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Research Article

Prevention of sevoflurane agitation in children undergoing congenital hernia repair, impact of adding dexmedetomidine to caudal analgesia

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KEYWORDS

Caudal analgesia;
Dexmedetomidine;
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Abstract *Background:* Postoperative agitation is a common problem in pediatric sevoflurane-based anesthesia. Dexmedetomidine has been described as a safe, long acting and effective additive in many anesthetic and analgesic techniques. The aim of present study was to evaluate the effect of adding dexmedetomidine to caudal lidocaine in sevoflurane-based anesthesia on the incidence and severity of emergency agitation (EA) in children after surgical repair of congenital hernia.
Patients and methods: A total of 48 pediatric patients aged 18–38 months ASA I, II scheduled for congenital hernia surgery were randomly enrolled into 2 groups: Group L patients ($n = 24$) received 1% lidocaine 0.7 ml kg, while Group D patients ($n = 24$) received 1% lidocaine 0.7 ml kg + dexmedetomidine 2 μg/kg. Postoperatively, emergency agitation and modified Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) scores were observed and recorded.
Results: The current study showed that the incidence and severity of agitation and modified CHEOPS scores were significantly lower in group D compared to group L. Also occurrence of EA in patients in group D was significantly lower.
Conclusion: The present study suggested that use of dexmedetomidine in addition to lidocaine was effective to control emergency agitation after sevoflurane anesthesia.

1. Introduction

Sevoflurane commonly used in pediatric anesthesia for inhalational induction and maintenance for its several advantages: decreased severity of airway irritation and cardiovascular depression [1]. However, emergence agitation (EA) in children after sevoflurane anesthesia is common, with a reported incidence up to 80% [2]. The exact cause of EA in children is unknown but several risk factors may be encountered such as: intrinsic characteristics of an anesthetic, rapid emergence from anesthesia, postoperative pain, preschool age, preoperative anxiety, and child temperament [2]. Multiple randomized controlled trials revealed that EA occurred more frequently with sevoflurane. Rapid awakening after sevoflurane anesthesia has been assumed to be a cause for this phenomenon [3]. Till now, there are guidelines around how to avoid emergence agitation. Several measures have been suggested. Anxiolytic premedications, e.g. midazolam or dexmedetomidine were

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used to get effective measures [4]. Dexmedetomidine has a fewer incidences of side effects, highly selective to receptors which might permit its application in relatively high doses for sedation and analgesia without causing vascular complications from activation of α 1-receptors [5,6]. One of the major advantages of dexmedetomidine over other sedatives is its minimal respiratory effects. Indeed, respiratory rate, Carbon Dioxide (CO_2) tension, and oxygen saturation are generally maintained during dexmedetomidine sedation in children. Dexmedetomidine provides an interesting quality sedation that permits arousal with gentle stimulation [7,8]. The aim of this study was to detect the efficacy of caudal dexmedetomidine – lidocaine to control emergency agitation after sevoflurane anesthesia in children after surgical repair of congenital hernia.

2. Patients and methods

After obtaining approval from the Clinical Research Ethics Committee of South Valley University Hospital and obtaining informed consent from the parents or guardian. A total of 48 pediatric patients with aged range between 18 and 38 months old, The American Society of Anesthesiologists (ASA) physical status I, II of both sex scheduled for elective congenital hernia surgeries were included. Any patient with a history of mental retardation or delayed development that may interfere with pain intensity assessment, known or suspected coagulopathy, congenital anomalies of the sacrum, infection at the site of injection and known or suspected allergy to any of the studied drugs, was excluded from this study.

This was randomized; double blind clinical study. Randomization and enrollment to dexmedetomidine or lidocaine was done by closed envelop. Collection of data was performed by the physician (A.M.). Drug preparation was done by the resident not involved in the study. Patients were randomly assigned to one of two groups: **Group L** patients ($n = 24$) received single dose caudal epidural analgesia using 1% lidocaine 0.7 ml/kg, while **Group D** patients ($n = 24$) received single dose caudal epidural analgesia using 1% lidocaine 0.7 ml/kg + dexmedetomidine 2 μg/kg.

2.1. Pre-operative evaluation

In all patients, age, body weight and baseline vital signs were recorded. History of previous anesthesia, surgery, medical illness, medications and allergy to used medication was recorded; physical examination and air way assessment were done. The following laboratory investigations were done as hemoglobin percentage, random blood sugar, urea, creatinine and urine analysis.

2.2. Anesthetic technique

All children were fasting for water 2 h, breast milk 4 h and light meals for 6 h. They had 24 G intravenous access line before arriving at operating room. All patients were premedicated with 0.01 mg/kg atropine I.M. 30 min before shifting to operation room.

On arrival to the operating room, the standard monitoring was used including pulse oximetry electrocardiography non-invasive blood pressure; and inhalational general anesthesia was induced using 8% sevoflurane in 100% oxygen. Atracurium 0.5 mg/kg was given IV to facilitate endotracheal intubation and maintain anesthesia using sevoflurane 1% with controlled mechanical ventilation.

2.3. Anesthetic procedure

The patients were placed in a right lateral position and single dose caudal epidural injection was done under strict aseptic precautions using 25 G needle. Proper position of the needle was confirmed by the pop sensed during penetration of the sacro-coccygeal ligament [9]. Then re-direct the needle flattened and advanced. Aspiration of blood or cerebrospinal fluid (C.S.F.) is performed; patients of group L were given 0.7 ml/kg lidocaine 1%, whereas patients of group D were given 0.7 ml/kg lidocaine 1% + dexmedetomidine parenteral preparation 2 μg/kg. By the end of surgery, reversal of remnant muscle relaxant was done by atropine 0.02 mg/kg and neostigmine 0.05 mg/kg IV.

2.4. Data collection and measurements

Heart rate and arterial pressure were recorded before operation and every 5 min until the end of surgery. On return, spontaneous ventilation extubation was established and patient was shifted to the post-anesthesia care unit (PACU). The time of surgery was recorded, the emergence time (defined as the time from end of surgery and closure of sevoflurane until extubation). The incidence of EA was evaluated using Aono's four point scale [10] (Table 1). Scores of one and two were noted as the absence of EA, and scores of three and four were defined as the presence of EA. The incidence and severity of agitation scores (AS) were measured upon admission to the PACU (AS 0) and in the PACU at 5 min (AS 5), at 15 min (AS 15) and at 30 min (AS 30). Postoperative pain was measured using the modified Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) in the PACU at (T0), (T5), (T15) and (T30). The ***duration of surgery*** (from the time of skin incision to the completion of the procedure), ***duration of sevoflurane anesthesia*** (from mask induction to the discontinuation of the inhaled anesthetic), ***duration of extubation*** (from the discontinuation of sevoflurane to the removal of endotracheal tube) and ***duration of PACU stay*** (from arrival to the PACU until discharge) were recorded. We record the adverse events such as respiratory depression, urinary retention, pruritus, hypotension, bradycardia, vomiting, laryngospasm, bronchospasm and oxygen desaturation. Vomiting was treated with metoclopramide 0.15 mg/kg i.e. and we record the incidence of vomiting. It was difficult to assess nausea in children.

2.5. Outcomes

The primary outcome measure was the improvement in emergency agitation in dexmedetomidine group. The secondary

Table 1 Aono's four point scale.

Calm	1
Not calm, but could be easily calmed	2
Moderately agitated or restless	3
Combative, exited, disorient	4

Table 2 Patients' criteria and anesthetic details.

Groups / Parameters	Group L n = 24	Group D n = 24	P value
Age (years) (mean±SD)	29.33±6.24	28.58±6.22	0.451
Sex (M:F) (N)	23:1	24:0	
Weight (kg) (mean±SD)	15.37±2.69	14.70±3.71	0.171
Duration of anesthesia (min) (mean±SD)	51.45±3.96	50.83±4.57	0.248
Duration of surgery (min) (mean±SD)	43.20±4.13	42.79±5.09	0.301

Values were presented as mean±SD.

outcome measures were duration of extubation and duration of post-anesthesia care unit stay.

2.6. Statistical analysis

Sample size estimation calculated that 24 patients were required in each group to detect 40% incidence of EA and about 10% reduction in EA for 0.05 levels of significance and power of 80%. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (IBM, Chicago, IL). Data were presented as mean ± SD. Analysis of data was performed by Chi-square, Fisher Exact tests, *T*-test and ANOVA. *T*-test was used to analyze parametric data between the two groups. Chi-square and Fisher's exact tests were used to compare non-parametric data. To compare EA in the two groups Chi-square or Fisher Exact tests were used. *P* values of <0.05 were considered significant.

3. Results

A total of 48 patients were studied, one (2.08%) of whom was female. Their age was ranging from 18 to 38 months. There were no significant differences among the two studied groups in patient characteristics, incidence of agitation before induction of anesthesia as well as the different durations of anesthesia and surgery (Table 2).

3.1. Primary outcome

The incidence and severity of EA were significantly lower in group D compared to group L at AS0, AS5, AS15 and AS30 (Table 3). The number of patients who developed severe EA was significantly lower in group D and compared to group L (Table 4). Modified CHEOPS was significantly lower in group D compared to group L at CHEOPS 0, CHEOPS 5, CHEOPS 15 and CHEOPS 30 (Table 3).

Table 3 Incidence of emergence agitation, modified children's hospital of eastern Ontario pain scale characteristics and recovery characteristics.

Groups / Parameters	Group L n = 24	Group D n = 24	P value
AONO's score			
• AS 0	1.71±0.95	1.20±0.41	0.0198
• AS 5	1.70±0.90	1.29±0.62	0.0218
• AS 15	1.69±0.89	1.37±0.64	0.0428
• AS 30	2.29±1.23	1.08±0.28	0.0001
Modified CHEOPS (mean±SD)			
• CHEOPS 0	4.83±1.20	4.12±0.85	0.0081
• CHEOPS 5	3.62±0.76	3.00±0.78	0.0006
• CHEOPS 15	3.33±1.00	2.41±0.50	0.0005
• CHEOPS 30	1.54±0.65	1.16±0.38	0.0093
Duration of extubation (min) (mean±SD)	5.33±0.91	5.12±0.79	0.134
Duration of PACU stay (min) (mean±SD)	37.50±3.91	38.0±4.11	0.598
Vomiting in PACU (*n*)	2	3	0.132

AONO's score; CHEOPS – Children's Hospital of Eastern Ontario Pain Scale; PACU – Post -anesthesia care unit.

Table 4 Show occurrence of emergency agitation in patients of both groups.

	Group L $n = 24$	Group D $n = 24$	P value
Time 0	14 (58.33%)	0 (0)	< 0.001
At 5 min	10 (41.66%)	2 (8.33%)	< 0.001
At 15 min	11 (45.83%)	2 (8.33%)	< 0.001
At 30 min	12 (50%)	0 (0)	< 0.001

Values were presented as number (%) of patients that developed emergency agitation.

3.2. Secondary outcomes

Time to emergence and extubation in group L was longer compared to group D. Time to discharge from the PACU was earlier in group L compared to group D with no statistically significant differences between them as regards two times (Table 3).

No statistically significant difference between the two groups as regards of vomiting.

4. Discussion

The current study aimed to evaluate the effect of caudal dexmedetomidine combined with lidocaine to control emergency agitation by sevoflurane in children undergoing congenital hernia repair.

In our study, the incidence and severity of agitation score were significantly lower in group D compared to group L. Previous studies [11–13] showed that dexmedetomidine reduces the incidence of EA after sevoflurane anesthesia in children because of their sedative and analgesic effects. In another study, done by El-Hennawy et al. [14]; dexmedetomidine and clonidine were administrated in a dose of 2 μg/kg as adjuvant with 0.25% bupivacaine caudally. They found that the duration of analgesia was significantly higher in the group receiving bupivacaine–dexmedetomidine mixture or bupivacaine–clonidine mixture than the group receiving bupivacaine alone [14]. Similar study was done by Neogi et al. [15] compared clonidine 1 μg/kg and dexmedetomidine 1 μ/kg as adjuncts to ropivacaine 0.25% for caudal analgesia in pediatric patients and concluded that addition of both clonidine and dexmedetomidine with ropivacaine administered caudally significantly increases the duration of analgesia [15]. Saadawy et al. compared caudal bupivacaine and dexmedetomidine in mixed dose and caudal bupivacaine alone. They showed that the incidence of agitation following sevoflurane anesthesia was significantly lower with dexmedetomidine. They found the duration of analgesia was significantly longer with dexmedetomidine administration [16]. No significant difference was found between both the groups as regards to hemodynamic variables. Dexmedetomidine produced better quality of analgesia and a prolonged duration of sedation ($P < 0.05$). Using caudal dexmedetomidine 2 μg/kg with sevoflurane anesthesia, we found the mean extubation time of group L was 5.33 ± 0.91 min and in group D was 5.12 ± 0.79 min, however, the difference between the two groups was statistically insignificant ($P > 0.05$) (Table 3).

In our study, the emergence agitation score (Table 3) of the group D was lower than that of group L. The difference between the means was statistically significant ($P < 0.05$). The observations showed that group L children were agitated and restless compared to group D children who were calm. This improves that caudally administered dexmedetomidine prevented the EA following sevoflurane administration significantly. Our results were similar to Bock et al. [17] and Boker et al. [18] studies that compared caudal clonidine 3 μg/kg B.W. and bupivacaine 0.25% respectively with dexmedetomidine 1 μg/kg B.W. and caudal bupivacaine 0.25% alone and showed that the incidence of agitation following sevoflurane anesthesia was significantly lower with dexmedetomidine and the duration of analgesia was significantly longer with dexmedetomidine administration [17,18]. Extubation Time and emergence time were statistically significantly longer in group D in comparison with group L. in agreement to other studies [19,20] showing that the time to awakening correlates negatively with EA scores. The statistically significant difference between group L and group D is of small magnitude and is not clinically significant. Children in both groups had comparable durations of PACU stay. The modified CHEOPS was significantly lower in group D compared to group L. Modified CHEOPS in each group decreased significantly over time. Kim et al. [21] and Ali and Abdellatif [3] reported similar results [21,3]. We observed from our study that there were no clinically significant postoperative complications such as respiratory depression, urinary retention, pruritus, hypotension and bradycardia. Vomiting was recorded in two cases of group L and three cases in group D. The results of our observations show that in addition to a good postoperative analgesia, dexmedetomidine has a favorable safety profile and stable hemodynamics, which are in agreement with the reports published by several other authors ([22–27]).

5. Conclusion

In our study we concluded that caudal dexmedetomidine 2 μg/kg achieved less incidence of EA following sevoflurane anesthesia with significant postoperative pain relief. We find dexmedetomidine to be a safe and effective adjuvant for caudal analgesia in pediatrics. It is recommended to perform more studies to evaluate the effect of dexmedetomidine with different doses with different concentrations of lidocaine with larger sample size to study incidence of EA of sevoflurane anesthesia.

Conflict of interest

The authors declare no conflict of interest about this study.

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