A RANDOMIZED EVALUATION OF INTRAVENOUS DEXAMETHASONE VERSUS ORAL ACETAMINOPHEN CODEINE IN PEDIATRIC ADENOTONSILLECTOMY: EMERGENCE AGITATION AND ANALGESIA

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Abstract

Background: Adenotonsillectomy is the most frequently performed ambulatory surgical procedure in children. Post operative agitation and inadequate pain control, for children undergoing adenotonsillectomy, can be a challenge. The aim of this study was to assess the effect of intravenous dexamethasone and oral acetaminophen codeine on emergence agitation and pain after adenotonsillectomy in children.

Methods: One hundred and five pediatric patients (3-7 years old), scheduled to undergo adenotonsillectomy under general anesthesia, were enrolled in the study. Thirty minutes before induction, patients were randomized to three groups. Group 1 received 0.2 mg/kg of intravenous dexamethasone and 0.25 ml/kg of oral placebo syrup. Group 2 received 20 mg/kg of oral acetaminophen codeine syrup and 0.05 ml/kg of intravenous saline. Group 3 received 0.25 ml/kg of oral placebo syrup and 0.05 ml/kg of intravenous saline. Emergence agitation and postoperative pain were assessed, recorded and compared.

Result: Agitation was less frequent in dexamethasone and acetaminophen codeine groups in comparison with placebo group, but there were not significant differences between the two groups.

The pain frequencies in the three groups were not significantly different.

Conclusion: The results of this study suggest that the administration of intravenous dexamethasone (0.2 mg/kg) and oral acetaminophen codeine (20 mg/kg) thirty minutes before anesthesia can significantly decrease the incidence and severity of agitation but does not have an effect on postoperative pain.

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Introduction

Adenotonsillectomy is the most frequently performed ambulatory surgical procedure in children[1,2]. Post operative agitation and inadequate pain control for children undergoing

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adenotonsillectomy can be a challenge. The underlying mechanisms for this agitation have not been identified[3,4]. Possible etiologic factors include a rapid recovery from sevoflurane, psychological immaturity, genetic predisposition, type of procedure, duration of anesthesia and concurrent medications[5,6,7]. Opioids[8], midazolam[9] and clonidine[10] have been administered for both prophylaxis and treatment of emergence agitation in children with different levels of goal achievement.

Although opiates are excellent analgesics in these patients, they are often contraindicated because of their potentially adverse effects on respiration and the central nervous system[11]. Acetaminophen and NSAIDs do not have these effects. Dexamethasone has been used as an antiemetic drug in patient undergoing chemotherapy with limited side effects[5]. It has been found to have a prophylactic effect on postoperative vomiting in children undergoing tonsillectomy[5]. Dexamethasone has combined antiemetic and anti-inflammatory effects that may decrease postoperative tissue injury, edema and pain after tonsillectomy.

Acetaminophen codeine is widely used for musculoskeletal pain, but few studies have evaluated it for tonsillectomy.

The aim of this study was to assess the effect of intravenous dexamethasone and oral acetaminophen codeine on emergence agitation and pain after adenotonsillectomy in children.

Methods

The study was approved by the local ethics committee and written informed consents were obtained from all parents. We conducted a randomized, prospective, blinded clinical trial from March 2009 to March 2010, in Alzahra Hospital, Isfahan, Iran.

We investigated 105 pediatric patients aged 3-7 years with ASA status I and II scheduled to undergo adenotonsillectomy with general anesthesia. Children with active lower and upper respiratory infection, history of asthma, allergy, and those who received antiemetics, steroids, antihistaminic or psychoactive drugs during the week before the surgery were excluded from the study

An anesthesiologist who contributed in our team used a random-number table to allocate the patients into three groups. Thirty minute before the anesthesia, the first group received 0.2 mg/kg of intravenous dexamethasone and 0.25 ml/kg of oral placebo syrup. The second group received 20 mg/kg of oral acetaminophen codeine syrup and 0.05 ml/kg of intravenous saline. The third group received 0.25 ml/kg of oral placebo syrup and 0.05 ml/kg of intravenous saline.

All drugs and data sheets were labeled with the randomization number of the patient. Patients, and the anesthesiologist who gave the scores, and the staff were unaware of the patient group assignment.

All operations were performed by one surgeon using a standard surgical technique. No premedication was administered. All patients received an identical anesthetic technique, consisting of atropine (0.02 mg/kg), fentanyl (2 µg/kg), sodium thiopental (5 mg/kg), and atracurium (0.5 mg/kg).

After intubation with appropriate tracheal tube anesthesia was maintained with N2O and O2 in a 50/50 ratio and isoflurane with %1.25 MAC. At the end of the surgery, reversal of neuromuscular blockage was performed through intravenous administration of 0.02 mg/kg of atropine and 0.04 mg/kg of neostigmine. In the recovery room, the patients were placed in slight head-down tonsil position. Extubation was performed when the patient responded to commands.

Patients were constantly supervised during their stay in the recovery room, and agitation and pain scores were assessed by an anesthesiologist, blinded to patient group assignment, during the first hour following the operation. Agitation was assessed using a 5 point scale[7] (1 = sleeping; 2 = awake, calm; 3 = irritable, crying; 4 = inconsolable crying; 5 = severe restlessness, disorientation, thrashing around) and pain assessments were made using a 5 point rating scale (1 = the child had no pain or was asleep; 2 = the child complained of mild pain but was not distressed by it; 3 = the child stated that his or her throat was very painful but was not distressed or the child was moderately tearful but consolable; 4 = the child was in considerable distress; 5 = the child was screaming and struggling violently).

Throughout the procedure and in the recovery room, heart rate, peripheral oxygen saturation and blood pressure were monitored.

The anesthesiologist was blinded to drugs, tracheal extubation time (time from the discontinuation of anesthetic gas to tracheal extubation), anesthesia time (the time from induction of anesthesia to discontinuation of anesthetic gas), recovery time (time span between entrance to recovery room and discharge from the recovery room) and duration of surgery. Agitation and pain scores were recorded. If agitated patients could not be calmed, the second investigator was allowed to administer midazolam; furthermore, if patients had uncontrolled pain, additional opioid was administrated.

Statistical analysis was performed through Mann Whitney, U-test for agitation and pain scores. Nominal and numerical data were analyzed through chi square, Fisher's exact test and unpaired student's T-test. Statistical significance was accepted for $p<0.05$, using SPSS 17.

Results

A total of 105 pediatric patients were studied; 35 patients were allocated randomly to each group.

There were no significant differences between the groups with respect to age, weight, height, gender and duration of surgery ($p<0.05$) (Table 1). There were no significant differences between the mean values of extubation time, anesthesia time and recovery time (duration of stay in PACU) in the three groups (Table 2). Agitation was less frequent in dexamethasone and acetaminophen codeine groups in comparison with the placebo group ($p = 0.016$, $p = 0.042$, respectively) (Table 3); but there were not significant differences between acetaminophen-codeine and dexamethasone groups.

The pain frequencies in the three groups were not significantly different ($p = 1$, $p = 0.142$, $p = 0.142$) (Table 3). Agitation and pain score means are shown in Table 4.

No adverse events such as laryngospasm, bronchospasm, hypotension, bradycardia, postoperative respiratory depression and hypoxia were noted in the three groups. Heart rate, blood pressure and spO_2 values before the surgery, by the time of admission to recovery unit and by recovery discharge were compared but showed no significant differences.

Discussion

Emergence agitation (EA) is one of the most common complications after adenotonsillectomy in pediatric patients. In epidemiologic study incidence of agitation after surgery were 5.3% in all age and 12-13% in children[4]. EA is a self-limiting phenomenon;

Table 1
Demographic and surgical data

Group	Mean age ± SD (year)	Mean weight ± SD (kg)	Mean Height ± SD (cm)	Gender (m; f) (N)	Mean Duration of surgery ± SD (min)
Placebo	4.66 ± 1.16	22.32 ± 8.51	108.36 ± 19.59	16; 19	39.12 ± 11.3
Dexamethasone	4.71 ± 1.33	23.56 ± 9.13	109.9 ± 19.3	17; 18	39.86 ± 11.5
Acetaminophen codeine	4.8 ± 1.41	23.84 ± 9.35	111.2 ± 18.3	15; 20	38.67 ± 11.2
P value	0.271	0.332	0.315	0.186	0.87

Table 2
Mean values of anesthesia, extubation and recovery times

Group	Mean Anesthesia time ± SD (min)	P value	Mean Extubation time ± SD (min)	P value	Mean Recovery time ± SD (min)	P value
Placebo	42 ± 11	0.87	36.57 ± 7	0.31	57.49 ± 9.1	0.33
Dexamethasone	42.29 ± 11.3		34.29 ± 7		54.71 ± 9.4	
Acetaminophen codeine	41.57 ± 11.1		34.86 ± 7.2		55.14 ± 9.1	

Table 3
comparison of agitation and pain frequencies between the groups. (= p value <0.05)*

Group	Agitation (Number of patients)		P value	Pain (Number of patients)		P value
	+	-		+	-	
Placebo Dexamethasone	30 21	5 14	0.016*	32 32	3 3	1.0
Placebo Acetaminophen codeine	30 23	5 12	0.042*	32 28	3 7	0.142
Dexamethasone Acetaminophen codeine	21 23	14 12	0.752	32 28	3 7	0.142

however, it can occasionally lead to harmful effects[14]. In rare cases, EA has lasted for longer than two days[15].

The results of this study indicate that administration of dexamethasone (intravenous) and acetaminophen codeine (oral) 30 minute before anesthesia, reduces agitation frequency. According to tables we did not observe any significant changes in extubation, recovery and anesthesia time and pain frequency between the three groups.

Although the causes of postoperative agitation following general anesthesia are not exactly known, risk factors such as preschool age, otolaryngologic procedures and using sevoflurane of desflurae, which provoke this phenomenon, are suggested[4,5,6]. Thus, we decided to investigate the efficacy of dexamethasone and acetaminophen codeine in adenotonsillectomy procedures and in preschool age children and in whom that the incidence of postoperative agitation is high. Although the reason for this high incidence is unknown, two articles suggested that a sense of suffocation during procedures on airway tract can result in remarkable frequency of agitation[16,17]. The incidence of postoperative agitation in children who received midazolam premedication increased according to lapin et al[9] and decreased according to coke et al[7]. Regarding the diversity of previous results, the present study focuses on the use of midazolam premedication.

Opioids remarkably decrease the incidence postoperative agitation[8]. However pain is not a cause of agitation by itself[18,19], it can be one of the most important factors resulting in the severity and frequency of agitation[14,20].

Effective analgesia following adenotonsillectomy is not easy to achieve and this might influence the high incidence of agitation in these patients. Although opioids are effective analgesic, they may increase the airway problem and nausea and vomiting[8]. Acetaminophen codeine and dexamethasone did not provide the expected level of analgesia in our study; 37% of the patients in dexamethasone and acetaminophen codeine groups and 42% of the patients

Table 4
Mean agitation and pain scores (= p value <0.05)*

Group	Mean agitation score ± SD	P value	Mean pain score ± SD	P value
Placebo	2.09 ± 1.2	0.011*	2.46 ± 1.0	0.193
Dexamethasone	1.34 ± 0.8		2.57 ± 1.0	
Acetaminophen codeine	1.49 ± 0.7		2 ± 1.2	

in control group required additional analgesia doses.

Acetaminophen codeine produced similar analgesia postoperatively as dexamethasone.

This investigation shows a decrease in the incidence of postoperative agitation in dexamethasone and acetaminophen codeine groups ($p<0.016$, $p<0.042$). Research has shown that the principle cause of agitation may be edema in airway tract, and dexamethasone and acetaminophen codeine reduce edema and agitation.

In conclusion, the administration of intravenous dexamethasone (0.2 mg/kg) and oral acetaminophen codeine (20 mg/kg) can significantly decrease the incidence and severity of agitation but does not have an effect on postoperative pain. This study may suggest that the control of edema with corticosteroids or other drugs can reduce postoperative agitation, and that pain cannot be the only reason for agitation.

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