2- afraid slightly but easily reassured, 3- afraid but challenging to be reassured, 4- screaming; crying; requires restraint (19).

Venous access was secured, and IV fentanyl 1 µg/kg was titrated very slowly. Airway maintenance was done using a laryngeal mask airway (LMA). Lactated ringer solution was administered according to the calculated fluid needs. Sevoflurane (1-2%) was adjusted to maintain anesthesia in an oxygen/air mixture (60%/40%) with spontaneous breathing. End-tidal carbon dioxide ($EtCO_2$) levels were monitored with a capnogram to maintain normocapnia. $EtCO_2$ > 45 mmHg was managed with assisted ventilation at any time during surgery.

Patients were subsequently placed in the lateral decubitus position for ultrasound-guided caudal block. After cleaning and draping by povidone-iodine and complete aseptic conditions were done, a high-frequency linear transducer was put transversely over the sacral cornu until the appearance of the 'frog-eye' sign. The probe was then turned longitudinally to obtain a sagittal view of the caudal space. A caudal block was performed using a short beveled, 23 G needle (view from the study) (Fig.1). Surgical intervention was started 15 minutes following the caudal injection of the drug mixture.

Arterial oxygen saturation (SPO_2), systolic blood pressure (SBP), and heart rate (HR) were noted and recorded every 5 minutes all through surgery. Intraoperative hemodynamics (NIBP, HR) were used to evaluate the efficacy and adequacy of analgesia. An increase in SBP or HR by>20% compared to the baseline readings 15 minutes following caudal block was regarded as failed analgesia. At the same time, inadequate analgesia was defined as a> 20 % increase in SBP or HR 45 minutes after surgical incision. Patients with failed or inadequate analgesia were managed with another dose of fentanyl, one ug/Kg intravenously (IV), and were subsequently excluded from the study. Intraoperative bradycardia or hypotension (a decrease by>30% in HR or SBP from the baseline readings) was treated with atropine, IV fluids, or ephedrine as needed.

At the end of the surgery, sevoflurane was discontinued, and inspired oxygen concentration was increased to 100%. LMA was removed when the child showed a facial grimace or made a purposeful movement while breathing regularly and spontaneously. The duration of surgery was noted (defined as the time from surgical incision till completion of surgery). The time of emergence was also recorded (defined as the time from discontinuation of sevoflurane till the removal of LMA). After removing LMA, patients were shifted to a quiet, dim-lighted post-anesthesia care unit (PACU). One parent was allowed to keep the patient company during the PACU stay.

All patients were continuously observed until their discharge from PACU. The observation was done by an anesthesiologist who was unaware of the drug injected. Oxygen saturation, SBP, and HR were noted every 15 minutes. The degree of ED was assessed at zero minutes, every 15 minutes, and up to 1 hour after PACU admission. Pediatric Anesthesia Emergence Delirium (PAED) scale from Bajwa and colleagues was used to evaluate the incidence and severity of agitation, and a score of 10/20 was regarded as delirium (20). If a child was agitated, his attending parent's first line of treatment was a consolation. After 5 minutes, if consolation failed, dexmedetomidine 0.4 µg/Kg IV bolus was given slowly over 10 minutes as the second line of treatment. The FLACC scale demonstrates five pain behaviors, including facial expression, leg movement, activity, crying, and controllability. It is commonly used because it is quick, versatile, and can be applied to different pediatric ages, including those with mental disabilities (21). The score range from 0 to 10 was used to evaluate the severity of postoperative pain. FLACC pain score was recorded at zero minutes, every 15 minutes, and up to 1 hour after PACU admission. FLACC score ≥ 5 was defined as a cut-off point for IV fentanyl administration as rescue medication (0.5 µg/Kg). The duration of the PACU stay was also recorded. Patients were discharged from PACU according to Modified Aldrete Scores; a score ≥ 9 was considered adequate for discharge. Side effects such as nausea, vomiting, bradycardia, hypotension, or respiratory depression (defined as SPO2< 95%) were noted and managed.

Our primary outcome was the degree of ED evaluated with a PAED score. Intraoperative

hemodynamics, postoperative pain scoring, postoperative dexmedetomidine and fentanyl requirements, and duration of PACU stay were all secondary endpoints.

Sample size justification: The sample size was calculated using G*power 3.1.9.2 software program. Depending on the Chi-Square test analysis of the ED proportions among the three studied groups, Cramer's V effect size of 0.36 at a degree of freedom of 2 was adopted (18). The power was set at 80% and the α-error at 0.05. The total sample size was 75, with 25 in each group.

Statistical analysis: It was performed using SPSS 23.0 for Windows (SPSS, Chicago, IL, USA). For quantitative parametric data, analysis of variance was used with posthoc tests to compare the three groups. Tukey's test was used if there was a significant difference between the groups. For quantitative nonparametric data, the Kruskal- Wallis test was used. The Chi-square test was used to compare qualitative data. Continuous parametric data were shown as mean SD, non-parametric data as median (IQR), and categorical data as numbers and percentages. P-values of 0.05 were regarded as significant.

Results

A total of 78 patients were selected for the study; three patients whose guardians declined to participate were excluded. The selected 75 patients were allocated to three equal groups (25 patients in each group). (Fig. 2). No statistically significant difference was found regarding the selected patients' demographic data nor the surgery duration or type **(**Table 1).

Pre- and intra-operatively, all patients' oxygen saturation, blood pressure, and heart rate were recorded every 5 to 45 minutes. The authors found no statistically significant difference in all these parameters between the three groups.

Post-operative oxygen saturation was recorded for one hour and showed no statistically significant difference between the three groups. However, the authors reported a statistically significant difference in heart rate and systolic blood pressure at 0 and 15 minutes postoperatively between the three groups, and higher values were recorded in group B followed by group BM then the lowest values were recorded in group BD (Table 2).

We measured the ED in the three groups at zero minutes and then every 15 minutes in the first hour postoperatively using the PAED scale. We found that Group BD recorded the least scores, followed by group BM and then group B, which showed the highest PAED scores during the first 15 minutes in PACU. None of the patients in group BD or BM developed ED (as defined by a score of 10/20 or more on the PAED scale). In contrast, around 20% of patients in group B scored ten or more on the PAED scale during the first 15 minutes postoperatively (Table 3) (Fig. 3). Regarding the FLAAC scores, this study concluded a comparable pain score between all three groups during the first hour postoperatively with no statistically significant difference (Table 4).

Regarding the time of emergence from

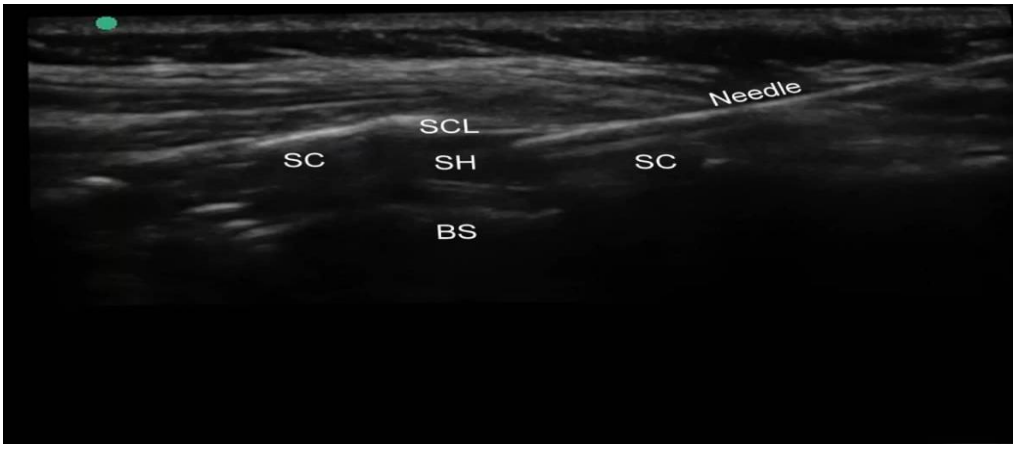

Figure 1. Ultrasound guided caudal block .BS:base of sacrum, SC:sacral cornua. SCL:sacrococcygeal ligament, SH: sacral hiatus.

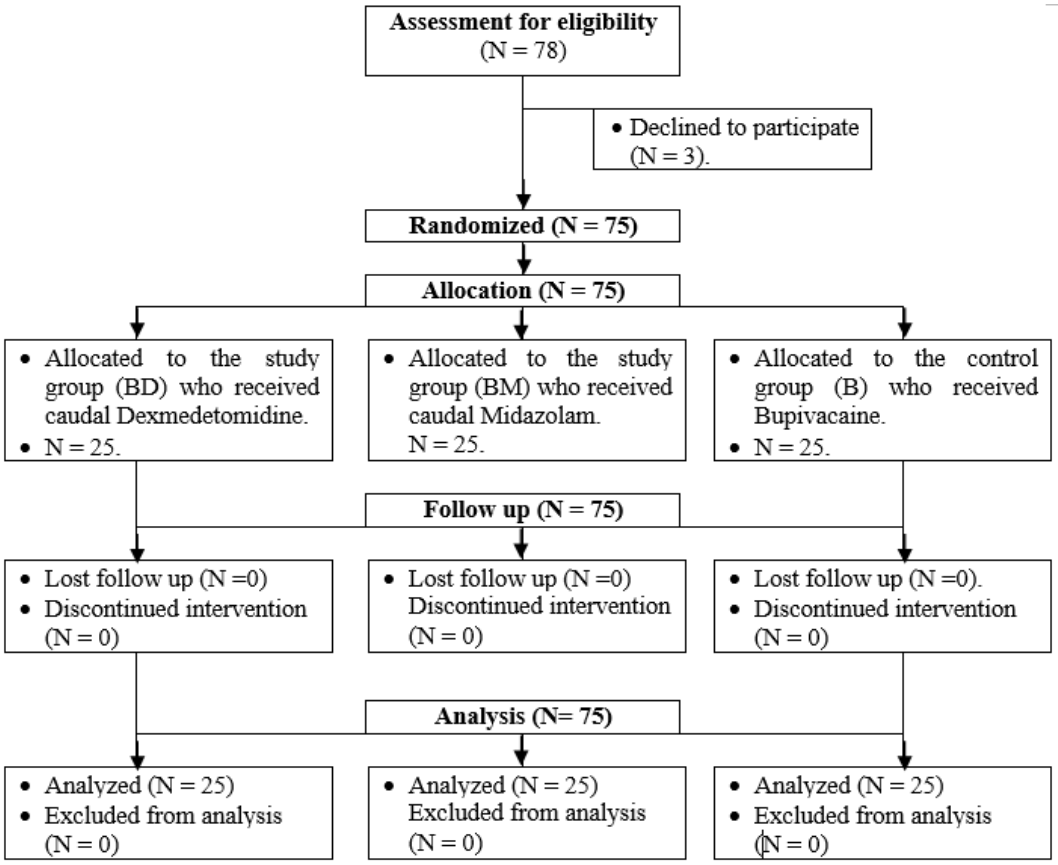

Figure 2. CONSORT patient flowchart.

sevoflurane anesthesia, there was no statistically significant difference between the three groups (Table 5). However, concerning the duration of PACU stay, we found that the control group had a statistically significant longer duration of PACU stay compared to BM and BD groups (Table 5).

Regarding the intra-or post-operative complications, no patients experienced hypotension or bradycardia in the three groups.

Discussion

In the current study, we tried to compare the effect of dexmedetomidine and midazolam when used as adjuvants with caudal bupivacaine on the incidence of

Table 1: Demographic data, duration, and type of surgery.

	Group BD (n=25)	***Group BM (n=25)***	***Group B (n=25)***	***p-value***
Age (year) (mean ± SD)	1.2 ± 4.2	1.1 ± 4.08	1.35 ± 4.3	0.87
Sex (M/F) (number)	16/9	15/10	13/12	0.681
Duration of the procedure (min)	10.47 ± 54.96	11.86 ± 53.2	10.91 ± 52.2	0.674
Type of operation:				
- Inguinal hernia	10	10	9	
- Another hernia	3	4	7	
- Hydrocele	8	6	5	0.740
- Hypospadias	3	5	4	
- Others	1	0	0	

Data are presented as numbers or mean±SD. P > 0.05 was considered statistically non-significant between the 3 groups.

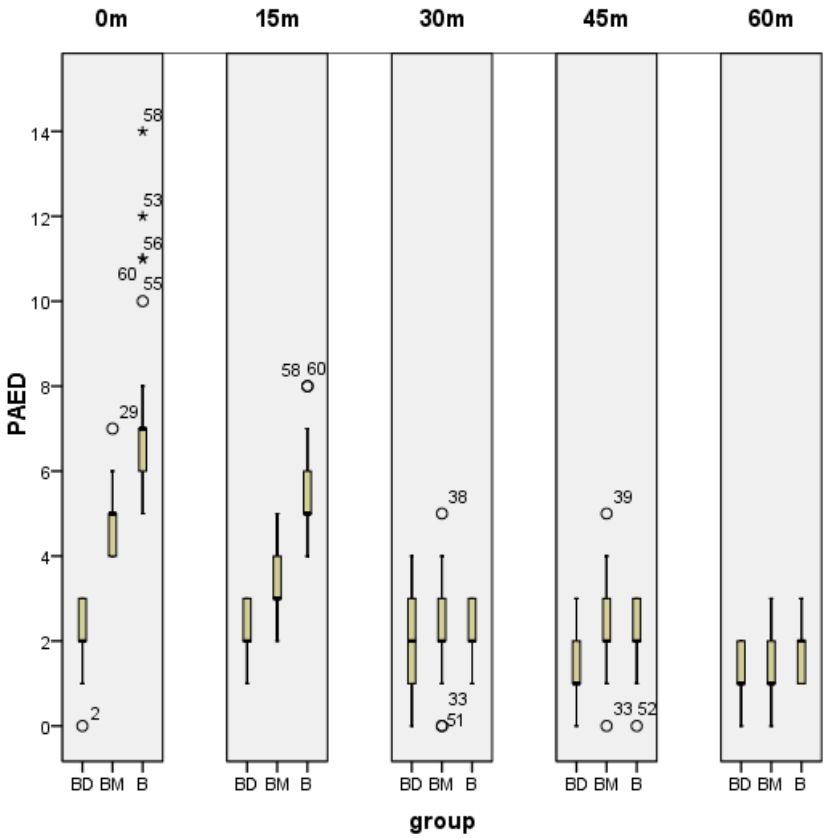

Figure 3. The middle black solid line represents the median, the upper & lower margins of each box represent the IQR, the whiskers are maximum and minimum values, and dots represent the number of patients with outlier data.

Table 2: Post-operative systolic blood pressure and heart rate.

	Post-operative systolic blood pressure				Post-operative heart rate			
	Group BD	**Group BM**	**Group B**	**P-value**	**Group BD**	**Group BM**	**Group B**	**P-value**
0m	2.15±86.3	10.5±102.4	8.9±111.64	<0.001*	3.71± 80.8	7.4±105.84	8.84± 108.5	< 0.001*
15m	1.7±86.6	92.44±5.1	8.4†±100.4	<0.001*	3.4±80.52	8.3†± 90.5	5.7†± 95.8	< 0.001*
30m	5.82±87.44	6.84±86.76	4.4±88.5	0.556	8.9±86	6.3±86.4	1.8±83.5	0.244
45m	6.7±88.5	3.9±86.1	5.6±89.9	0.052	7.9±84.6	7.5±85.2	2.2±83.4	0.636
60m	3.19±89.8	4.8±87.12	6.3±88.44	0.323	7.224±84.12	7.52±85.2	2.1±83.5	0.43

The data is presented as mean± SD. P > 0.05 was considered statistically insignificant when comparing the three groups. * P< 0.05 was considered statistically significant when comparing the three groups. When compared to the baseline value, P <0.05 was considered statistically significant.

emergence delirium (ED) in pediatric patients undergoing lower abdominal or perineal surgeries under sevoflurane based anesthesia. Our study indicated that both caudal dexmedetomidine and caudal midazolam were safe and efficacious in decreasing the incidence and severity of ED; furthermore, dexmedetomidine was more efficacious with the least PAED scores. The emergence time and length of PACU stay were not prolonged with both adjuvants, and pain FLACC scores were compared with the control group during the first hour postoperatively.

Dexmedetomidine enhances the local anesthetic effects without serious adverse effects. It possesses a

Table 3: Post-operative Pediatric Anesthesia Emergence Delirium Scale (PAED).

	Post-operative Pediatric Anesthesia Emergence Delirium Scale (PAED)			
	Group BD (n=25)	***Group BM (n=25)***	***Group B (n=25)***	***p-value***
0m	2 (2-3)	5 (4-5)	7(6-7)	<0.001*
15m	2 (2-3)	3 (2-4)	5 (4-6)	<0.001*
30m	2 (1-3)	2 (2-3)	2 (2-3)	0.346
45m	1 (1-2)	2 (1-3)	2 (2-3)	0.19
60m	1 (1-2)	1 (1-2)	2 (1-2)	0.198

Data are presented as median (IQR). P > 0.05 was considered statistically non-significant between the 3 groups. * P <0.05 was considered statistically significant between the 3 groups.

Table 4: Post-operative Face, Legs, Activity, Cry, and Consolability (FLACC) pain scale.

	Post-operative Face, Legs, Activity, Cry, and Consolability (FLACC) pain scale			
	Group BD (n=25)	***Group BM (n=25)***	***Group B (n=25)***	***p-value***
0m	2 (1-3)	2 (1-2)	2 (1-2)	0.766
15m	2 (1-3)	2 (1-2)	2 (1-2)	0.443
30m	1 (0-2)	2 (0-3)	1 (1-2)	0.304
45m	1 (1-2)	1 (0-2)	1 (1-2)	0.411
60m	1 (0-2)	1 (0-2)	1 (1-2)	0.572

The data is presented as the median (IQR). P > 0.05 was considered statistically insignificant when comparing the three groups. * P< 0.05 was considered statistically significant when comparing the three groups.

Table 5: The time to emergence, Number of patients who received postoperative IV Dexmedetomidine, and post-anesthesia care unit (PACU) stay.

	Group BD (n=25)	***Group BM (n=25)***	***Group B (n=25)***	***p-value***
Time to emergence (minutes)	.56±5.55	1.2±5.16	0.84±5.28	0.624
No. of patients received Dexmedetomidine	0	0	5	0.005*
PACU stay (minutes)	3.06±22	3.44 ±20.6	6.68‡±31.76	<0.001*

The data is presented as mean SD. P > 0.05 was considered statistically insignificant when analyzing different groups. * The difference between the three groups was considered statistically significant at P< 0.05.

highly selective alpha2 adrenoceptor agonist effect, particularly for the 2A subtype, that renders it a more effective sedative, anxiolytic, and analgesic when compared to clonidine. Moreover, the unwanted cardiovascular effects from alpha-1 receptor activation can be avoided (22).

Unlike the intravenous route, when $alpha_2$ agonists are used as adjuvants with local anesthetics in the caudal epidural route, they provide an analgesic effect without unwanted excessive sedation, probably due to sparing the supraspinal CNS sites from too much drug exposure. Based on the hypothesis mentioned above, we used dexmedetomidine via the caudal route in our study to avoid excessive sedation that may lead to prolonged emergence time and lengthy PACU stay (22).

Following the discovery of benzodiazepine receptors in the spinal cord, it had been suggested that midazolam could be introduced as an adjuvant to local anesthetic agents intrathecally, caudally, or epidurally

to enhance postoperative pain relief (23). Midazolam modulates nociceptive responses by interaction with specific gamma-aminobutyric acid (GABA) receptors in the spinal cord and brain. It has also been suggested that caudal midazolam may interact with opiate receptors (24, 25).

This study found that the patients who received caudal dexmedetomidine as an adjuvant to bupivacaine recorded the least scores regarding the ED using PAED score, followed by midazolam and then bupivacaine alone. Following our results, Mohamed et al., *2015* (26) reported that caudal dexmedetomidine (2 µg/Kg) added to lidocaine in congenital hernia repair reduced the incidence of emergence agitation.

Sanwatsarkar and co-workers 2017 (24) reported that mean sedation scores were higher in the control group compared to the patients who received clonidine and midazolam with bupivacaine in the caudal block in pediatric infraumbilical surgeries under sevoflurane anesthesia, who had lower comparable mean sedation scores. This study inspired us to compare the effect of another alpha$_2$ agonist like dexmedetomidine with midazolam in preventing ED when added to caudal bupivacaine. In our study, dexmedetomidine showed statistically significantly lower PAED scores compared to midazolam at 0 and 15 minutes postoperatively. Dexmedetomidine is eight times more specific than clonidine to alpha$_2$ receptors, which might explain the different results.

Also, Yao and colleagues 2018 (27) found that both caudal and IV dexmedetomidine reduced the incidence of ED similarly compared to the control group in patients undergoing unilateral inguinal hernia repair. Anand and his co-workers 2011 (28) concluded that caudal dexmedetomidine (2 µg/Kg) with 0.25% ropivacaine (1 ml/Kg) for pediatric lower abdominal surgeries produced less incidence of emergence agitation following sevoflurane anesthesia which is consistent with our results.

In controversy to our results, Cho and his co-workers 2020 (29) compared the effect of intravenous dexmedetomidine and midazolam injected 5 minutes before the end of surgery to prevent ED in children undergoing tonsillectomy. They found that intravenous dexmedetomidine and midazolam were equally effective. This could be attributed to the different routes of administration and the different doses used (1.5 µg/Kg in the current study versus 0.3 µg/Kg).

Al et al., 2016 (30) reported that compared to IV administration, caudal dexmedetomidine during caudal bupivacaine anesthesia provided better behavior scores with decreased emergence agitation. In our study, we did not use the IV route. However, similarly, we found a decreased incidence of emergence delirium with caudal dexmedetomidine.

This study found no statistically significant difference between dexmedetomidine, midazolam, and bupivacaine in emergence Time. In agreement with these results, Cho and his co-workers (29) found emergence time comparable in all groups when they compared IV dexmedetomidine and midazolam to prevent ED. Mohamed et al. (26) found no clinically significant difference in Emergence Time when analyzing the impact of adding caudal dexmedetomidine to lidocaine, which is consistent with our results.

Also, Yao and colleagues 2018 (27) found that caudal and IV dexmedetomidine reduced the incidence of emergence agitation similarly to the control group in patients undergoing unilateral inguinal hernia repair. Anand and his co-workers 2011 (28) concluded that caudal dexmedetomidine (2 µg/Kg) with 0.25% ropivacaine (1 ml/Kg) for pediatric lower abdominal surgeries produced less incidence of emergence agitation following sevoflurane anesthesia which is consistent with our results.

In controversy to our results, Cho and his co-workers 2020 (29) compared the effect of intravenous dexmedetomidine and midazolam injected 5 minutes before surgery to prevent ED in children undergoing tonsillectomy and found that intravenous dexmedetomidine and midazolam were equally effective. This could be attributed to the different routes of administration and the different doses used (1.5 µg/Kg in the current study versus 0.3 µg/Kg).

Al et al., 2016 (30) reported that compared to IV administration, caudal dexmedetomidine during caudal bupivacaine anesthesia provided better behavior scores with decreased emergence agitation. In our study, we did not use the IV route. However, similarly, we found a decreased incidence of emergence delirium with caudal dexmedetomidine.

This study found no statistically significant difference between dexmedetomidine, midazolam, and

bupivacaine in emergence time. In agreement with these results, Cho and his co-workers (29) found emergence time comparable in all groups when they compared IV dexmedetomidine and midazolam to prevent ED. Mohamed et al. (26) found no clinically significant difference in emergence time when analyzing the impact of adding caudal dexmedetomidine to lidocaine, which is consistent with our results.

However, in contrast to our results, Anand and colleagues (28) reported that patients who received ropivacaine plus dexmedetomidine had a mean emergence time of 5.4±1.8 minutes, while patients who received ropivacaine scored 4.0±1 minute with a statistically highly significant difference between the two groups ($P \leq 0.001$). This could be attributed to the fact that we used a lower dose of caudal dexmedetomidine (1.5 µg/Kg) compared to the dose they used (2 µg/Kg).

Our study found that FLAAC scores were comparable between all three groups during the first hour postoperatively. Similarly, Sanwatsarkar and his colleagues (24) found no clinically significant difference in FLAAC pain scores postoperatively during the first 3 hours when comparing caudal midazolam and clonidine.

Regarding the duration of PACU stay, we found that the patients who received bupivacaine only had a statistically significant longer duration of PACU stay compared to patients who received adjuvants midazolam and dexmedetomidine. In contrast, Mohamed A et al. (24) reported a comparable length of PACU to stay between the group that received caudal dexmedetomidine with lidocaine and the control group. This could be attributed to the IV dexmedetomidine that we used postoperatively as a rescue medication to treat ED in the control group resulting in over-sedation, and prolonged PACU stay.

We reported no cases of bradycardia or hypotension either postoperatively or intraoperatively. Although Al and colleagues 2016 (30), reported that four patients in the IV dexmedetomidine group developed bradycardia and hypotension during surgery, no complications were recorded in the caudal dexmedetomidine and bupivacaine alone groups. That is one of the reasons why we preferred to use the caudal route instead of the IV route for dexmedetomidine administration in our study.

Limitations of the study: Our study was a single-center experience, so multi-center research is suspected to give us more accurate results, especially with a larger number of patients involved in the study giving more reliable results.

Conclusion

Dexmedetomidine and midazolam are safe and efficient in decreasing the incidence and severity of ED when used as an adjuvant to bupivacaine in caudal-block after sevoflurane-based anesthesia in pediatric patients. Furthermore, dexmedetomidine was more efficient with the least PAED score, reflecting less incidence of ED with no need for postoperative analgesia. Dexmedetomidine is recommended to be used as an adjuvant to bupivacaine in the pediatric caudal block.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

1. Sethi S, Ghai B, Ram J, Wig J. Postoperative emergence delirium in pediatric patients undergoing cataract surgery--a comparison of desflurane and sevoflurane. Paediatr Anaesth. 2013;23(12):1131-7.
2. Shukry M, Clyde MC, Kalarickal PL, Ramadhyani U. Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? Paediatr Anaesth. 2005;15(12):1098-104.
3. Chen L, Yu L, Fan Y, Manyande A. A comparison between total intravenous anaesthesia using propofol plus remifentanil and volatile induction/ maintenance of anaesthesia using sevoflurane in children undergoing flexible fibreoptic bronchoscopy. Anaesth Intensive Care. 2013;41(6):742-9.
4. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology. 2004;100(5):1138-45.
5. Malarbi S, Stargatt R, Howard K, Davidson A. Characterizing the

behavior of children emerging with delirium from general anesthesia. Paediatr Anaesth. 2011;21(9):942-50.
6. Moore AD, Anghelescu DL. Emergence Delirium in Pediatric Anesthesia. Paediatr Drugs. 2017;19(1):11-20.
7. Menser C, Smith H. Emergence Agitation and Delirium: Considerations for Epidemiology and Routine Monitoring in Pediatric Patients. Local Reg Anesth. 2020;13:73-83.
8. Mizuno J, Nakata Y, Morita S, Arita H, Hanaoka K. [Predisposing factors and prevention of emergence agitation]. Masui. 2011;60(4):425-35.
9. Wang W, Huang P, Gao W, Cao F, Yi M, Chen L, et al. Efficacy and Acceptability of Different Auxiliary Drugs in Pediatric Sevoflurane Anesthesia: A Network Meta-analysis of Mixed Treatment Comparisons. Sci Rep. 2016;6:36553.
10. Ydemann M, Nielsen BN, Wetterslev J, Henneberg S, Lauritsen T, Steen N, et al. Effect of clonidine to prevent agitation in children after sevoflurane anaesthesia: a randomised placebo controlled multicentre trial. Dan Med J. 2016;63(6).
11. Sun L, Guo R, Sun L. Dexmedetomidine for preventing sevoflurane-related emergence agitation in children: a meta-analysis of randomized controlled trials. Acta Anaesthesiol Scand. 2014;58(6):642-50.
12. Goyal V, Kubre J, Radhakrishnan K. Dexmedetomidine as an adjuvant to bupivacaine in caudal analgesia in children. Anesth Essays Res. 2016;10(2):227-32.
13. Chen J, Li W, Hu X, Wang D. Emergence agitation after cataract surgery in children: a comparison of midazolam, propofol and ketamine. Paediatr Anaesth. 2010;20(9):873-9.
14. Oriby ME. Comparison of Intranasal Dexmedetomidine and Oral Ketamine Versus Intranasal Midazolam Premedication for Children Undergoing Dental Rehabilitation. Anesth Pain Med. 2019;9(1):e85227.
15. Yang X, Hu Z, Peng F, Chen G, Zhou Y, Yang Q, et al. Effects of Dexmedetomidine on Emergence Agitation and Recovery Quality Among Children Undergoing Surgery Under General Anesthesia: A Meta-Analysis of Randomized Controlled Trials. Front Pediatr. 2020;8:580226.
16. Cho EJ, Yoon SZ, Cho JE, Lee HW. Comparison of the effects of 0.03 and 0.05 mg/kg midazolam with placebo on prevention of emergence agitation in children having strabismus surgery. Anesthesiology. 2014;120(6):1354-61.
17. Mahajan R, Batra YK, Grover VK, Kajal J. A comparative study of caudal bupivacaine and midazolam-bupivacaine mixture for post-operative analgesia in children undergoing genitourinary surgery. Int J Clin Pharmacol Ther. 2001;39(3):116-20.
18. Kim HY. Statistical notes for clinical researchers: Chi-squared test and Fisher's exact test. Restor Dent Endod. 2017;42(2):152-5.
19. Tate JA, Devito Dabbs A, Hoffman LA, Milbrandt E, Happ MB. Anxiety and agitation in mechanically ventilated patients. Qual Health Res. 2012;22(2):157-73.
20. Bajwa SA, Costi D, Cyna AM. A comparison of emergence delirium scales following general anesthesia in children. Paediatr Anaesth. 2010;20(8):704-11.
21. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs. 1997;23(3):293-7.
22. Fares KM, Othman AH, Alieldin NH. Efficacy and safety of dexmedetomidine added to caudal bupivacaine in pediatric major abdominal cancer surgery. Pain Physician. 2014;17(5):393-400.
23. Aliena SP, Lini C, Chirayath JJ. Comparison of postoperative analgesic effect of caudal bupivacaine with and without ketamine in Pediatric subumbilical surgeries. J Anaesthesiol Clin Pharmacol. 2018;34(3):324-7.
24. Yang Y, Yu LY, Zhang WS. Clonidine versus other adjuncts added to local anesthetics for pediatric neuraxial blocks: a systematic review and meta-analysis. J Pain Res. 2018;11:1027-36.
25. Gooty S, Priyanka DSR, Pula R, Pakhare V, Ramachandran G. A Comparative Study of Effect of Oral Melatonin Versus Oral Midazolam as Premedicant in Children Undergoing Surgery Under General Anesthesia. J Cell Mol Anesth. 2022;7(3):160-7.
26. Mohamed AA. Prevention of sevoflurane agitation in children undergoing congenital hernia repair, impact of adding dexmedetomidine to caudal analgesia. Egypt J Anaesth. 2015;31(3):227-31.
27. Yao Y, Yu C, Zhang X, Guo Y, Zheng X. Caudal and intravenous dexmedetomidine similarly prolong the duration of caudal analgesia in children: A randomized controlled trial. Paediatr Anaesth. 2018;28(10):888-96.
28. Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivacaine in paediatric lower abdominal surgeries. Indian J Anaesth. 2011;55(4):340-6.
29. Cho EA, Cha YB, Shim JG, Ahn JH, Lee SH, Ryu KH. Comparison of single minimum dose administration of dexmedetomidine and midazolam for prevention of emergence delirium in children: a randomized controlled trial. J Anesth. 2020;34(1):59-65.
30. Al-Zaben KR, Qudaisat IY, Alja'bari AN, Ababneh OA, Yousef AM, Al-Shudifat AM. The effects of caudal or intravenous dexmedetomidine on postoperative analgesia produced by caudal bupivacaine in children: a randomized controlled double-blinded study. J Clin Anesth. 2016;33:386-94.