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The minimum effective intravenous dose of ondansetron for prevention of postoperative nausea and vomiting after adenotonsillectomy in dexamethasone pretreated children

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Abstract

Postoperative nausea and vomiting (PONV) remains a distressing and common problem after tonsillectomy with an incidence ranging from 40-73% in those who did not receive prophylactic antiemetic. This study was done to identify the minimum effective IV dose of ondansetron to decrease the incidence and severity of PONV in the dexamethasone (150ug/kg) pretreated children undergoing adenotonsillectomy. In this prospective, randomized, double-blinded, placebo-controlled study, 150 children (3-12 years old) received dexamethasone 150μg/kg IV (maximum 8mg) premedication were randomly assigned to receive either placebo (saline) or ondansetron in a dose of 25, 50, 75 or 150μg/kg IV immediately after induction of anesthesia. All children received standardized perioperative care, including surgical and anesthetic techniques, IV fluid, postoperative analgesic and rescue antiemetic (RAE). The incidence and severity of PONV were recorded in a standardized fashion at the intervals 0-2, 2-12 and 12-24h postoperatively. The time to first postoperative analgesic, total analgesic consumptions, the need for rescue antiemetic (RAE), the fast tracking time (FTT), the time to first oral intake and parent's satisfaction score were recorded as clinically true outcome measures. The five treatment groups were similar with respect to patients's characteristics and operative data. There was no significant difference with respect to the incidence ($P>0.05$) or severity ($P>0.05$) of PONV between the placebo and 25μg/kg ondansetron group during the study period (0-24h). The incidence of early (0-2h), delayed (2-12h), and late (12-24) PONV were significantly less in the 50 ($P<0.05$), 75 ($P<0.05$) and 150 ($P<0.05$) μg/kg ondansetron groups compared with placebo. The incidence of 24h PONV was 43, 37, 13, 10 and 7% in placebo, 25, 50, 75 and 150μg/kg ondansetron groups, respectively. The PONV severity scores (0-3) were significantly less ($p<0.05$) in children who received ondansetron in a dose of 50μg/kg or more compared with the placebo. There was no statistically significant difference with respect to the incidence ($P>0.05$) or the severity ($P>0.05$) of PONV between the 50, 75 and 150μg/kg ondansetron groups. The time to first postoperative analgesic, the total postoperative analgesic consumptions, the need for RAE, the time to first oral intake and the fast tracking time (FTT) were significantly less ($P<0.05$) in children who received 50, 75 and 150 μg/kg ondansetron in comparison with placebo. The parent's satisfaction scores were significantly high ($P<0.05$) for those children who received ondansetron in a doses of 50μg/kg or more compared with placebo. There was no significant difference with respect to the clinically true outcome measures in children who received ondansetron in dose of 50μg/kg or more. In conclusion, ondansetron 50μg/kg IV was the minimum effective IV dose to decrease the incidence and severity of PONV in dexamethasone (150μg/kg IV) pretreated children undergoing adenotonsillectomy. This dose was associated with a significant reduction in the time to first postoperative analgesic, total analgesic consumptions, the need for rescue antiemetic (RAE), the time to first oral intake, the fast tracking time (FTT) and a high parent's satisfaction scores. Increasing the dose of ondansetron to 150μg/kg provided no significant benefits in reducing the incidence or severity of PONV in dexamethasone (150μg/kg IV) pretreated children undergoing adenotonsillectomy.

Introduction

Tonsillectomy with or without adenoidectomy is one of the most frequently performed surgical procedure in children and is associated with an incidence of postoperative nausea and vomiting (PONV) ranging between 40-73%. Thus, prophylactic antiemetic therapy is highly indicated in this high risk group of children [1].

Dexamethasone has been reported to be an effective, low cost and long lasting prophylactic antiemetic for prevention of PONV in children undergoing ambulatory adenotonsillectomy [2-5]. Also, it has combined analgesic and anti-inflammatory effects that may decrease postoperative edema and subsequently may improve oral intake after adenotonsillectomy [6, 7].

Previous studies on ondansetron antiemetic potential in children have produced conflict results [8-13]. Different single IV doses of ondansetron have been used to decrease the incidence of PONV in children undergoing tonsillectomy [8-12]. The combination of dexamethasone with ondansetron is likely to be the most effective prophylactic antiemetic intervention currently available for the control of PONV after tonsillectomy [13].The dose effectiveeness of intravenous ondansetron when used as a prophylactic antiemetic for prevention of PONV in dexamethasone pretreated children undergoing tonsillectomy is not well defined. Moreover, a number of studies and meta-analysis that evaluated the effects of ondansetron on PONV reported non-clinically true outcome measures, such as the incidence of PONV and the number of emetic episodes per patient, rather than more clinically important true outcome measures, such or fast tracking time (FTT), parent's satisfaction score and hospital readmission [14].

The aim of this study was to evaluate the effects of four different single IV doses of ondansetron (25, 50, 75 and 150μg/kg) on the incidence and severity of PONV in dexamethasone (150μg/kglV) pretreated children scheduled for electro-dissection adenotonsillectomy under general anesthesia. The second objective was to specify the safety and clinical effectiveness of these 4 different doses with clinically true outcome measures such as the time to first postoperative analgesic, total analgesic consumptions, the need for rescue antiemetic (RAE), the time to first oral intake, the fast tracking time (FTT)), and parent's satisfaction scores.

Patients and Methods

After obtaining hospital review board approval and written informed parent consent, 150 children, 3-12 yr of age, American Society of Anesthesiologist (ASA) physical status I or II, scheduled for adenotonsillectomy were enrolled in this prospective, randomized, double-blinded, placebo-controlled study. Children who had received antiemetics, antihistaminics, steroids or psychoactive drugs within 24 h of surgery were excluded. Children with a history of an adverse drug reaction to any of the medications used in the anesthetic management outlined below were not eligible to participate in this study. Children did not consume milk or solid food for at least 6h before operation; clear fluids were allowed until 3h before induction.

Children were not premedicated. Intravenous (IV) line was established and all children received fentanyl 1μg/kg IV and dexamethasone 150μg/kg IV (maximum dose 8mg). Anesthesia was induced with sevoflurane 8% end-inspired concentration and 50% nitrous oxide in oxygen via a face mask. Patients >8yr of age had IV induction with propofol 2mg/kg. After induction of anesthesia, patients were randomly assigned to 5 equal groups (30 patients each) by a computer-generated random number-table to receive a single IV dose of either saline (placebo) or ondansetron 25, 50, 75 or 150μg/kg. The study medications were prepared, by an anesthesiologist who was not involved in any subsequent assessment to a fixed volume of 2ml in identical syringes

(ondansetron and saline were indistinguishable in appearance) to maintain the double-blind nature of the study. Tracheal intubation was facilitated by mivacurium (0.3mg/kg). Anesthesia was maintained with sevoflurane 1-5% end-inspired concentrations (adjusted to maintain heart rate and blood pressure within 20% of the baseline value) and 50% nitrous oxide in oxygen. Ventilation was mechanically controlled and adjusted to maintain end-tidal CO_2 value between 30-35 mmHg throughout the surgery. Intraoperotive IV fluid compromised lactated Ringer's solution, replacing half of the fluid deficit plus maintenance fluid. Neuromuscular block was maintained with supplemental mivacurium as clinically indicated. All children received paracet-amol 30mg/kg rectally approximately 10 min before the end of surgery and repeated every 6hrs for the first 24h postoperatively. Residual neuromuscular blockade was allowed to recover spontaneously in all patients, without pharmacological reverse of the muscle relaxant. Children were tracheally extubated when they had demonstrated satisfactory motor power and wakefulness. After operation, all children were transferred to the postanesthesia care unit (PACU) where standard monitoring was established and children were observed for a period of at least 2h.

In the PACU, management of IV fluid, postoperative pain and PONV were standardized. Postoperative IV fluid compromised lactated Ringer's solution, replac-ing the remaining of the fluid deficit plus maintenance fluids. Postoperative analgesia (fentanyl 0.5μg/kg IV) bolus doses were provided if old children reported pain or if young children cried. The time to first dose of fentanyl and the total fentanyl consumptions were recorded. Metoclopramide 150μg/kg IV was given as rescue antiemetic (RAE) when the child experienced more than 15 min of nausea, or two emetic episodes. If PONV persisted for 20 minutes after administration of metoclopramide, a second rescue antiemetic consisting of IV droperidol 0.015 mg/kg (minimum, 0.65m; maximum 1.25mg) was administered. The total number of children who requested for RAE was recorded. Oral fluids were offered and encouraged by the nursing staff during the recovery period to the children. The time to first oral intake and the quality of swallowing were also recorded.

All incidences of PONV in the first 24 postoperative hours at the intervals of 0-2h (early PONV), 2-12h (delayed PONV), and 12-24h (late PONV) were recorded. The severity of PONV over the first 24 postoperative hours was assessed using the numeric scoring system for PONV[(14)] (0=no nausea or vomiting 1= nausea but no vomiting, 2=vomiting once 3 = two or more episodes of vomiting).The incidence and severity of PONV were recorded in PACU (0-2h) by the anesthesiologist who provided the intraoperative care and by a trained anesthesia nurse in the surgical ward (2-24h).

Nausea was defined as a subjective feeling of the urge to vomit. Vomiting was defined as the forceful expulsion of gastric contents through the mouth. Vomiting and retching were grouped together under common term “emetic episodes”. Episodes of vomiting occurring less than five min. apart were considered one episode. If there were more than 4 episodes of emesis within the 24h observation period, the emesis was considered severe. Those children, who had severe PONV (score 3) in the first 2 post-operative hours of their PACU stay, were observed in the PACU until they remained PONV free for 1h.

The time to achieve eligibility for discharge from PACU to the ward (fast tracking time) (FTT) was calculated as the time from the discontinuation of sevoflurane to the time at which the child had a patent airway without assistant, stable vital signs, mild or no PONV, adequate pain control and Aldrete recovery score 9 (score of 0-10: 0, 1 and 2 to activity, respiration, circulation, color and consciousness with score of 9 indicating eligibility for transfer from PACU) [15].

Finally, at the end of the 24h observation period, the primary caretaker was asked to give a global assessment of

the entire postoperative experience of the child (parent's satisfaction score) using an 11-point verbal numeric scoring system (0=not at all satisfied, 10=full satisfied). The details of any adverse effects through the study period (0-24h) such as headache, constipation, or drowsiness were also recorded.

Statistical Analysis

The previous reported incidence of PONV after adenotonsillectomy in children was ranging between 40% and 73% [(1)]. Sample size was determined assuming that the acceptable difference in vomiting is 20%. The alpha error was set at 0.05, and type II error was set as 0.20. Therefore, this study was targeted for a sample size of 150 patients (30 in each group). Data were analyzed using one-way analysis of variance with a linear contrast, X test. Severity of PONV between the ondansetron 25, 50, 75, and 150μg/kg groups and the placebo group was compared by chi-square analysis and the Fisher exact test with a Yates' correction as appropriate. Data were presented as the mean ± SD or number and percentage. P value < 0.05 was considered statistically significant.

Results

Patient characteristics and operative data such as patient age, gender, weight, ASA physical status, duration of surgery, anesthesia and recovery times, perioperative fluid and number of children induced with propofol were similar among three groups (table 1).

Table (2) represented the incidence of PONV in the first 24 postoperative hours at the intervals of 0-2h (early PONV), 2-12h (delayed PONV), and 12- 24h (late PONV). There was no significant difference (P>0.05) between the placebo and the 25μg ondansetron group with respect to the incidence of PONV at the entire study period. A reduction in the incidence of early (0-2h), delayed (2-12h) and late (12-24h) PONV were observed in the 50 (P<0.05), 75 (P<0.05) and 150μg/kg (P<0.05) ondansetron groups compared with placebo. No significant difference (P>0.05) was recorded as regard to the incidence of PONV between the ondansetron 50, 75 and 150μg/kg groups at all time intervals.

Table (3) represented the PONV severity scores (0-3) in the entire study period (0-24h). The episodes of vomiting per child were ranging from 0-5. There was no significant difference (P>0.05) between the placebo and the 25μg ondansetron group with respect to PONV severity scores at the entire study period. All PONV severity scores were significant less (p<0.05) in children who had received ondansetron in dose of 50μg/kg or more compared with the placebo group. There were no significant differences (P>0.05) with respect to PONV severity scores between the 50μg, 75 and 150μg ondansetron groups.

Table (4) represented the clinically true outcome measures in the entire study period (0-24h). There was no significant difference in the clinically true outcome measures between children who received 25/μg/kg ondansetron or placebo. The time to first fentanyl analgesic, the total fentanyl consumptions, number of children requested for RAE, the time to first oral intake and the PACU stay (FTT) were significantly less in children who received 50 (P<0.05), 75 (P<0.05) or150 (P<0.05) μg/kg ondansetron in comparison with placebo. The parent's satisfaction scores were significantly higher (P<0.05) for those children who received ondansetron in a doses of 50μg/kg or more compared with the placebo. There was no significant difference in the clinically true outcome measures between children who received 50, 75 or150/μg/kg ondansetron.

Children who received ondansetron in a doses of 50μg/kg or more had statistically significant (p<0.05) more incidence of drowsiness (table 5).

Table (1): Patients demographic and Operative Data

Demographic and Operative Data	Placebo Group	Ondansetron Groups			
		25μg/kg	50μg/kg	75μg/kg	150μg/kg
No. of patients	30	30	30	30	30
Age (yr)	6.8±2.8	6.6±2.9	6.6±3.1	6.1±3.4	6.2±3.4
Gender (M/F)	15/15	16/14	13/17	14/16	14/16
Weight (kg)	19.4±8.0	20.5±8.7	19.5±7.6	19.3±10.0	20.6±10.2
ASA status I or II	28/2	27/3	30/0	28/2	29/1
Duration of anesthesia (min)	45.8±14.6	48.4±13/3	47.4±12.1	46.2±14.2	48.4±13.4
Duration of surgery (min)	30.0±12.7	32.4±13.4	33.0±14.4	31.0±13.0	33.4±14.0
Recovery time (min)	8.7±14.7	10.3±15.3	9.7±11.3	9.4±10.1	8.2±9.4
Perioperative IV fluid(ml/kg)	17.1±5.5	18.8±5.9	16.8±5.7	15.4±6.7	16.1±6.6
Children induced with propofol (N0.)	7	5	6	6	7

Age, weight, ASA physical status, anesthetic, surgical and recovery times, perioperative IV fluid were presented as the mean ± SD. ASA physical status, gender and propofol inductions, were presented as the number of children. The demographic and operative data were comparable in all groups ($p>0.05$).

Table (2): Incidence of PONV: Number of Patients (%)

Incidence of PONV (0-24h)	Placebo Gr. (n=30)	Ondansetron Groups			
		25(μg/kg) (n=30)	50(μg/kg) (n=30)	75(μg/kg) (n=30)	150(μg/kg) (n=30)
0-2h (early PONV)	7 (23.33)	6 (20.00)	4 (13.33)*	3 (10.00)*	2 (6.66)*
2-12h (delayed PONV)	8 (26.66)	6 (20.00)	3 (10.0) *	2 (6.66) *	3 (10.00)*
12-24h (late PONV)	7 (23.33)	6 (20.00)	3 (10.00)*	3 (10.00)*	2 (6.66)*
0-24h (24h PONV)	13 (43.33)	11 (36.66)	4 (13.33)*	3 (10.00)*	2 (6.66)*

The values were presented as the number of children (%)

There was no significant difference ($P>0.05$) between the placebo and the 25μg ondansetron group with respect to the incidence of PONV at the entire study period (0-24). A reduction in the incidence of early (0-2h), delayed (2-12h) and late (12-24h) PONV were observed in the 50 ($P<0.05$), 75 ($P<0.05$) and 150μg/kg ($P<0.05$) ondansetron groups compared with placebo group. No significant difference ($P>0.05$) was recorded as regard to the incidence of PONV between the ondansetron 50, 75 and 150μg/kg groups at all time intervals.

PONV (postoperative nausea and vomiting)

* = $P<0.05$

Table (3): PONV severity score during the study period (0-24h)

PONV severity score (0-3)	Placebo Gr. (n=30)	Ondansetron Groups			
		25(µg/kg) (n=30)	50(µg/kg) (n=30)	75(µg/kg) (n=30)	150(µg/kg) (n=30)
0 (no)	16 (53.33)	14 (46.66)	25 (83.33)*	26 (86.66)*	24 (80.00)*
1 (mild)	5 (16.66)	6 (20.00)	1 (3.33)*	2 (6.66)*	1 (3.33)*
2 (moderate)	4 (13.33)	3 (10.00)	2 (6.66)*	0 (0.00)*	2 (6.66)*
3 (severe)	7 (23.33)	5 (16.66)	1 (3.33)*	1 (3.33)*	2 (6.66)*

The values were presented as the number of children (%)

The episodes of vomiting per child were ranging from 0-5. There was no significant difference (P>0.05) between the placebo and the 25µg ondansetron group with respect to PONV severity scores at the entire study period. All PONV severity scores were significantly less (p<0.05) in children who had received ondansetron in dose of 50µg/kg or more compared with the placebo group. There were no significant differences (P>0.05) with respect to PONV severity scores between the 50µg, 75 and 150µg ondansetron groups.

The numeric scoring system for PONV [14] (**0** = no nausea or vomiting **1** = nausea but no vomiting, **2** = vomiting once **3** = two or more episodes of vomiting)**.**

PONV (postoperative nausea and vomiting).

* = P<0.05

Table (4): The clinically true outcome measurements (0-24h)

	Placebo	Ondansetron group			
		25µg/kg	50µg/kg	75µg/kg	150µg/kg
Time to first dose of fentanyl (min)	11 ± 2	13 ± 3	23 ± 1*	21 ± 4*	22 ± 2*
Total consumed fentanyl (mg) in the PACU	51 ± 7	56 ± 6	25 ± 9*	28 ± 4*	27 ± 8*
Number of children requested for RAE (No.)	16	14	6*	7*	5*
Time to first oral intake (min)	360 ± 70	390 ± 45	183 ± 27*	185 ± 41*	184 ± 36*
PACU stay (FTT) min	154 ± 23	157 ± 36	128 ± 12*	127 ± 12*	122 ± 14*
Children with good to excellent oral intake (%)	45	56	81*	86*	84*
Parent's satisfaction score (0-10)	5.7 ± 1.6	5.8 ± 1.5	8.7 ± 1.3*	8.9 ± 1.6*	8.1 ± 1.2*

Values were expressed as Mean ± SD, number or %

The time to first postoperative fentanyl analgesia, the total postoperative fentanyl consumptions, number of children who requested for RAE, the time to first oral intake and PACU stay (FTT) were significantly less (P<0.05) in children who received 50, 75 or 150 µg/kg ondansetron in comparison with placebo. The parent's satisfaction scores were significantly higher (P<0.05) for those children who received ondansetron in a doses of 50µg/kg or more compared with the placebo. There was no significant difference between children who received 50, 75 or150/µg/kg ondansetron with respect to the clinically true outcome measures.

PONV = Postoperative nausea and vomiting.

RAE = Rescue antiemetics.

*P<0.05

Table (5): Side effects during the study period (0-24h)

SIDE EFFECTS	Placebo Group	Ondansetron Groups			
		25mg/kg	50mg/kg	75mg/kg	150mg/kg
		(n=30)	(n=30)	(n=30)	(n=30)
Headache	2	2	1	2	2
Constipation	0	0	1	1	2
Drowsiness	1	0	0	3*	4*

Values were presented as number of patients

Children who received ondansetron in a doses of 75μg/kg or more had statistically significant ($p<0.05$) more incidence of drowsiness in comparison to placebo.

* = $P<0.05$

Discussion

The present study demonstrated that ondansetron 50μg/kg IV is the minimum effective IV dose to decrease the incidence and severity of PONV in dexamethasone (150μg/kg IV) pretreated children undergoing adenotonsillectomy. This dose was associated with reduction of post-adenotonsillectomy PONV from 43% to 13% in dexamethasone (150μg/kg IV) pretreated children. This dose was also associated with a significant reduction in the time to first postoperative analgesic, total analgesic consumptions, the need for rescue antiemetic (RAE), the time to first oral intake, the fast tracking time (FTT) and with high parent's satisfaction scores. Increasing the dose of ondansetron to 150μg/kg provided no significant benefits in reducing the incidence or severity of PONV after adenotonsillectomy in dexamethasone (150μg/kg IV) pretreated children.

Postoperative nausea and vomiting (PONV) not only causes distress to the patient, tension on sutures, and potential bleeding at the operative site, but also may lead to delayed discharge from ambulatory surgical centers, fluid and electrolyte imbalance, and unanticipated hospital admission[16]. Although much attention has been paid to the prevention of PONV during the last decade, the optimal antiemetic regimen for children in the surgical setting has still not been established [1]. PONV after adenotonsillectomy in children is a complex and multifactorial, such as patient characteristics, operative procedure, anesthetic technique, postoperative pain and perioperative fluid therapy. In the current study, the groups were comparable with respect to patient characteristics, surgical procedure, anesthetic technique, and perioperative analgesics and intravenous fluid. Therefore, the differences in the incidence and severity of PONV and the clinically true outcome measures among the groups in this study can be attributed only to the difference in the dose of ondansetron administered. The four ondansetron doses selected for this study cover the range of preemptive IV ondansetron doses (25-150μg/kg) that have been evaluated in pediatric surgical sitting [8-14]. In this study, high dose of ondansetron (150μg/kg) was selected because it has been shown that, this dose effectively reduced post tonsillectomy vomiting [8, 9].Lowe dose ondansetron 25μg/kg was selected because there was evidences that this dose may have antiemetic efficacy in pediatric ambulatory surgery [14].

Several studies have substantiated the efficacy of various antiemetic agents in the treatment of post-tonsillectomy vomiting. Ferrari and Donlon [17] reduced the incidence of vomiting from 70% to 47% by using

0.15mg.kg^{-1} metoclopramide. Stene and his colleagues [18] demonstrated less dramatic results, with higher dose of metoclopramide (0.25mg.kg$^{-1)}$ and reported incidences of vomiting 54% in their treatment group and 69% in the control group. Sten[18] and his colleagues also investigated the ondansetron in preventing post-tonsillectomy emesis and reported PONV incidence of 26%. In another study, Litman and his colleagues [19] demonstrated that 0.15mg.kg^{-1} ondansetron reduced the incidence of vomiting from 73% to 23%. Similar results were obtained by Furst and Rodarte [20] who reported a decrease in post-tonsillectomy vomiting from 62% to 27%. In each of these studies, the primary anesthetic agent was either halothane or isoflurane. These studies differed in several aspects: exclusion of patients with a history of motion sickness, use of non-depolarizing muscle relaxants, different opioid analgesic regimens and whether the patient's stomachs were emptied at the conclusion of the procedure. Interestingly, despite the differences in the experimental protocols these studies had similar incidences of vomiting in their control and treatment groups.

The present study demonstrated a decrease in 24h post-tonsillectomy PONV from 43% to 13% by utilizing ondansetron 50μg/kg IV in dexamethasone (150μg/kg IV) pretreated children. Splinter and Rhine[13] demonstrated a 30% incidence of PONV in patients who received ondansetron 50μg/kg IV plus 150μg/kg dexamethasone. In Wtacha study[9], the incidence of pre-discharged emesis in 50μg/kg ondansetron group was relatively higher (19%) than in this study (13%). That study [9] demonstrated that, ondansetron as a sole prophylactic antiemetic in a dose of 50μg/kg was more effective than either placebo or 10μg/kg but not less effective than 100μg/kg dose for control of PONV in a heterogeneous pediatric population. In that study, the effectiveness of 75 and 150μg/kg ondansetron were not studied. Studies of blood levels after intravenous administration of ondansetron in healthy children during anesthesia have shown that a theoretical intravenous dose of 50μg/kg ondansetron in a child will provide a similar area under the plasma concentration-time curve as a dose of 4mg which is the minimally effective antiemetic dose in adults [21].

In the present study, the incidence of 24h PONV in the placebo group (Dexamethasone pre-treated children) was 43%. This incidence was in keeping with the result of Henzi and his colleagues [1]. Several factors may have contributed to the low incidence of PONV observed in the placebo group of the present study. First is the preemptive use of dexamethasone, Second, the use of mivacuronium might have reduced the PONV in this study by allowing spontaneous recovery from the neuromuscular block without reversal of neuromuscular blockade with less incidence of PONV. Third, may be the propofol-based induction of anesthesia in older children. Barst and his colleagues [22] reported a decreased from 55% to 21% in post-tonsillectomy vomiting by utilizing a propofol-based anesthetic instead of gaseous agent and without utilizing antiemetic agents.

In the present study, the time to first postoperative analgesic, total analgesics consumptions, the need for rescue antiemetic (RAE), the fast tracking time (FTT), the time to first oral intake and parent's satisfaction score were recorded as clinically true outcome measures. These true clinical outcome measures were found to be significantly better in children who received 50μg/kg ondansetron or more compared with those children who received placebo or 25μg/kg ondansetron. Moreover, dexamethasone premedication was associated with improved oral intake after surgery. The unexpected readmissions to the hospital due to PONV as another clinically true outcome measure could not be assessed in this study because all of our patients were observed in the hospital for 24h postoperatively.

Cost is increasingly a focus in health care[23]. In the present study, 50μg/kg ondansetron dose not only have the same efficacy of the higher doses on decreasing

the incidence and severity of PONV, but it is less costly than the higher doses (75and150μg/kg). In addition, the low dose (50μg/kg) ondansetron was associated with lower nursing costs because of markedly less incidence of PONV, short FTT and less need for RAE.

In **Conclusion**, ondansetron 50μg/kg IV is the minimum effective IV dose to decrease the incidence and severity of PONV in dexamethasone (150μg/kg IV) pretreated children undergoing adenotonsillectomy. This dose is associated with a significant reduction in the time to first postoperative analgesic, total analgesic consumptions, the need for rescue antiemetic (RAE), the time to first oral intake, the fast tracking time (FTT) and a higher parent's satisfaction scores. Increasing the dose of ondansetron to 150μg/kg provides no significant benefits in reducing the incidence or severity of PONV after adenotonsillectomy.

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تحديد أقل جرعة وريدية مؤثرة من عقار الأوندانسترون لمنع القيء والغثيان بعد عملية استئصال اللوزتين واللحمية في الأطفال السابق تحضريهم قبل الجراحة بعقار الديكساميثازون

يظل القيء والغثيان بعد عملية استئصال اللوزتين مشكلة شائعة الحدوث بمعدل يصل إلى 40-73% في الأطفال الذين لم يحضورا بعقارات مانعة للقيء في فترة ما قبل الجراحة. وقد تمت هذه الدراسة لتحديد أقل جرعة مؤثرة من عقار الأوندانسترون لمنع القيء والغثيان بعد عملية استئصال اللوزتين واللحمية في الأطفال السابق تحضريهم قبل الجراحة بعقار الديكساميثازون بمعدل 150 ميكروجرام /كجم.

في هذه الدراسة المستخدم بها الطريقة العمياء المزدوجة مع وجود مجموعة ضابطة (بلاسيبو) وزع 150 طفلا تتراوح أعمارهم بين 3- 12 سنة وتم حقنهم بعقار الديكساميثازون بجرعة 150 ميكروجرام /كجم (وبحد أقصى 8 مجم) توزيعاً عشوائيا إلى 5 مجموعات في فترة التحضير للجراحة.(30 طفل لكل مجموعة) بعد بدء التخدير الكلي بغاز السيفوفلورين 8% أو بعقار البروبفول 2 مجم/كجم. في أطفال المجموعة الضابطة (البلاسيبو) تم حقن الأطفال بجرعة 2 مل من محلول ملحي. أما أطفال المجموعات الأربعة الباقية فقد تم حقنهم وريدا بجرعة 2 مل تحتوى على 25،50، 75 أو 150ميكروجرام /كجم من عقار الأوندانسترون.

وتم مطابقة القياسات الجراحية والتخديرية والسوائل الوريدية ومسكنات الألم بعد الجراحة وكذلك مضادات التقيء والغثيان في الفترات من صفر-2 ساعة ، 2-12 ساعة و12-24ساعة في فترة ما بعد الجراحة ـ كما تم قياس وقت أول طلب للطفل لمسكنات ألم ما بعد الجراحة وكذلك الكمية الكلية المستهلكة لمخدر الألم ما بعد الجراحة خلال فترة الدراسة (24ساعة). وكذلك تم حساب نسبة الاحتياج إلى أدوية منع القيء وفترة بقاء الطفل في وحدة العناية بعد التخدير ووقت أول تناول للطفل للسوائل عن طريق الفم. وفي نهاية الدراسة تم قياس مدي رضاء الأباء عن الدواء المستخدم في المعالجة التخديرية كما سجل أي مضاعفات للدواء.

وقد أثبت نتائج البحث عدم وجود أي فروق ذات دلالة إحصائية بين المجموعة الضابطة (البلاسيبو) ومجموعة 25 ميكروجرام أوندانسترون بالنسبة لمعدل وشدة حدوث قيء وغثيان ما بعد الجراحة خلال فترة الدراسة (24 ساعة).

وكان معدل حدوث قيء وغثيان ما بعد الجراحة أقل إحصائيا من المجموعة الضابطة في مجموعات الأوندانسترون 50، 75، 150 ميكروجرام / كجم خلال جميع فترات الدراسة. وكان المعدل الكلي لحدوث القيء خلال فترة الدراسة (24ساعة) 43% ، 37% ، 13% ، 10% ، 7% في المجموعات :الضابطة، 25 ، 50، 75 و 150 ميكروجرام /كجم أندوانسترون على الترتيب. وكان مقياس شدة قيء وغثيان ما بعد الجراحة أقل من المجموعة الضابطة في الأطفال الذين حقنوا بكمية من الأوندانسترون أكثر من 50 ميكروجرام /كجم. ولم يسجل أي اختلاف ذو دلالة إحصائية بالنسبة لمعدل وشدة

قيء وغثيان ما بعد لجراحة بين الأطفال الذين تناولا جرعات أكثر من 50 ميكرو جرام / كجم من الأوندانسترون .

وسجل انخفاض احتياج الأطفال إلى مسكنات الألم ومضادات التقيء في فترة ما بعد الجراحة في الأطفال الذين تناولوا جرعات أكثر من 50 ميكروجرام/جم كما قصرت فترة بقاء هؤلاء الأطفال في وحدة العناية بعد التخدير وكان تناولهم للسوائل بعد الجراحة أسرع من الأطفال الذين تناولوا محلول الملح أو الأندانسترون بجرعة أقل من 50 ميكروجرام /كجم. كما سجل أباء هؤلاء الأطفال مقاييس أعلى بالنسبة لرضاهم عن المعالجة التخديرية وسلوك أبنائهم في فترة الدراسة (24ساعة). ولم يكن هناك أي فروق ذات دلالة إحصائية في كل القياسات السابقة بين مجموعات 50 ، 75 ، 150 ميكروجرام /كجم أندوانسترون.

وتستنتج هذه الدراسة أن 50ميكروجرام / كجم من عقار الأندوانسترون هل أقل جرعة وريدية يمكن حقنها للأطفال المحضرين قبل الجراحة بعقار الديكساميثازون بجرعة (150 ميكروجرام /كجم) لمنع حدوث قيء وغثيان ما بعد جراحة إزالة اللوزتين واللحمية.