Original Article

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Oral Clonidine Premedication Reduces Nausea and Vomiting in Children after Appendectomy

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Abstract

Objective: Clonidine is an α2-agonist which is used as a sedative premedication in children. There are conflicting results in the published literature about the effect of clonidine on the incidence of post operative nausea and vomiting (PONV). We therefore decided to evaluate the effect of oral clonidine given preoperatively on the incidence of PONV in children after appendectomy.

Methods: sixty children, 5-12 years old, classified as American Society of Anesthesiologists physical status I and II, who were scheduled for appendecectomy were enrolled in this randomized double blinded clinical trial. Patients were randomly assigned into two groups of 30 patients. Patients in clonidine group were given 4 μg.kg -1 clonidine in 20 cc of apple juice and patients in control group were given only 20 cc of apple juice 1 hour before transporting to operating room. The protocol of general anesthesia and postoperative analgesia was the same for two groups. Incidence of PONV and antiemetic usage of patients were assessed during 0-24 hours after anesthesia.

Findings: The patients' characteristics were similar in two groups. Patients who had received clonidine had significantly less episodes of PONV and also less rescue antiemetic usage than patients in control group.

Conclusion: we showed that oral clonidine at a dose of 4 μg.kg -1 administered preoperatively is associated with a reduced incidence of postoperative vomiting in children who have undergone appendectomy.

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Key Words: Clonidine; Appendectomy; Vomiting; Clinical trial

Introduction

Nowadays, post-operative nausea and vomiting (PONV) sound to be the leading cause of morbidity and discomfort among pediatric surgical patients[1]. PONV may at least direct patients to have longer stay at hospital after surgery but some more serious consequences such as bleeding, wound dehiscence, dehydration, electrolyte disturbance and/or pulmonary aspiration of gastric contents can be resulted by severe types of PONV[2,3]. The incidence of PONV is higher in pediatric patients than in adults[2,4]. It has been reported that up to 40% of children undergoing

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appendicectomy who have not received any antiemetic drug may have PONV[5]. Clonidine, an α2-adrenoceptor agonist, is an effective premedicant which has been shown to decrease the incidence of PONV in children undergoing strabismus surgery[6,7], but its efficacy for prevention of PONV after appendectomy in pediatric patients has not been studied yet. We therefore decided to evaluate the effect of oral clonidine given preoperatively on the incidence of PONV in children after appendectomy.

Subjects and Methods

Following approval of institutional review board of Medical Faculty of Tehran University of Medical Sciences and written parental consent, 60 children, with American Society of Anesthesiologists physical status I,II, aged 5-12 years, who were scheduled for appendectomy were enrolled in this randomized double blinded clinical trial. This study was carried out at Bahrami Children's Hospital, Tehran from February to November 2009. We excluded patients with perforated appendicitis, history of gastrointestinal diseases, motion sickness, and unexpected cardiac or respiratory events during or after the surgery and also those patients who had received antiemetic within 24 hours before surgery. A random number table was used to allocate patients into clonidine and placebo groups. Patients in clonidine group were given 4 μg.kg -1 clonidine in 20 cc of apple juice and patients in control group were given only 20 cc of apple juice 1 hour before transporting to operating room. Standard monitoring included electrocardiography, noninvasive blood pressure, and pulse oximetry and capnography. Heart rate and systolic and diastolic blood pressures were measured before and after anesthesia induction and after tracheal intubation in patients of the two groups. Anesthesia was induced with 2 μg.kg -1 fentanyl, 5 mg.kg -1 sodium thiopental, and 2 mg.kg -1 succynyl choline and maintained with isoflorane, fentanyl, atracurium and nitrous oxide. Lactate ringer was administered to all of patients before induction of anesthesia (5ml.kg -1) and during the surgery with regard to hemorrhage intensity and body fluid loss. Twenty minutes before the end of the procedure, all patients were given paracetamol 30 mg.kg -1 rectally. At the end

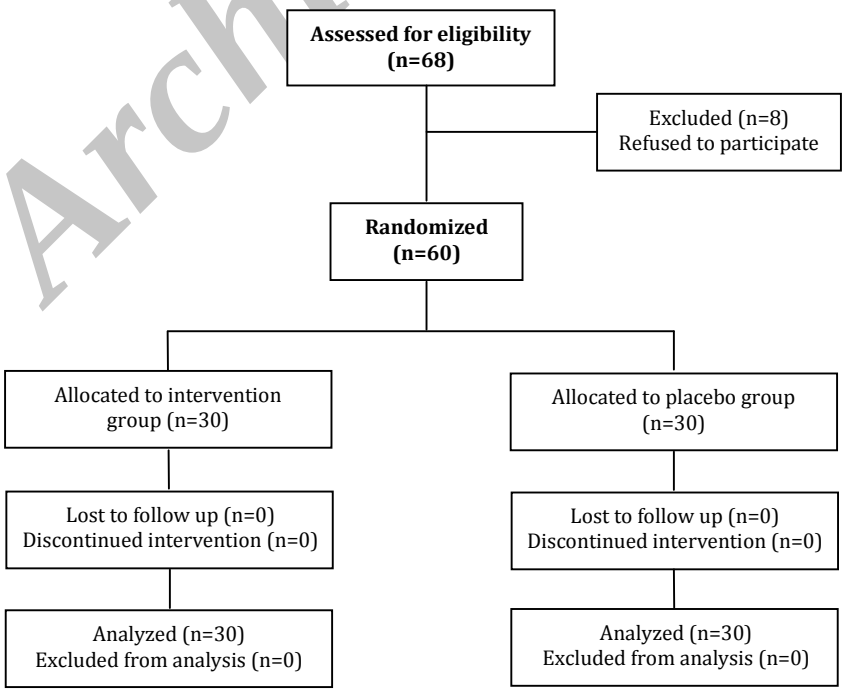

Fig. 1: Flow diagram of patients

Table1: Characteristics of the patients in two groups

Variables	Clonidine (n=30) Mean (SD)	Placebo (n=30) Mean (SD)	*P* value
Mean age (yrs)	7.5(2.9)	8.1(2.7)	0.436
Sex (males)	19 (63.3%)	18 (60%)	0.791
Mean weight (kg)	27.9(11.3)	24.2(6.6)	0.128
Mean time of surgery (min)	53.4(15.5)	52.6(19.5)	0.861
Preanesthetic mean heart rate	113(15)	111(14)	0.607
Mean systolic pressure	101(19)	103(13)	0.631
Mean diastolic pressure	69.5(8)	68(10)	0.791

SD: Standard Deviation

of surgery muscle relaxation was reversed by 50 µg.kg-1 neostigmine along with 20 µg.kg-1 atropine. Bupivacaine 0.5% was infiltrated on incision site at the skin closure.

The children were extubated at the end of surgery when awake and then transferred to the post anesthesia care unit. At the surgical ward patients were given 15 mg.kg-1 paracetamol every 4 hour within 24 hours after the surgery. The episodes of vomiting as well as antiemetic usage were observed and recorded for 24 hours after the surgery. When two or more episodes of emetic symptoms occurred, intravenous metoclopramide 0.2 mg.kg-1 was administered slowly. All intra and postoperative observations were made by trained technicians and nursing staff who were blinded to which study group the patients had been allocated.

Data were expressed as simple count or mean [±SD]. Statistical analysis of patients data from the two study groups was conducted using analysis of variance for repeated measurements (ANOVA), Fisher's exact test, or Chi square test where appropriate. Statistical calculations were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). A power analysis based on the result of a similar study[5] and our pilot study under the present protocol showed that sample size of 30 patients in each group deemed to have a power of 80% to detect a difference in PONV between groups with a significance value of $P<0.05$.

Findings

Sixty patients were recruited in this study and no patient was excluded or lost from the study. Patients' characteristics were similar in the two Groups (Table 1). There was no statistically significant difference between the groups with respect to sex, age and weight. Also there was no significant difference in the mean values of systolic and diastolic blood pressures and heart rate and total time of surgery between the two study groups (Table 1). Patients who had received clonidine had significantly less episodes of PONV than patients in control group ($P<0.001$)(Table 2). Difference between patients in the two study groups with respect to number of patients who were given rescue antiemetic drug was also statistically significant (Table 2). No clinically significant adverse effect such as bradycardia and hypotension was seen during perioperative period.

Table 2: Number of patients with nausea and vomiting and requiring rescue antiemetic medication during 24 h after anesthesia

	Clonidine (n = 30) n (%)	Placebo (n = 30) n (%)	*P* value
No PONV	23(76.7)	7(23.3)	<0.001
Nausea	7(23.3)	23(76.7)	<0.001
Vomiting	5(16.7)	21(70)	<0.001
Rescue	3(10%)	10(19.3)	<0.001

Discussion

To the best of our knowledge this is the first study aimed to evaluate the effect of premedication with clonidine to prevent PONV in patients undergoing appendectomy. We showed that oral clonidine with the dose of 4 mg.kg-1 in children undergoing appendectomy can significantly decrease the incidence of PONV as compared with control group (70% vs. 16.7%). The incidence of post operative vomiting in control group of our study was 70% which is higher than the result of a similar study[5]. The reason for this high incidence of PONV is not known to us.

PONV is a multifactorial complication of anesthesia and surgery which accounted for 13-42% of all post-operative complications in pediatric surgical patients[1].

Many drugs (antihistamines, butyrophenones, dopamine receptor antagonists) have been attempted to prevent and treat PONV, but undesirable adverse effects, such as excessive sedation, hypotension, dry mouth, dysphoria, hallucinations and extrapyramidal signs have occasionally been noted[2].

Clonidine is an α2-agonist which is used as a sedative premedication in children[1]. Due to the lower costs of clonidine in comparison with other drugs such as opioid and benzodiazepines, as well as less complications of clonidine, it has been proposed as an effective drug for preoperative period. It has been shown that this drug can provide preoperative sedation, suppress cardio-vascular responses to laryngoscopy and tracheal intubation and reduces anesthetic requirement. Moreover, clonidine has been reported to reduce shivering both after general and spinal anesthesia and the incidence of PONV has been shown to be reduced after both systemic and epidurally administered clonidine[10,11]. However, there are conflicting results in the published literature about the effect of clonidine on the incidence of PONV. Some investigations in adults concluded that oral clonidine can reduce the incidence of PONV[12-15], but in children the results are somewhat different. Our results are consistent with the two earlier studies who examined the effect of clonidine in children undergoing strabismus surgery and showed that preoperative oral clonidine at a dose of 4 μg.kg-1 is associated with a reduced incidence of postoperative vomiting in this group of patients [6,7].

In contrast, some other investigators reported no significant antiemetic effect of clonidine given orally to children[16,17]. The difference between the above mentioned results may be related to the nature and origin of vomiting during perioperative period.

In addition to age, sex, a history of PONV and motion sickness and also type of surgery which accounted as uncontrollable risk factors for PONV, there are anesthesia-related factors under control of anesthetists that have impact on the incidence and severity of PONV[1]. It seems that the variety number of factors affecting the incidence of PONV in adults and children can be accounted for the different results of investigations evaluating the effect of clonidine on PONV. The mechanism of antiemetic effect of clonidine has not been yet clearly specified but some investigators believe that antiemetic effect of clonidine can result from its sedative and anxiolytic action which can directly reduce anesthetic and analgesic requirement of patients in perioperative period. It also has been suggested that clonidine can decrease PONV through its inhibitory action on sympathetic outflow and catecholamine release which can then block triggering of nausea and vomiting[18].

One of the most important systemic side effects of clonidine is hypotension along with bradycardia in adults which have not been considered as main post-operative complications among children[17,18]. However, none of the patients in our study experienced such episodes of severe hemodynamic change.

In our study all patients were comparable regarding demographic data, anesthetic technique, surgical procedure and postoperative medications, therefore the difference between the study groups with respect to incidence of PONV can be attributed to premedication with oral clonidine.

In this study we used oral clonidine with the dose of 4 μg.kg-1 which has been shown that it can reduce the incidence of PONV[6,7]. Because of slow onset (0.5-l h) and a long duration (12 h) of action [8], we administered oral clonidine to patients in intervention group one hour before transporting

patients to the operating room.

Our study had a few limitations. In the present study the level of sedation and discharge time was not studied. Because of sedative effect of clonidine, further studies are required to elucidate if clonidine prolongs hospital stay in patients receiving clonidine in the perioperative period. However, to verify the antiemetic effect of clonidine in postoperative period, we need to design similar studies with larger sample size in appendectomy patients and also other pediatric surgical populations.

Conclusion

We have shown that oral clonidine at a dose of 4 µg/kg-1 administered preoperatively is associated with a reduced incidence of postoperative vomiting in children who have undergone appendectomy.

Acknowledgment

The proposal of this manuscript was approved in the research committee of the department of anesthesiology and critical care of Tehran University of Medical Sciences, and registered in the Iranian Registry of Clinical Trials with following number: IRCT201011225225N1. All nurses and colleagues at the anesthetic departments and the surgical wards of Bahrami Children's Hospital, Tehran, are gratefully acknowledged for their kind co-operation during this study.

Conflict of Interest: None

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