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ORIGINAL ARTICLE

Effect of Ondansetron versus Intraperitoneal or Intravenous Dexamethasone on Postoperative Nausea, Vomiting and Pain in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Background: Even with all the advantages that come with having a laparoscopic cholecystectomy, like quicker recovery times and shorter hospital stays, there is still a significant rate of postoperative nausea, vomiting, and pain, which lowers patient satisfaction. The purpose of this research was to evaluate the effectiveness of ondansetron versus intravenous or intraperitoneal dexamethasone in preventing pain, nausea, and vomiting following laparoscopic cholecystectomy.

Methods: This comparative prospective randomized double-blinded clinical trial was conducted at the Anesthesia, Intensive Care, and Pain Management Department of Zagazig University Hospitals. The study included 120 Patients undergoing laparoscopic cholecystectomy randomly allocated into four groups: Group A (control group, n=30) received no ondansetron or dexamethasone; Group B (intravenous Ondansetron group, n=30); Group C (intraperitoneal dexamethasone, n=30); and Group D (intravenous dexamethasone, n=30).

Results: Both ondansetron and dexamethasone, either intraperitoneal or intravenous effectively showed comparable effect to reduce postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. But regarding postoperative pain, both intraperitoneal and intravenous dexamethasone, offers superior postoperative pain management compared to ondansetron and saline controls.

Conclusions: Intraperitoneal dexamethasone may be a promising alternative for preventing postoperative complications and improving patient outcomes following laparoscopic cholecystectomy**.**

Keywords: Ondansetron, Dexamethasone, Nausea and Vomiting, Pain, Laparoscopic Cholecystectomy

INTRODUCTION

Patients benefit from a number of minimally invasive surgical techniques, such as a quicker recovery, a shorter hospital stay, and a quicker return to normal activities. One such approach is laparoscopic cholecystectomy. However, a notable issue that can have a detrimental impact on patient satisfaction and perhaps result in unfavorable side effects is the high frequency of postoperative nausea and vomiting (PONV) and postoperative pain (POP) [1].

After anesthesia, PONV is one of the most common adverse effects. Up to 70% of "high-risk" patients and 30% of unselected patients experience it [2]. It has been determined that a number of variables, including female gender, a history of PONV, motion sickness in the past, nonsmoking status, opiate use, and lengthy surgical procedures, raise the risk for PONV [3]. PONV causes wound

dehiscence, raises intracranial pressure, increases intraocular pressure, and lengthens hospital and recovery room stays [4].

The drug ondansetron is classified as an antagonist of the serotonin 5-hydroxytryptamine 3 (5-HT3) receptors. Its main use is to stop vomiting after receiving chemotherapy. It is believed that ondansetron affects both peripheral and central nerves. By reducing vagus nerve activity, ondansetron inhibits the vomiting center in the medulla oblongata as well as the serotonin receptors in the chemoreceptor trigger zone (CTZ) [5].

Dexamethasone is a glucocorticoid that is well-known for its antiemetic properties. It's yet unknown exactly how dexamethasone works. The effects of dexamethasone on the central nervous system and vomiting center at the medulla oblongata, such as changes in blood-brain barrier permeability to certain blood proteins, changes in the activity of neurotransmitters like dopamine and serotonin, or suppression of prostaglandin production, could provide an explanation [6].

While having some side effects, including the risk of postoperative infections and temporary hyperglycemia, dexamethasone was used in a single dose with varying amounts (e.g., 4, 6, and 8 mg) in different combinations via intravenous (IV) route of injection in the majority of prior studies to prevent PONV [6].

In an effort to lessen patient discomfort during the first 24 hours following surgery, some researchers have been looking for more efficient ways to lower PONV, pain, and the frequent use of analgesic and antiemetic drugs in recent years. Lower discomfort and PONV have been linked to a single intraperitoneal (IP) dexamethasone injection during gynecological procedures. According to research, compared to intravenous injection, intraperitoneal dexamethasone injection is linked to less adverse effects, such as headaches and dizziness [1].

We hypothesized that there are differences between administration of intravenous ondansetron, intravenous or intraperitoneal dexamethasone in preventing postoperative nausea, vomiting and pain after laparoscopic cholecystectomy.

METHODS

This comparative prospective randomized double blinded clinical trial was conducted at Anesthesia, intensive care, and pain management department of Zagazig University Hospitals.

Written informed consents from the patients were taken. The protocol was applied for approval from the institutional review board (IRB number 10610-4-4-2023).

Randomization and allocations:

To prevent bias in the results of this research, a double-blind method will be used in which test information will be kept confidential and hidden from examining anesthesiologist and the patient until the end of the research, the patients were randomly allocated into four groups by computer generated random number

Inclusion criteria included patients willing to sign informed consent, patients underwent elective laparoscopic cholecystectomy under general anesthesia, age: between 21 and 65 years, sex: both Male and female, patients belonging to ASA I or II, BMI ≤ 35kg/m2 and duration of surgery less than 2 hours.

Exclusion criteria included patients with gastrointestinal disorders, pregnant and lactating women, women during menstruation, patients with a history of motion sickness, patients with CNS disorders, particularly cerebellar problems, patients who used opioids, steroids, or antiemetic drugs within a week prior to the operation, patients taking antidepressants and patients with history of allergy to ondansetron or dexamethasone, BMI > 35kg/m2 are among the groups of patients who should be excluded from consideration for this procedure.

Groups of study:

Group A (control group) (n=30): patients received 10 ml saline directly injected in the peritoneum of the gallbladder's bed by the surgeon and 10 ml saline intravenous by a physician.

Group B (intravenous Ondansetron group) (n=30): Patients who received 10 ml saline directly injected in the peritoneum of the gallbladders bed by the surgeon and 4mg ondansetron diluted in 10 ml saline intravenous by a physician.

Group C (intraperitoneal dexamethasone) (n=30): Patients who received 8 mg dexamethasone diluted in 10 ml saline directly injected in the peritoneum of the gallbladders bed by the surgeon and 10 ml saline intravenous by a physician.

Group D (intravenous dexamethasone) (n=30):

Patients who received 10 ml saline directly injected in the peritoneum of the gallbladders bed by the surgeon and 8 mg dexamethasone diluted in 10 ml saline intravenous by a physician.

Preoperative:

A day prior to surgery, all patients underwent a thorough history taking, a comprehensive pre-anesthetic examination, and investigations to determine their suitability and eligibility. These included a clinical examination that included vital signs, cardiac, chest, and body mass index (BMI), which was computed by dividing the patient's weight in kilograms by the square of their height in meters. Complete blood count, bleeding time, PT, PTT, liver and kidney function, HCV Ab, HBV Ag, and random blood glucose were among the laboratory tests carried out. Preoperative fasting for anesthesia was as follows: 2 hours fasting to clear fluids, 6 hours fasting to light meal and 8 hours fasting to heavy meal.

Intraoperative:

A peripheral intravenous line (18G) was established, and intravenous fluids was given according to 4,2, 1 rule applies (4 ml/kg/hr for the first 10 kg, 2 ml/kg/hr for the second 10 kg, and 1 ml/kg/hr). The patient's mean blood pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SPO2) were tracked and recorded using a non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximeter. Intravenous injections of 2 mg/kg propofol and 2 ug/kg fentanyl were used to induce general anesthesia. An intravenous injection of 0.8 mg/kg rocuronium assisted tracheal intubation, and controlled breathing was initiated, with tidal volume and respiratory rate adjusted to maintain an EtCO2 between 35 and 45 mmHg. Every 20 to 30 minutes, rocuronium (0.2 mg/kg), a muscle relaxant, and 1.5% MAC isoflurane were used to maintain anesthesia. Hemodynamic parameters throughout surgery, such as heart rate, mean arterial blood pressure, and peripheral oxygen saturation, were continuously tracked. The investigated medications were administered intraperitoneally and intravenously right before the laparoscope trocar was removed at the conclusion of the procedure. The inhalational anesthetic was discontinued, and the muscle relaxant was replaced with a combination of 0.01 mg/kg of atropine and 0.05 mg/kg of neostigmine. When the patient was completely conscious, extubation was carried out. After being moved to the Post Anesthesia Care Unit (PACU), the patient's length of stay there was documented using the Modified Aldrete Score method which consists of five key parameters (movements, breathing, Blood pressure, Consciousness and SpO2), and the patient's heart rate, mean blood pressure, breathing rate, and SPO2 were all monitored. To be released from the PACU, a score greater than nine was needed **[7].** Then, the patients were observed for the objectives of the study for the 1st 24 hours, including complaining of PONV and postoperative pain and their severity.

Vomiting was defined as the violent release of stomach contents from the mouth, and nausea as a subjectively unpleasant feeling connected to the consciousness of the want to vomit **[8].** Every 15 minutes during the first hour and at 2, 4, 6, 8, 12, and 24 hours later, the incidence and severity of postoperative nausea and vomiting as well as the first time it occurred were evaluated and documented in the PACU and Surgery Ward.

The severity of vomiting was assessed by the Bellville scoring scale **[9]** which uses a simple numeric system to rate the intensity of nausea and vomiting as follows: The lack of nausea and vomiting = 0, Nausea=1, Nausea with belching = 2, Vomiting = 3**.** For severe nausea, 10 mg of metoclopramide intravenously was given as a rescue antiemetic. The total amount of antiemetic dosages and ingestion over a 24-hour period were noted. The visual analog scale (VAS), which has a score range of 0 for no pain and 10 for the greatest possible agony, was used to measure the amount of discomfort **[10],** in which the patients were asked to report the severity of pain at 2, 4, 8, 12, and 24 hours after laparoscopy. If VAS ≥3 rescue analgesia, intravenous 30 mg ketorolac, was administered and time of first rescue analgesia was recorded. Total doses and total consumption of analgesia per 24 hours were recorded. Patient hemodynamics (heart rate and mean arterial blood pressure) were measured at 2, 4, 6, 8, 12, and 15-minute intervals during the first hour.

Sample size calculation:

Assuming the mean severity of nausea at 2 hours was 1.76+_0.5 vs 1.42+_0.5 in intravenous vs intra peritoneal dexamethasone **[1].** At 80% power and 95% CI, the estimated sample was 92 cases,23 cases in each group. The size was raised to 120 cases (30 cases in each group) to compensate for drop cases. Calculated by Open Epi.

Statistical Analysis

SPSS version 29.0 was used for data processing, including data entry, tabulation, and analysis. The present study employed many statistical methods to analyze its data, including the student "t" test, Mann Whitney test, Chi-square test (X2), and Z-test for percentage.

RESULTS

Regarding demographic characteristics of included patients, no significant differences were found in age distribution across the Groups ($p > 0.05$). Also, there were no significant disparities in gender distribution, with males constituting approximately 40-46.67% and females 53.33-60% across all groups ($p > 0.05$). ASA classification showed no significant differences in distribution among the groups, with the majority falling under ASA class I and fewer in ASA class II ($p > 0.05$). Surgery and anesthesia duration showed no significant differences among the groups ($p > 0.05$). Patients in the study groups had their baseline vital signs measured; there were no discernible variations between the groups' mean arterial pressure, heart rate, respiratory rate, and oxygen saturation ($p > 0.05$). **(Table 1**)

There was no discernible variation in the intraoperative MAP at various intervals between the groups under investigation during the intraoperative phase ($p>0.05$)**.** As shown in table (2), Heart rate (HR) measurements at different intraoperative intervals did not show significant differences between the four groups ($p > 0.05$). As shown in table (2), There were no appreciable changes in oxygen saturation values between the four groups at various intraoperative intervals ($p > 0.05$). **(Table 2)**

There was no discernible variation in the MAP at different time points between the groups under investigation during the post-operative phase ($p>0.05$). In post-operative period, there was no significant difference between the studied groups regarding HR at different intervals ($p>0.05$). The post-operative respiratory rate data analysis across the study groups at various time points did not show significant differences between the groups ($p > 0.05$). At different times after surgery, the groups' post-operative SpO2 did not significantly differ from one another ($p>0.05$). **(Table 3)**

Regarding VAS, no significant difference found between group A and group B at all time points ($P1>0.05$). At **15 minutes**, there was no discernible difference between groups C and D ($P6>0.05$). The groups' VAS scores differed significantly from one another ($P < 0.001$). Groups C and D had significantly lower scores compared to Groups A and B. Significant P-values for pairwise comparisons were: P2= 0.0014*, P3= 0.0001*, P4= 0.0021*, P5= 0.0001*. At **30 minutes**, there was no discernible difference between groups C and D ($P6>0.05$). Groups C and D had significantly lower scores than Groups A and B, indicating a significant difference between the groups ($P = 0.0014$). P-values that were significant for pairwise comparisons were: P2=0.0149*, P3= 0.023*, P4= 0.0265*, P5= 0.04*. At **45 minutes**, no significant difference found between group C and group D ($P6>0.05$). The VAS scores differed significantly among the groups ($P < 0.001$). Groups C and D had significantly lower scores than Groups A and B. Significant P-values for pairwise comparisons were: P2< 0.001*, P3< 0.001*, P4< 0.001*, P5< 0.001*. At **4 hours**, no significant difference found between group C and group D ($P6>0.05$). There was a significant difference in VAS scores ($P < 0.001$). Groups C and D had significantly higher scores compared to Groups A and B. Significant P-values for pairwise comparisons were: P2 <0.001*, P3< 0.001*, P4 <0.001*, P5< 0.001*. At **6 hours**, stared to show significant difference between group C and group D (P6=0.0127). A significant difference was observed ($P < 0.001$), with Groups C and D showing significantly lower scores than Groups A and B. Significant P-values for pairwise comparisons were: P2= <0.001*, P3= 0.0022*, P4= <0.001*, P5 = 0.0022*, P6= 0.0127*. At **8 hours**, the VAS scores differed significantly among the groups ($P < 0.001$). Groups C and D had significantly lower scores than Groups A and B. Significant P-values for pairwise comparisons were: P2 <0.001*, P3 < 0.001*, P4 <0.001*, P5 <0.001*, and continued to show a significant difference between group C and group D (P6< 0.001*). At **12 hours**, Group C had significant lower VAS score compared to group D, a significant difference was found ($P < 0.001$). Group C had significantly lower scores compared to other Groups. Significant P-values for pairwise comparisons were: P2= <0.001*, P4= <0.001*, P6< 0.001*. no significant difference between group D and group A and B (P3, P5 >0.05). At **24 hours**, Group C's VAS score was much lower than Group D's, indicating a substantial difference in VAS scores ($P < 0.001$). Group C had significantly lower scores compared to Groups A

and B. Significant P-values for pairwise comparisons were: P2= <0.001*, P4= <0.001*, P6= <0.001*. no significant difference between group D and group A and B (P3, P5 >0.05). **(Figure 1)**

The requirement for Rescue Analgesia at the first time varied significantly amongst the groups (P < 0.001). Group A and B showed a significantly lower time regarding first time Rescue Analgesia need compared to Group C and D (P2, P3, P4. P5 <0.05). Regarding second time Rescue Analgesia need among the groups, there was no significant between group A and B (P = 0.6407). However, there was a significant difference in the 24-hour total analgesic dose among the groups (P < 0.001). Group A and B received a significantly higher total analgesic dose compared to Group C and D (P2, P3, P4. P5 <0.05).

Regarding the time of start of nausea, there was a statistically significant difference between the groups under investigation (P< 0.001), where Group A showed a significantly decrease in time of onset of nausea compared to other Groups (P1, P2, P3 <0.05). Also, there was statistically significant difference between the studied groups regarding Time of Rescue Antiemetic (Hr) (P< 0.001), with significant decreases observed in Group A compared to other Groups (P1, P2, P3 <0.05). Regarding Patients Who Needed Rescue Antiemetic, there was a statistically significant difference (P <0.001) between the groups under study; 63.33% of patients in Group A needed rescue antiemetic, whereas 6.67% of patients in Groups B and C and 13.33% of patients in Group D needed it **(Table 4)**

The Bellville scoring scale showed statistically significant differences between the groups under study at various intervals (30, 45 minutes, 1, 2, 4 hours) (p<0.05) with best results reported in group B while at 6 h, 8 ,12 and 24 there was no difference between the groups. At 30, 45 minutes, 1, 2, 4 hours, Group A showed significant increase in mean Bellville score value compared to other three groups (P1, P2, P3 <0.05). Additionally, there was no discernible difference between groups B's mean Bellville score values, C, D (P>0.05). **(Figure 2)**

Regarding postoperative complications, there were no cases of headache reported in any group. The incidence of drowsiness was similar across all groups, ranging from 6.67% to 16.66%, with no significant difference observed (P = 0.637). Likewise, anxiety incidence was consistent across groups, ranging from 6.67% to 10%, showing no discernible difference (P = 0.637). Every patient was released, and none of the groups experienced any serious side effects (P > 0.05). **(Table 5)**

Table 1: Baseline data among the studied four groups.

		Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F/X2)
Age (Years)		42.5 ± 9.53	44 ± 9.8	42.43 ± 9.08	43.57 ± 11.66	0.909
BMI (kg/m2)		29.78 ± 1.46	30.58 ± 1.38	30.28 ± 1.45	30.28 ± 1.36	0.195
Sex	**Male**	14 (46.67%)	12 (40%)	13 (43.33%)	12 (40%)	0.945
	Female	16 (53.33%)	18 (60%)	17 (56.67%)	18 (60%)	
ASA ps	**I**	22 (73.33%)	24 (80%)	21 (70%)	23 (76.67%)	0.828
	II	8 (26.67%)	6 (20%)	9 (30%)	7 (23.33%)	
Surgery duration (min)		50.5±10.7	51.2±10.3	50.3±10.5	51.1±10.4	0.758
Anesthesia duration (min)		65±7.2	66.2±7.9	68±6.9	67.5±7.5	0.432
MAP (mmHg)		90.5 ± 3	90.2 ± 2.97	90.18 ± 3.18	90.35 ± 3.05	0.976
		P1= 0.708, P2= 0.688, P3= 0.847, P4= 0.978, P5= 0.856, P6= 0.835				
HR (Beat/min.)		86.77 ± 4.14	86.73 ± 4.01	86.87 ± 3.52	86.9 ± 3.83	0.998
		P1= 0.974, P2= 0.922, P3= 0.896, P4= 0.896, P5= 0.870, P6= 0.974				
RR (Breath/min.)		15.8 ± 1.7	15.53 ± 1.65	15.77 ± 1.75	15.63 ± 1.47	0.913
		P1= 0.9204, P2= 0.99, P3= 0.9782, P4= 0.9423, P5= 0.9954, P6= 0.9876				
SPO2 (%)		97.99 ± 0.58	97.97 ± 0.54	97.99 ± 0.65	97.96 ± 0.59	0.996
		P1= 0.881, P2= 0.983, P3= 0.831, P4= 0.898, P5= 0.949, P6= 0.848				

Table 2: Intra operative vital signs among the studied four groups**.**

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)
MAP (mmHg)					
15 min.	80.34 ± 1.46	79.76 ± 2.26	80 ± 3.24	80.59 ± 3.83	0.694
	P1= 0.433, P2= 0.646, P3= 0.744, P4= 0.744, P5= 0.267, P6= 0.433				
30 min.	83.27 ± 2.21	84.64 ± 2.94	84.08 ± 2.41	84.39 ± 3.76	0.231
	P1= 0.072, P2=0.231, P3=0.122, P4= 0.432 P5= 0.634, P6= 0.366				
45 min.	93.37 ± 1.82	93.69 ± 3.26	93.24 ± 3.69	93.28 ± 3.84	0.952
	P1= 0.707, P2= 0.886, P3= 0.917, P4= 0.604, P5= 0.631, P6= 0.969				
60 min.	92.6 ± 2.31	93.45 ± 3.1	93.43 ± 4.29	94.23 ± 4.81	0.437
	P1= 0.394, P2= 0.400, P3= 0.101, P4= 0.991, P5= 0.426, P6= 0.419				
HR (Beat/min.)					
15 min.	109.93 ± 2.17	110.93 ± 2.91	110.07 ± 2.17	111.2 ± 1.94	0.103
	P1= 0.105, P2= 0.828, P3= 0.141, P4= 0.159, P5= 0.664, P6= 0.066				
30 min.	100.4 ± 2.82	99.87 ± 2.62	99.93 ± 2.45	99.63 ± 2.54	0.725
	P1= 0.438, P2= 0.497, P3= 0.266, P4= 0.923, P5= 0.734, P6= 0.662				
45 min.	90.07 ± 2.54	90 ± 2.61	89.43 ± 1.98	89.93 ± 2.43	0.741
	P1= 0.916, P2= 0.318, P3= 0.833, P4= 0.371, P5= 0.916, P6= 0.430				
60 min.	79.83 ± 2.21	80.73 ± 2.72	79.9 ± 2.09	79.33 ± 2.15	0.144
SPO2 (%)					
	P1= 0.140, P2= 0.912, P3= 0.410, P4= 0.171, P5= 0.122, P6= 0.351				
15 min.	99.23 ± 0.8	99.1 ± 0.79	98.7 ± 0.9	99.03 ± 0.8	0.092
	P1= 0.539, P2= 0.076, P3= 0.357, P4= 0.067, P5= 0.758, P6= 0.126				
30 min.	99.1 ± 0.83	98.8 ± 0.75	98.93 ± 0.89	99.1 ± 0.79	0.435
	P1= 0.165, P2= 0.439, P3= 1, P4= 0.535, P5= 0.165, P6= 0.439				
45 min.	99.2 ± 0.91	99 ± 0.86	99.03 ± 0.8	98.83±0.82	0.436
	P1= 0.370, P2= 0. 455, P3= 0.102, P4=0.881, P5= 0.455, P6= 0.370				
60 min.	99.2 ± 0.83	98.9 ± 0.83	99 ± 0.77	99.03 ± 0.8	0.56
	P1= 0.160, P2= 0.348, P3= 0.434, P4= 0.639, P5= 0.531, P6= 0.876				

Table 3: Post operative vital signs among the studied four groups**.**

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)
MAP (mmHg)					
15 min	95.42±2.73	95.78±2.21	95.11±2.05	95.36±2	0.723
	P1=0.623, P2=0.564, P3=0.985, P4=0.914, P5=0.741, P6= 0.699				
30 min	97.52±4.5	98.18±3.04	96.53±3	97.92±2	0.226
	P1=0.174, P2=0.987, P3=0.212, P4=0.332, P5=0.468, P6=0.570				
45 min	96.13±7.11	95.94±7.08	93.89±8.61	96.38±8.54	0.594
	P1= 0.472, P2= 0.522, P3= 0.185, P4= 0.609, P5= 0.541, P6= 0.231				

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)
1 h	96.07±7.24	95.86±7.32	95.99±8.79	97.53±7.81	0.823
	P1= 0.987, P2= 0.850, P3= 0.711, P4= 0.838, P5= 0.711, P6= 0.819				
2 h	92.72±6.37	92.78±6.27	93.18±7.28	94.37±7.61	0.777
	P1= 0.99, P2= 0.997, P3= 0.655, P4= 0.996, P5= 0.452, P6= 0.687				
4 h	94.29±7.07	94.04±6.96	93.64±8.38	94.74±7.67	0.953
	P1= 0.834, P2= 0.921, P3= 0.612, P4= 0.733, P5= 0.766, P6= 0.666				
6 h	96.7±5.78	96.11±5.7	94.52±6.24	95.71±6.56	0.562
	P1= 0.133, P2=0.547, P3=0.541, P4=0.456, P5=0.597, P6= 0.687				
8 h	97.76±5.67	96.68±4.34	95.08±4.74	96.5±4.85	0.219
	P1= 0.331, P2= 0.418, P3= 0.054, P4= 0.871, P5= 0.331, P6= 0.258				
12 h	95.59±4.98	95.64±5.02	94.13±6.49	96.53±5.73	0.420
	P1= 0.430, P2=0.219, P3=0.666, P4=0.315, P5=0.223, P6= 0.422				
24 h	94.63±5.94	94.98±5.9	95.89±7	96.93±5.46	0.467
	P1= 0.461, P2=0.327 P3=0.516, P4=0.808, P5=0.489, P6= 0.144				
HR (Beat/min.)					
15 min	108.23±3	106.93±3.37	106.63±3.91	107.63±2.98	0.249
	P1= 0.134, P2=0.166, P3=0.387, P4=0.128, P5=0.318, P6= 0.248				
30 min	93.83±3.78	93.1±4.02	92.2±2.7	93.63±2.25	0.220
	P1= 0.333, P2=0.235, P3=0.315, P4=0.210, P5=0.287, P6=0.322				
45 min	94.6±3.82	93.43±4.04	93.9±3.58	93.83±2.49	0.639
	P1= 0.673, P2=0.588, P3=0.601, P4=0.612, P5=0.557, P6=0.684				
1 h	93.83±3.78	93.1±4.02	92.2±2.7	93.63±2.25	0.220
	P1= 0.387, P2=0.156, P3=0.413, P4=0.289, P5=0.529, P6=0.192				
2 h	93.27±2.46	92.63±3.32	93.07±4.27	93.27±2.46	0.855
	P1= 0.798, P2=0.614, P3=852, P4=0.678, P5=0.755, P6=0.865				
4 h	94.37±3.74	93.43±4.04	93.9±3.58	93.83±2.49	0.785
	P1= 0.352, P2=0.619, P3=0.598, P4=0.749, P5=0.807, P6=0.682				
6 h	94.6±3.61	93.53±3.99	93.77±3.85	94.13±2.29	0.662
	P1= 0.585, P2=0.610, P3=0.585, P4=0.497, P5=0.723, P6=0.694				
8 h	95.03±4.25	93.63±4.09	93.9±3.85	94.2±2.19	0.489
	P1= 0.633, P2=0.258, P3=0.547, P4=0.325, P5=0.511, P6=0.992				
12 h	93.8±3.66	93.63±4.09	93.9±3.85	94.2±2.19	0.938
	P1= 1.0, P2=0.751, P3=0.829, P4=0.925, P5=0.854, P6=772				
24 h	94.13±4.26	93.5±3.95	93.7±3.79	93.9±2.44	0.921
	P1= 0.411, P2=0.900, P3=0.844, P4=0.735, P5=0.681, P6=0.989				
Respiratory rate (breaths per minute)					
15 min	17.5 ± 2.81	18.77 ± 3.41	16.97± 2.81	18.5 ± 2.88	0.080
	P1= 0.110, P2=0.498, P3=0.205, P4=0.078, P5=0.735, P6=0.053				
30 min	16.5 ± 2.78	17.93 ± 3.66	16.07± 2.77	17.27 ± 2.98	0.103
	P1= 0.078, P2=0.592, P3=0.343, P4=0.098, P5=0.410, P6=0.139				
45 min	16.23 ± 2.64	17.3 ± 3.59	15.77± 2.73	16.83 ± 3.14	0.243
	P1= 0.185, P2=0.561, P3=0.455, P4=0.058, P5=0.561, P6=0.185				
1 h	15.73 ± 2.08	15.17 ± 2.37	14.57± 3.45	14.03 ± 4.14	0.19

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)
	P1= 0.491, P2=0.157, P3=0.123, P4=0.466, P5=0.169, P6=0.516				
2 h	15.83 ± 2.03	15.47 ± 2.39	15.47± 3.19	15.37 ± 3.65	0.931
	P1= 0.630, P2=0.630, P3=0.539, P4=1, P5=0.895, P6=0.895				
4 h	15.67 ± 2.09	15.4 ± 2.29	15.03± 1.47	15.27 ± 2.56	0.722
	P1= 0.636, P2=0.262, P3=0.478, P4=0.515, P5=0.813, P6=0.679				
6 h	15.77 ± 1.78	15.57 ± 2.06	15.27± 1.86	15.33 ± 2.21	0.765
	P1= 0.702, P2=0.340, P3=0.408, P4=0.566, P5=0.655, P6=0.899				
8 h	15.7 ± 1.86	15.83 ± 2.78	14.93± 2.19	15.7 ± 2.67	0.473
	P1= 0.833, P2=0.227, P3=1.0, P4=0.157, P5=0.833, P6=0.227				
12 h	15.83 ± 2	16.17 ± 2.45	15.47± 1.91	16.6 ± 2.11	0.220
	P1= 0.552, P2=0.513, P3=0.173, P4=0.213, P5=0.440, P6=0.110				
24 h	15.8 ± 2.02	16.5 ± 2.17	15.6 ± 1.82	16.67 ± 2.17	0.138
	P1= 0.196, P2=0.711, P3=0.110, P4=0.097, P5=0.757, P6=0.05				
SPO2 %					
15 min	97.2 ± 0.83	97.07 ± 0.89	97.17± 0.86	97.27 ± 0.68	0.826
	P1= 0.537, P2=0.877, P3=0.757, P4=0.643, P5=0.355, P6=0.643				
30 min	97.03 ± 0.75	97.13 ± 0.88	97.13± 0.76	97.13 ± 0.72	0.949
	P1= 0.627, P2=0.627, P3=0.627, P4=1, P5=1, P6=1				
45 min	96.83 ± 0.78	97 ± 0.93	96.93± 0.77	96.9 ± 0.75	0.887
	P1= 0.435, P2=0.639, P3=0.755, P4=0.755, P5=0.639, P6=0.876				
1 h	97.27 ± 1.15	97.53 ± 1.09	97.37± 1.28	97.33 ± 0.94	0.828
	P1= 0.367, P2=0.735, P3=0.821, P4=0.573, P5=0.498, P6=0.910				
2 h	97.53 ± 1.06	97.3 ± 1	97.2 ± 0.91	97.6 ± 1.08	0.392
	P1= 0.383, P2=0.214, P3=0.803, P4=0.708, P5=0.263, P6=0.136				
4 h	97.6 ± 1.02	97.67 ± 1.14	97.5 ± 1.02	97.8 ± 1.14	0.758
	P1= 0.815, P2=0.725, P3=0.482, P4=0.558, P5=0.639, P6=0.293				
6 h	97.5 ± 1.18	97.33 ± 1.04	97.7 ± 1	97.5 ± 0.99	0.626
	P1= 0.549, P2=0.472, P3=1.0, P4=0.189, P5=0.549, P6=0.472				
8 h	97.43 ± 1.26	97.7 ± 1.13	97.5 ± 1.06	96.97 ± 0.87	0.075
	P1= 0.353, P2=0.816, P3=0.105, P4=0.485, P5=0.065 P6=0.056				
12 h	97.53 ± 1.2	97.67 ± 1.19	97.57 ± 1.23	97.63 ± 1.11	0.973
	P1= 0.669, P2=0.915, P3=0.749, P4=0.749, P5=0.915, P6=0.831				
24 h	97.27 ± 1.15	97.13 ± 1.09	97.37± 1.14	97.77 ± 1.05	0.160
	P1= 0.648, P2=0.732, P3=0.089, P4=0.425, P5=0.112, P6=0.172				

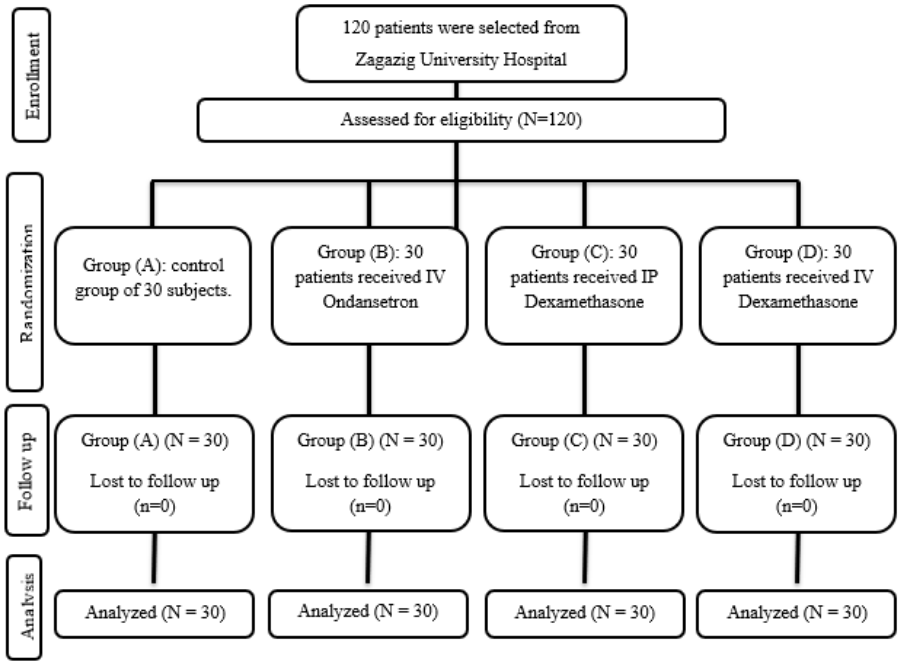
Table 4: Follow up of rescue analgesic and rescue antiemetics among included patients in the studied four groups**.**

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)/ (X^2)
Number of patients needed rescue analgesic	30(100%)	30(100%)	30(100%)	30(100%)	-----
First time rescue analgesia (Hr)	0.4 ± 0.34	0.39 ± 0.31	3.67 ± 2.07	3.53 ± 2.72	< 0.001*
	P1= 0.99, P2< 0.0001*, P3< 0.0001*,				

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (F)/ (X^2)
	P4< 0.0001*, P5< 0.0001*, P6= 0.9892				
Second time rescue analgesia (Hr)	7.9±1.7	8.1±1.6	---	----	0.6407
24h total analgesics dose (mg)	60± 13.75	60 ± 14.62	30 ± 12.83	30 ± 13.75	< 0.001*
	P1= 0.854, P2< 0.001*, P3= 0.001, P4< 0.001*, P5= 0.001*, P6=0.623				
Time of onset Nausea (Hr)	0.94±0.57	3.7±3.46	3.55±2.59	4.1±4.65	<0.001*
	P1=0.008*, P2=0.015*, P3<0.001*, P4=0.336, P5=0.354, P6=0.123				
Time of Rescue Antiemetic (Hr)	1.8± 0.48	3.2 ± 1.71	3.6 ± 1.8	4.6 ± 1.5	<0.001*
	P1<0.001*, P2<0.001*, P3<0.001*, P4= 0.718, P5= 0.718, P6= 0.470				
Patients who required rescue antiemetic	19 (63.33%)	2 (6.67%)	2 (6.67%)	4 (13.33%)	<0.001* (X^2)

Table 5: Patient postoperative adverse effect occurrence and number of patients discharged after 24 hours among the studied four groups.

	Group (A) (n = 30)	Group (B) (n = 30)	Group (C) (n = 30)	Group (D) (n = 30)	P. Value (X^2)
Headache	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Drowsiness	4 (13.33%)	5 (16.66%)	2 (6.67%)	2 (6.67%)	0.637
Anxiety	2 (6.67%)	3 (10%)	3 (10%)	3 (10%)	0.96
Discharge after 24 hr	30 (100%)	30 (100%)	30 (100%)	30 (100%)	-



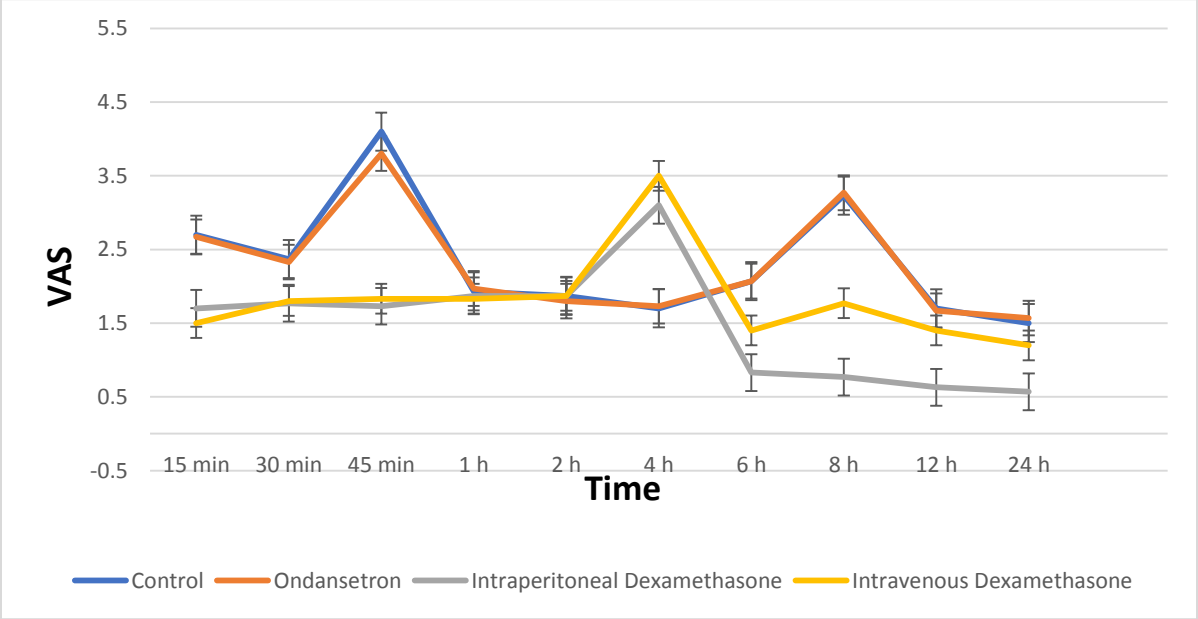


Figure 1: Patient VAS score at different intervals among the studied four groups

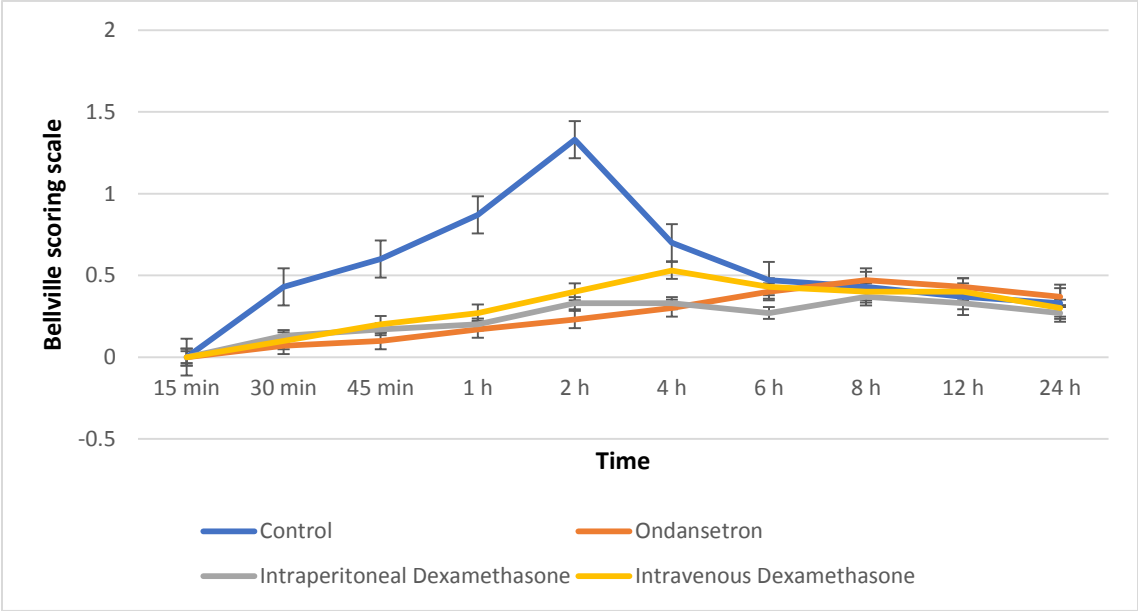


Figure 2: Patient Bellville scoring scale at different intervals among studied four groups

DISCUSSION

There were no discernible disparities in the four groups' demographics according to our analysis: Control (Group A), Ondansetron (Group B), Intraperitoneal Dexamethasone (Group C), and Intravenous Dexamethasone (Group D). Mean ages ranged from 42.43 ± 9.08 to 44 ± 9.8 years ($p > 0.05$), mean BMI values ranged from 29.78 ± 1.46 to 30.58 ± 1.38 kg/m² ($p > 0.05$), and gender distribution was similar, with males comprising 40-46.67% and females 53.33-60% across all groups ($p > 0.05$). ASA classification was also comparable, with most patients classified as ASA I and fewer as ASA II ($p > 0.05$). Additionally, there were no discernible variations between the groups in the lengths of the surgeries or anesthesia ($p > 0.05$).

MAP, HR, RR, and (SpO2) among the study groups during the intraoperative and postoperative phases did not significantly differ, according to our findings. These findings suggest that neither intravenous ondansetron nor dexamethasone, whether administered intravenously or

intraperitoneally, had a significant impact on cardiovascular or respiratory parameters during or after laparoscopic cholecystectomy.

These results align with the findings of Abdelaziz, et al. [11] who compared between an Ondansetron group and a Control group and found no significant differences in between the two groups' systolic and diastolic blood pressure or postoperative respiratory rate.

Similarly, Nazemroaya, et al. [1] investigated the effects of administering dexamethasone intraperitoneally (IP) versus intravenously (IV) on PONV. Among the three study groups, there were no notable variations in heart rate, oxygen saturation, mean arterial pressure, or length of surgery. In addition to the results of Abdelaziz et al. and our own investigation, Nazemroaya et al. [1] underscores the safety and efficacy of ondansetron and dexamethasone in the management of PONV without adversely affecting cardiovascular or respiratory parameters during or after laparoscopic cholecystectomy.

The four groups' VAS scores, as well as the amount and timing of rescue analgesia, varied significantly, according to our study. Specifically, Groups C and D had consistently lower VAS scores compared to Groups A and B at most time points, but intraperitoneal dexamethasone (Group C) generally provided the most effective pain relief compared to the other groups indicating better pain control and show that intravenous dexamethasone (Group D) had some efficacy, though not as markedly as intraperitoneal administration. This aligns with findings from other studies.

At 15- and 30-minutes post-surgery, Groups C and D, which received intraperitoneal dexamethasone and intravenous dexamethasone, respectively, had lower VAS scores compared to Groups A (control) and B (ondansetron). This finding suggests that dexamethasone may offer superior early pain relief compared to ondansetron, which aligns with studies suggesting that corticosteroids can reduce postoperative pain, potentially through anti-inflammatory mechanisms. For instance, the study by Apfelbaum, et al. [12] observed that corticosteroids like dexamethasone reduced postoperative pain intensity by decreasing inflammation and edema. Similarly, a recent meta-analysis by De Oliveira, et al. [13] supports the use of dexamethasone at doses more than 0.1 mg/kg intravenously is effective for improved pain management in laparoscopic surgeries.

In line with our findings, Jamil and Qaisar [14] who found that 0.1 mg/kg intravenous dexamethasone significantly reduced postoperative pain compared to a placebo. The pain scores were lower in the group receiving dexamethasone, and there was a notable reduction in the need for additional analgesics.

Our study found ondansetron (Group B) less effective compared to dexamethasone in managing postoperative pain, this result in accordance with Abdelaziz, et al. [11] explored the efficacy of ondansetron in controlling postoperative pain following laparoscopic cholecystectomy. Their research revealed that ondansetron did not provide significant pain relief compared to placebo or standard analgesics. This study reinforced the understanding that ondansetron is effective in managing nausea but does not influence postoperative pain levels.

At 4 hours, Groups C and D had significantly higher VAS scores compared to Groups A and B. However, by 6, 8 hours, Groups C and D consistently showed lower VAS scores compared to Groups A and B, with the lowest scores observed in Group C which showed significantly lower VAS score when to other groups.

The rebound in VAS scores at 4 hours for Groups C and D could indicate a transient increase in pain or a decline in the effectiveness of dexamethasone over time. However, the consistent lower VAS scores from 6 hours onward in these groups suggest that both dexamethasone formulations provide better long-term pain relief compared to ondansetron and the control.

This observation aligns with research findings by Walters, et al. [15] who found that sustained-release dexamethasone intracanalicular depot (.4 mg) effective for managing ocular pain and inflammation post-cataract surgery. and indicated that dexamethasone’s long-term anti-inflammatory effects could contribute to sustained pain relief.

Intraperitoneal dexamethasone likely provides superior pain relief through several mechanisms. By being administered directly into the peritoneal cavity, dexamethasone exerts its anti-inflammatory effects locally, reducing inflammation at the surgical site and surrounding tissues. This localized action decreases the release of pro-inflammatory

cytokines and mediators, which are known to contribute to pain and hypersensitivity post-surgery. The drug's potent glucocorticoid activity helps to stabilize cell membranes, inhibit the proliferation of immune cells, and reduce the production of inflammatory mediators. As a result, compared to systemic or ondansetron therapies, intraperitoneal dexamethasone more directly addresses the underlying inflammatory processes, which can successfully lower pain intensity and the need for further analgesics [16].

Our findings are in accordance with Mohtadi, et al. [17] who examined the analgesic effects of dexamethasone administered intraperitoneally versus intravenously in patients having laparoscopic cholecystectomy. The research findings indicate that intraperitoneal dexamethasone was superior to intravenous administration in terms of pain alleviation during the postoperative phase. This is indicated by the significantly lower VAS scores and decreased opioid intake.

Our study demonstrated that Groups C and D, which received dexamethasone, showed a delay in the need for rescue analgesia and didn't receive a second dose of rescue analgesic. This may indicate that potential synergistic effects of combining ketorolac and dexamethasone for postoperative pain management in laparoscopic surgeries and dexamethasone was effective in prolonging the time before additional analgesic interventions were required. This delayed need for rescue analgesia suggests that dexamethasone might offer more sustained pain relief compared to ondansetron and control group.

This result in accordance with Razi et al. [18] investigated the effectiveness of a ketorolac and dexamethasone combination regimen for treating pain in patients with renal colic. The outcomes showed that when ketorolac and dexamethasone were given together, the pain was better controlled than when they were given separately. The study noted that patients receiving the combination therapy had lower VAS pain scores and required less additional analgesics during the postoperative period. The researchers attributed this enhanced pain control to the synergistic effects of ketorolac's nonsteroidal anti-inflammatory action and dexamethasone's corticosteroid-mediated anti-inflammatory response.

This result in accordance with Xu, et al. [19] found that dexamethasone can significantly prolong the analgesic effect postoperatively, aligning with your findings of delayed rescue analgesia.

Our study showed that Groups C and D, who received dexamethasone received lower total analgesic dose, this suggests that these groups required less additional analgesia overall. This can be attributed to the more effective pain control provided by dexamethasone, reducing the need for supplementary analgesics.

In line with our findings, Li, et al. [20] noted that dexamethasone's anti-inflammatory properties could reduce the total need for postoperative analgesics, which supports the finding of lower analgesic requirements in patients.

Additionally, Elsakka, et al. [21] Researched the impact of various corticosteroids on pain following surgery and demonstrated that intraperitoneal dexamethasone and hydrocortisone helped alleviate patients' shoulder and abdominal discomfort. As a result, this lessened the requirement for analgesics to be given to patients following laparoscopic cholecystectomy without having a major negative impact. These findings align with our results, indicating that dexamethasone, particularly when administered intravenously or intraperitoneally, effectively reduces postoperative pain without significant adverse effects.

Regarding PONV, our research showed that at 30, 45, and 60 minutes, Group A (the control group) had a considerably higher Bellville scoring scale than the other three groups, 1, 2, 4 hours, highlighting the effectiveness of ondansetron and dexamethasone in managing PONV. Groups C and D (Dexamethasone): Both showed benefits and not significantly different from each other or Group B in the early period, suggesting that both forms of dexamethasone are effective but may not offer additional benefits over ondansetron in the immediate postoperative period.

According to our findings, group B's Bellville score was significantly lower than group A's, which is consistent with the literature supporting ondansetron's efficacy in the immediate postoperative period. This result in accordance with Gan et al. [22] suggested that ondansetron is particularly effective in the immediate postoperative period.

When compared to Groups A, intraperitoneal dexamethasone (Group C) significantly improved the nausea and vomiting scores. This outcome is

consistent with Xu et al. [23] reported that dexamethasone significantly reduced postoperative nausea and vomiting, reflected by lower Bellville scores, which aligns with your results showing that dexamethasone groups experienced less nausea compared to the control group

Our results showed significant lower Bellville score in group D compared to group A, in line with our findings, Rehman, et al. [24] shown that PONV were considerably reduced by 4 mg of IV dexamethasone compared to the control group. The dexamethasone group exhibited significantly lower scores for nausea at various time intervals postoperatively compared to the control group. Moreover, the dexamethasone group had a significant decrease in the need for rescue antiemetic medicine, demonstrating the effectiveness of IV dexamethasone in lowering PONV after surgery.

At Intermediate Postoperative Period Six to twenty-four hours later, no discernible variations were seen between the groups, suggesting that the effect of antiemetic treatments may diminish over time. This supports findings from various studies indicating a reduction in the effectiveness of single dose antiemetics over extended periods.

There may be pharmacological reasons for the observed variations in PONV and the requirement for rescue antiemetic medicine between the study groups. The selective serotonin 5-HT3 receptor antagonist Ondansetron (Group B) is known to inhibit serotonin receptors centrally in the chemoreceptor trigger zone and peripherally on vagal nerve terminals to produce its antiemetic effects [25]. Similarly, dexamethasone possesses anti-inflammatory properties and may act through multiple mechanisms, including inhibition of prostaglandin synthesis and modulation of neurotransmitter release. The significantly lower Bellville scores and reduced need for rescue antiemetics observed in patients receiving ondansetron (Group B) and intraperitoneal and intravenous dexamethasone (Group C and D) compared to the control group (Group A) could be explained by the synergistic antiemetic actions of these medications, which likely mitigate the incidence and severity of PONV [26].

Our findings showed both intravenous ondansetron and dexamethasone, whether given intravenously or intraperitoneally, were not significantly different in their Bellville scores, and they were similarly successful in lowering the incidence of nausea and vomiting following surgery.

Our finding in accordance with Xu, et al. [23] who investigated the efficacy of intraperitoneal dexamethasone against intravenous ondansetron in reducing nausea and vomiting during laparoscopic procedures. The study demonstrated that both antiemetic regimens had similar outcomes in terms of reducing nausea and vomiting, with comparable Bellville scores across both groups at various time intervals and found no statistically significant difference between the two treatments in terms of the total number of emesis episodes or the need for additional antiemetic therapy. This implies that dexamethasone and ondansetron are equally useful in preventing PONV.

Our finding partly agreed with Maitra, et al. [27] research that found that for the prevention of PONV in patients having laparoscopic procedures, both ondansetron and dexamethasone are useful. According to the investigation, dexamethasone outperformed ondansetron in avoiding PONV, especially when it came to lowering the frequency of nausea and vomiting. The study showed that dexamethasone was superior to ondansetron alone in reducing postoperative symptoms, whether it was administered alone or in conjunction with it.

Our findings are rather partly consistent with several other studies. Nazemroaya, et al. [1] showed that within the first 24 hours following surgery, IP dexamethasone injection significantly decreased the occurrence of nausea when compared to the control group. In addition, the IP group experienced much less postoperative vomiting than the IV and control groups. In comparison to the IV and control groups, IP treatment also markedly decreased the degree of pain and nausea.

Our results showed that group A not only had higher nausea and vomiting scores but also experienced a shorter time to onset of nausea and a greater need for rescue antiemetics, with 63.33% of patients requiring additional medication which is consistent with Abdelaziz, et al. [11] found that patients who took ondansetron had a significantly decreased frequency of PONV recorded at 8 and 24 hours compared to the control group ($p = 0.023$ and 0.016, respectively). During the research period, 52% of the patients who got ondansetron did not develop nausea or vomiting. In the ondansetron group, 4% of patients experienced severe nausea or

vomiting at 8 hours after surgery; however, in the same group, no patients reported any nausea or vomiting at 24 hours. In the control group, severe PONV was observed in 33.33% of patients at 8 hours and in 4.17% of patients at 24 hours.

Similarly, Rehman, et al. [24] also proved that dexamethasone was effective in lowering PONV. Up to 24 hours after surgery, 81.7% of patients in the dexamethasone group did not have PONV, according to their observations, compared to 56.7% in the control group.

Munir, et al. [28] furthermore discovered that the incidence of nausea and vomiting was considerably decreased when dexamethasone was added to ondansetron. 81.25% of patients who took dexamethasone + ondansetron did not develop nausea or vomiting after surgery, according to their report, compared to only 6.25% in the ondansetron alone group.

Similarly, Lopez-Olaondo, et al. [29] and Bano, et al. [30] found that when ondansetron and dexamethasone were used together, PONV was significantly lower than when ondansetron was used alone or a placebo. According to Lopez-Olaondo et al., 84% of patients in the group receiving ondansetron and dexamethasone experienced a full recovery, while just 20% of patients in the placebo group did. According to Bano et al., 81.6% of patients in the combination group and 60.4% of patients in the dexamethasone group did not have nausea and vomiting after surgery.

Our study found no reported cases of headache in any of the groups. The incidence of drowsiness and anxiety was similar across all groups, with drowsiness ranging from 6.67% to 16.66% and anxiety from 6.67% to 10%, showing no significant differences (P = 0.637), (P = 0.96) respectively among the groups. Additionally, all patients were discharged with no significant adverse effect. These findings suggest that the treatments administered did not significantly affect the occurrence of drowsiness, anxiety, or discharge timing.

Similarly, in the study by Jo, et al. [31] It looked at the prevalence of headache and dizziness in women having laparoscopic cholecystectomy who took 8 mg of dexamethasone to avoid postoperative nausea and vomiting. Specifically, dexamethasone was associated with 1 case of headache and 4 cases of dizziness. These findings are consistent with our study, highlighting the overall low incidence of side effects across both studies.

In contrast, in the study by Ismail, et al. [6] Eight milligrams of dexamethasone were administered intravenously (40 patients) or intraperitoneally (40 patients) to the patients. In comparison to the IP group (7.5%), the IV group experienced a greater rate of adverse effects (27.5%), with headache and dizziness being the most frequently reported symptoms (P = 0.037). However, in our investigation, the frequency of adverse events was similar in every group, indicating no significant differences in adverse effects between dexamethasone either intravenously or intraperitoneally.

CONCLUSIONS

In conclusion, our study demonstrated that both ondansetron and dexamethasone, either intraperitoneal or intravenous, effectively showed comparable effect to reduce postoperative nausea and vomiting in cholecystectomy patients using laparoscopic surgery. But regarding postoperative pain, both intraperitoneal and intravenous dexamethasone, offers superior postoperative pain management compared to ondansetron and saline controls. The results emphasize the role of dexamethasone in both reducing inflammation and providing pain relief, particularly in the early postoperative period, but at late postoperative period, Intraperitoneal dexamethasone shows superior efficacy in pain management compared to ondansetron and intravenous dexamethasone, with no significant adverse effects observed. These findings suggest that intraperitoneal dexamethasone may be a promising alternative for preventing postoperative complications and improving patient outcomes following laparoscopic cholecystectomy. However, to validate these findings and assess the long-term impacts of these treatments, more research with bigger sample sizes is necessary.

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Competing interests:

The authors declare that they have no competing interest.

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