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The effect of intravenous administration of ondansetron on analgesia time of caudal block in circumcision cases: A randomized controlled trial

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Abstract

We investigate whether there was any effect of intravenous ondansetron administered for postoperative nausea vomiting prophylaxis on the duration of caudal block action in patients who undergo circumcision surgery. 66 ASA I–II patients aged 4 to 10 and scheduled for circumcision surgery were included in this prospective, randomized controlled study. We administered 0.1 mg/kg ondansetron IV to Group Ondansetron patients before caudal block and same amount of serum physiologic for Group Control patients. After anesthesia induction caudal block with 1 ml/kg 0.25% bupivacaine administered. We evaluated postoperative analgesia durations in each group. There were no difference between groups for number of patients which were painless for first 4 hours and 8 hours, total analgesic requirements for first 24 hours, total time for first analgesic requirements. We concluded that iv ondansetron given at 0.1 mg/kg dose before caudal block with bupivacaine can be used safely without a significant effect on the duration of block-induced analgesia.

Keywords: Caudal block, ondansetron, postoperative analgesia

Introduction

Caudal epidural block is a technique used as an adjunct to general anesthesia for postoperative analgesia in pediatric patients, especially those with infraumbilical, perineal and lower extremity surgery [1]. It is a commonly used block in infraumbilical pediatric surgery because it reduces the need for perioperative and postoperative analgesia, reduces the need for general anesthesia, accelerates the awakening, suppresses the surgical neurohumoral stress response and can be performed easily [2].

Although postoperative nausea and vomiting (PONV) are frequent and morbidity-related complication in children, PONV is still present in almost twice the frequency of adults, 33.2–82%. For this reason, prophylactic applications are primarily at the foreground instead of treatment [3]. 5-HT₃ antagonists, especially ondansetron, are indicated as the first choice among antiemetic drugs used for PONV prophylaxis and treatment alone or for multimodal prophylaxis [3]. There are studies reporting different results regarding the effect of 5-HT₃ antagonists on sensorial block level due to spinal anesthesia in recent years. Mowafi et al. [4] found that iv granisetron accelerates the recovery of sensory

block in spinal anesthesia with bupivacaine and Fassoulaki et al. [5] reported that ondansetron was antagonizing the sensorial block in spinal anesthesia with lidocaine. However, some studies have reported that systemic ondansetron has no effect on the block formed by spinal anesthesia [6,7].

We investigate whether there was any effect of intravenous ondansetron administered for postoperative nausea vomiting prophylaxis on the duration of caudal block action in patients who undergo circumcision surgery.

Material and Method

Following ethical committee approval from institutional Ethical Committee (No: KA 16/165), 66 American Society of Anesthesiology (ASA) stage I–II patients aged 4 to 10 and scheduled for circumcision surgery were included in this prospective, randomized controlled study. Written consent was obtained from all patients and their parents. The study was registered to the Australian New Zealand Clinical Trial Registry (No: ANZCTR126160000957493). The study was conducted in 3rd level university hospital between June 2016 and August 2017. Patients' age, height, body weight, body mass index were recorded. Children were excluded in these conditions; refusal for participation in the study, the presence of one of the caudal block contraindications, patients with body mass index > 30,

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hypersensitivity to the study drug, a history of neurological or neuromuscular disease.

All children were premedicated with oral 0.5 mg/kg midazolam 30 min before surgery and were routinely monitored. Peripheral i.v. access was secured and IV 1 mcg/kg fentanyl, 2 mg/kg propofol were administered. Anesthesia was maintained with sevoflurane via ballon mask ventilation. Children were positioned left lateral decubitus position and an expert anesthesiologist performed caudal block with 1 ml/kg 0.25% bupivacaine via appropriate size iv cannula. At the end of surgery, if the patient felt pain over 5/10 according to the Facies Pain Scale-Revised scale [8], the caudal block was considered unsuccessful and the patient was excluded from the study. Patients were randomized by computer generated random sequence number method and divided into two groups to receive ondansetron or not. We administered 0.1 mg/kg ondansetron IV to Group Ondansetron patients before caudal block and same amount of serum physiologic for Group Control patients. At the end of the operation patients taken to postanesthesia care unit. Patients' pain level was assessed with the Facies Pain Scale-Revised scale per hour for the first 8 hours. If patients required additional analgesic, 15 mg/kg IV paracetamol was given. Blind observer recorded patients who were painless observed during the first 4 and 8 hours, total analgesic requirement, the first analgesic requirement and the need for rescue analgesic use, the first walking and miction time and nausea-vomiting. Patients were externed after eight hours from surgery and parents recorded parameters for 24 hours.

Statistical Analysis

The study was designed to be able to detect 1 hour analgesic duration time difference between groups for clinical significance. A power calculation based on these assumption together with an α of 0.05 and a β of 0.9 resulted in the need for 33 patients in each group. Compliance of data to normal distribution was examined with the single sampling Kolmogorov Smirnov test. In the comparison between groups, Student t test was used for the variables which distributed normally and Mann Whitney U test for other variables. Statistically significance was defined as $p < 0.05$.

Results

66 children, 33 in each group, were enrolled in the study. There were no statistically significant differences in demographic characteristics and durations of surgery and anesthesia between groups (Table 1).

Table 1. Demographic characteristics of patients and durations of surgery and anesthesia

	Group Ondansetron	Group Control	p value
Age (year)	6,87±1,34	7,35±1,19	0.750
ASA (I/II)	33/0	32/1	0.924
Height (cm)	124,54±10,20	125,14±9,24	0.948
Weight (kg)	24±6,44	23,57±5,18	0.851
Duration of surgery (min)	18,06±4,55	18,92±4,78	0.749
Duration of anesthesia (min)	21,48±4,77	22±4,83	0.449

Values are given as mean and standard deviation or as number of patients.

There were no difference between groups for number of patients which were painless for first 4 hours and 8 hours, total analgesic requirements for first 24 hours, total time for first analgesic requirements between groups (Table 2).

Table 2. Data on caudal block analgesia durations

	Group Ondansetron	Group Control	p value
Number of patients without pain for the first 4 hours (n)	31	29	0,260
Number of patients without pain for the first 8 hours (n)	26	23	0.165
Total painless time (hour)	17,03±8,63	16,09±9,41	0.195
Number of first 24-hour additional analgesic dose (n)	1,21±1,08	1,64±1,25	0,169

Values are given as mean and standard deviation or as number of patients.

Although there was no significant difference between the groups in terms of postoperative walking time, it was observed that the control group had earlier first voiding time ($p=0.003$). No significant difference was found in the number of patients with PONV (Table 3).

Table 3. PONV, first walking and voiding times

	Group Ondansetron	Group Control	p value
PONV (number of patients)	3	4	0,548
First Walking time (hour)	4,33±3,03	3,35±1,52	0.07
First voiding time (hour)	5,93±3,31	3,57±1,87	0.003*

Values are given as mean and standard deviation or as patient numbers.

*Significant difference between groups

Discussion

According to the results of this study, ondansetron applied iv during anesthesia induction did not cause any change in the duration of analgesia with caudal block in pediatric patients. This is the first study to examine the effect of ondansetron on central blocks in the pediatric age group. Controversial results have been obtained in previous studies in adults. First study in this subject, Fassoulaki et al. [5] showed that ondansetron given 4 mg oral 1 day before surgery and 4 mg IV 15 minutes prior to spinal anesthesia antagonizes sensory block without effect on motor block. In a similar study, granisetron, another 5-HT₃ antagonist, with 1 mg IV dose showed a significant increase in sensory regression time compared to the control group, not affecting the motor block [4]. Following these two studies, it was demonstrated that 8 mg ondansetron oral the night before and 8 mg intravenous administration before spinal anesthesia did not have any effect on spinal anesthesia with ropivacaine [6]. Similarly, 4 mg of ondansetron given 15 minutes before spinal anesthesia has been shown to have no effect on spinal anesthesia induced by hyperbaric bupivacaine [7].

There are a large number of 5-HT₃ receptors at the spinal level. These receptors are located in the superficial laminae and substantia gelatinosa at the spinal cord. Although the role of spinal serotonergic mechanisms in pain modulation is complex, the role of 5-HT₃ receptors in antinociception has been demonstrated in various animal studies. It has been shown that selective 5-HT₃

agonists given intrathecally in rats exhibit antinociceptive activity by providing GABA release [9], which is also antagonized by 5HT3 receptor antagonists. In humans, the cerebrospinal fluid levels of serotonin after spinal bupivacaine are increased 3-fold [10]. Increased serotonin levels directly hyperpolarize the membrane of the substantia gelatinosa, the presynaptically released excitatory neurotransmitter inhibits glutamate and enhances the release of inhibitor neurotransmitter released from interneurons [11]. In contrast, 5-HT3 receptors can act as mediators in both central spinal and peripheral pathways in pain modulation [12]. There is not absolute evidence of serotonergic pathway maturation in children, for this reason it will not be realistic to comment on this issue.

Risk factors for PONV in pediatric patients include PONV, family history of PONV, anesthesia duration > 30 min and strabismus surgery. In the presence of a single risk factor, the PONV risk is 11.6%, but when three risk factors coexist, this rate rises to 42.3% [13]. In addition to drug applications such as dexamethasone and 5-HT3 antagonists, the risk of PONV can be reduced by avoiding volatile anesthetics, reducing postoperative opioids, and using regional methods [14]. In our study, no difference was found between PONV rates between the group receiving ondansetron and the control group. In addition, lower nausea and vomiting rates were observed compared to the rates reported in the literature. This is due to the short duration of the surgery, the use of caudal block and volatile anesthetics with low MAC and the lack of postoperative opioid analgesic requirement.

This study has some limitations. While studies on the effects of ondansetron on spinal anesthesia in adults have been carried out on sensory block duration and motor block duration, our study was evaluated only analgesic duration due to pediatric age group. In addition, patients were given a standard prophylactic dose of 0.1 mg/kg of ondansetron, which could be administered one night before an additive dose or another dose comparison can be studied in another study.

Conclusion

In conclusion, we conclude that iv ondansetron given at 0.1 mg/kg dose before caudal block with bupivacaine can be used safely without a significant effect on the duration of block-induced analgesia.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

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