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Emergence Agitation in Children Undergoing Lower Abdominal Day Care Procedures with Sevoflurane and Dexmedetomidine

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Abstract
Background and Objective: *The incidence of emergence agitation in children under sevoflurane anaesthesia varies between 10% - 80%. Other factors such as pain, anxiety, personal character, type of surgery, rapid recovery from anaesthesia and type of anaesthesia also predispose to emergence agitation. In context to this a double blinded randomized controlled trial was done to study the effect of intra operative prophylactic intravenous dexmedetomidine infusion in children aged 1–6 years undergoing herniotomy and circumcision as a day care procedure under general anaesthesia combined with caudal epidural block as compared to placebo infusion.*
Methods and Material: *A total of 70 children (35 in each group) were selected. One group received intravenous dexmedetomidine at a dose of 1mcg/kg over 10 minutes followed by 0.1 mcg/kg/hour and the control group received saline. Intraoperative sevoflurane consumption, duration of anaesthesia, emergence agitation, sedation, pain in the Post Anaesthetic Care Unit and any adverse effects were noted. The data was analysed using SPSS software.*
Results: *In this study emergence agitation, pain score, sevoflurane consumption, duration of anaesthesia and first oral intake were significantly reduced in dexmedetomidine group compared to saline group. Sedation score was significantly higher in dexmedetomidine group compared to saline group (p= <0.001).*
Conclusions: *Dexmedetomidine 1 µg/kg bolus over 10 minutes, followed by 0.1µg/kg/h infusion prevents emergence agitation.*
Keywords: *Dexmedetomidine, Emergence agitation, Sevoflurane.*

Introduction

Emergence Agitation (EA) or Emergence Delirium (ED) is often described as a transient phenomenon of dissociated state of consciousness in which the child is irritable, non-compromising, uncooperative, incoherent and inconsolably crying, moaning, kicking or thrashing.[1.]Agitation on emergence from anaesthesia may not only cause injury to the child but may also lead to accidental removal of surgical dressings, intravenous catheters and drains needing extra nursing care as well as supplemental sedative and or analgesic medications, which may delay the patient discharge from hospital[1]. This restless behaviour upon emergence makes the parents feel unhappy with the quality of recovery from

anaesthesia.

The incidence of EA ranges from 10-50% and may be as high as 80%[1]. EA usually occurs within the first 30 min of recovery from anaesthesia and is usually self limiting (5–15 min) and often resolves spontaneously[2-4]. Maximum incidence is seen in preschool children.

A variety of factors have been suggested to play a potential role in the development of EA. Sevoflurane, a popular inhalational anaesthetic used frequently in paediatric anaesthesia is frequently associated with EA in children[5-9].

Over the years several pharmacological agents have been tried to reduce the occurrence and severity of emergence agitation. Dexmedetomidine is a potent α_2 adrenergic receptor agonist with eight times higher affinity for $\alpha_2$adrenoceptor than clonidine. It acts on the pontine locus coeruleus and decreases sympathetic nervous system outflow. Intraoperative administration of dexmedetomidine has shown to effectively reduce emergence agitation in children because of its anxiolytic and analgesic properties without respiratory depression. Not many studies in south Indian population are available on this regard especially in day care surgeries. This is the rationale for selecting this study, which aims at studying the effect of intravenous dexmedetomidine in reducing EA in children receiving sevoflurane anaesthesia.

Subjects and Methods

The study is a double blinded randomized controlled trial done over a period of one year at the postgraduate teaching institution. Ethical permission was obtained from the institutional review board (IRB). A written informed consent in the local language was obtained from the parents of all the participants. Children with American Society of Anesthesiology (ASA) physical status 1 aged 1- 6 years, weight less than or equal to 25kg, of both sexes, scheduled for herniotomy or circumcision as a daycare procedure were included in the study. Children with mental retardation, developmental delay, spinal anomalies, neurological disease, respiratory tract infection, coagulation disorder were excluded from the study.

Sample size calculation was based on previous study[10]. In this study proportion of emergence agitation in placebo group is 55% and proportion of emergence agitation in study group is 5%. For an $\alpha = 0.05$ and a power of 90%, the sample size in each group was calculated to be 18. However as the total number of children undergoing day care procedures within study duration in the inpatient department of this institution satisfying the inclusion criteria was much more than required sample size a total of thirty five study subjects were enrolled in each group, thereby including a sample size of seventy. Parents of children were blinded to the study, as they did not know in which group their child was assigned. The investigator was also blinded to the study. So the study medication was given to the investigator, by the nurse, after labelling a treatment code number. The treatment code number was noted in the proforma. The treatment code was decoded at the end of the study duration of one year. Prior to surgery a thorough clinical examination of the patient was performed. Each subject was allocated a serial code number. The patients were randomly assigned to one of the two groups by using random number table.

The grouping was as follows

Group A: Dexmedetomidine infusion group

Group B: Normal saline infusion group

Drugs used in the study were prepared in the anaesthesia preparation room and coded with a treatment code number by a nurse. No prophylactic premedication was given for the prevention of emergence agitation. For one group, dexmedetomidine was mixed in normal saline to make 1 µg/ml in a 50 ml syringe. For other group, normal saline was prepared in a 50 ml syringe. All children were kept nil per oral before surgery as per standard fasting protocol. Children with parents were moved to the premedication room with their toys. On arrival in the pre medication room, the patient's baseline heart rate, blood pressure, oxygen saturation and respiratory rate were recorded after settling in the premedication room. In the operating room, anaesthesia was induced with facemask with 7% sevoflurane in oxygen at a gas flow of 1.5 -2

times the minute ventilation using open circuit. The induction scale was assessed based on mask acceptance 1 = accept mask readily 2 = slight fear of mask easily calmed 3 = not calmed with reassurance 4 = terrified, crying, agitated. Score of 1 or 2 were considered to be satisfactory induction. After the loss of consciousness, intravenous access was achieved. After that sevoflurane concentration was reduced to 1.5% – 2%. The blinded anaesthetic practitioner accordingly administered the coded infusion to each group. The coded infusion of 1 ml/kg was administered intravenously over 10 minutes using a syringe pump, followed by a 0.1ml/kg/h infusion until the end of surgery in both groups. Anaesthesia was maintained with face mask and adjusting the sevoflurane concentration. After the bolus dose, caudal block was performed with 1 ml/kg of 0.25% bupivacaine in both groups. As soon as caudal block was done, the operation was started. No additional analgesics were given during operation. Respiration was maintained spontaneously throughout the operation. Intra operatively sevoflurane concentration was titrated based on immobility and hemodynamic parameters such as heart rate and blood pressure. When the surgical closure was started, sevoflurane and coded infusion administrations were discontinued. Oxygen through the facemask was continued. The facemask was removed when the patient became awake. End tidal sevoflurane, mean arterial pressure (MAP) and heart rate (HR) were recorded just before coded drug administration (T0, baseline), just after coded drug loading of 1 ml/kg (T1), 10 min after coded drug loading (T2), start of operation (T3), 10, 20, 30 min after the start of operation (T4, T5, T6), and at the end of operation (T7). Atropine 0.01 - 0.02 mg/kg was administered during the procedure when the HR decreased more than 30% of baseline value (T0). The patients were monitored in the post anaesthetic care unit (PACU) by the investigator and their parents, both of whom were blinded to the child's group allocation. Because most of the emergence agitation episodes occurred within 30 min of PACU arrival, emergence agitation was assessed at arrival and every 5 min for up to 30 min in PACU. Emergence agitation was rated using a four-point scale modified by Watcha et al (1=calm, 2=crying, but can be consoled, 3=crying and cannot be consoled, 4=agitated and thrashing around). If a child fell asleep, this was defined as a score of 0. Children with scores of 3 or 4 were considered to have had an emergence agitation episode. Postoperative pain was assessed with the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) upon PACU arrival, at 30 min, 60 min, and 120 min postoperatively. 0.5 μg/kg of fentanyl was administered when CHEOPS score was ≥7. Sedation level was assessed with the Ramsay's sedation scale upon PACU arrival and at 30,60,120 minutes post operatively (1= anxious and agitated or restless, or both; 2=co-operative, oriented, and calm; 3=responsive to commands only; 4= exhibiting brisk response to light glabellar tap or loud auditory stimulus; 5=exhibiting a sluggish response to light glabellar tap or loud auditory stimulus; and 6=unresponsive). The first oral intake time and adverse events if any were also noted. The observations made were tabulated and analysed using statistical package for social sciences (SPSS) software (Version 16.0 SPSS Inc, Chicago, IL, USA).

Results

Patients in both groups were comparable with respect to basic variables such as age, sex, weight and duration of surgery.

Table 1 Comparison of induction score

	Group A	Group B	Total	P Value
Satisfactory	20	17	37	0.569
Unsatisfactory	15	18	33	
	35	35	70	

Table 2 Comparison of emergence agitation score (EAS)

EAS score	Group A (N=35)		Group B (N=35)		Mann-Whiney U test
	Median	Inter quartile range	Median	Inter quartile range	P
At arrival	2	0-2	3	3-3	<0.001
After 5 min	2	2-2	3	3-3	<0.001
After 10 min	2	1-2	3	3-3	<0.001
After 15 min	1	1-1	3	2-3	<0.001
After 20min	1	1-1	3	2-3	<0.001
After 25 min	1	1-1	2	2-3	<0.001
After 30 min	1	1-1	2	2-3	<0.001

At all times the median emergence agitation score was significantly greater in Group B children (P < 0.001)

Table 3 Comparison of intra operative end tidal sevoflurane concentration

Intra operative End tidal sevoflurane	Group A (N=35) Mean	Group B (N=35) Mean	P
Before Dexmed	2.23	2.26	0.18
After Dexmed	2.04	2.18	0.00
After 10min	1.60	2.07	0.00
After 20min	1.21	2.00	0.00
After 30min	0.88	1.99	0.00
At the end	0.44	1.90	0.00

After the administration of dexmedetomidine sevoflurane consumption was significantly reduced in group A.

Table 4 Comparison of pain score between groups

CHEOPS score	Group A (N=35)		Group B (N=35)		Mann-Whitney U test	
	Median	Inter quatile range	Median	Inter quartile range	Z	P
On arrival	7	6-7	7	7-8	3.833	<0.001
After 30min	6	6-6	7	7-8	6.205	<0.001
After 60min	5	5-6	7	7-7	6.176	<0.001
After 120 min	4	4-5	6	5-7	5.965	<0.001

Pain score was significantly reduced in group A (P<0.001).

Table 5 Comparison of sedation score between groups

	Group A(N=35) Median	Group B(N=35) Median	P
At arrival	3	1	<0.001
After 30 min	2	1	<0.001
After 60 min	2	1	<0.001
After 120 min	2	2	<0.001

Sedation score was significantly higher in group A (P<0.001).

Mean Duration of anaesthesia (induction to facemask removal) in group A was 57.86 minutes and in group B was 64.20 minutes. It was significantly reduced in group A (p = < 0.001)

Mean Duration for first oral intake (induction to oral intake) in group A was 4.87hours and in group B was 5.96 hours. It was significantly reduced in group A (p = < 0.001)

Discussion

Emergence agitation, a post operative behavioural disorder, occurs frequently in children during recovery from anaesthesia. This is commonly associated with sevoflurane anaesthesia. The major concerns for anaesthetists in recent years are to improve the recovery quality of anaesthesia, reduce the incidence of complications in recovery period and shorten the duration in post anaesthesia care unit. Dexmedetomidine, a potent selective α_2-adrenergic agonist is reported to significantly reduce emergence agitation frequency after sevoflurane anaesthesia in children. Because dexmedetomidine has sedative, hypnotic and analgesic properties, it can reduce the dose of hypnotics, opioids, analgesics and anaesthetics required to be concomitantly administered during anaesthesia without producing respiratory depression. Na Young Kim et al study[10] shows that intraoperative use of dexmedetomidine is effective in attenuating sevoflurane induced emergence agitation. They concluded that intraoperative infusion of dexmedetomidine reduced sevoflurane requirements and decreased emergence agitation without delaying discharge in children undergoing ambulatory surgery. However, attention should be taken in regard to bradycardia and hypotension.

The first outcome studied in our study was the emergence agitation score. Emergence agitation was assessed using a four-point scale modified by Watcha et al. Emergence agitation was significantlyreduced in dexmedetomidine group compared to saline group at all time.

Postoperative pain was assessed with the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) upon PACU arrival, at 30 min, 60 min, and 120 min postoperatively. It was found that pain score was significantly reduced in group A compared to group B (p=< 0.001).

Sedation was assessed with the Ramsay's sedation scale upon PACU arrival and at 30, 60, 120 minutes post operatively. It was found that sedation score was significantly higher in dexmedetomidine group compared to saline group (p= <0.001). Similar results are also seen in Na Young Kim et al study[10] in which sedation scores are higher in dexmedetomidine group at PACU arrival and after

30 minutes.

It was found that there was no significant difference in the sevoflurane consumption between the two groups before the administration of dexmedetomidine. But after the administration of dexmedetomidine sevoflurane consumption was significantly reduced in group A. This may be the reason for decreased emergence agitation in dexmedetomidine group. Similar results are also seen with Lin He et al study[11].

In our study it was found that Mean Duration of anaesthesia (induction to face mask removal) in group A was significantly reduced in dexmedetomidine group (p = < 0.001) First oral intake time is also significantly reduced in dexmedetomidine group.

In this study it was found that there was significant difference present in the mean heart rate between the two groups. Mean heart rate was lower in dexmedetomidine group compared to saline group. But it was present even before the administration of dexmedetomidine. None of them needed any intervention. In one child dexmedetomidine was stopped due to bradycardia. Then the heart rate returned to normal. Atropine was not used. This was the only one adverse effect seen during this study. There was no statistical significance in mean arterial blood pressure between dexmedetomidine group and saline group intra operatively. Hammer G B et al [12] study on the Effects of dexmedetomidine on Cardiac electrophysiology in children showed that dexmedetomidine significantly depressed sinus and atrioventricular nodal function in paediatric patients.Heart rate decreased and arterial blood pressure increased during administration of dexmedetomidine.

In this study only short duration procedures were involved. So the duration of exposure to sevoflurane was less in these children. Emergence agitation was more with long duration of exposure and other type of surgery like tonsillectomy. Depth of anaesthesia was not assessed with any measures other than clinical features like immobility. So the reliability of decrease in the sevoflurane consumption associated with dexmedetomidine infusion is uncertain. In this study postoperative pain was assessed. But caudal block was not confirmed with ultrasound. It can act as a confounding factor.

In conclusion intraoperative prophylactic use of intravenous dexmedetomidine 1 μg/kg bolus over 10 minutes followed by 0.1 μg/kg/h infusion reduced the sevoflurane induced emergence agitation in children undergoing lower abdominal day care surgeries. Dexmedetomidine prevents sevoflurane induced emergence agitation.

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