An-Najah National University

Faculty of Graduate Studies

ONDANSETRON VERSUS KETOROLAC WITH ONDANSETRON FOR THE PROPHYLAXIS OF POSTOPERATIVE NAUSEA AND VOMITING IN PEDIATRIC PATIENTS UNDERGOING STRABISMUS SURGERY

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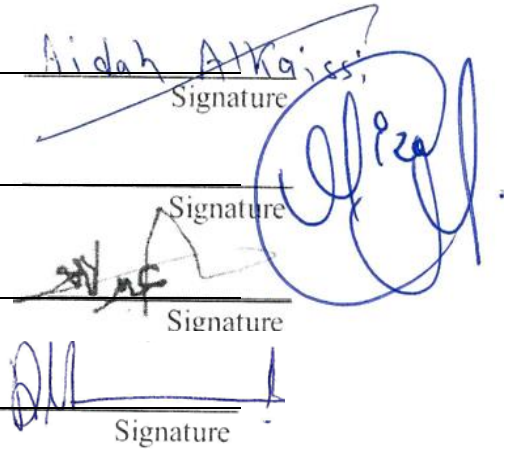

Dedication

I would like to express my sincere gratitude to my parents, wife, children, relatives, and friends for their unwavering support and unceasing encouragement during my years of study and for their assistance with the research and writing of this thesis. Without them, this achievement would not have been feasible. Thank you very much.

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Declaration

I, the undersigned, declare that I submitted the thesis entitled:

ONDANSETRON VERSUS KETOROLAC WITH ONDANSETRON FOR THE PROPHYLAXIS OF POSTOPERATIVE NAUSEA AND VOMITING IN PEDIATRIC PATIENTS UNDERGOING STRABISMUS SURGERY

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

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Signature: _____

Date: 27/05/2024

List of Contents

List of Tables

List of Figures

List of Appendices

ONDANSETRON VERSUS KETOROLAC WITH ONDANSETRON FOR THE PROPHYLAXIS OF POSTOPERATIVE NAUSEA AND VOMITING IN PEDIATRIC PATIENTS UNDERGOING STRABISMUS SURGERY

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Abstract

Background: Nausea and vomiting after strabismus surgery are frequent side effects that can cause electrolyte imbalance, dehydration, sub-conjunctival hemorrhage, and problems with surgical attachment. These ailments may necessitate re-admission, lengthen post-anesthesia care, and increase hospital stays and expenses.

Aims: Evaluating the effects of Ondansetron by itself versus Ondansetron plus Ketorolac on pain thresholds, the frequency of postoperative nausea and vomiting, and the consequent requirement for rescue antiemetic and analgesic drugs in pediatric strabismus patients.

Methods: Seventy pediatric patients (ASA I and II, ages 3 to 12) were split into two groups for elective strabismus surgery under general anesthesia: 40 for Ondansetron and 30 for Ondansetron plus Ketorolac. Postoperative nausea, vomiting, pain, and need for rescue medication were assessed from 30 minutes to 8 hours.

Results: Results from the PACU showed that the Ondansetron group (n=13, 32.5%) had a substantially higher incidence of surgical site pain than the combined Ondansetron and Ketorolac group (n=3, 10%; p= 0.042). Nevertheless, there were no significant variations between the two groups in terms of postoperative nausea, vomiting, retching, or the need for rescue drugs.

In the pediatric ward, all of the complications are significantly lower in prevalence in the combined group compared to the ondansetron group, including vomiting (0.0% vs 22.5%), p-value = 0.008), nausea (6.7% vs 32.5%, p-value = 0.017), retching (0.0% vs 22.5%, p-value = 0.008), surgical site pain (13.3% vs 42.5%, p-value = 0.009), use of

analgesics (6.7% vs 35.0%, p-value = 0.008) and rescue antiemetic (0.0% vs 27.5%, p-value = 0.002), respectively.

In 8 hours postoperatively, there is a significantly lower incidence in the combined group compared to the ondansetron group in terms of nausea (0.0% vs 10%, p-value = 0.013), retching (0.0% vs 10%, p-value = 0.013), and the use of rescue medications (0.0% vs 10%, p-value = 0.013), while no significant differences in the Incidence of vomiting (0.0% vs 7.5%, p-value = 0.125) and use of analgesics (3.3% vs 10%, p-value = 0.284), respectively.

Conclusion: Ketorolac, administered as an adjuvant to Ondansetron in pediatric strabismus patients, has been shown to reduce pain and the subsequent need for analgesics and rescue antiemetic drugs, as well as postoperative nausea and vomiting.

Keywords: Ketorolac; Ondansetron; strabismus surgery; Postoperative Nausea; Vomiting; Pain; Rescue medications.

Chapter One

Introduction and Theoretical Background

1.1 Introduction

The exploration of nausea and vomiting spans a rich and storied tradition in research, dating back through generations of medical inquiry. One major challenge facing pediatric anesthesiologists today is the prevention and management of postoperative nausea and vomiting (PONV) in children[1]. Although the physiology of emesis is now better understood, PONV is still a significant cause of morbidity, even with the advent of new anesthetics and antiemetic medications[2, 3]. The strategy for reducing this complication is multifaceted and consists of appropriate preoperative planning, a thoughtful strategy for intraoperative antiemetic prophylaxis, the selection of suitable anesthetic agents and techniques, and a well-defined postoperative care plan.

Antiemetics prevent or treat PONV by acting on many receptor sites. This is likely why several studies have shown that combining multiple antiemetic medications is typically more effective and causes fewer adverse effects than merely raising the dosage of a single antiemetic. A multimodal approach to PONV should not be restricted to medication therapy alone. Instead, it should include a comprehensive strategy that begins before surgery and continues during the procedure with risk reduction techniques, to which preventive antiemetics are added based on the patient's estimated risk for PONV.

Recent theoretical developments have revealed that strabismus surgeries are regarded as a distinct risk factor contributing to postoperative nausea and vomiting (PONV)[4]. The incidence of PONV after strabismus surgery ranges from 37% to 90% without administration of any prophylactic antiemetic drugs. [4]

The occurrence of PONV increases post-anesthesia care unit (PACU) stay time [5], increased health care costs, [6] also PONV can increase the risk of complications such as dehydration, electrolyte imbalance, sub-conjunctival hemorrhage, loosening of surgical attachments, increased hospitalization period, and maybe hospital re-admission. [7]

The mechanisms of frequent PONV after strabismus surgery include the oculo-emetic reflex, a vagally mediated reflex related to eye muscle manipulation, and a change in visual perception after the surgery. [7]

The factors contributing to PONV in pediatric patients vary from those in adult patients. [8]. The major risk factors for PONV in pediatric surgery include surgery type (e.g., strabismus surgery and tonsillectomy), age >3 years, duration of anesthesia >30 min, and a personal or first-degree relative history of PONV. [8].

Postoperative nausea and vomiting (PONV) frequently manifest as a prevalent and uncomfortable consequence following strabismus surgery [9]. Numerous studies have demonstrated the effectiveness of ondansetron, a 5HT3 antagonist, in alleviating PONV in children undergoing strabismus surgery. Most research in this patient population has focused on assessing the efficacy of ondansetron administered at the induction of anesthesia [10]. Pre-emptive inhibition of 5HT3 receptors before the arrival of emetic cues associated with ocular manipulation is thought to be more effective than later treatment[10].

Ondansetron, a 5-HT3 receptor antagonist, is commonly used to prevent PONV after strabismus surgery[11]. However, recent research suggests that Ketorolac, a nonsteroidal anti-inflammatory drug (NSAID), might offer additional benefits in reducing PONV. A study showed that the administration of Ketrolac has the same analgesic effects as pethidine but significantly decreases the incidence of PONV in the first 24 hours. [12]

The current study aimed to compare the effect of Ondansetron versus Ketorolac with Ondansetron on pain thresholds, the frequency of postoperative nausea and vomiting, and the consequent requirement for rescue antiemetic and analgesic drugs in pediatric strabismus patients.

1.2 Literature Review

Strabismus operations are considered to be an independent risk factor for postoperative nausea and vomiting (PONV). Previous research showed that the incidence of PONV after strabismus surgery ranges from 37% to 90% without administration of any prophylactic antiemetic drugs. [4]

In 1997, a double-blind, randomized, placebo-controlled trial was conducted to investigate the effectiveness of Ondansetron and metoclopramide in preventing postoperative vomiting after strabismus surgery in children. [13] The study enrolled 176 children slated for elective strabismus surgery, who were randomly allocated to one of three groups: normal saline placebo, Ondansetron 0.15 mg/kg, and metoclopramide 0.25 mg/kg given intravenously. At 24 hours, vomiting was observed in 43 of 60 children (71.7%) in the normal saline group, 22 of 64 children (34.4%) with (P<0.001) in the ondansetron group, and 32 of 52 children (61.4%) in the metoclopramide group. In addition, the incidence of postoperative vomiting was greater in children aged 9-12 years (64.4%) and 5-8 years (63%) compared to children aged 1-4 years (25%) in all three groups (P0.001). The frequency of postoperative vomiting was significantly reduced in the ondansetron group compared to the placebo group at all time intervals within 24 hours, while in the third group (metoclopramide), the frequency of emesis was significantly higher only from 6 to 24 hours after surgery when compared it with ondansetron group that no patient vomited at this interval.

An additional prospective literature source reveals that a randomized double-blinded study, conducted to explored the impact of ondansetron administration timing on antiemetic effectiveness in children undergoing elective strabismus surgery. [10] The study included 120 children aged from one to 15 years with ASA physical status I&II who had been scheduled for elective strabismus surgery. Children were divided into two groups; Group 1 received 100 µg/kg of Ondansetron at induction and normal saline at the end of the procedure, while Group 2 was given saline during induction and 100 µg/kg of Ondansetron after the procedure. Within 24 hours, vomiting was reported in 35% (21 out of 60) of patients in Group 1 and 33.3% (20 out of 60) in Group 2 (P=1.00). There was no notable disparity in vomiting occurrence between the two groups throughout the time intervals of (0-2h), (2-6h), and (6-24h). Also, both groups had an equal need for rescue antiemetics (P=0.7144). PONV prophylaxis after strabismus surgery has been proven highly effective with Ondansetron, a 5HT3 antagonist. The documented prevalence of PONV following ondansetron prophylaxis ranged from 6% to 20%.

In the study, 35 percent of people in Group 1 and 33.3 percent in Group 2 experienced emesis. This greater rate could be attributable to the institute's higher baseline rate of nausea and vomiting following strabismus surgery (70 to 80 percent), which might be associated with opioid pain relief medication. The greater prevalence of PONV could also be attributed to patients' 24-hour inpatient care, which allowed to better capture events that would otherwise be based on parent reports in centers doing this procedure on a day-stay basis. The findings of this study show that Ondansetron demonstrated comparable advantages in preventing PONV and reducing the necessity for antiemetic treatment, whether administered during anesthesia induction or post-strabismus surgery in pediatric patients.

In 1998, a study was conducted to investigate the effect of timing ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. [11] This study included 164 women having an ASA physical status grade I or II and who had been scheduled for outpatient laparoscopic surgeries. The participants were randomly assigned to one of four antiemetic therapy groups. Patients in Group A were given saline before induction and saline at the end of surgery, while those in Group B were given Ondansetron 2 mg before induction and Ondansetron 2 mg at the end of surgery. In comparison, participants in Group C received 4 mg of ondansetron before induction and saline at the conclusion of surgery, while those in Group D were administered saline before induction and received 4 mg of ondansetron at the end of surgery.

The findings indicate that both groups receiving a single IV dosage of 4 mg ondansetron experienced lower levels of nausea compared to the placebo group while inside the PACU. However, only when Ondansetron 4 mg IV was provided at the conclusion of the operation was the incidence of vomiting considerably reduced. Also, the requirement for rescue antiemetics in the PACU was similar in all four groups receiving treatment. The occurrence and intensity of PONV were notably diminished throughout the 24-hour follow-up period when Ondansetron 4 mg IV was administered at the conclusion of the surgery.

Additionally, the study discovered a notable decrease in the occurrence of nausea when 4 mg of ondansetron IV was administered at the conclusion of surgeries lasting more than 60 minutes. The incidence of non-emetic postoperative side effects did not differ

significantly across the four treatment groups. The quality of sleep, time taken off work by a caregiver, and time to return to work after release from the ambulatory surgery unit were not substantially different among the four groups. Compared to the placebo and ondansetron split-dose groups, the time to tolerating normal fluids and regular meals was considerably reduced when Ondansetron 4 mg IV was administered at the conclusion of the surgery.

Patient satisfaction levels varied significantly among the different groups, with a higher percentage of patients in the group receiving ondansetron at the conclusion of the surgery reporting high satisfaction compared to the placebo group. That administering ondansetron at the conclusion of the surgery demonstrated greater efficacy in preventing PONV and enhancin oth early and late recovery in women undergoing outpatient laparoscopy. Although PONV incidence was lowered, rescue antiemetic requirements were reduced, and the period from the conclusion of surgery until 25% of patients had PONV.

Another randomized, double-blind, placebo-controlled study conducted was designed to evaluate the relative efficacy of prophylactic Ondansetron 4 mg IV if given prior to general anesthesia induction or at the conclusion of surgery to an outpatient group at high risk of developing postoperative vomiting and nausea (PONV). [14] Seventy-five adult ASA physical status I and II patients ranging in age from 20 to 70 years were randomly allocated to one of three antiemetic drug groups after having ambulatory otolaryngologic procedures such as endoscopic sinus, middle ear, or mastoid surgeries. The participants were separated into three groups: Group I was given normal saline at the induction and saline at the conclusion of the surgery, Group II was given Ondansetron 4 mg at the induction and saline at the conclusion of the surge, and Group III was given saline at the induction and ondansetron 4 mg at the conclusion of the surgery.

The results show no significant differences in the incidence of postoperative nausea in the postoperative recovery room (Group I 80%, Group II 68%, and Group III 60%) even though fewer individuals in Group III suffered vomiting (4% versus 12% in Group I and 20% in Group II). Also, the study finds that when Ondansetron 4 mg IV was delivered at the end of the operation, it greatly reduced the requirement for rescue antiemetics in the PACU, but on the other hand, Ondansetron administered prior to anesthesia

induction did not decrease the requirement for rescue antiemetic drugs in the recovery room considerably.

Also, the study revealed that a higher proportion of female patients in Groups I and III required rescue antiemetics, and in Group III, a larger percentage of female patients experienced nausea compared to male patients (83% vs. 38%, $P < 0.05$). In all three treatment groups, female patients exhibited significantly higher rates of postoperative nausea (83% vs 58%, $P < 0.05$) and the need for rescue antiemetics (71% vs 35%, $P < 0.01$) in the postoperative recovery room compared to male patients.Finally, although time had no influence on the incidence of nausea or vomiting in outpatients undergoing otorhinolaryngologic surgery when Ondansetron was administered at the end of the procedure, the requirement for rescue antiemetics was considerably decreased.

Early and late vomiting are related to a very high incidence (>40 percent) of strabismus surgery. [15] Postoperative vision distortion, residual tension on the intraocular muscles [15], The possibility of an oculo-emetic reflex [15], postoperative pain [16], and the use of opioid analgesics [17] are all factors that contribute to the elevated incidence of PONV following strabismus surgery.

The chemoreceptor trigger zone is stimulated by eyeball movement, which triggers a centrally mediated trigeminovagal reaction in which numerous neurotransmitters are produced. Antiemetic treatment is based on blocking these neurotransmitter receptors. [18]

In several studies on PONV after strabismus surgery, antiemetics were administered prior to manipulating the eyeball, based on the hypothesis that preemptively blocking the oculo-emetic reflex would enhance their effectiveness. Droperidol administered at induction, according to studies by Smith et al. [19] and Jones et al. [20], reduced the incidence of PONV after strabismus surgery to a clinically tolerable level. [21] On the other hand, no effect of Droperidol timing on antiemetic efficacy was found.

In 1997, a study was conducted to look into the frequency of postoperative nausea and vomiting (PONV) and the oculo-cardiac reflex (OCR) in people after strabismus surgery. [22] Ninety-seven adult patients, ASA physical status I–III, ages 18 to 86, are scheduled for elective strabismus surgery. The patients were then randomly allocated to

one of the following groups: (A) induction with 5mg/kg thiopentone IV followed by maintenance with 1-1.5 percent isoflurane and a N20 in oxygen mixture (60:40%); (B) induction with 3-kg propofol IV followed by a continuous IV infusion of propofol (10–14 mg/kg/hr) and N20 in oxygen mixture (60:40%); (C) induction with 3mg/kg propofol IV followed by a continuous IV infusion of propofol (10–14 mg/kg/hr) and oxygen in air.

The findings indicate that propofol, both with and without N20, tended to have a decreased incidence of PONV compared to thiopentone-isoflurane. Additionally, there was no significant difference in the incidence of OCR between the propofol N20 and TIVA group. Therefore, independent of the anesthetic method used, people who were administered prophylactic atropine before strabismus surgery exhibited a reduced risk of experiencing oculocardiac reflex and PONV.

A study shows that a reflex mechanism for PONV exists following strabismus surgery. However, although being beneficial against the development of oculocardiac reflex, Klockgether-Radke et al. [21] and Chisakuta et al. [23], found that atropine pre-administration during strabismus surgery in children does not lower the incidence of emetic symptoms. Because sustained and repeated stimulation causes the oculocardiac reflex to tire, a study conducted by Donlon, the researcher employed atropine when bradycardia is persistent and severe.[24]

In 2014, a study has been proposed that the central nervous system's α-adrenergic mechanism causes nausea and vomiting. In addition, they mention how an elevated incidence of postoperative vomiting is linked to some general anesthetics, which raise circulating catecholamine levels. [25] When using levodopa to treat Parkinson's disease, nausea is a significant barrier.[26] Dopamine, its active metabolite, functions as an α- and β-adrenergic stimulant. Catecholamine levels in the blood rise in response to pain and trauma. It is frequently seen that people with injuries also experience nausea.

In 1976, a study was conducted to provide additional insight into the potential relationship between opiate effects and pain and nausea during the early postoperative phase. [16] One hundred four patients underwent procedures on their upper abdomen (80) or lower abdomen (24). The patients ranged in age from 18 to 89, with a mean age

of 60 years. There were 37 male and 67 female patients. The premedication consisted of hyoscine and morphine.

Droperidol 2.5 to 7.5 mg was also administered to half of patients early in the anesthetic. In the postoperative ward, every patient was monitored throughout the night. Whenever a patient complained of pain, they were randomly assigned to receive either 2 mg of ketobemidone or 4 mg of morphine intravenously. Before the analgesic was administered, the level of pain (severe, moderate, or mild) and the presence or absence of nausea or vomiting were noted. The patient was questioned once more about the presence or absence of pain and nausea ten minutes following the intravenous opiate injection at the moment of greatest effect. An extra dose of half the initial dose was administered immediately if the patient was still experiencing severe or moderate pain after the first analgesic injection, and after ten minutes, pain and nausea were assessed once more.

The findings indicate that, following abdominal surgeries, 104 patients had nausea related to pain. In 10% of the patients, nausea episodes unrelated to pain were reported. Of the 61 patients, 114 occurrences of simultaneous pain and nausea were noted. In 80% of the cases, the intravenous injection of either ketobemidone or morphine alleviated both the pain and nausea. It was rare for pain alleviation to be accompanied by nausea persistence, and if pain treatment was insufficient, nausea persisted. We conclude that in the early postoperative phase, nausea is frequently present together with pain and can be effectively treated in a significant number of cases by administering appropriate amounts of opiates intravenously.

In 2001, a study including 29 pediatric inpatient surgery cases was carried out using a case-control design. [27] The patients were treated prospectively with a routine IV ketorolac (0.5 mg/kg) every 6 hours with supplemented morphine sulfate. Every six hours, 0.5 mg/kg of ketorolac tromethamine was injected IV. The first dose was given during surgery, right before the wound was closed. Every three to four hours, 0.1–0.5 mg/kg of morphine sulfate was injected IV and titrated to achieve the ideal level of effect. To treat postoperative fever and as a supplement to analgesia in the postoperative period, acetaminophen was given orally or per rectum at a dose of 10 to 15 mg/kg. It was also noted that any signs of respiratory depression, urinary retention,

nephrotoxicity, and bleeding complications are adverse effects of morphine sulfate and ketorolac.

The results show that during the first 48 hours following surgery, patients who received ketorolac in addition to morphine showed a significant decrease in morphine needs. Regardless of the method of analgesia (nurse delivered or patient controlled), a significant reduction in the usage of morphine was observed in patients who received ketorolac. Also, it was noted that ketorolac adjuvant did not modify the adverse effects of morphine, such as respiratory depression, vomiting, or urine retention. When ketorolac was given to the patient, there was no significant rise in bleeding or nephrotoxicity.

In pediatric strabismus surgery, opioid administration is linked to a significant prevalence of PONV. [28] Researchers investigated the effects of IV ketorolac against morphine for pediatric outpatients after strabismus surgery in a double-blind, randomized, prospective study. Forty-two ASA I and II children, ranging in age from 2 to 12 years, were randomly assigned to receive either ketorolac 0.75 mg kg IV or morphine 0.1 mg kg IV together with metoclopramide 0.15 mg kg.” Pain was measured every 15 minutes till discharge, and within the first 24 hours, the frequency of nausea and vomiting was documented. The results show that recovery times and pain behavior scores didn't significantly differ between the two groups. In the first 24 hours, 19% of the participants in the ketorolac group and 71% of the morphine group experienced nausea and vomiting ($P<0.001$). After comparing ketorolac to morphine and metoclopramide, we found that ketorolac was associated with reduced postoperative nausea and vomiting for pediatrics undergoing strabismus surgery.

Also in 1999, conducted a study to assess and compare the analgesic and emetic effects of ketorolac and pethidine and to determine the medication's suitability for this type of surgery. [29] This study enrolled 52 children in ASA class I, ages 2.5 to 15. Children were randomly divided into two groups: the participants in group P received pethidine IV (0.5 mg kg), and participants in group K received ketorolac (0.9 mg kg). Pain was measured at 0 hours, 1/2 hours, and 1 hour after arriving at the PACU. PONV incidence was measured for the first 24 hours and at several intervals (0–2 hours, 2–6 hours, and 6–24 hours).

The study found that pain assessments at 0 hours, 1/2 hours, and 1 hour after arrival at the PACU were identical in groups K and P. Group K PONV was significantly lower than group P's at all periods, except for 6–24 hours when there was no statistically significant difference. Group K observed a considerably decreased overall incidence of PONV within the first 24 hours compared to group P ($P<0.001$). None of the patients receiving ketorolac suffered severe vomiting, compared to eleven patients in group P. Neither ketorolac nor pethidine-related side effects were present in any of the participants in either group. There was sufficient anesthesia, and both groups' postoperative analgesic needs were equal.

Another study demonstrate that ketorolac is highly suitable for managing postoperative pain in children, either independently or in conjunction with opioids or local anesthetics, due to its potent analgesic properties and relatively minimal incidence of side effects such as respiratory depression and nausea/vomiting. [30] a lower dose of IV pethidine (0.5 mg/kg) was administered as an intraoperative analgesic, followed by oral ibuprofen or IM diclofenac for postoperative pain management. In an experiment, using ketorolac or acetaminophen instead of pethidine for intraoperative pain may have further lowered the incidence of PONV. Another study of two groups, propofol-fentanyl and propofol-ketorolac, shows an equally successful in avoiding postoperative nausea and vomiting in children undergoing strabismus surgery whether propofol-ketorolac or propofol-fentanyl anesthesia is used, also intraoperative oculocardiac reflex does not significantly differ between the two groups. [31] Another study show that both the ketorolac group and fentanyl group had the same low incidence of PONV at every step of the follow-up. [32] Alo postoperative pain scores were comparable, but the ketorolac group's agitation scores in the post anesthesia care unit were noticeably higher than the fentanyl group in children undergoing adenotonsillectomy surgery.

1.3 Theoretical Background

1.3.1 Concepts and Operational Definitions

Nausea: is an uncomfortable sensation associated with wanting to throw up but not explosive muscular movement.[33]

Vomiting: It refers to the vigorous contraction of the abdominal and diaphragm muscles, resulting in the ejection of upper gastrointestinal contents through the mouth.[33]

Retching: when no stomach contents are expelled even with expulsive muscular exertions [33], and it is characterized by multiple, precisely regulated rhythmic contractions of the abdominal wall, respiratory, and diaphragm muscles without any stomach contents being expelled. Retching occurs when the stomach is empty and there are expulsive efforts, but the stomach contents are not expelled.[34]

Strabismus: Strabismus (crossed eyes) is any condition of misalignment of the visual axes and is also known as squint. Children suffering from strabismus are between 1% to 3%. Various factors lead to strabismus development among children, including prematurity. General diseases are associated with an increased risk for amblyopia, ocular pathologies, and a family history of strabismus.[35].

Strabismus Surgery:

Strabismus surgery is a surgical procedure that involves loosening or tightening the eye muscle to restore normal alignment of the eyes.

Numerous treatment choices are available, such as pharmacological injections of botulinum toxin or bupivacaine, traditional corrective surgery, adjustable suture surgery, and minimally invasive procedures.[36]

Postoperative nausea and vomiting:

Nausea is an unpleasant vomiting feeling unrelated to expelling gastric muscle movement.[37] Vomiting is a forceful expulsion of a small amount of content from the upper gastrointestinal by mouth.[37]

Postoperative nausea and vomiting (PONV) is the event of nausea and vomiting experienced by the patient within the first 24 hours after surgery.

Physiology of PONV:

Because of the intense vomiting coupled with dehydration, postoperative hemorrhage, pulmonary aspiration, and wound reopening, PONV represent a prominent source of

morbidity in pediatric patients. Children are more likely than adults to experience PONV, even though the mechanisms behind it are similar to those of adults.[38]

The two most common surgical procedures assisted in pediatrics are adeno-tonsillectomy and strabismus repair. Adeno-tonsillectomy involves swallowing blood, while strabismus surgery stimulates the extraocular muscle. These surgical procedures are the primary cause of postoperative nausea and vomiting (PONV).[38]

The CNS vomiting centers include the emetic center, area postrema, nucleus of the solitary tract, and chemoreceptor trigger zone. The chemoreceptor trigger zone is situated within the area postrema, located at the base of the fourth ventricle outside the blood-brain barrier, in close proximity to the emetic center.[38]

The vomiting center controls the entire process involving nausea, retching, and vomiting. Stimulation can be initiated from the outside, such as the oropharynx, mediastinum, gastrointestinal tract, renal pelvis, peritoneum, or genitalia, or from the inside, such as the cerebral cortex, labyrinthine, otic, or vestibular apparatus, sensory tactile stimulation of the posterior pharynx may occur due to endotracheal intubation or the application of oral or nasal airway devices, potentially triggering the oculocardiac reflex alongside extraocular muscle movements.[38]

High concentrations of enkephalin, opioids, and dopamine (D2) receptors are present in the chemoreceptor trigger zone. The area postrema harbors significant concentrations of opioids, D2 receptors, serotonin (5-hydroxytryptamine; 5-HT), and neurokinin-1 (NK-1) receptors. Moreover, the nucleus of the solitary tract primarily showcases enkephalin, histamine, muscarinic, cholinergic, and NK-1 receptors.[38]

Substances like medications, electrolytes, and metabolic compounds stimulate the emetic neuro-receptor areas, acting as detectors for these stimuli. This leads to the transmission of impulses to the vomiting center, thereby triggering the initiation of the vomiting reflex.[39]

The vomiting reflex comprises two phases: the pre-ejection stage, marked by sensations of nausea accompanied by symptoms such as chills, sweating, dilated pupils, heightened salivation, and tachycardia are all orchestrated by sympathetic and parasympathetic

nerves. The ejection stage is marked by retching and the expulsion of stomach contents through vomiting.[33]

Risk factors of PONV

- **Patient factors:**

- **History of PONV**

A prior occurrence of PONV in the children or their family members (father, mother, or siblings).[40] or a history of motion sickness, has been recognized as a significant predictor of PONV. This factor can elevate the risk of experiencing PONV by two to three times.[41]

- **Age**

The incidence of PONV declines with age, peaking between the ages of 6 and 16 near the end of childhood. This age group is frequently vomiting more than any other, and they are monitored regardless of the procedure performed.[42]

- **Obesity**

Because excess fat tissue stores anesthetic drugs and because adipose tissue produces more estrogen, PONV is more common in those with higher BMIs.[33] When BMI levels exceed 30, patients experience heightened abdominal pressure, which correlates with an elevated risk of PONV.[43]

- **Opioids**

The high prevalence of PONV is driven by opioids that activate the chemoreceptor triggering zone, which sends afferents to the vomiting center.[42] Opioids also slow down the motility of the gastrointestinal tract, which decreases emptying time and may result in elevated PONV. They also stimulate the vestibular and otic zones of motion.[42]

- **Inhalational anesthetic agents**

PONV is associated with all inhalants, although the use of sevoflurane may be linked to a reduced incidence of PONV. Although the nature of nitric oxide is still debatable,

PONV makes it seem appealing. However, the lack of nitrous oxide presents more chances for intraoperative awareness.[44]

According to several studies, 25% of patients develop postoperative nausea and vomiting (PONV) following general anesthesia using volatile anesthetics; however, the frequency of PONV dropped to 20% when total intravenous anesthesia (TIVA) such as propofol was used in place of volatile anesthesia. There is evidence to suggest that propofol may have antiemetic effects as well.[45]

Nitrous oxide often reduces the amount of volatile anesthetic, although doing so comes with a 28% higher risk of vomiting.[42]

- **The airway management**

Face mask ventilation may be the cause of stomach distention, which may trigger the vomiting reflex and increase the risk of postoperative nausea and vomiting (PONV). Using a nasogastric tube during per-operative gastric evacuation did not decrease the incidence of PONV. However, it does not appear that airway management is the primary factor influencing PONV.[46]

➢ **Surgical factors:**

- **Surgical Technique**

The vomiting reflex is regulated by the vomiting center situated in the medulla oblongata. Inputs to this center originate from the facial mucosa and the posterior oropharynx. Stimulation in these areas can trigger the trigeminal nerve, potentially heightening the risk of PONV. Patients undergoing tonsillectomy may be susceptible to swallowing blood from the surgical site, possibly due to the neck extension position. This position might enable the hypopharynx and laryngopharynx to open, changing cricopharyngeal pressure and causing the gastrointestinal tract to ingest blood. This mechanism could induce irritation and increase the risk of PONV.[42]

- **Strabismus Surgery**

The primary reason for the morbidity following pediatric strabismus surgery is PONV. After strabismus surgery, the incidence of PONV without any prophylaxis ranges from

41% to 88%. The primary factor for re-admission and lengthening hospital stays following strabismus is PONV.[47]

Afferent impulses activate the oculo-chemical reflex pathway, raising the risk of POV. These stimuli are transmitted from peripheral to central vomiting centers, eliciting responses from the area postrema via the glossopharyngeal and vagal nerves. This process aids in comprehending the etiology and mechanism of PONV.[38]

PONV Prophylaxis

PONV Prophylaxis is defined as a process of guarding against the development of PONV by a treatment or applying an action that affects the mechanism of occurrence. Many prophylactic actions can be used to prevent PONV, including reducing baseline risk, using interventions, medication, and non-pharmacologic techniques.[48]

Many risk factors induce PONV among patients undergoing surgery. For adults commonly used the Koivuranta risk score and the Apfel risk scores for patients undergoing anesthesia, the Apfel simplified risk score is based on four main factors: female sex, history of PON, nonsmoking status, and use of postoperative opioids.[49]

The commonly used simplified risk score for children undergoing anesthesia is based on four main factors: duration of surgery >30 minutes, patient age >3 years, patient or family history of POV/PONV, and strabismus surgery.[8]

- **Reduce baseline risk**

Many studies in the pediatric population confirmed that total intravenous anesthesia (TIVA), fluid therapy, and avoiding opioids would reduce baseline risk for POV/PONV in children. [50] & [51] & [52]

Another study shows that the administration of Ketrolac has the same analgesic effects as pethidine but significantly decreases the incidence of PONV in the first 24 hours.[12]

Another study shows that strabismus surgery with total intravenous anesthesia will increase the risk of bradycardia due to oculo-cardiac reflex, and it is recommended to replace it with inhalational anesthetics with one prophylactic antiemetic drug.[53]

Another study shows that the administration of intravenous paracetamol for patients undergoing strabismus surgery will decrease the incidence of PONV within the first 24 hours after the surgery.[54]

- **Interventions medication**

According to the POV/PONV risk scale, there are many recommendations for medication use as a prophylaxis for PONV in children and adults. When the risk is extremely low, there is no need to administer antiemetic prophylaxis. However, prophylaxis drug is strongly recommended for patients at high risk of PONV.

Many studies support that propofol TIVA will reduce the incidence of PONV.[53] Also, the same study shows that propofol will reduce the incidence of PONV at the same rate compared to using a single prophylaxis drug.[53]

Another study supported that the use of a single dose of aprepitant (NK1 Receptor Antagonists) was superior to Ondansetron for the prevention of vomiting during the first 48 hours after surgery, but no significant differences for nausea control for both drugs, [55] but another study supported that use a single dose of aprepitant was superior to Ondansetron for reducing of nausea severity at the first 48 hours after surgery.[56]

One of the safest antiemetic medications for kids is Ondansetron, a 5-HT3 antagonist that helps prevent PONV, especially when used with dexamethasone.[38] In children with tonsillectomy or strabismus correction, intravenous Ondansetron 0.05-0.15 mg / kg or oral ondansetron 0.1 mg/kg was considerably more efficacious than placebo in preventing PONV. Prophylactic administration of Ondansetron at a dose of 0.1 mg/kg reduced PONV in pediatric patients, independent of surgical or anesthetic factors, and led to shorter stays in the PACU.[38]

The prophylactic application of dexamethasone for PONV: Randomized controlled trials have shown that dexamethasone acts as an antiemetic compared to a placebo, without any clinically significant toxicity or adverse effects in patients. Furthermore, when combined with a 5-HT3 receptor antagonist, dexamethasone exhibits outstanding prophylactic efficacy against PONV.[38] On the other hand, according to other research, combining intravenous ondansetron 50 μg/kg with intravenous dexamethasone 150 μg/kg significantly reduced PONV compared to using the medicine alone.[38]

A meta-analysis study found that significantly reduced the incidence of PONV in children receiving one type of prophylaxis drug (dexamethasone or Ondansetron).[12] This same study also found that it significantly reduced the incidence of PONV in children receiving a combination of two prophylaxis drugs (dexamethasone and Ondansetron) compared with receiving a single prophylaxis drug.[12]

Metoclopramide is an antiemetic that acts on multiple models.[57] It has prokinetic and antiemetic properties and operates on central dopamine and serotonin receptors.[58] Metoclopramide was first prescribed to alleviate nausea and vomiting associated with radiation therapy, chemotherapy, and migraines.[57] In contemporary times, it is used to treat gastroparesis, heartburn, gastrointestinal reflux, and lower preoperative stomach contents.[59]

Although Droperidol has more side effects than other antiemetic medications and may cause the QT interval to lengthen on an ECG when taken excessively, well-controlled randomized and comparative clinical trials, have shown that the risk of QT prolongation is significantly reduced when Droperidol is combined with a 5-HT3 receptor antagonist.[60]

Nonsteroidal anti-inflammatory drugs (NSAIDs) like ketorolac have strong analgesic properties and a low frequency of side effects. Ketorolac is more effective than codeine and just as effective as the main opioid analgesics, including morphine, according to numerous clinical trials treating postoperative pain in children. Clinical trials involving both adults and children reveal that combining ketorolac with opioids improves the efficacy and quality of pain management, while reducing the likelihood of opioid-related side effects such as ileus, respiratory depression, nausea, and vomiting. After abdominal surgery, patients treated with ketorolac recover their bowel function more quickly than those treated with opioids. Ketorolac reduces tissue nociceptors' hypersensitization following surgery and reversibly inhibits cyclo-oxygenase. It also inhibits thromboxane formation, accounting for its reversible antiplatelet actions.[30]

- **Non-pharmacologic technique**

Acupuncture techniques have been reported to effectively reduce the incidence of PONV. A randomized, double-blind study supports that the administration of acupuncture compared to dexamethasone will provide the same antiemetic effect among pediatrics undergoing tonsillectomy.[61]

Transcutaneous electrical acupoint stimulation is a painless, effective, and convincing way to treat and prevent PONV in pediatric tonsillectomy when used on children under general anesthesia.[62]

1.3.2 Problem Statement

Patients often cite pain, nausea, and vomiting as their primary postoperative worries, especially among pediatric populations. The incidence of PONV in children, varying from 33.2% to 82%, can be twice as prevalent as in adults.[63]

Nausea and vomiting are among the most prevalent adverse events in the postoperative period, particularly in patients undergoing strabismus surgery. This event is associated with a wide range of complications for the patient and hospital, such as dehydration, electrolyte imbalance, sub-conjunctival hemorrhage, loosening of surgical attachments, increased post anesthesia care unit (PACU) stay time, increased hospitalization period, maybe hospital re-admission and increased health care costs.

A simplified risk score was developed, incorporating four predictors: previous experience of PONV or family history, anesthesia duration (> 30 min), patient age (> 3 years), and undergoing strabismus surgery. For instances with none, one, two, three, or four of these risk factors, the associated occurrences of PONV were 9%, 10%, 30%, 55%, and 70%.[40]

Due to this wide range of adverse effects regarding PONV, we need to provide a prophylactic method to minimize the incidence of PONV after strabismus surgery.

1.3.3 Significance of the Study

Data suggests that postoperative nausea and vomiting may be associated with patient dissatisfaction, longer stay in post-anesthesia care unit,[5] hospital re-admission,[7] increased treatment cost,[6] and hospital complications.

PONV stand out as the most commonly encountered issues by patients after surgery. The estimated incidence of PONV ranges from 10% to 30% of all patients and reaches 80% in high-risk individuals,[49] espite numerous significant studies on postoperative nausea and vomiting and the use of antiemetic agents, the incidence remains high, estimated between 33.2% and 82% in childhood,[52] Thus, postoperative nausea and vomiting represent the most common complication affecting children, with a prevalence rate twice as high as in adults.[63]

This complication is the most feared by patients and their families, more than pain, and this experience is reflected in decreased patient satisfaction. Adult Populations at the highest risk for developing PONV are patients with a history of PONV, non-smokers, females, patients with motion sickness, younger populations, and type of surgical procedure. Pediatric Populations at the highest risk for developing PONV are duration of surgery >30 minutes, age >3 years, personal or first-degree relative history of POV/PONV, and strabismus surgery.[48]

The mechanisms of frequent PONV after strabismus surgery include the oculo-cardic reflex, a vagally mediated reflex related to eye muscle manipulation during surgery, and alterations in visual perception postoperatively.[4] Many complications may occur, such as dehydration, electrolyte imbalance, subconjunctival hemorrhage, the loosening of surgical attachments, delayed hospital discharge, and hospital re-admission.[7]

To ensure optimal and efficient management of PONV, it is imperative to understand the risks associated with PONV in adults and POV in children. This includes identifying interventions that lower the baseline risk for PONV, evaluating the effectiveness of single antiemetic or combination therapies for PONV prophylaxis, and assessing the efficacy of non-pharmacological interventions.[48]

This study is significant because it will increase the familiarity of the anesthetist regarding the new protocol that can be used as a prophylactic of PONV among patients undergoing strabismus surgery; therefore, reduce the consequential burden like redo the surgery, long hospitalization, and low satisfaction.

1.3.4 Study Purpose and Objectives

1.3.4.1 Aims of the study

The current study aims to compare the effect of Ondansetron versus Ketorolac with Ondansetron for postoperative nausea and vomiting prophylaxis among pediatric patients undergoing strabismus surgery and its impact on the postoperative requirement for rescue antiemetic and analgesic medications.

1.3.4.2 Primary Outcome Measures

Complete response refers to the absence of nausea and vomiting, the incidence and severity of nausea, as well as the frequency of vomiting and retching within 8 hours following surgery.

1.3.4.3 Secondary outcome measures

Using rescue antiemetic drugs and experiencing pain following surgery.

1.3.5 Study Objectives

- This study compared the complete response, incidence, and severity of nausea as well as frequency of vomiting and retching between Ondansetron groups versus Ketorolac with Ondansetron groups in pediatric patients undergoing strabismus surgery.

- This study compared the postoperative pain and rescue antiemetic and analgesic medication between Ondansetron versus Ketorolac with Ondansetron groups in pediatric patients undergoing strabismus surgery.

1.3.6 Research questions

This study will answer the following questions:

- Does administering IV ketorolac and IV Ondansetron together 15 minutes before the conclusion of surgery help patients having strabismus surgery by increasing complete response (no nausea, no vomiting, no retching, no need for rescue antiemetic medication), minimizing the frequency and intensity of PONV, as well as minimizing postoperative pain and the need for antiemetic and analgesic medications?

- Does administering IV Ondansetron alone 15 minutes before the conclusion of surgery effectively increase complete response (no nausea, no vomiting, no retching, no need for rescue antiemetic medications), reduce PONV incidence and severity, postoperative pain, and the need for antiemetic and analgesic drugs in patients having strabismus surgery?

1.3.6 Hypothesis

- There is no statistically significant difference at the level of ($\alpha \leq 0.05$) regarding complete response (no nausea, no vomiting, no retching, no need for antiemetic rescue medication) between ketorolac with Ondansetron and Ondansetron groups.

- There is no statistically significant difference at the level of ($\alpha \leq 0.05$) related to the incidence and intensity of PONV between ketorolac with Ondansetron and Ondansetron groups.

- There is no statistically significant difference at level of ($\alpha \leq 0.05$) related to postoperative pain between ketorolac with Ondansetron and Ondansetron groups.

- There is no statistically significant difference at the level of ($\alpha \leq 0.05$) related to rescue antiemetic and analgesic medication consumptions between ketorolac with Ondansetron and Ondansetron groups.

- There is no statistically significant difference at level of ($\alpha \leq 0.05$) related to patients' satisfaction with their therapy between the ketorolac with Ondansetron and Ondansetron groups.

Chapter Two

Methods

2.1 Study design

The study aims to evaluate a risk-adapted PONV prophylaxis in pediatric patients undergoing strabismus surgery. Thus, the researcher used an observational study conducted in the operation room, post Anesthesia Care Unit (PACU), and after 8 hours in the pediatric surgical ward at An-Najah National University Hospital.

The researcher used an observational study design to examine the relationship among variables and used a structured instrument to collect information.

This study lacks random selection procedures since the pediatric patients undergoing strabismus surgery selected were Purposive and confined to the An-Najah National University Hospital. A quantitative approach was used in this study to analyze the results because it emphasizes objectivity in data collection and analysis of information. It also allows analyzing data using numerical information through statistical procedures.

The study included children with an Eberhart risk score of three or above for POV, indicating high-risk characteristics. It indicates that after strabismus surgery, there is a 42.3% chance that any child may experience postoperative vomiting. The participants were divided into two prophylactic treatment groups: Ondansetron (n=40) and Ondansetron in combination with ketorolac (n=30). The variables studied are complete response (no nausea, no vomiting, no retching, no need for rescue antiemetic medications), the occurrence and intensity of nausea, incidence of vomiting and pain, requirement for rescue antiemetic therapy, and rescue analgesia.

2.2 Study population

The target population of this study is the total number of pediatric patients 3-12 years old, ASA physical status I and II, who are undergoing elective strabismus surgery at An-Najah National University hospitals from 1st June to 1st December in 2023.

2.3 Site and setting

The study took place in the operating room, PACU, and pediatric surgical ward at An-Najah National University Hospital in the West Bank, Palestine.

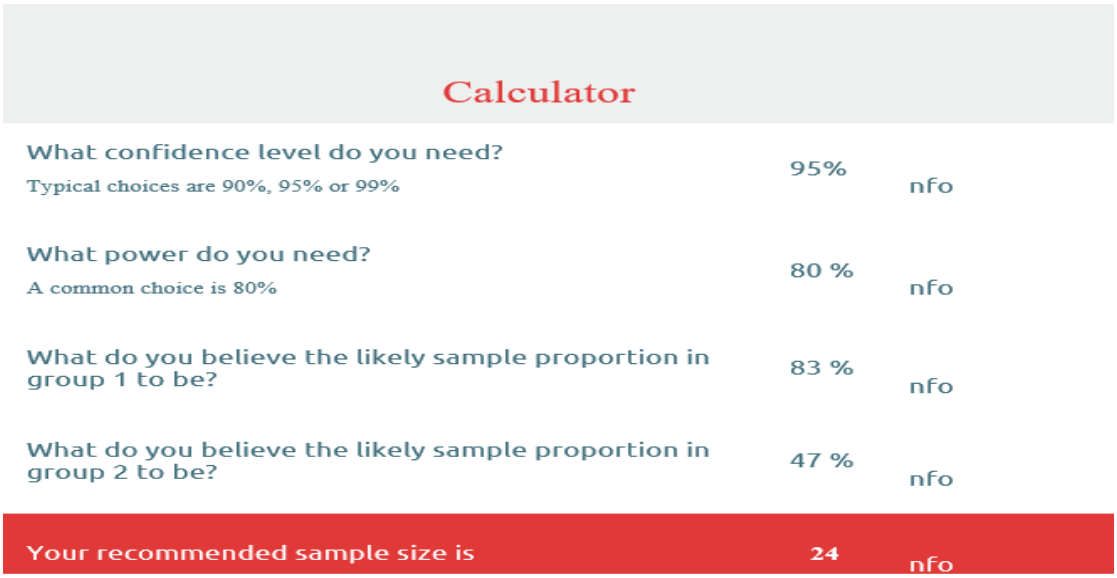
2.4 Sampling method and approach

Most nursing studies employ non-probability sample strategies due to their cost-effectiveness and convenience.[64] The sample size is known as the number of people in a sample.[64] The researchers employed a non-probability purposive sampling technique in their investigation. Purposive sampling involves choosing a sample that is indicative of the qualities or features that the researcher is interested in based on the specific objective of the study. Because purposive sampling relies on the idea that a researcher's understanding of the population can be utilized to manually choose which cases to include in the sample,[64] the researcher deliberately chose as many participants as feasible.

Based on a study by Senthilkumar Sadhasivam et al. (2000) to examine the prophylactic Ondansetron in the Prevention of postoperative nausea and vomiting following pediatric strabismus surgery, the sample size for the current study was determined using the Select statistical service calculator.[65] It was found that the incidences of PONV were 83% in the placebo group and 47% in the ondansetron group at 75 microgram/kg. This computation indicates that each group needs 24 patients. To account for the dropout and depending on the clinical practice's conditions, this is an observational study with a purposeful sample. Thirty patients were added to the combination group, and forty were added to the ondansetron group.

Figure 1

Select statistical service calculator for sample size



2.5 Inclusion & Exclusion criteria

➢ **Inclusion criteria**

- Patients ASA I-II were undergoing elective strabismus surgery under general anesthesia.
- Female and male patients.
- Age 3 to 12 years.
- Children who have previously experienced motion sickness or PONV.
- With a risk score ≥30 % for PONV.

➢ **Exclusion criteria:**

- Bleeding diathesis.
- People for whom it is contraindicated to use NSAIDs.
- Patients who were nauseated or who were vomiting either before the operation.
- Patients who received antiemetics or NSAID 24 hours preoperatively.
- Patient history of gastroesophageal reflux.

2.6 Instruments of study

➢ **Demographic characteristics:**

Age, anesthesia duration, weight, surgery duration, and total dose of perioperative drugs.

➢ **Outcome measurements:**

The primary outcome measured was the incidence of postoperative nausea and vomiting (PONV) and pain, which were assessed 8 hours after surgery. A patient was deemed to experience PONV if nausea, vomiting, or retching were recorded during any of the postoperative evaluations.

The secondary outcome will focus on assessing the severity PONV and pain. PONV, measured with a 10 VAS-N scale, represented by five or six simple cartoon faces depicting varying levels of discomfort. A score of ≥4 on the VAS-N scale indicates the need for nausea treatment. Pain severity will be measured using VAS-P , also featuring five or six cartoon faces illustrating different levels of pain intensity. A score of ≥4 on the VAS-P scale indicates the need for pain management.

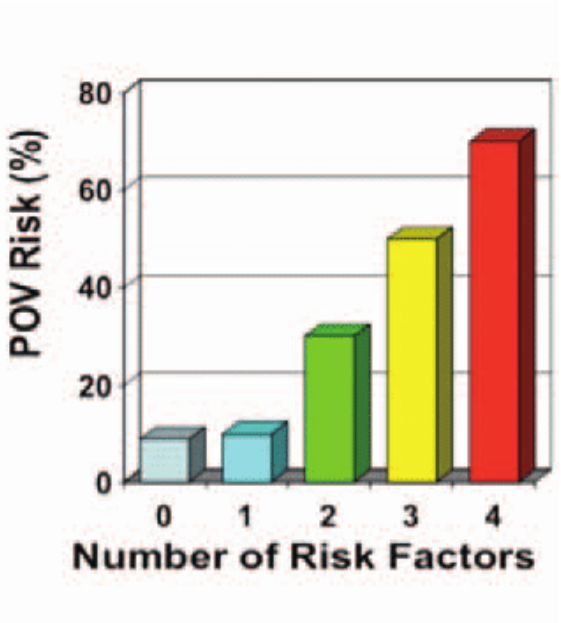
➢ **Risk score for PONV:**

Previous work by Eberhart et al,[8] a simplified risk score consisting of four predictors for PONV or POV in pediatric patients was developed. These risk factors include a history of PONV or a positive family history, anesthesia duration (>30 minutes), age (≥3 years), and undergoing strabismus surgery. The incidence rates of PONV corresponding to the presence of none, one, two, three, or all four of these risk factors were 9%, 10%, 30%, 55%, and 70%, respectively. Furthermore, excluding strabismus, the incidence will be present in only one risk factor, 11.6% if two risk factors are 28.2%, and up to 42.3% in the presence of three risk factors.[63]

Figure 2

Simplified risk score for POV in Children

Risk Factors	Points
Surgery ≥ 30 min.	1
Age ≥ 3 years	1
Strabismus surgery	1
History of POV or PONV in relatives	1
Sum =	0 . . . 4



Dependent & Independent Variable

- **Dependent Variable:**

- Rescue antiemetic medication: Dexamethasone 0.15 mg/kg.
- Rescue painkiller medication: Paracetamol 15 mg/kg.
- Intensity and incidence of nausea, vomiting, retching, and pain in the post-anesthesia care unit.
- Intensity and incidence of nausea, vomiting, and pain in the pediatric ward.
- Complete response (no nausea, no retching, no vomiting, no rescue antiemetic medications)

- **Independent Variables:**

- Received of I.V Ondansetron versus Ketorolac with Ondansetron.

- **Outcome measurements:**

The primary outcomes were complete response (no nausea, no retching, no vomiting, no rescue antiemetic medications), the incidence and intensity of nausea, and frequency of vomiting and retching, which were assessed 8 hours postoperative. A patient was classified as experiencing postoperative nausea and vomiting (PONV) if they exhibited symptoms such as nausea or vomiting, retching, and the requirement for rescue antiemetic medication during any of the postoperative evaluations. Nausea severity was measured with a -10 VAS-N scale, represented by five or six simple cartoon faces illustrating various levels of discomfort. A score of ≥4 on the VAS-N scale served as the cutoff point indicating the need for nausea treatment.

Secondary outcomes included the occurrence and severity of pain, evaluated using a VAS-P eaturing five or six simple cartoon faces representing different emotional states. A cutoff point of ≥4 on the VAS-P scale indicated the need for pain management. Rescue antiemetic and rescue analgesia were recorded.

- **Validity of the questionnaire:**

The checklist was tested and verified by a panel of five arbitrators (two anesthesiologists, one ophthalmologist, one PACU nurse, and one statistician) after all team members unanimously agreed on the checklist.

2.7 Data collection

The researcher collected data by employing direct observation and follow-up from hospital admission till 8 hours after surgery. Then, the data was filled in the checklist created by the researcher. PONV measured with a -10 VAS-N scale shows five or six simple cartoon faces beginning with emotion; a cut-off point of≥ 4 on the VAS-N scale indicates treatment nausea. Pain measured with a VAS-P shows five or six simple cartoon faces beginning with emotion; the cut-off point is ≥ 4 on the VAS-P scale, which indicates pain treatment. At intervals of 0 - 2 hours, 2 - 4 hours, and 4 - 8 hours, all emetic episodes are recorded throughout the first 8 hours of the postoperative period in the hospital. Demographic data, anesthesia time, or surgery duration were recorded.

2.8 Assessment and Anesthesia Protocol

- **Anesthesia protocol**

Instruction for preoperative fasting was given as fasting for 3 hours for clear fluids. A 22 gauge of IV catheter is inserted, and infusion with lactated Ringer's solution commenced. Pre-oxygenation with 100 percent oxygen for 3-5 minutes started. Induction is carried out with fentanyl at 1-2 µg/kg, propofol (1-2.5 mg/kg). The endotracheal tube is placed according to age. General anesthesia is maintained with isoflurane 1 to 2.4 MAC with air and oxygen 1L/min.

Perioperative monitoring was maintained with an end-tidal carbon dioxide monitor, electrocardiogram, oxygen saturation monitor, temperature monitor, and automatic blood pressure recorder. Anesthesia was maintained with air oxygen and Isoflurane. Lactated Ringer's solution was used intraoperatively for the maintenance of intraoperative fluids. The fluid requirement was calculated according to body weight. Patients received approximately 60 ml plus 1 ml/kg/hr. The fluid deficit was calculated. During the second hour, one-quarter of the fluid deficit was replaced. Ondansetron is given in group (1), and an equivalent volume of Ondansetron and ketorolac is given in

group (2) fifteen minutes before the end of surgery IV. In the end, the patient was extubated after gaining consciousness.

- **Assessment of nausea and vomiting in the Postoperative Anesthetic Care Unit (PACU)**

Nausea was assessed using 10 VAS-N scale featuring six simple cartoon faces depicting different levels of discomfort. A cutoff point of ≥4 on the VAS scale indicated varying degrees of nausea severity: 0-1 (no nausea), 1+/-4 (mild), 4+/-7 (moderate), and 7+/-10 (severe).

Zero for no nausea; two for mild, annoying nausea; four for nagging, uncomfortable, troublesome nausea; six for distressing, miserable nausea; eight for intense, dreadful, horrible nausea; 10 for worst possible, unbearable (vomit), excruciating nausea.

- The patients were requested to evaluate their level of nausea until their discharge from the PACU.

- Vomiting was noted by the nurses, as was the need for antiemetic's (Dexamethasone 0.15 mg/kg).

- **Assessment of nausea and vomiting after discharge from PACU**

Nausea/vomiting was recorded a time after discharge from PACU to the pediatric surgical ward until 8 h after surgery, which the study terminated at this time.

- **Assessment of pain in the Postoperative Anesthetic Care Unit (PACU)**

Pain is assessed using a 10 VAS-P Scale, which is 0-1 (no pain), 1+/-4 (mild), 4+/-7 (moderate), and 7+/-10 (severe).

- The patients were asked to assess their degree of pain until discharge from the PACU.

- The pain was noted by the nurses, as was the need for rescue medication perfalgan®15 mg/ kg IV.

- **Rescue antiemetic medication**

If the nausea is more than ≥ 4 on the VAS-N scale and/or vomiting twice and above. Decort ® (Dexamethasone 0.15 mg/kg) given.

- **Rescue medication for pain (analgesia)**

If the pain is more than ≥ 4 on the VAS-P scale, Perfalgan® (Paracetamol 15 mg/kg I.V) is given.

2.9 Procedure

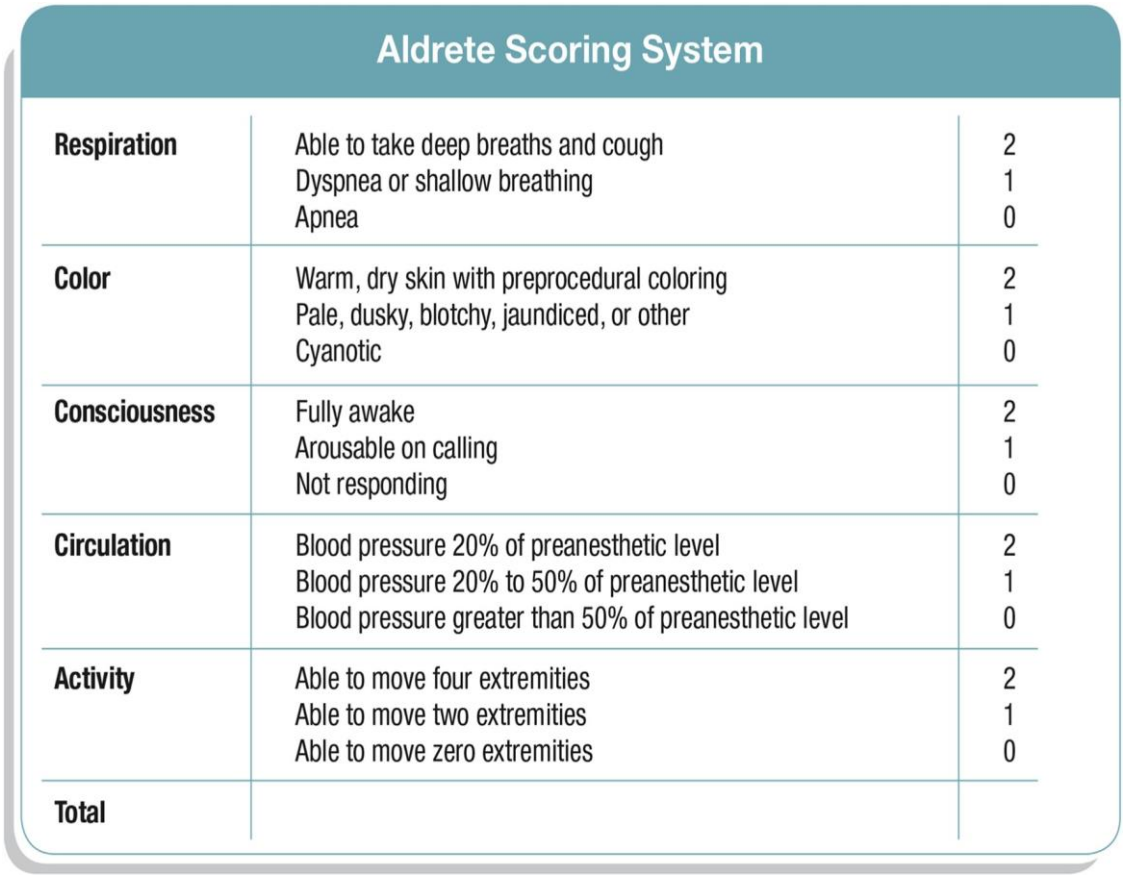
Seventy children, ASA physical status I and II, aged 3 to 12 years and scheduled for elective strabismus surgery, enrolled in the study after receiving institutional approval and parental informed agreement. Before surgery, all children are fasted for meals (8 to 10 hours) and clear liquids for up to three hours. There is no premedication administered.

Isoflurane 1 to 2.4 MAC with air and oxygen are used to induce anesthesia and was delivered through a facemask. The trachea was intubated, and a muscle relaxant was given. Fentanyl used to provide analgesia. Anticholinergic prophylaxis is not administered to prevent the oculocardiac reflex. If the reflex persists for more than 30 seconds and is severe (heart rate less than 50 beats per minute), it is managed with intravenous atropine at a dose of 7µ g/kg IV (with a minimum dose of 0.1 mg). Additionally, lactated Ringer's solution was administered to address the calculated fluid deficit.

Neostigmine 50 µg/kg is used to counteract residual neuromuscular inhibition. All of the children were extubated and transported to the PACU when the neuromuscular blockade was successfully reversed. Aldrete's recovery score (scale 0 to 10) (Aldrete & Kroulik, 1970) is used to assess anesthetic recovery in PACU. Five characteristics are evaluated in this score: level of activity, color, respiration, circulation, and consciousness. Each parameter is scored 0, 1, or 2, and patients scoring 9 or greater are eligible to be transferred from the high-dependency PACU to the surgical ward (Figure 2).

Figure 3

Aldrete scoring system



Aldrete Scoring System		
Respiration	Able to take deep breaths and cough Dyspnea or shallow breathing Apnea	2 1 0
Color	Warm, dry skin with preprocedural coloring Pale, dusky, blotchy, jaundiced, or other Cyanotic	2 1 0
Consciousness	Fully awake Arousable on calling Not responding	2 1 0
Circulation	Blood pressure 20% of preanesthetic level Blood pressure 20% to 50% of preanesthetic level Blood pressure greater than 50% of preanesthetic level	2 1 0
Activity	Able to move four extremities Able to move two extremities Able to move zero extremities	2 1 0
Total		

The children were divided into two observational groups. Group 1 was given Ondansetron 0.15 mg/kg at fifteen minutes before the end of surgery, and children in group 2 were given Ondansetron 0.15 mg/kg and ketorolac 0.5 mg/kg in the same period.

As is standard procedure, children are held in the ward for the first 8 hours after surgery. Nausea is a subjectively unpleasant sensation that occurs when a person is conscious of the desire to vomit. The forceful evacuation of stomach contents from the mouth was defined as vomiting.

An emetic episode is defined as a period of nausea, vomiting, or any combination of these symptoms that occurs in rapid succession (less than one minute between events). If there was a one-minute gap between episodes of nausea, vomiting, or a combination of the two, they are considered independent episodes. At intervals of 0 to 2 hours, 2 to 4 hours, and 4 to 8 hours, all emetic episodes are recorded throughout the postoperative

period in the hospital. In both groups, the time from the onset of the first episode of emesis was recorded. As a rescue antiemetic, children who experience two or more emetic episodes are given (Dexamethasone 0.15 mg/kg IV).

When children complain of discomfort and are thought to be crying because they are in pain (i.e., when their cries could not be stopped by food, a caregiver present, or if they were associated with thrashing and rubbing their eyes), an intravenous dose of perfalgan (15 mg/kg) is administered.

2.10 Statistical analysis

The Statistical Package for Social Sciences Software (SPSS) Version 23 was used for the data analysis in this study. The researcher performed descriptive statistics (including frequencies, percentages, means, and standard deviations) for all variables, indicators, parameters, and measurements examined in the study. The statistical tests used to analyze the results and to test the research hypotheses assuming that the P-Value ≤ 0.05 is deemed significant are:

- The Chi-Square test was used to test the differences in percentages between the two study groups for the qualitative variables such as Gender, Age, Residence, BMI, Eberhart risk score, Surgery type, Frequency of vomiting, Incidence of vomiting, Incidence of nausea, Retching, Frequency of retching, Having pain on the area of surgery, Analgesic, Rescue antiemetic (Dexamethasone IV), Satisfaction about the given treatment, and Recommendation the treatment to other patients.

- The two independent samples T-test: test the differences in means between the two study groups for the quantitative variables such as Age, Weight, Height, BMI, Anesthesia duration, Surgery duration, Medications during the Operation, Frequency of vomiting, Intensity of nausea using VAS-N, Frequency of retching, Intensity of pain by using VAS-P, Satisfaction about the given treatment.

2.11 Ethical considerations

To maintain ethical and legal standards, permission to conduct this study was obtained from the hospital administration at An-Najah National University Hospital and the hospital's Clinical Research Center. The study received accreditation from both the Institutional Review Board (IRB) of An-Najah National University and the Ethics

Committee of An-Najah National University Hospital, the institution where the study took place. The study adhered to the ethical principles outlined in the World Health Organization Declaration of Helsinki for Human Medical Research.Additionally, parents/guardians in the study received an explanation about the purpose and method of the study, and their informed consent was obtained prior to the start of data collection.

Chapter Three

Results

3.1 Study Sample

A study sample of 70 pediatric patients undergoing strabismus surgery was selected and distributed into two groups: the first group contained 40 patients given Ondansetron only, and the second group contained 30 patients given a combination of Ketorolac with Ondansetron. Generally, the study sample included 41 males (p=58.6%) and 29 females (p=41.4%), and the ages in the sample were distributed as about 23% for the age group 3-5 years, 30% for the age group 6-9 years, and about 47% for the age group 10 – 12 years. About 39% of the patients in the study sample have a history of PONV in previous surgeries. 60% of the patients in the study sample have three Eberhart risk scoress, 40% have four Eberhart risk scores, and most of the patients have squint 3 muscle surgery type (p=63%). The average anesthesia duration was about 127 minutes, and the average surgery duration for the patients was about 89 minutes.

Table 1

*Comparisons between the study groups in the Personal Data (N=70) **

Variable	Ondansetron only		Combined		Total		P-value
	N	%	N	%	N	%	
Male	22	55	19	63.3	41	58.6	
Female	18	45	11	36.7	29	41.4	
Age							
3-5 years	15	37.5	1	3.3	16	22.9	0.000**
6-9 years	14	35	7	23.3	21	30	
10 – 12 years	11	27.5	22	73.3	33	47.1	
Weight	26.83 ± 12.24		44 ± 13.81		34.19 ± 15.43		0.000
Height	114.1 ± 21.8		140.27 ± 22.25		125.31 ± 25.43		0.000
BMI	20.24 ± 4.6		22.83 ± 8.05		21.35 ± 6.39		0.093
Hx of PONV in previous surgeries	10	25	17	56.7	27	38.6	0.007
Age equal or above 3 years	40	100	30	100	70	100	-----
Anesthesia > 30 min	40	100	30	100	70	100	-----
Eberhart risk score							
Three	29	72.5	13	43.3	42	60	0.014
Four	11	27.5	17	56.7	28	40	
squint 1 muscle	2	5	0	0	2	2.9	
squint 2 muscle	11	27.5	9	30	20	28.6	0.465**
squint 3 muscle	26	65	18	60	44	62.9	
squint 4 muscle	1	2.5	3	10	4	5.7	
Anesthesia duration	122.88 ± 37.14		131.67 ± 31.36		126.64 ± 34.82		0.299
Surgery duration	84.25 ± 28.75		96.33 ± 22.93		89.43 ± 26.91		0.063

* The P-values are related to the two independent sample T-test for quantitative variables and the Chi-square test for Qualitative variables; the numbers in the table represent (Mean ± Standard deviation) or N(%).

** The P-value of the Chi-square test is based on the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5.

The results in Table (1) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) in the following variables: Age, Weight, Height, Eberhart risk score, and the History of PONV in previous surgeries.

Regarding the Age, the results show that the mean of the ages in the Ondansetron-only group (Mean=6.93) is significantly lower than the mean of the ages in the Combined group (Mean=10.37). Also, the percentage of the age group (3-5 years) in the Ondansetron-only group (n=15, p=37.5%) is significantly higher than that in the Combined group (n=1, p=3.3%), while the percentage of the age group (10 – 12 years) in the Ondansetron only group (n=11, p=27.5%) is significantly lower than that in the Combined group (n=22, p=73.3%), the P-value of the test is 0.000.

Regarding the Weight, the results show that the mean of the weights in the Ondansetron-only group (Mean=26.83) is significantly lower than the mean of the weights in the Combined group (Mean=44), and the P-value of the test is 0.000. Also, regarding the Height, the results show that the mean of the patients' heights in the Ondansetron-only group (Mean=114.1) is significantly lower than the mean of the patients' heights in the Combined group (Mean=140.27), the P-value of the test is 0.000.

Regarding the History of PONV in previous surgeries, the results show that the percentage of patients with a history in the Ondansetron-only group (n=10, p=25%) is significantly lower than that in the Combined group (n=17, p=56.7%), the P-value of the test is 0.007.

Finally, regarding the Eberhart risk score, the results show that the percentage of patients with score three in the Ondansetron-only group (n=29, p=72.5%) is significantly higher than that in the Combined group (n=13, p=43.3%). In comparison, the percentage of patients with a score of four in the Ondansetron-only group (n=11, p=27.5%) is significantly lower than that in the Combined group (n=17, p=56.7%), the P-value of the test is 0.014.

Table 2

Comparisons between the study groups in Medications during the Operation (N=70) *

Variable	Group			P-value
	Ondansetron only	Combined	Total	
Total Fentanyl (µg)	34.58 ± 20.64	63.5 ± 30.85	46.97 ± 29.14	0.000
Total Propofol (mg)	102.88 ± 55.12	144 ± 60.09	120.5 ± 60.46	0.004
Total Rocuronium	16.6 ± 9.74	29.13 ± 17.35	21.97 ± 14.8	0.000
Total Perfalgan	301 ± 266.06 (n=10)	433.33 ± 28.87 (n=3)	331.54 ± 237.9 (n=13)	0.422
Zofran dose	2.62 ± 0.93	3.69 ± 0.69	3.08 ± 0.99	0.000
Ketorolac dose	-----	21.77 ± 6.73	21.77 ± 6.73	-----

* The P-values are related to the two independent sample T-test for quantitative variables; the numbers in the table represent (Mean ± Standard deviation).

The results in Table (2) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) in the following supplied medications during the operation: Total Fentanyl, Total Propofol, Total Rocuronium, and Ondansetron dose. This is driven to reject the study hypotheses regarding these medications.

Regarding the total Fentanyl, the results show that the mean of the total Fentanyl supplied in the Ondansetron-only group (Mean=34.58) is significantly lower than the mean of the total Fentanyl supplied in the Combined group (Mean=63.5), the P-value of the test is 0.000.

Regarding the total Propofol, the results show that the mean of the total Propofol supplied in the Ondansetron-only group (Mean=102.88) is significantly lower than the mean of the total Propofol supplied in the Combined group (Mean=144), the P-value of the test is 0.004.

Regarding the total Rocuronium, the results show that the mean of the total Rocuronium supplied in the Ondansetron-only group (Mean=16.6) is significantly lower than the mean of the total Rocuronium supplied in the Combined group (Mean=29.13), the P-value of the test is 0.000.

Finally, regarding the Zofran doses, the results show that the mean of the total Zofran doses supplied in the Ondansetron-only group (Mean=2.62) is significantly lower than the mean of the total Zofran doses supplied in the Combined group (Mean=3.69), the P-value of the test is 0.000.

Table 3

Comparisons between the study groups in the Postoperative parameters at the PACU (N=70) *

Variable	Group		Total	P-value
	Ondansetron only N=40	Combined N=30		
Incidence of vomiting	1(2.5%)	1(3.3%)	2(2.9%)	0.836
Frequency of vomiting:	2 ± 0	1 ± 0	1.5 ± 0.71	-----
1	0/1(0%)	1/1(100%)	1/2(50%)	0.157
2	1/1(100%)	0/1(0%)	1/2(50%)	
Incidence of nausea	3(7.5%)	1(3.3%)	4(5.7%)	0.457
Intensity of nausea using VAS-N	6 ± 2	10 ± 0	7 ± 2.58	0.225
Retching	3(7.5%)	0(0%)	3(4.3%)	0.125
Frequency of retching:	1.33 ± 0.58	-----	1.33 ± 0.58	-----
1	2/3(66.7%)	-----	2/3(66.7%)	-----
2	1/3(33.3%)	-----	1/3(33.3%)	
Having pain on the area of surgery	13(32.5%)	3(10%)	16(22.9%)	0.042**
Intensity of pain by using VAS-P	6.46 ± 3.07	8.67 ± 1.15	6.88 ± 2.92	0.251
Analgesic	8(20%)	3(10%)	11(15.7%)	0.255
Rescue antiemetic	2(5%)	1(3.3%)	3(4.3%)	0.733

* The P-values are related to the two independent sample T-test for quantitative variables and the Chi-square test for Qualitative variables; the numbers in the table represent (Mean ± Standard deviation) or N (%). Framing Scores for Different Reward Sizes.

** The P-value of the Chi-square test is based on the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5.

The results in Table (3) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) only in having pain in the area of surgery. This is driven to reject the study hypothesis regarding having pain in the area of surgery in the Postoperative parameters at the PACU. The results show that the

percentage of patients who had pain in the area of surgery in the Ondansetron-only group (n=13, p=32.5%) is significantly higher than the percentage of patients who had pain in the area of surgery in the Combined group (n=3, p=10%), the P-value of the test is 0.042.

Figure 4

Comparison in the incidence of nausea, vomiting, and retching between the Ondansetron only and combined groups in the PACU

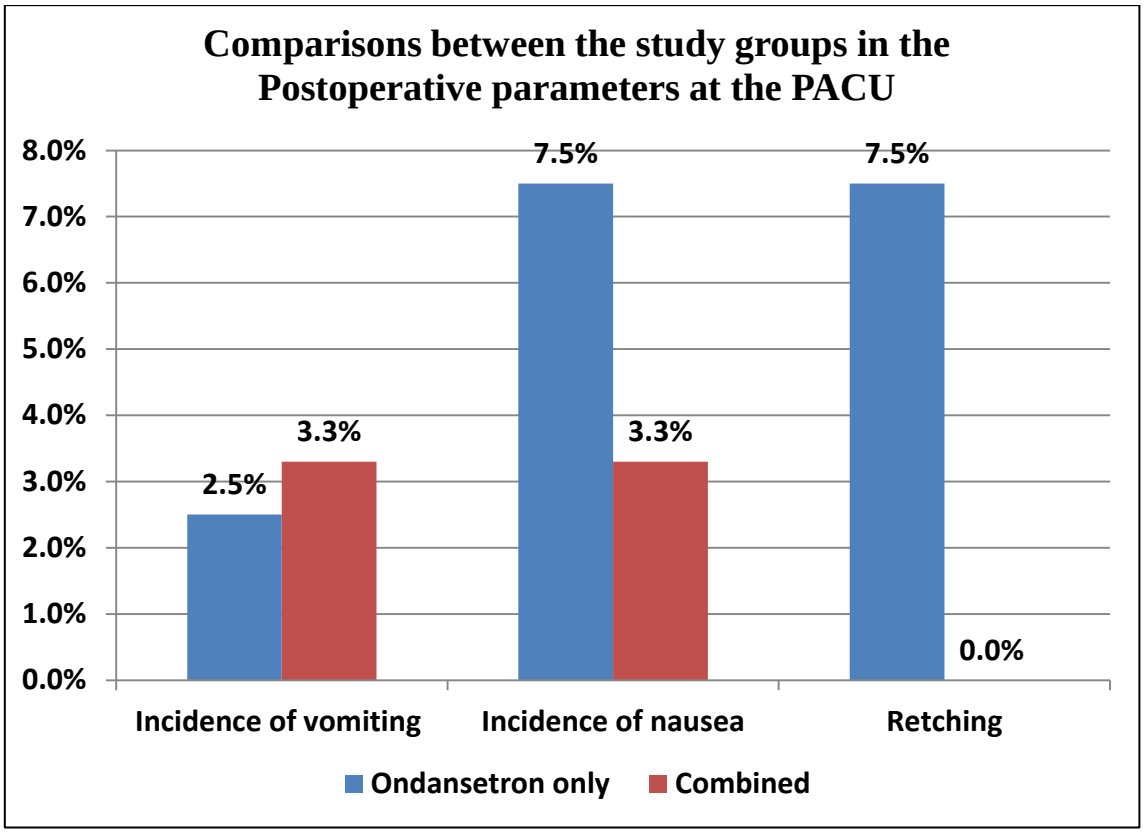


Figure (4) shows that the the percentage of the incidence of vomiting at the PACU is 2.5% in the Ondansetron only group while it is 3.3% in the combined group. Also, the percentage of the incidence of nausea is 7.5% in the Ondansetron only group while it is 3.3% in the combined group. Finally, the percentage of the retching is 7.5% in the Ondansetron only group while no retching were in the combined group.

Table 4

*Comparisons between the study groups in the Postoperative parameters at the Pediatric Ward (N=70) **

Variable	Group		Total	P-value
	Ondansetron only N=40	Combined N=3		
Incidence of vomiting	9(22.5%)	0(0%)	9(12.9%)	0.008**
Frequency of vomiting:	1 ± 0	-----	1 ± 0	-----
1	9/9(100%)	-----	9/9(100%)	-----
Incidence of nausea	13(32.5%)	2(6.7%)	15(21.4%)	0.017**
Intensity of nausea using VAS-N	5.92 ± 3.3	4 ± 0	5.67 ± 3.13	0.439
Retching	9(22.5%)	0(0%)	9(12.9%)	0.008**
Frequency of retching:	1.22 ± 0.44	-----	1.22 ± 0.44	-----
1	7/9(77.8%)	-----	7/9(77.8%)	-----
2	2/9(22.2%)	-----	2/9(22.2%)	
Having pain on the area of surgery	17(42.5%)	4(13.3%)	21(30%)	0.009**
Intensity of pain by using VAS-P	7.53 ± 2.15	6.25 ± 2.06	7.29 ± 2.15	0.295
Analgesic	14(35%)	2(6.7%)	16(22.9%)	0.008**
Rescue antiemetic (Dexamethasone IV)	11(27.5%)	0(0%)	11(15.7%)	0.002**

* The P-values are related to the two independent sample T-test for quantitative variables and the Chi-square test for Qualitative variables; the numbers in the table represent (Mean ± Standard deviation) or N (%).

** The P-value of the Chi-square test is based on the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5.

The results in Table (4) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) only in the following postoperative parameters at the Pediatric Ward: Incidence of vomiting, Incidence of nausea, Retching, Having pain on the area of surgery, Analgesic, and Rescue antiemetic (Dexamethasone IV). This is driven to reject the study hypotheses regarding these parameters.

Regarding the Incidence of vomiting, the results show that the percentage of patients with an incidence of vomiting in the Ondansetron-only group (n=9, p=22.5%) is significantly higher than the percentage of patients with an incidence of vomiting in the Combined group (n=0, p=0%), the P-value of the test is 0.008.

Regarding the Incidence of nausea, the results show that the percentage of patients with an incidence of nausea in the Ondansetron-only group (n=13, p=32.5%) is significantly higher than the percentage of patients with an incidence of nausea in the Combined group (n=2, p=6.7%), the P-value of the test is 0.017.

Regarding the Retching, the results show that the percentage of patients with Retching in the Ondansetron-only group (n=9, p=22.5%) is significantly higher than the percentage of patients with Retching in the Combined group (n=0, p=0%), the P-value of the test is 0.008.

In terms of pain around the surgical site, the results indicate that a significantly higher proportion of patients in the Ondansetron-only group (n = 17, p = 42.5%) than in the Combined group (n = 4, p = 13.3%) experienced pain around the surgical site; the test's P-value is 0.009.

Regarding Analgesics, the results show that the percentage of patients who had analgesics in the Ondansetron-only group (n=14, p=35%) is significantly higher than the percentage of patients who had analgesics in the Combined group (n=2, p=6.7%), the P-value of the test is 0.008.

Finally, regarding the Rescue antiemetic (Dexamethasone IV), the results show that the percentage of patients with rescue antiemetic in the Ondansetron-only group (n=11, p=27.5%) is significantly higher than the percentage of patients with rescue antiemetic in the Combined group (n=0, p=0%), the P-value of the test is 0.002.

Figure 5

Comparison of the incidence of vomiting, nausea, and retching in the pediatric ward between the ondansetron-only and Combined groups

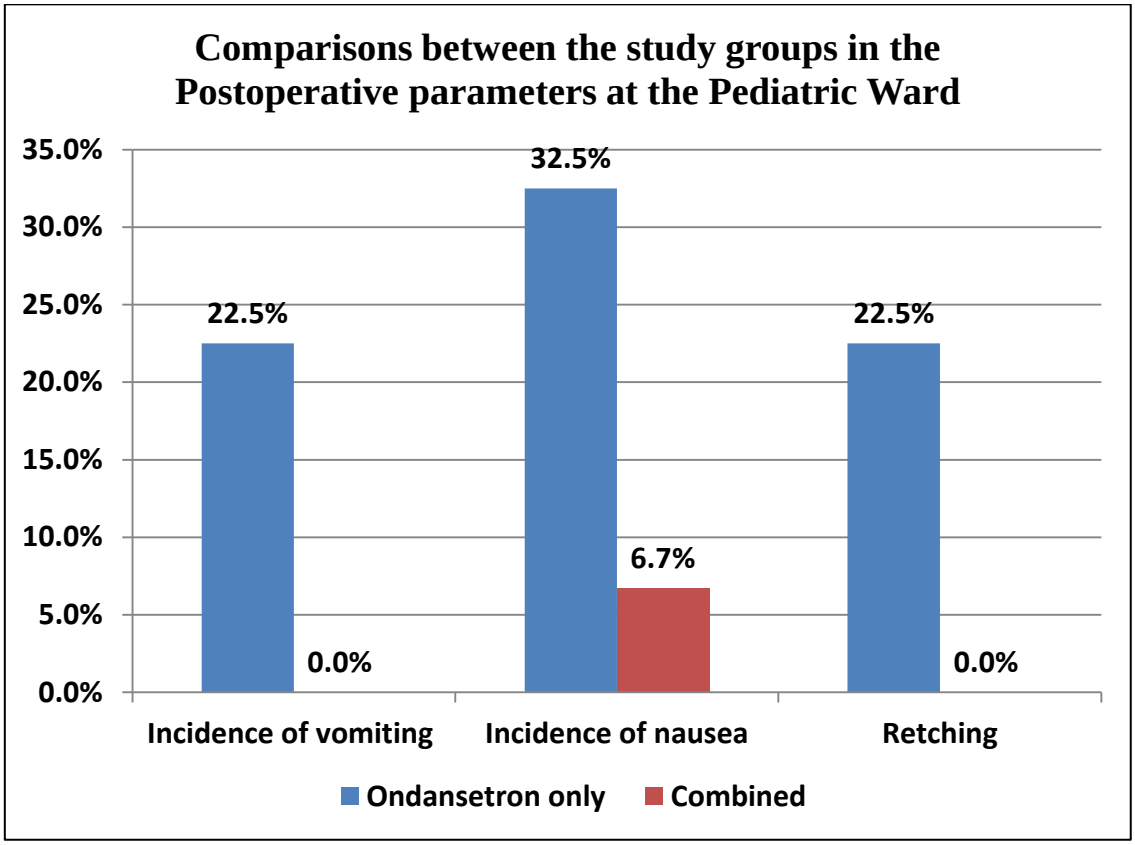


Figure (5) shows that the the percentage of the incidence of vomiting at the the Pediatric Ward is 22.5% in the Ondansetron only group while there were no incidence of vomiting in the combined group. Also, the percentage of the incidence of nausea is 32.5% in the Ondansetron only group while it is 6.7% in the combined group. Finally, the percentage of the retching is 22.5% in the Ondansetron only group while no retching were in the combined group.

Table 5

Comparisons between the study groups in the 8 hours' postoperative parameters (N=70) *

Variable	Group			P-value
	Ondansetron only N=40	Combined N=30	Total	
Incidence of vomiting	3(7.5%)	0(0%)	3(4.3%)	0.125
Frequency of vomiting:	1 ± 0	-----	1 ± 0	-----
1	3/3(100%)	-----	3/3(100%)	-----
Incidence of nausea	4(10%)	0(0%)	4(5.7%)	0.013*
Intensity of nausea using VAS-N	6.75 ± 3.59	-----	6.75 ± 3.59	-----
Retching	4(10%)	0(0%)	4(5.7%)	0.013*
Frequency of retching:	1 ± 0	-----	1 ± 0	-----
1	4/4(100%)	-----	4/4(100%)	-----
Having pain on the area of surgery	3(7.5%)	2(6.7%)	5(7.1%)	0.893
Intensity of pain by using VAS-P	7 ± 1.73	6 ± 2.83	6.6 ± 1.95	0.647
Analgesic	4(10%)	1(3.3%)	5(7.1%)	0.284
Rescue antiemetic	4(10%)	0(0%)	4(5.7%)	0.013*
Satisfaction about treatment	4.28 ± 0.64	4.8 ± 0.41	4.5 ± 0.61	0.000*
Very unsatisfied	0(0%)	0(0%)	0(0%)	
Unsatisfied	1(2.5%)	0(0%)	1(1.4%)	
Neither	1(2.5%)	0(0%)	1(1.4%)	0.003*
Satisfied	24(60%)	6(20%)	30(42.9%)	
Very satisfied	14(35%)	24(80%)	38(54.3%)	
Recommendation the treatment to another patients	39(97.5%)	30(100%)	69(98.6%)	0.383

* The P-values are related to the two independent sample T-test for quantitative variables and the Chi-square test for Qualitative variables; the numbers in the table represent (Mean ± Standard deviation) or N(%).

The results in Table (5) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) only in the following 8 hours' postoperative parameters: Incidence of nausea, Retching, Rescue antiemetic (Dexamethasone IV), and in Satisfaction about the given treatment. This is driven to reject the study hypotheses regarding these parameters.

Regarding the Incidence of nausea, the results show that the percentage of patients with an incidence of nausea in the Ondansetron-only group (n=4, p=10%) is significantly higher than the percentage of patients with an incidence of nausea in the Combined group (n=0, p=0%), the P-value of the test is 0.013.

Regarding the Retching, the results show that the percentage of patients with Retching in the Ondansetron-only group (n=4, p=10%) is significantly higher than the percentage of patients with Retching in the Combined group (n=0, p=0%), the P-value of the test is 0.013.

Regarding the Rescue antiemetic (Dexamethasone IV), the results show that the percentage of patients with rescue antiemetic in the Ondansetron-only group (n=4, p=10%) is significantly higher than the percentage of patients with rescue antiemetic in the Combined group (n=0, p=0%), the P-value of the test is 0.013.

Finally, regarding satisfaction with the given treatment, the results show that the mean of satisfaction scale for patients in the Ondansetron-only group (Mean=4.28) is significantly lower than the mean of satisfaction scale for patients in the Combined group (Mean=4.8), the P-value of the test is 0.000. Also, the percentage of the very satisfied patients in the Ondansetron-only group (n=14, p=35%) is significantly lower than the percentage of the very satisfied patients in the Combined group (n=24, p=80%), the P-value of the test is 0.003.

Figure 6

Comparison of the incidence of vomiting, nausea, and retching in the 8 hours following surgery between the Ondansetron only and the combined groups

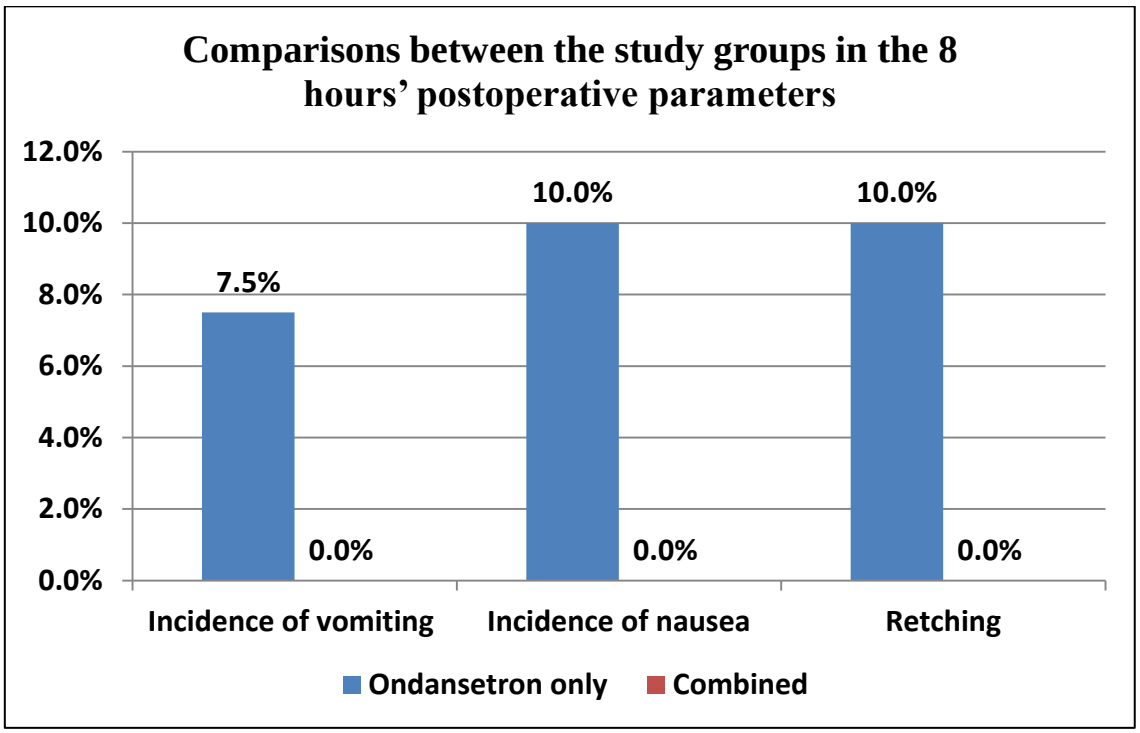


Figure (6) shows that the the percentages of the the 8 hours' postoperative incidence of vomiting, incidence of nausea, and retching are 7.5%, 10%, and 10% respectively in the Ondansetron only group, while no incidence of vomiting, incidence of nausea, and retching were in the combined group.

Table 6

*Differences in the Postoperative Vomiting, Nausea, and Retching at the PACU according to (Gender, Age, History of PONV in previous surgeries, Eberhart risk score, Surgery type, and Surgery duration) (N=70) **

Variable	Incidence of vomiting					Incidence of nausea					Retching				
	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value
Gender															
Male	1	2.4	40	97.6	1.000	1	2.4	40	97.6	0.300	1	2.4	40	97.6	0.566
Female	1	3.4	28	96.6		3	10.3	26	89.7		2	6.9	27	93.1	
Age															
3-5 years	0	0	16	100	0.713	1	6.3	15	93.8	1.000	1	6.3	15	93.8	1.000
6-9 years	0	0	21	100		1	4.8	20	95.2		1	4.8	20	95.2	
10 – 12 years	2	6.1	31	93.9		2	6.1	31	93.9		1	3	32	97	
Hx of PONV in previous surgeries															
Yes	1	3.7	26	96.3	1.000	1	3.7	26	96.3	1.000	1	3.7	26	96.3	1.000
No	1	2.3	42	97.7		3	7	40	93		2	4.7	41	95.3	
Eberhart risk score															
One	0	0	0	0	1.000	0	0	0	0	0.645	0	0	0	0	1.000
Two	0	0	0	0		0	0	0	0		0	0	0	0	
Three	1	2.4	41	97.6		3	7.1	39	92.9		2	4.8	40	95.2	
Four	1	3.6	27	96.4		1	3.6	27	96.4		1	3.6	27	96.4	
Surgery type															
1 squint muscle	0	0	2	100	0.608	0	0	2	100	1.000	0	0	2	100	0.654
2 squint muscle	1	5	19	95		1	5	19	95		0	0	20	100	
3 squint muscle	1	2.3	43	97.7		3	6.8	41	93.2		3	6.8	41	93.2	
4 squint muscle	0	0	4	100		0	0	4	100		0	0	4	100	
Surgery duration															
less than 90 minutes	1	4.3	22	95.7	1.000	1	4.3	22	95.7	1.000	0	0	23	100	0.546
90 minutes or more	1	2.1	46	97.9		3	6.4	44	93.6		3	6.4	44	93.6	

* The P-values are related to the Chi-square test adjusted by the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5. The numbers in the table represent N(%).

The results in Table (6) above show that there are no significant differences at 0.05 level in the Postoperative Vomiting, Nausea, and Retching at the PACU according to (Gender, Age, History of PONV in previous surgeries, Eberhart risk score, Surgery type, and Surgery duration). All the P-values in the table are higher than 0.05.

Table 7

*Differences in the Postoperative Vomiting, Nausea, and Retching at the Pediatric Ward according to (Gender, Age, History of PONV in previous surgeries, Eberhart risk score, Surgery type, and Surgery duration) (N=70) **

Variable	Incidence of vomiting					Incidence of nausea					Retching				
	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value
Gender															
Male	6	14.6	35	85.4	0.726	11	26.8	30	73.2	0.244	5	12.2	36	87.8	1.000
Female	3	10.3	26	89.7		4	13.8	25	86.2		4	13.8	25	86.2	
Age															
3-5 years	4	25	12	75		5	31.3	11	68.8		3	18.8	13	81.3	
6-9 years	2	9.5	19	90.5	0.330	7	33.3	14	66.7	0.047	3	14.3	18	85.7	0.656
10 – 12 years	3	9.1	30	90.9		3	9.1	30	90.9		3	9.1	30	90.9	
Hx of PONV in previous surgeries															
Yes	1	3.7	26	96.3	0.139	2	7.4	25	92.6	0.035	1	3.7	26	96.3	0.139
No	8	18.6	35	81.4		13	30.2	30	69.8		8	18.6	35	81.4	
Eberhart risk score															
One	0	0	0	0		0	0	0	0		0	0	0	0	
Two	0	0	0	0	0.075	0	0	0	0	0.085	0	0	0	0	0.075
Three	8	19	34	81		12	28.6	30	71.4		8	19	34	81	
Four	1	3.6	27	96.4		3	10.7	25	89.3		1	3.6	27	96.4	
Surgery type															
squint 1 muscle	0	0	2	100		0	0	2	100		0	0	2	100	
squint 2 muscle	2	10	18	90	0.764	4	20	16	80	1.000	2	10	18	90	0.764
squint 3 muscle	6	13.6	38	86.4		10	22.7	34	77.3		6	13.6	38	86.4	
squint 4 muscle	1	25	3	75		1	25	3	75		1	25	3	75	
Surgery duration															
less than 90 minutes	4	17.4	19	82.6	0.463	6	26.1	17	73.9	0.545	4	17.4	19	82.6	0.463
90 minutes or more	5	10.6	42	89.4		9	19.1	38	80.9		5	10.6	42	89.4	

* The P-values are related to the Chi-square test adjusted by the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5. The numbers in the table represent N(%).

The results in Table (7) above show that there are significant differences at 0.05 level in the Postoperative Nausea at the Pediatric Ward according to Age; the results show that the percentage of patients who had nausea from the age group 3-5 years (n=5, p=31.3%) and the percentage of patients who had nausea from the age group 6-9 years (n=7, p=33.3%) are significantly higher than the percentage of patients who had nausea from the age group 10 – 12 years (n=3, p=9.1%), the P-value of the test is 0.047.

Also, the results in the table above show that there are significant differences at 0.05 level in the Postoperative Nausea at the Pediatric Ward according to the history of PONV in previous surgeries; the results show that the percentage of patients who had nausea and history of PONV in previous surgeries (n=2, p=7.4%) is significantly lower than the percentage of patients who had nausea without history of PONV in previous surgeries (n=13, p=30.2%), the P-value of the test is 0.035.

Table 8

*Differences in the in the 8 hours' Postoperative Vomiting, Nausea, and Retching according to (Gender, Age, History of PONV in previous surgeries, Eberhart risk score, Surgery type, and Surgery duration) (N=70) **

Variable	Incidence of vomiting					Incidence of nausea					Retching				
	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value	Yes	%	NO	%	P-value
Gender															
Male	1	2.4	40	97.6	0.566	2	4.9	39	95.1	1.000	2	4.9	39	95.1	1.000
Female	2	6.9	27	93.1		2	6.9	27	93.1		2	6.9	27	93.1	
Age															
3-5 years	0	0	16	100	1.000	0	0	16	100	0.807	0	0	16	100	0.807
6-9 years	1	4.8	20	95.2		1	4.8	20	95.2		1	4.8	20	95.2	
10 – 12 years	2	6.1	31	93.9		3	9.1	30	90.9		3	9.1	30	90.9	
Hx of PONV in previous surgeries															
Yes	1	3.7	26	96.3	1.000	2	7.4	25	92.6	0.637	2	7.4	25	92.6	0.637
No	2	4.7	41	95.3		2	4.7	41	95.3		2	4.7	41	95.3	
Eberhart risk score															
One	0	0	0	0	1.000	0	0	0	0	1.000	0	0	0	0	1.000
Two	0	0	0	0		0	0	0	0		0	0	0	0	
Three	2	4.8	40	95.2		2	4.8	40	95.2		2	4.8	40	95.2	
Four	1	3.6	27	96.4		2	7.1	26	92.9		2	7.1	26	92.9	
Surgery type															
squint muscle 1	0	0	2	100	1.000	0	0	2	100	1.000	0	0	2	100	1.000
squint muscle 2	1	5	19	95		1	5	19	95		1	5	19	95	
squint muscle 3	2	4.5	42	95.5		3	6.8	41	93.2		3	6.8	41	93.2	
squint muscle 4	0	0	4	100		0	0	4	100		0	0	4	100	
Surgery duration															
less than 90 minutes	1	4.3	22	95.7	1.000	1	4.3	22	95.7	1.000	1	4.3	22	95.7	1.000
90 minutes or more	2	4.3	45	95.7		3	6.4	44	93.6		3	6.4	44	93.6	

* The P-values are related to the Chi-square test adjusted by the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5. The numbers in the table represent N(%).

The results in Table (8) above show that there are no significant differences at 0.05 level in the 8 hours' Postoperative Vomiting, Nausea, and Retching according to (Gender, Age, History of PONV in previous surgeries, Eberhart risk score, Surgery type, and Surgery duration). All the P-values in the table are higher than 0.05.

Table 9

*Comparisons between the study groups in the Whole term of the postoperative parameters (N=70) **

Variable	Group			P-value
	Ondansetron only N=40	Combined N=30	Total	
Complete response (no nausea, no vomiting, no retching, no rescue medication)	19(47.5%)	27(90%)	46(65.7%)	0.000
Early Complete response (0–3 hr)	37(92.5%)	29(96.7%)	66(94.3%)	0.457
Late Complete response (3-8 hr)	20(50%)	28(93.3%)	48(68.6%)	0.000
PONV+Retching+ Rescue medication (postoperative nausea and vomiting and retching and rescue medication)	9(22.5%)	0(0%)	9(12.9%)	0.008**
Vomiting (only)	13(32.5%)	1(3.3%)	14(20%)	0.002**
Nausea (only)	17(42.5%)	3(10%)	20(28.6%)	0.003**
Retching (only)	13(32.5%)	0(0%)	13(18.6%)	0.000**

* The P-values are related to the Chi-square test for Qualitative variables; the numbers in the table represent N (%).

** The P-value of the Chi-square test is based on the Fisher's Exact Test to account for the low frequency of some categories where the expected count could be less than 5.

The results in Table (9) above show that there are significant differences at 0.05 level between the study groups (Ondansetron only, Combined) in the following variables: Complete response, Late Complete response, PONV+Retching+ Rescue medication, Vomiting (only), Nausea (only), Retching (only).

The results show that the percentage of complete response patients in the whole postoperative term in the Ondansetron-only group (n=19, p=47.5%) is significantly lower than the percentage in the Combined group (n=27, p=90%), the P-value of the test is 0.000.

The results show that the percentage of early complete response patients in the Ondansetron-only group (n=37, p=92.5%) is not significantly different from the percentage in the Combined group (n=29, p=96.7%), the P-value of the test is 0.457. On the other hand, the results show that the percentage of late complete response patients in the Ondansetron-only group (n=20, p=50%) is significantly lower than the percentage in the Combined group (n=28, p=93.3%), the P-value of the test is 0.000.

The results show that the percentage of PONV patients in the whole postoperative term in the Ondansetron-only group (n=9, p=22.5%) is significantly higher than the percentage in the Combined group (n=0, p=0%), the P-value of the test is 0.005.

The results show that the percentage of patients with vomiting only in the whole postoperative term in the Ondansetron-only group (n=13, p=32.5%) is significantly higher than the percentage of vomiting in the Combined group (n=1, p=3.3%), the P-value of the test is 0.002. Also, the results indicate that a substantially higher percentage of patients in the Ondansetron-only group (n=17, p=42.5%) experienced nausea during the whole postoperative term than in the Combined group (n=3, p= 10%)%), the P-value of the test is 0.003. Finally, the results show that the percentage of patients with retching only in the whole postoperative term in the Ondansetron-only group (n=13, p=32.5%) is significantly higher than the percentage of retching in the Combined group (n=0, p=0%), the P-value of the test is 0.000.

Figure 7

Comparison of combined and Ondansetron-only groups in all postoperative measures for the entire term

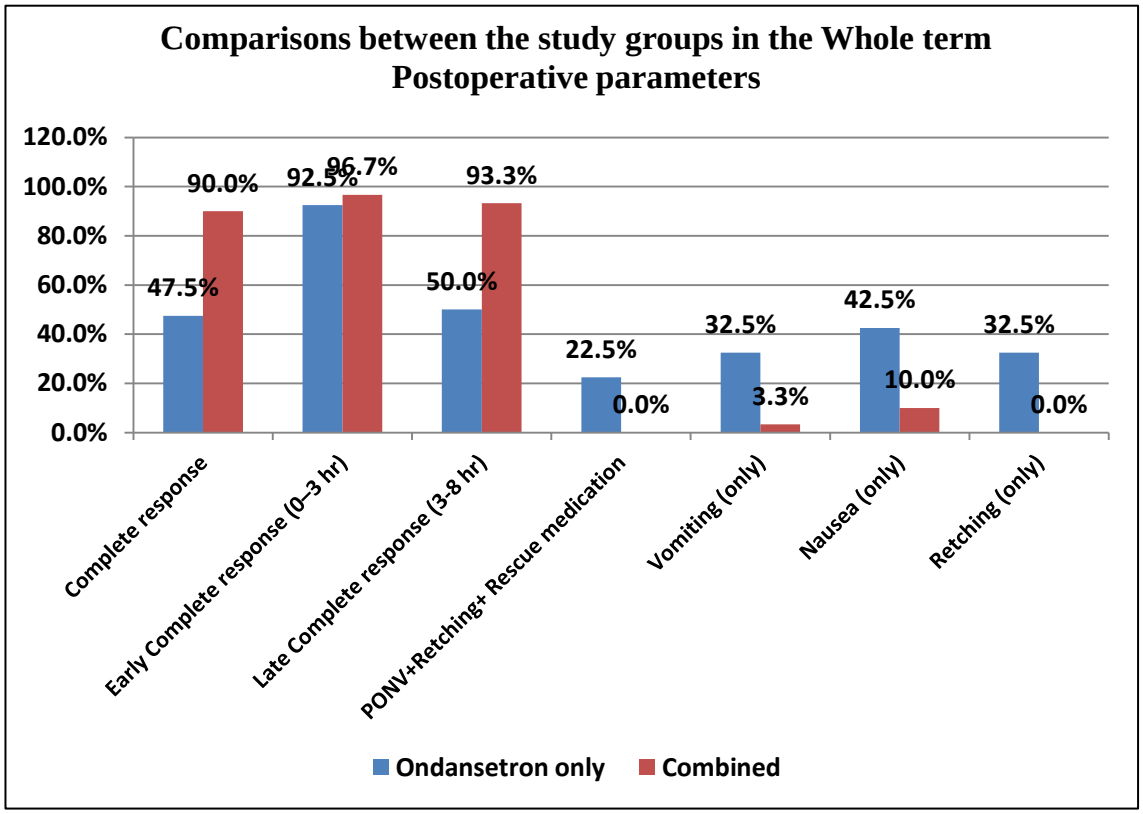


Figure (7) shows that the the percentage of the complete response in the whole term increased from 47.5% in the Ondansetron only group to 90% in the combined group. Also, the the percentage of the late complete response in the whole term increased from 50% in the Ondansetron only group to 93.3% in the combined group, while the percentage of the late complete response in the whole term increased very slightly from 92.5% in the Ondansetron only group to 96.7% in the combined group.

On the other hand, Figure (7) showes that the PONV+Retching+ Rescue medication percentages decreased from 22.5% in the Ondansetron only group to 0% in the combined group, the vomiting (only) percentages decreased from 32.5% in the Ondansetron only group to 3.3% in the combined group, the nausea (only) percentages decreased from 42.5% in the Ondansetron only group to 10% in the combined group, and the retching (only) percentages decreased from 32.5% in the Ondansetron only group to 0% in the combined group.

Chapter Four

Discussions and Conclusions

4.1 Discussion

The following part is dedicated to discussing the results of the current study, which is done by comparing its findings with previous literature's findings and providing a comprehensive critique from the researcher's point of view.

4.1.1 Demographic data

The majority of the variables in the two groups' demographic data are comparable. It indicates that the patients are distributed between both groups mostly homogeneously, decreasing the possibility of bias counteracting the collection bias due to purposive sampling and descriptive, non-interventional study design.

Regarding age, there were notable variations across the study groups in the current investigation. Examining the relationship between age and the frequency of nausea and vomiting, it was found that while age was a risk factor for postoperative nausea, it was not a risk factor for PV. Clinical investigations have shown that toddlers are less sensitive to emetic cues than school-aged children and adolescents.[66]

4.1.2 Multimodal PONV prophylaxis

In the current study, the combination treatment resulted in a higher percentage of patients with a complete response (defined as no nausea or emesis or retching and no need for rescue antiemetic) during the first 8 hours post-surgery) 27(90%) compared to those who received only Ondansetron19(47.5%), p=0.000. Comprehensive recommendations for the management of postoperative nausea and vomiting (PONV) in adult and pediatric populations are provided by the Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting (PONV), which are created by an international panel of experts based on evidence.

These recommendations place a strong emphasis on the need to recognize high-risk individuals, control baseline PONV risks, and make well-informed decisions regarding PONV prophylaxis and rescue therapy. They focus on the evidence supporting more recent medications and the application of general multimodal PONV prophylaxis, which

includes combination therapy, especially in young patients who have several PONV risk factors.[48]

A study compares the safety and effectiveness of ondansetron plus dexamethasone versus ondansetron alone for PONV prophylaxis in patients with elective laparoscopic surgery.[67] According to this trial, ondansetron plus dexamethasone worked better together than ondansetron alone to prevent postoperative nausea and vomiting. Compared to patients who got only Ondansetron, a greater proportion of patients who received the combination treatment experienced a full response, which is defined as no nausea or emesis and no need for rescue antiemetic within the first 24 hours post-surgery. While this study provides useful information, it's important to keep in mind that it was conducted on adults receiving laparoscopic surgery rather than on children undergoing strabismus surgery. The relevant findings may not be as applicable due to the differences in surgical procedures and patient demographics.

A review paper by K Y Ho et al.[68] that discusses the effectiveness of multimodal antiemetic therapy in reducing the risk of postoperative nausea and vomiting (PONV). The review emphasizes the part that patient, surgical, and anesthetic factors play in the risk of PONV. According to the study's findings, a multimodal approach that incorporates both pharmaceutical and non-pharmacological therapy lowers PONV. This approach is particularly beneficial for treating PONV in patients with a high number of risk factors.

4.1.3 Dose response of Ondansetron

In the present study, 150µg/kg of ondansetron at a dose of 0.15 mg/kg was used; this dose is similar to one that examined ondansetron's efficacy in preventing PONV in young children after strabismus surgery. According to the study, a routine preventive dose of 75 micrograms/kg of Ondansetron is just as effective as a dose of 150 micrograms/kg in preventing PONV and improving postoperative outcomes in children undergoing strabismus correction. The incidence of PONV was shown to be significantly reduced in the groups receiving 75, 100, and 150 micrograms/kg of Ondansetron compared to the placebo group. Furthermore, these groups had shorter stays in the post-anesthesia care unit and better parental assessment scores for their child's perioperative experience.[69]

Another pertinent research paper is entitled "Prophylactic Ondansetron in Prevention of postoperative nausea and vomiting following pediatric strabismus surgery: a dose-response study." In children having strabismus correction, this study evaluated the efficacy of ondansetron in avoiding postoperative nausea and vomiting (PONV). One hundred and eighty children participated in the study, which looked at different ondansetron dosages and discovered that 75 micrograms/kg of the drug was just as effective as 150 micrograms/kg in preventing PONV. Important new information regarding the dosage and efficacy of ondansetron for PONV in pediatric strabismus surgery is provided by this study.[69]

4.1.4 Time of administration of preventative antiemetics for PONV

In agreement with Cruz et al.'s (2008) investigation on the best time to give ondansetron to surgical patients to prevent postoperative nausea and vomiting (PONV), preventive drugs were given in the current study fifteen minutes before the procedure finished. In order to take part in the prospective, randomized, double-blind study, participants needed to fulfill a minimum of two PONV risk criteria. Before the procedure, patients were given dexamethasone and split into two groups. One group received ondansetron before anesthesia was induced, whereas the other group received it 30 minutes before the procedure was finished. The study found that ondansetron was more effective at preventing late postoperative nausea and vomiting (PONV) when given 30 minutes prior to the procedure's conclusion than when it was given immediately before anesthesia was induced. This information can help optimize PONV care, especially for pediatric patients who have many PONV risk factors.

4.1.5 Ondansetron as an antiemetic medication

In the research article "Vomiting after strabismus surgery in children: ondansetron vs. propofol," the cost and efficiency of two different anesthetic regimens for preventing vomiting in children having strabismus surgery were examined. This trial, which involved 300 youngsters, investigated the use of ondansetron in one regimen and propofol in another. The outcomes demonstrated that both methods were equally effective as antiemetics.[70]

The majority of patients in the current study had their squint three muscles corrected; these patients were divided into two groups: those receiving ondansetron (n = 26; 65%) and those receiving combination therapy (18%); the number of muscles operated on may have an impact on the incidence of PONV. This result is in line with the conclusions of the Splinter et al.[70] investigation. The efficacy of low-dose ondansetron plus dexamethasone compared to high-dose ondansetron alone was assessed in this trial. Ultimately, compared to the high-dose ondansetron group, there was a decreased incidence of vomiting in the low-dose ondansetron + dexamethasone group. Numerous other variables that may have an effect on the frequency of vomiting were also examined in the study, including the patient's age and the number of muscles they had surgery on.

4.1.6 Ketorolac

Pain after a range of surgical procedures, including surgery for strabismus in children, is commonly managed with nonsteroidal anti-inflammatory medications (NSAIDs), such as ketorolac. The primary justification for use it in this instance is its analgesic properties. Although ketorolac effectively treats postoperative pain, there is currently a lack of research on its potential to reduce postoperative nausea and vomiting (PONV). Due to its potent analgesic effects, ketorolac may be able to assist in the effective treatment of pain, which has been shown to lower PONV rates. But it's important to balance the benefits against any potential risks, especially for young children.

There are a variety of precise rules and suggestions regarding the usage of ketorolac, and it's important to take surgical specifics and patient considerations into account.[28] Munro and colleagues studied the analgesic and emetic effects of intravenous ketorolac and morphine in kids undergoing strabismus surgery. Forty-two children were randomized to receive either morphine or ketorolac. The results showed no differences in the groups' recovery times or pain levels. The ketorolac group, on the other hand, had a significantly lower incidence of nausea and vomiting than the morphine group. This study indicates that ketorolac is an effective analgesic for pediatric strabismus surgery and is related with lower postoperative nausea and vomiting when compared to morphine and metoclopramide.[28]

The use of ketorolac, a nonsteroidal anti-inflammatory medication (NSAID), for treating postoperative pain in children is examined in the article "Ketorolac for pediatric postoperative pain. A review" by A Di Massa et al.[71] The study highlights the pharmacological and pharmacokinetic characteristics and adverse effects of ketorolac, taking into account the differences in parameters, doses, administration techniques, treatment duration, side effects, precautions, and pharmacological interactions between children and adults. According to the study's findings, children's postoperative pain management with ketorolac is effective.

In children undergoing strabismus surgery, a study was done to compare the effects of intravenous ketorolac against pethidine on postoperative analgesia and postoperative nausea and vomiting (PONV). The trial had 52 children randomized to receive either ketorolac or pethidine. This suggests that ketorolac may be an effective analgesic for juvenile strabismus surgery while also reducing the risk of PONV.[29]

Nevertheless, in a study conducted by Mendel et al.[17], children classified as ASA I and II, aged 1 to 10, undergoing strabismus surgery, were randomized to receive intravenous ketorolac (0.9 mg/kg), fentanyl (1 microgram/kg), or saline placebo (2 mL) in a double-blind design, all while under a standard general anesthesia. The incidence of postoperative vomiting was considerably reduced in patients receiving ketorolac or placebo as compared to fentanyl, both in the day surgery unit (DSU) ($P = 0.03$) and overall (DSU plus home) ($P = 0.005$). When comparing patients receiving ketorolac or placebo to fentanyl, the intensity (number of episodes) of post-operative vomiting was considerably reduced in the DSU, at home (within the first 24 hours following hospital release), and overall ($P < 0.01$).

A very high incidence (>40%) of early and late vomiting is linked to strabismus surgery.[72] Postoperative distortion of vision,[18] residual strain on the intraocular muscles,[15] the potential existence of an oculo-emetic reflex,[18] postoperative pain,[16] and the use of opioid analgesics,[17] are the factors responsible for this high incidence of PONV following strabismus surgery. A centrally mediated trigeminovagal reaction is triggered by manipulation of the eyes, releasing a variety of neurotransmitters in the chemoreceptor trigger zone. Antiemetic medication is based on blocking the receptors for these neurotransmitters.[18]

Postoperative vomiting is still widespread in daily practice despite the significant attention it has received. Children receiving strabismus surgery have the greatest rate of postoperative vomiting (88%).[73] According to Lerman et al.[18], extraocular muscle surgery resets the emetic threshold, which results in emesis following oral consumption. Comparing antiemetic treatments is challenging because some researchers.[74] link retching to vomiting, while other researchers.[75] do not. We did not regard retching as being the same as vomiting.

It has been demonstrated that the 5HT3 antagonist ondansetron prevents postoperative PONV following pediatric strabismus surgery. Following ondansetron prophylaxis, reports of PONV incidence ranged from 6% to 20% [10, 72, 76, 77]. In the current study, the incidence of PONV was 0(0%) in the combined group and 9(22.5%) in the ondansetron group.

A 5-hydroxytryptamine type 3 receptor antagonist called ondansetron has been demonstrated to be useful in lowering postoperative vomiting related to strabismus surgery.[72] Our findings show that when ondansetron and ketorolac were administered to children after strabismus surgery, they had an impact on preventing PONV and decreasing the need for rescue antiemetics. Our findings imply that administering ondansetron to inhibit receptors increased efficacy beforehand. Given that ondansetron has a brief half-life of 2.8 ±0.6 hours, two recent investigations looked at how the time of its administration affected its antiemetic effectiveness. Ondansetron given at the conclusion of surgery was more successful in preventing PONV and promoting both early and late recovery in women undergoing outpatient laparoscopy.[11]

The study's outcome measures were reduced PONV incidence and a lower need for rescue antiemetics during the latter stages of recovery. While timing did not appear to impact the incidence of nausea or emesis in outpatients receiving otorhinolaryngologic surgery, ondansetron provided at the procedure's conclusion dramatically decreased the rescue antiemetics requirement.[14]

The current study noted numerous possible risk factors concerning the Eberhart risk score preoperatively. Concern was given to four separate risk factors for PV: age >/=3 years, strabismus surgery, duration of surgery >/=30 min, and a positive history of PV in the children or PV/postoperative nausea and vomiting in family members (parents,

siblings, or mother). The study covered participants who had three or more risk factors. The incidence of PV for the observed 0, 1, 2, 3, and 4 risk variables was 10%, 30%, 55%, and 70%.[8] It indicates that each patient who was included in the research had a POV risk score of 55% to 70%. As the current study's endpoint, PONV may be observed for up to eight hours after surgery. According to the current study, patients with four risk factors in the ondansetron group 11(27.5%) compared to 17(56.7%) in the combination group, p=0.014, and patients with three risk factors in the ondansetron group 29(72.5%) compared to 13(43.3%) in the combined group. These outcomes are consistent with a systematic study of antiemetic prophylaxis in children having strabismus correction, which found that an extremely high incidence (up to 87%) was seen in many studies.[17]

4.1.7 Analgesia

In the current study, pain in the incision area in the PACU was 13(32.5%) in the ondansetron group compared to 3(10%) in the combination group (p=0.042). In the ward, pain was 17(42.5%) in the ondansetron group compared to 4(13.3%) in the combination group (p= 0.009). These results are consistent with research.[28] that found that compared to morphine, ketorolac has been demonstrated to be a less common cause of postoperative emesis following strabismus surgery and to be an effective analgesic. These results differ from research.[17], which found that when saline placebo was used instead of ketorolac or fentanyl during pediatric strabismus surgery, there was no difference in the postoperative vomiting or amount of analgesic needs.

4.1.8 PACU Phase

In the PACU phase, it is noticed that significant differences are more apparent in terms of post-operative pain (p-value = 0.042), in which the ondansetron group of patients has a significantly higher prevalence of these variables than in the combined group of patients. This pattern has continued to happen in the pediatric ward, in addition to the significantly higher prevalence of PONV, retching, and the use of analgesics and rescue medications, which means that all of the study variables are significantly higher in prevalence among patients of the ondansetron-only group than in the combined group (p-value < 0.017). On the other hand, this pattern has changed when it comes to the 8-hour postoperative phase, where the prevalence rates were significantly higher among patients of the ondansetron group in terms of PONV and retching, as well as the use of

rescue medications (p-value < 0.05). In comparison, patients in the ondansetron group had marginally greater rates of postoperative pain and the corresponding usage of analgesics (p-value > 0.05).

The explanation for the previously explained pattern is that pain and the associated use of analgesics can be described as the main issue among patients during the three phases. At the same time, PONV does not immediately appear and is not a significant concern among the patients before transferring to the pediatric ward, as the prophylactic effect of intraoperative agents may cause it. The latter indicates that PONV is more quickly resolved among patients with combined therapy than in the ondansetron group.

In the current study, the highest incidence of nausea among patients in the ondansetron group was 32.5%, compared to 6.7% in the combined groups, during the pediatric ward phase, while the highest prevalence rate for vomiting was 22.5% vs 2.5%, respectively. This is a critical point to discuss, as it indicates that any of the provided treatments is kind of effective in protecting from PONV following a strabismus surgery, which is generally lower than the incidence rates that were reported by Williams and Conroy [4], who stated that PONV occurs in 37% to 90% among these patients without the use of prophylactic antiemetic drugs. When compared to the previously stated rates by Madan, Perumal [78], the current study stated that the prevalence of PONV was between 2.5% and 32.5% among patients who received ondansetron only, while the previous study found a rate that ranged from 6% to 20%, which shows a wider range of prevalence rates of PONV among patients in the current study.

The peak percentage of PONV in the current study is generally lower than in the previous study.[78] It is also worth noting that the current study used paracetamol as the main analgesic rescue medication, while a previous study by Shende and Mandal [13] stated that their rates of PONV were relatively higher among the patients who received ondansetron because they used opioid analgesic rescue medications, which are known to be associated with nausea and vomiting, and therefore contributing to some level of bias, which was successfully avoided in the current study. On the other hand, shared factors that cannot be modified are also present in the current and previous studies,[15, 16] including postoperative vision distortion, residual tension on the intraocular muscles, and possibility of a coulometric reflex,[15] as well as the inevitable postoperative pain.[16]

The principal investigator of the current study assured that the protocol of administering ondansetron and/or ketorolac at the end of the surgery, or within a short time before that, not at the beginning of the surgical procedure, which has shown to result in significantly lower incidence PONV, as proven by previous studies, although done on other types of surgeries rather than strabismus, like laparoscopy,[11] and otorhinolaryngologic surgeries.[14] The findings related to lower rates of PONV according to the timing of administration of ondansetron are easier to conclude than the findings of administering droperidol, as some studies found its efficacy on decreasing PONV if administered earlier in the surgery, before the manipulation of eyeball.[19, 20] In contrast, others found the opposite, where no significant differences in PONV were found according to the administration timing,[21, 22] which can be related to using a different agent. The current study was also conducted with the recommendation of not using atropine prior to the surgery, which was thought to have a prophylactic effect against PONV but disproved by Klockgether-Radke, Demmel [21] and Chisakuta and Mirakhur [23].

Although the previous study by Forrest, Heitlinger [30] was conducted on patients with abdominal surgeries, its findings regarding the decreased incidence of reversible antiplatelet actions are still favorable in the current study. This outcome, among others, encouraged the researcher to compare the effects of the use and not using ketorolac among strabismus surgery pediatric patients. As stated earlier, the use of opioids was not favorable because they are linked to a higher incidence of PONV, specifically among pediatric patients who undergo strabismus surgeries, as proven by Munro, Riegger [28], which supports abandonment of opioid use as analgesic rescue medication in the current study, as well as that its effect is comparable to the effect of pethidine in alleviating postoperative pain with less PONV incidence.[29, 30]

In addition, the findings of Keidan, Zaslansky [32] state the higher incidence of post-anesthesia agitation among patients who received ketorolac compared to fentanyl. The same applies to the investigation of postoperative pruritis, which was found to be decreased when ondansetron and ketorolac were used among patients undergoing cesarean section surgery.[79]

4.1.9 Patient satisfaction with the treatment

The majority of patients (54.3%) and 42.9%, respectively, express very satisfaction or satisfaction with the treatment they have received. This reflects the proper choices of antiemetics and rescue medications chosen by the specialists, as well as the proper ongoing assessment, evaluation, and interventions of the nursing team, which elevates the reputation of the targeted settings. The mentioned results are a crucial part of the audit system that hospitals should implement regularly to continuously evaluate surgical outcomes, detect weaknesses, and try to improve them. As a result, almost all patients (98.6%) have stated that they recommend the treatment provided to other patients. In addition, the findings of the Aldrete scores underscore the favorable postoperative recovery outcomes among patients who underwent strabismus surgery, as evidenced by uniformly high Aldrete scores across various physiological parameters.

4.2 Conclusion

In the later phases of recovery after strabismus surgery, the combination of ondansetron and ketorolac provided greater analgesia, increased complete response, decreased PONV, and a need for analgesic and antiemetic drugs. The less severe postoperative vomiting associated with ketorolac may be attributed to decreased patient exposure to opioid analgesics. Intravenous acetaminophen seemed to provide enough analgesia in pediatric strabismus patients.

4.3 Recommendations

Based on the discussion of the current study's results, the researcher recommends:

1. The use of ketorolac in addition to ondansetron to alleviate PONV and pain among pediatric patients who undergo strabismus surgery was observed to be associated with lower PONV, pain, and the use of analgesics and rescue medications, especially in the pediatric ward.

2. The conduct of further studies that apply the same approach to other types of pediatric and adult surgeries to improve patient outcomes in terms of postoperative care will also improve their experience and satisfaction level.

3. The conduct of further interventional studies to compare the outcomes in terms of PONV between patients who receive antiemetics at the beginning and end of the strabismus surgeries, which will help contribute to the body of science in this field.

4. The conduct of further studies that apply the same approach to investigate the agitation scores among strabismus pediatric patients.

5. The conduct of further studies to investigate the occurrence of pruritus among pediatric patients undergoing strabismus surgeries.

6. Increase the level of awareness among open ward nurses and healthcare professionals about the importance of continuous education regarding the optimal analgesics and rescue medications to be used among pediatric patients, as well as the use of non-pharmacological methods of PONV and pain control.

4.4 Limitations

The study was mainly limited to the following factors:

1. There is an inability to control the study variables fully, as the study was implemented using an observational rather than interventional design, which is mostly related to the surgeons' and anesthesiologists' preferences that are hard to modify.

2. Although no significant differences in patients' characteristics were found between both groups in terms of gender and BMI category, the study was limited by the significantly higher percentages of patients with a positive history of PONV among patients in the combined group. On the other hand, this limitation is self-issued, as the surgeons' and anesthesiologists' preferences were to recruit those patients in the combined group to give a higher chance of decreasing PONV. Controlling these variables may have given results with a higher proving confidence.

List of Abbreviations

Abbreviation	Meaning
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CRNA	Certified Registered Nurse Anesthetist
CTZ	Chemoreceptor Trigger Zone
Hx	History
I.V	Intravenous
MAC	Minimum Alveolar Concentration
NK-1	neurokinin-1
NSAID	Non-steroidal anti-inflammatory drugs
OR	Operation Room
PACU	Post Anesthesia Care Unit
PONV	Postoperative Nausea and Vomiting
SPSS	Statistical Package for the Social Sciences
TIVA	Total Intravenous Anaesthesia
VAS-N	Visual Analog scale for Nausea
VAS-P	Visual Analog scale for Pain
5-HT	5-hydroxytryptamine

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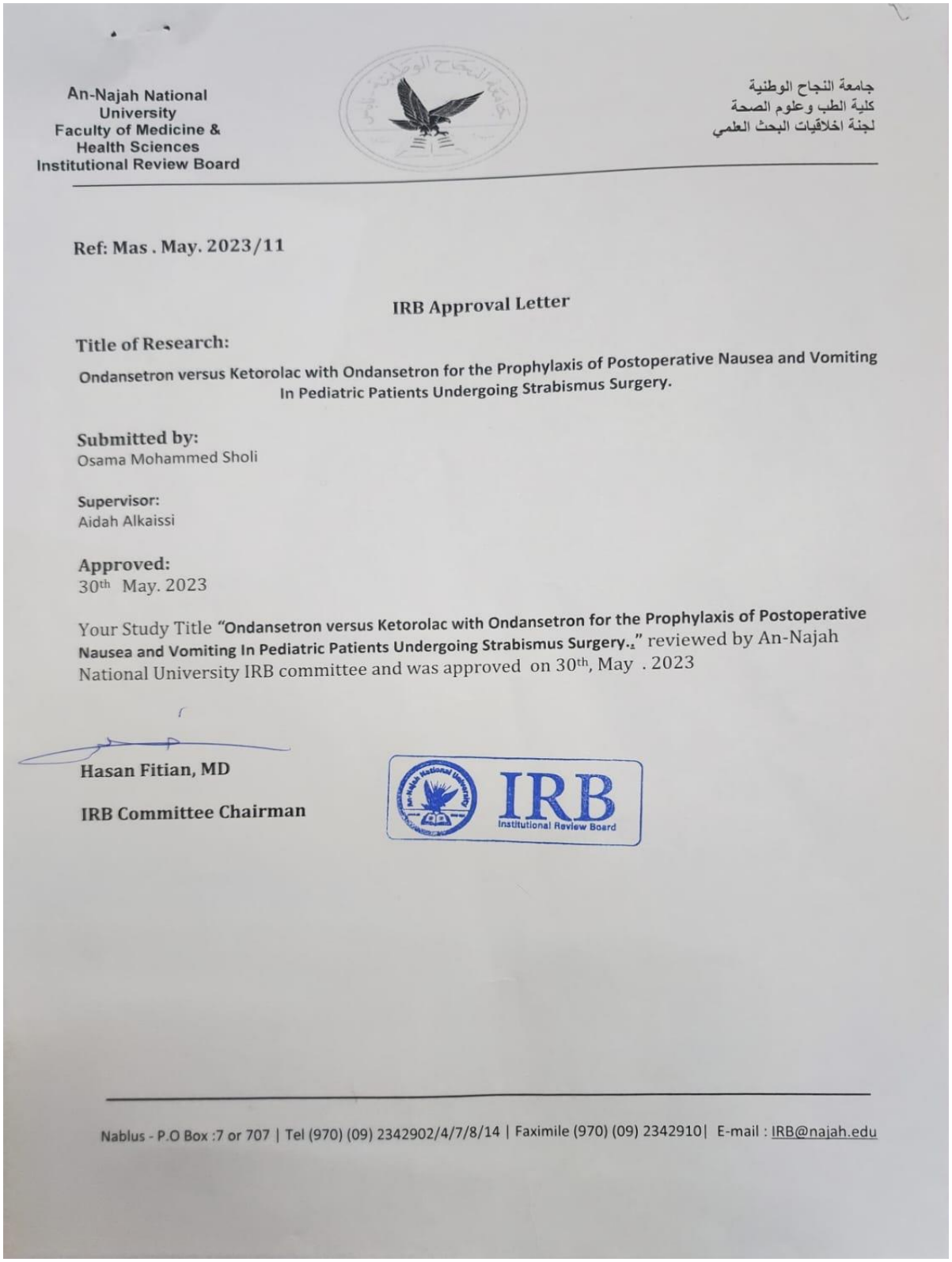
Appendices

Appendix A

IRB Approval Letter



An-Najah National University
Faculty of Medicine & Health Sciences
Institutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref: Mas . May. 2023/11

IRB Approval Letter

Title of Research:

Ondansetron versus Ketorolac with Ondansetron for the Prophylaxis of Postoperative Nausea and Vomiting In Pediatric Patients Undergoing Strabismus Surgery.

Submitted by:
Osama Mohammed Sholi

Supervisor:
Aidah Alkaissi

Approved:
30th May. 2023

Your Study Title "Ondansetron versus Ketorolac with Ondansetron for the Prophylaxis of Postoperative Nausea and Vomiting In Pediatric Patients Undergoing Strabismus Surgery.," reviewed by An-Najah National University IRB committee and was approved on 30th, May . 2023

Hasan Fitian, MD

IRB Committee Chairman

IRB Institutional Review Board

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910| E-mail : IRB@najah.edu

Appendix B

Collecting Data Sheet

استبيان لمرضى الحول

1. اسم المريض	
2. رقم المريض في البحث	
3. رقم ملف المريض في المستشفى	
4. الجنس	
5. العمر	
6. مكان الاقامة	
7. رقم الهاتف/ الجوال	
8. الوزن (كلغرام)	
9. الطول (سم)	
10. BMI	
11. وجود عمليات سابقة مع حدوث غثيان وتقيء لدى المريض او احد افراد العائلة (Hx of PONV)	
12. العمر أكثر او يساوي 3 سنوات	
13. مدة التخدير اكثر من 30 دقيقة Duration of anesthesia (> 30 min)	
14. ما هي نسبة ان يكون الطفل معرض للغثيان والقيء (Eberhart risk score)	
15. نوع العملية	
16. مده التخدير (دقيقة)	
17. مده الجراحة (دقيقة)	

أثناء العملية

Total intra operative drugs	
1. Total Fentanyl/ µg:	
2. Total Propofol/mg:	
3. Total Rocuronium:	
4. Total dexamethasone:	
5. Total Perfalgan:	
6. Other medications:	

Postoperative

Checklist

Section 1: On arrival to PACU and 30 min after operation :

No	Questions	30 Min After Operation	
1	Incidence of vomiting?	( ) Yes	( ) No
2	Frequency of vomitin		
3	Incidence of nausea	( ) Yes	( ) No
4	Intensity of nausea using VAS-N:		
5	Are you retching?	( ) Yes	( ) No
6	Frequency of retching		
7	Do you have pain on the area of surgery	( ) Yes	( ) No
8	Intensity of pain by using VAS-P:		
9	Analgesic	( ) Yes	( ) No
10	Rescue antiemetic (Dexamethasone IV)	( ) Yes	( ) No

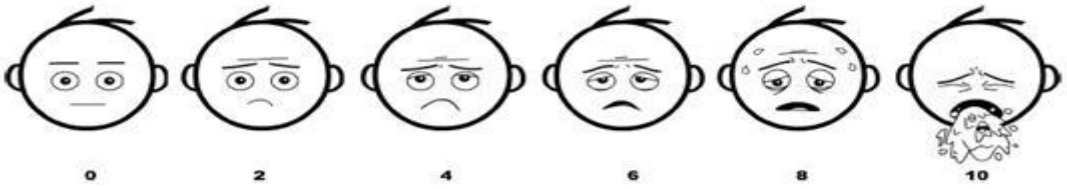
Section 2: At pediatric ward

No	Questions	pediatric ward	
1	Incidence of vomiting?	( ) Yes	( ) No
2	Frequency of vomiting		
3	Incidence of nausea	( ) Yes	( ) No
4	Intensity of nausea using VAS-N:		
5	Are you retching?	( ) Yes	( ) No
6	Frequency of retching		
7	Do you have pain on the area of surgery	( ) Yes	( ) No
8	Intensity of pain by using VAS-P:		
9	Analgesic	( ) Yes	( ) No
10	Rescue antiemetic (Dexamethasone IV)	( ) Yes	( ) No

Section 3: 8 h after operation

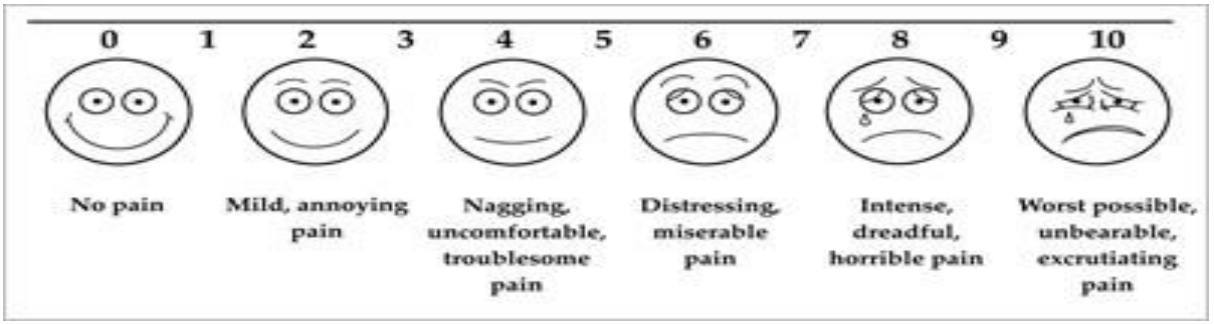
No	Questions	At Discharge From Hospital	
1	Incidence of vomiting?	( ) Yes	( ) No
2	Frequency of vomiting		
3	Incidence of nausea	( ) Yes	( ) No
4	Intensity of nausea using VAS-N:		
5	Are you retching?	( ) Yes	( ) No
6	Frequency of retching		
7	Do you have pain on the area of surgery	( ) Yes	( ) No
8	Intensity of pain by using VAS-P:		
9	Analgesic	( ) Yes	( ) No
10	Rescue antiemetic (Dexamethasone IV)	( ) Yes	( ) No
11	Do you satisfied about treatment that given to you?	1- ( ) Very unsatisfied	
		2- ( ) Un satisfied	
		3- ( ) Neither satisfied nor un satisfied	
		4- ( ) Satisfied	
		5- ( ) Very satisfied	
12	Do you recommend this treatment to another patient?	( ) Yes	( ) No

Measure of nausea using VAS-N:



No nausea Mild,annoying Nagging, Distressing, Intense, Worst possible,

Measure of pain using VAS-P:



Aldrete score (Post Anesthesia Recovery Score (PAR-Score))

Parameters	Description of the patient	Score
Activity level	Moves all extremities voluntarily/on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respiration	Breathes deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulation (blood pressure)	Is 20 mmHg > preanesthetic level	2
	Is 20 to 50 mmHg > preanesthetic level	1
	Is 50 mmHg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level > 90% when breathing room air	2
	Requires supplemental oxygen to maintain level > 90%	1
	Has level < 90% with oxygen supplementation	0

*Maximum total score is 10; a score of ≥9 is required for discharge.

Appendix C

Consent form

موافقة للاشتراك في البحث العلمي للوصي على الطفل

اسم الباحث: أسامة محمد شولي.

عنوان البحث: اوندانستيرون مقابل كيتولاك مع اوندانستيرون للوقاية من الغثيان والقيء بعد الجراحة في مرضى الأطفال الذين يخضعون لجراحة الحول.

مكان إجراء البحث: مستشفى النجاح الوطني الجامعي / نابلس.

أ- وصف البحث العلمي وهدفه وتفسير مجرياته:

يهدف هذا البحث إلى مقارنة تأثير إعطاء اوندانستيرون مقابل اعطاء كيتولاك مع اوندانستيرون للوقاية من الغثيان والقيء بعد الجراحة بين مرضى الأطفال الذين يخضعون لجراحة الحول وتأثيره على استهلاك الأدوية الإنقاذية المضادة للقيء وتسكين الألم بعد العملية الجراحية.

ب- الفوائد التي قد تنتج عن هذا البحث:

معرفه مدى تأثير كلا من إعطاء اوندانستيرون مقابل اعطاء كيتولاك مع اوندانستيرون في التقليل حالات القيء والغثيان بعد عمليه جراحة الحول مما يساعد على التقليل من استخدام الأدوية المستخدمه في تقليل القيء والغثيان وبالتالي التقليل من استهلاك الأدوية الإنقاذية المضادة للقيء

وتسكين الألم و تقليل وقت المكوث في قسم الإنعاش بعد التخدير و زيادة الرضا لدى المريض وتقليل التكاليف الماديه عليه

سرية معلوماتك: في حال وافقت على المشاركة في هذه الدراسة، سيبقى إسمك طي الكتمان . لن يكون لأي شخص، ما لم ينص القانون على ذلك، حق الإطلاع على الاستمارة بعد تعبئتها

علما بان هذه المعلومات لن تستخدم الا لغرض البحث العملي فقط و بدرجة عالية من السرية و الخصوصية.

ج. حقك فى الانسحاب: من حقك الانسحاب من البحث في أي وقت دون إبداء أسباب دون أى عواقب سلبية عليك

موافقة الباحث:

لقد شرحت بالتفصيل للمشترك في البحث العلمي (.....) طبيعته ومجرياته وتأثيراته السلبية. ولقدأجبت على كل أسئلته بوضوح على خير ما أستطيع. وسوفأعلم المشترك بأي تغيرات في مجريات هذا البحث أو تأثيراته السلبية أو فوائده في حال حصولها أثناء البحث.

إسم الباحث المولى **توقيع الباحث المولى**

على موافقة المشترك للحصول على موافقة المشترك_____

التاريخ: _____

موافقة والدي الطفل المشترك:

نحن والدي الطفل .....لقد قمنا بقراءة استمارة القبول هذه وفهمنا مضمونها. تمت الإجابة على أسئلتنا جميعها. وبناء عليه فأننا، أحرار مختارين، نوافقإجراء هذا البحث و موافق على اشتراك طفلنا فيه، و إننانعلم أن الباحث سيكون مستعد للإجابة على تسائلاتنا، وإذا شعرنا لاحقا أن الأجوبة تحتاج إلى مزيد من الإيضاح فسوف نتصل بأحد أعضاء البحث كما نعرف تمام المعرفة بأننا احارر في جعل ابننى ينسحب من هذا البحث متى شئنا حتى بعد التوقيع على الموافقة دون أن يؤثر ذلك على العناية الطبية المقدمة له.

التاريخ _____

اسم الباحث : اسامة محمد طاهر شولي

رقم هاتف : 0598243588

بريد الكتروني : osama.shuli@hotmail.com

Appendix D

Certificate of English Proofreading and Editing

Certificate of English Proofreading and Editing

This certificate confirms that the thesis mentioned below was proofread by an expert in academic English and edited by a native speaker.

The following issues were corrected: grammar, punctuation, sentence structure, and phrasing.

The Faculty of Graduate Studies at An-Najah National University can contact us for a copy of the edited document the author submitted.

Title

Ondansetron Versus Ketorolac with Ondansetron for The Prophylaxis of Postoperative Nausea and Vomiting in Pediatric Patients Undergoing Strabismus Surgery

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جـامعـــة النجاح الوطنية

كليـــة الد ارســـات العليـــا

اوندانستيرون مقابل كيتولاك مع اوندانستيرون للوقاية من الغثيان والقيء بعد الجراحة في مرضى الأطفال الذين يخضعون لجراحة الحول

إعداد

أسامة محمد شولي

إشراف

د. عائدة القيسي

د. نزار سعيد

قدمت هذه الرسالة استكمالا لمتطلبات الحصول على درجة الماجستير في تمريض التخدير، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

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اوندانستيرون مقابل كيتولاك مع اوندانستيرون للوقاية من الغثيان والقيء بعد الجراحة في مرضى الأطفال الذين يخضعون لجراحة الحول

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الملخص

الخلفية: يعد الغثيان والقيء بعد جراحة الحول من الآثار الجانبية التي يمكن أن تسبب عدم توازن المحلول الكهربائي، الجفاف، نزيف تحت الملتحمة وارتخاء الروابط الجراحية. قد تتطلب هذه الآثار الجانبية إعادة الدخول الى المستشفى، إطالة الإقامة في وحدة رعاية ما بعد التخدير، زيادة الإقامة في المستشفى وزيادة تكاليف الرعاية الصحية.

الأهداف: تقييم تأثيرات أوندانسيترون بمفرده مقابل أوندانسيترون بالإضافة إلى كيتورولاك على الألم، وتواتر الغثيان والقيء بعد العملية الجراحية، وما يترتب على ذلك من استهلاك أدوية الإنقاذ المضادة للقيء والمسكنات بعد العملية الجراحية لدى مرضى الأطفال الذين يخضعون لجراحة الحول.

المنهجية: تم تقسيم سبعين مريضًا من الأطفال (ASA I وII، أعمارهم تتراوح بين 3 إلى 12 عامًا) لمجموعتين لإجراء جراحة الحول الاختيارية تحت التخدير العام: 40 لأوندانسيترون و30 لأوندانسيترون بالإضافة إلى كيتورولاك. تم تقييم الغثيان والقيء، الألم والحاجة إلى أدوية الإنقاذ بعد العملية الجراحية من 30 دقيقة إلى 8 ساعات.

النتائج: في PACU، أظهرت النتائج أن مجموعة أوندانسيترون (ن = 13، ع = 32.5٪) كان لديها معدل أعلى من آلام في منطقة الجراحة من مجموعة أوندانسيترون وكيتورولاك مجتمعة (ن = 3، ع = 10٪)، القيمة الاحتمالية 0.042. ولم تكن هناك اختلافات بين المجموعتين من حيث الغثيان، والتقيؤ، والتهوع، أو الحاجة إلى أدوية الإنقاذ.

في قسم الأطفال، يظهر أن جميع المضاعفات أقل في المجموعة المشتركة مقارنة بمجموعة أوندانسيترون، بما في ذلك القيء (0.0% مقابل 22.5%)، القيمة الاحتمالية =0.008، والغثيان (6.7% مقابل 32.5%)، القيمة الاحتمالية 0.017، التهوع (0.0% مقابل 22.5%)، القيمة الاحتمالية 0.008، ألم الموقع الجراحي (13.3% مقابل 42.5%)، القيمة الاحتمالية 0.009، استخدام المسكنات (6.7% مقابل 35.0%)، قيمة الاحتمالية 0.008، ومضاد للقيء الإنقاذي (0.0% مقابل 27.5%)، قيمة الاحتمالية 0.002، على التوالي.

بعد الجراحة بـ 8 ساعات، يظهر أن هناك معدل أقل في المجموعة المشتركة مقارنة بمجموعة أوندانسيترون من حيث الغثيان (0.0% مقابل 10%)، القيمة الاحتمالية 0.013، التهوع (0.0% مقابل 10%)، القيمة الاحتمالية 0.013، واستخدام أدوية الإنقاذ (0.0% مقابل 10%)، القيمة الاحتمالية 0.013، في حين لم يتم العثور على فروق ذات دلالة إحصائية في حدوث القيء (0.0% مقابل 7.5%)، القيمة الاحتمالية 0.125، واستخدام المسكنات (3.3% مقابل 10%)، القيمة الاحتمالية 0.284، على التوالي.

الاستنتاج: تبين أن الكيتورولاك الذي يتم إعطاؤه كمساعد للأوندانسيترون في مرضى الحول عند الأطفال يقلل الألم والحاجة إلى أدوية مسكنة ومضادة للقيء، وكذلك الغثيان والقيء بعد العملية الجراحية.

الكلمات المفتاحية: كيتورولاك؛ أوندانسيترون؛ جراحة الحول؛ القيء والغثيان بعد العملية الجراحية؛ ألم؛ أدوية الإنقاذ.