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Effect of Dexmedetomidine on Emergence Characteristics in Children Undergoing Adenotonsillectomy Using Sevoflurane Anaesthesia

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Abstract

Background: Sevoflurane, a widely used volatile anaesthetic in children is associated with an increased risk of emergence agitation. Agitation can lead to increased bleeding from the operative sites, pulling out drains or catheters and often a major cause of dissatisfaction for parents and health care providers. Dexmedetomidine, a newer alpha 2 adrenoreceptor agonist, hassedative, analgesic and anxiolytic actions. *Aim*: This study was to evaluate the effect of a single dose of dexmedetomidine given before extubation, on reducing emergence agitation. *Method and Materials*: In this prospective study, 60 children aged 3–8 years, scheduled for adenotonsillectomy were divided into two groups. Induction and maintenance of anaesthesia was with sevoflurane. One among the two groups received dexmedetomidine 0.3mcg in 10ml normal saline 10 minutes before extubation and the other group did not receive dexmedetomidine. Emergence agitation was assessed on a 5 point Watcha scale. Adverse airway events during extubation like coughing or breath holding and adverse hemodynamic effects such as bradycardia, hypotension and the time taken for recovery were also assessed. *Results:* Incidence and severity of emergence agitation was significantly reduced in children who received dexmedetomidine prior to extubation (p value <0.05). No significant difference was noted in the incidence of adverse airway events, adverse hemodynamic effects and time taken for recovery. *Conclusions:* A single dose of dexmedetomidine 0.3 mcg, given prior to extubation significantly reduces the emergence agitation seen after sevoflurane anaesthesia. Administration of dexmedetomidine was not associated with any adverse effects on hemodynamics or recovery.

Keywords: Sevoflurane; Dexmedetomidine; Emergence Characteristics; Adenotonsillectomy.

Introduction

Adenotonsillectomy is one of the most frequently performed surgical operations in children. Rapid emergence from anaesthesia is desirable to allow the child full airway control after extubation. Sevoflurane is one such inhalational anaesthetic agent used having a rapid induction and rapid recovery profile. It is pleasant, non pungent, non irritant to airways and is considered the inhalational agent of choice in children. However, sevoflurane has been associated with an increased incidence of emergence agitation [1,2].

Emergence agitation is characterized by aggressive behaviour such as thrashing, crying or struggling that develops during the awakening from anaesthesia. It can cause increased bleeding from surgical sites and dislodgement of catheters and drains. This can be disastrous in children causing post tonsillectomy bleeding which can be disastrous and life threatening.

Over years, several pharmacological agents have been studied to reduce the occurrence and severity of emergence agitation. Opiods like fentanyl, intravenous anaesthetic drugs such as propofol, ketamine and alpha$_2$ agonists clonidine and dexmedetomidine were found to be effective in reducing this agitation [3].

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Dexmedetomidine, a selective alpha$_2$ adrenergic receptor agonist provides sedation, analgesia and anxiolysis with minimum effects on respiratory drive. This study was to evaluate its efficacy on reducing the post anaesthesia emergence agitation and providing a smooth recovery in children undergoing adenotonsillectomyin whom anaesthesia was induced and maintained with sevoflurane.

Methods

In this prospective study, we included 60 children, aged 3-8 yrs, of either sex, weighing 12-24kg belonging to American Society of Anaesthesiologists Physical Status (ASA-PS) 1 posted for elective adenotonsillectomy. After obtaining approval from the institutional ethics committee and informed consent from parents, the study was initiated. Total study population was randomly assigned to two groups (Group C and Group D) of 30 each.

The exclusion criteria included children belonging to ASA-PS 2 or above, those with hypersensitivity to dexmedetomidine, and those with cognitive delay, psychological or neurological disorder that limits their ability to communicate with nursing personnel.

After a thorough preanaesthetic check up, preoperative fasting of 8 hours for solid food and 3 hours for clear fluids were advised.General anaesthesia was induced with inhalation of 8% sevoflurane in 50% nitrous oxide and oxygen. After induction, intravenous line was secured and ringer lactate infusion started. Analgesia was provided with fentanyl 1mcg/kg intravenously and paracetamol rectal suppository 30mg/kg. Ondansetron (0.1mg/kg) and dexamethasone (0.1mg/kg) were used for prophylaxis against Post Operative Nausea and Vomiting (PONV). Electrocardiogram (ECG), Noninvasive Blood Pressure (NIBP), Pulse Oxymetry(SPO2) and End Tidal Carbon dioxide (EtCO2) were monitored. Maintenance of anaesthesia was also with sevoflurane 1.5-3% adjusted to keep blood pressure and heart rate values within 20% of baseline values (+/- 20%). Vecuronium bromide was used for maintenance of muscle relaxation.At the completion of surgery, residual muscle relaxation was reversed with neostigmine 0.05mg/kg and atropine 0.02mg/kg intravenously.

Children in Group C did not receive dexmedetomidine and were extubated once they were awake and following commands. Approximately 10 minutes before extubation, children in Group D received dexmedetomidine 0.3 mcg/kg diluted in 10ml normal saline intravenously. This was infused over 10 minutes such that the end of infusion is the approximate time for extubation.

The primary outcome studied was emergence agitation. We used a 5 point Watcha scale to assess agitation (Table 1)

Table 1: Watcha Scale

Score 1	Sleeping
Score 2	Awake, calm
Score 3	Irritable, crying
Score 4	Inconsolable crying
Score 5	Severe restlessness, disorientation or thrashing around

Agitation was further assessed in the Post Anaesthesia Care Room (PACU), every 5 minutes for the first 30 minutes after extubation. A score >3 in Watcha scale was considered as significant agitation. Parental presence in PACU was first attempted for managing agitation. If that failed, midazolam at incremental doses of 0.02mg/kg IV was given.

Children complaining of localized pain were not considered to have emergence agitation and rescue analgesics were administered. An objective scoring system for pain assessment was not used as emergence agitation and pain often have similar clinical manifestations and it would be technically difficult to implement the pain scoring systems in an agitated young child.

Other parameters studied included adverse airway events during extubation such as significant breath holding (holding breath >20s), severe coughing (more than 4 coughs and saturation <95%) and adverse events related to dexmedetomidine such as bradycardia, hypotension. Tracheal extubation time (time to extubation after cutting off anaesthetic gases), time to emergence (first eye opening to command after cutting off anaesthetic gases) and time to discharge from PACU were also compared between the two groups.

The observations made were tabulated and analyzed using computer software, Statistical Package for Social Sciences. The data were expressed in its frequency, percentage, mean and standard deviation. Independent Sample t test, Mann-Whitney U test, chi square test and Fisher's Exact test were used to find the associations and comparisons between different parameters. For all statistical evaluations, a two-tailed probability of value, < 0.05 was considered significant.

Results

The results obtained were tabulated as follows and were analysed. There were no significant (P>0.05) differences between the two groups with respect to age, sex, weight and duration of surgery (Table 2).

The incidence of significant agitation (Score>3) was compared between the two groups during extubation as well as every 5 minutes for the first 30 minutes following extubation. During extubation, among the children who did not receive dexmedetomidine, 56.7% had significant agitation where as the incidence was 20% in the dexmedetomidine group. This difference was statistically significant (P < 0.001).Similar results were obtained during the next 30 minutes of assessment and children in dexmedetomidine group continued to have markedly lower agitation scores (P <0.003) (Table 3).

Table 2: Demographic and surgical data

	No Dexmedetomidine group (n=30)	Dexmedetomidine group (n=30)
Age (year)	5.4 ± 1.6	5.3 ± 1.6
Weight (kg)	16.6 ± 3.7	16.7 ± 3.2
Duration of surgery(min)	71.5 ± 9.3	71 ± 8.8
Sex (M:F)	15 : 15	15 : 15

Values given are mean ±SD

Table 3: Incidence of significant emergence agitation

Time	Group (n=30)	
	No Dexmedetomidine N (%)	Dexmedetomidine N (%)
At Extubation	17 (56.7)	6 (20)
After Extubation		
5 mins	20 (66.7)	5 (16.7)
10 mins	10 (53.3)	4 (13.3)
15 mins	12 (40)	3 (10)
20 mins	8 (26.7)	4 (13.3)
25 mins	9 (30)	3 (10)
30 mins	9 (30)	3 (10)

P value < 0.003

Table 4: Incidence of other adverse events

Adverse event	Group (n=30)	
	No dexmedetomidine N (%)	Dexmedetomidine N (%)
Coughing	6 (20)	2 (6.7)
Breath holding	1 (3.3)	0 (0)
Bradycardia	0 (0)	1 (3.3)
Hypotension	0 (0)	0 (0)

P value > 0.05

Table 5: Time to extubation and emergence from anaesthesia, Time to discharge from PACU

Time (min)	No dexmedetomidine group	Dexmedetomidne group
Time to extubation	9.3 ± 2.6	10.2 ± 3.3
Time to emergence	5.1 ± 1.3	5.7 ± 2.5
Time to discharge from PACU	64.8 ± 5.2	61.4 ± 6.1

P>0.05, Values given are mean ± SD

The Incidence of Other Untoward Events were also Compared between the Two Groups

Adverse airway events during extubation such as coughing and breath holding were less in the dexmedetomidine group but the difference was not statistically significant (P>0.05). Incidence of bradycardia and hypotension was not significantly increased in dexmedetomidine group. Dexmedetomidine administration did not cause any delay in recovery. The time to emergence, time to

extubation and the time to discharge from PACU were similar in both groups (Table 5).

Discussion

The results of this study indicate that the administration of dexmedetomidine at a dose of 0.3mcg IV, 10 minutes before extubation, reduces the incidence of emergence agitation after sevoflurane anaesthesia.

Emergence agitation, is a frequent phenomenon in children recovering from general anaesthesia with a reported incidence of upto 80% [4]. Mechanism behind this phenomenon is complex and not fully understood. The factors that contribute include age, anxiety, temperament, type of surgery, duration of surgery or anaesthesia, and postoperative pain. Earlier pain was considered to be the most important cause for agitation. But increased emergence agitation was found with sevoflurane when used for non-painful procedures such as Magnetic Resonance Imaging (MRI) scanning [5,6].

Higher incidence seen with the use of sevoflurane is often attributed to rapid emergence from anaesthesia because of its lower blood gas solubility. Some other inherent properties of the gas may have an effect on this, as increased agitation is not seen with propofol which also provides a fast emergence [7].

The incidence of emergence agitation is more in preschool children and those undergoing otorhinolaryngological procedures like adenotonsillectomy [8]. The increased incidence in adenotonsillectomy is independent of postoperative pain and is often postulated to be due to a sense of suffocation combined with the presence of blood or secretions in the oral cavity [9]. Thus we decided to evaluate the effect of dexmedetomidine on emergence agitation seen after adenotonsillectomy done under sevoflurane anaesthesia.

There is no well established prophylaxis or treatment for postoperative agitation but the incidence of this excitatory behavior seems to be reduced by perioperative use of sedative-analgesic drugs. Premedication with midazolam, probably due to its dissociative effect on memory, has produced conflicting results. Following midazolam premedication, the incidence of agitation increased according to Lapin et al [10] and decreased according to Cole et al [11]. Because of such conflicting reports, we reserved oral midazolam premedication for very anxious children and they were excluded from the study.

Auoad *et al* observed that a single pre-extubation dose of propofol 1 mg / kg IV was effective in reducing agitation but at the cost of slightly prolonged recovery [12]. Ira todd et al in their double blinded trial concluded that fentanyl at a dose of 2.5 ± 0.62 mcg / kg, given at the time of induction effectively reduces agitation [13]. Clonidine, because of its sedative-analgesic actions, was extensively studied in the management of emergence agitation. Kulka et al found a reduction in agitation from 80% in control group to 10% in clonidine group, when clonidine 2mcg IV was administered 5 minutes after beginning of surgery [14].

Dexmedetomodineis the dextro-stereoisomer of medetomidine with eight times more affinity than clonidine for $alpha_2$ adrenoceptors ($alpha_2$: $alpha_1$ ratio 1600: 1).Unlike opioids or benzodiazepines it has minimal effect on respiration. Its short context sensitive half time also ensures that recovery from anaesthesia will not be affected much with the administration of dexmedetomidine. These factors make dexmedetomidine a promising agent in the management of emergence agitation.

Ibacache et al studied two different doses of dexmeditomidine 0.15 mcg and 0.3 mcg given at the time of induction of anaesthesia on reducing emergence agitation [15]. They concluded that 0.15 mcg dose was ineffective whereas 0.3 mcg / kg dexmedetomidine reduced emergence agitation seen after sevoflurane anaesthesia (p value <0.05) without any significant adverse effects. They also came up with an observation that even though 0.5 mcg / kg dexmedetomidine may be more effective for reducing emergence agitation, it might be associated with a greater incidence of adverse hemodynamic events such as bradycardia.

Shukry M et al compared the effect of a perioperative infusion of dexmedetomidine 0.2 mcg / kg / hour with placebo and found out that the incidence as well as severity of emergence delirium was significantly reduced in children who received dexmedetomidine [16]. There was no significant difference in pain scores or time taken for extubation.

In our study we evaluated the effect of a single pre-extubation dose of dexmedtomidine 0.3 mcg / kg on reducing agitation. The rationale behind using this pre-extubation single dose was that since the context sensitive half time of dexmedetomidine is short (4 minutes for a 10 minute infusion), it may have maximum effect on reducing agitation when it is given just before extubation. Also, similar studies using pre-extubation single doses had pointed out that there is

more hemodynamic stability and less interference with recovery from anaesthesia, with this approach. In our study, dexmedetomidine effectively reduced agitation without causing any hemodynamic adverse effects or delay in recovery.

Our finding is in agreement with the study of Essam Manna et al who found that a pre-extubation single dose of fentanyl 1mcg/kg and dexmedetomidine 0.3 mcg IV were both equally effective in reducing agitation when compared to placebo [17]. At this dose, there was no delay in recovery or any serious hemodynamic adverse effects and they concluded that 0.3 mcg of dexmedetomidine is an effective as well as a safe dose.

In our study, the incidence of adverse airway events during extubation like coughing, breath holding were not significantly different in two groups. Gulen Guler *et al* observed that dexmedetomidine 0.5 mcg/kg IV given 5 minutes before the end of surgery, significantly reduced not only agitation and pain scores but also the occurrence of adverse airway events in children undergoing adenotonsillectomy using sevoflurane anaesthesia [18]. The larger dose (0.5 mcg/kg) used may have reduced coughing and made extubation smooth but at the cost of a significant delay in time to emergence and time to extubation.

Though dexmedetomidine produces some reduction in heart rate and blood pressure, hemodynamically significant bradycardia or hypotension is uncommon [19]. If such hemodynamic adverse effects occur, it is well amenable to treatment with atropine and ephedrine [20]. In our study, one child in the dexmedetomidine group developed significant bradycardia (>20% drop from baseline) and that was promptly reversed with atropine. None of the children developed hypotension.

It is difficult for an agitated child to cooperate for assessment of pain using a visual or numerical pain scale. Observational or behavioural scales are also difficult because emergence agitation and postoperative pain have similar clinical manifestations. Hence a simple subjective assessment was used to detect the presence of significant localized pain in throat and managed accordingly. Limitation of our study is that pain may be a confounding variable as objective pain assessment was not done.

Till date, there are no well established recommendations regarding the most appropriate dose of dexmedetomidine as well as the timing of its administration for reducing agitation. More research may be needed to establish whether a pre-extubation single dose is better than continuous infusion as well as to find out the most effective and safe dose.

Conclusion

In our study, we found that a single dose of dexmedetomidine 0.3 mcg/kg IV given 10 minutes before extubation reduced the incidence of postoperative agitation in children undergoing adenotonsillectomy using sevoflurane anaesthesia. This did not produce any significant adverse hemodynamic effects and the recovery from anaesthesia was unaffected.

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