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Comparison Between Oxycodone and Pregabalin as Preemptive Analgesia for Postoperative Pain Control: A Randomized Controlled Trial

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ABSTRACT

Preemptive analgesia is an intervention that provides analgesia preoperatively to reduce postoperative pain. Several medications have been studied as adjuvant therapy to general anesthesia, such as Pregabalin and oxycodone. However, only some studies have compared two options at the same time. Hence, the study aimed to assess the effectiveness of a single oral preemptive dose of Pregabalin versus oxycodone as preemptive analgesia on the short-term postoperative pain score. This three-armed, double-blinded, randomized controlled trial (RCT) was conducted from August 2021 to July 2022 in Nablus-Westbank-Palestine at the An-Najah National University Hospital (NNUH) surgery department. Patients undergoing Laparoscopic Cholecystectomy, Submucosal Resection, Breast Lumpectomy, or Median Laparotomy were recruited if they met inclusion criteria and were randomized to one of three arms. The medications were given 30 minutes before the induction of general anesthesia. Pain score, sedation score, vital signs, side effects, time to first use of rescue analgesia, total analgesic consumption, time to first use of antiemetic and total antiemetic consumption were reported 30 minutes preoperatively and at 0, 1, 4, and 8 hours postoperatively. A total of 168 patients were randomized to the control group, i.e., multivitamins group (n=56), Oxycodone group (n=55), or Pregabalin group (n=57). At 0 hours and 1 hour postoperatively, the mean pain score was the lowest in the pregabalin group and the highest in the placebo group. At 4 hours postoperatively, the mean pain score was the lowest in the placebo group and the highest in the pregabalin group. At 8 hours postoperatively, the mean pain score was the lowest in the pregabalin group and the highest in the oxycodone group. No significant changes in vital signs were recorded between the different groups. However, preemptive use of Oxycodone or Pregabalin, compared to placebo, did not significantly reduce postoperative pain levels or opioid consumption. In conclusion, oxycodone and Pregabalin as preemptive analgesia do not reduce early postoperative pain levels and/or opioid consumption, but they are safe options.

Keywords: Preemptive Analgesia; Oxycodone; Pregabalin; Opioid; Laparoscopic Cholecystectomy; Submucosal resection; Breast lumpectomy; Median laparotomy.

INTRODUCTION

Postoperative pain is a significant issue that impacts patients' rehabilitation and health-related quality of life, as experienced by a high number of patients undergoing surgical procedures. Moreover, there is a high possibility for acute pain to develop into chronic pain and for hypersensitivity and hyperexcitability to occur. Therefore, it is important to reduce postoperative pain; otherwise, it will increase the amount of morbidity and mortality [1,2]. Postoperative pain is a global concern, with despite efforts and policies, severe and enduring pain persists in clinical settings [3]. Unrelieved pain costs patients' comfort and can lead to psychological, physiological, and socioeconomic consequences, including chronic pain and poor quality of life [4].

Preemptive analgesia is an intervention that provides analgesia before initiating painful stimuli to reduce or prevent subsequent pain by blocking the establishment of altered central processing of afferent input, which amplifies hyperalgesia and allodynia after surgery[5]. It has been shown to minimize perioperative stress, postoperative morbidity, narcotic consumption, and hospital stay. It also increases patient satisfaction [6,7].

Both central and peripheral pain receptor sensitization are thought to contribute to postoperative pain. Blocking these receptors and preempting sensitization prevents hyperalgesia, lowering medication requirements[8]. Opioids are the most commonly used analgesics in the perioperative setting[9]. Unfortunately, they are commonly associated with serious adverse effects. Therefore, several drugs have been used as adjuvant therapy to general anesthesia to minimize opioid consumption in the postoperative period. This avoids its side effects [6]. Such drugs are pregabalin and oxycodone[10,11].

Several recent studies have presented the positive effects of preemptive analgesia on postoperative pain, especially when pregabalin and oxycodone were used. However, they were only on specific or similar types of surgeries. At the same time, most of the studies in the literature were about preventive analgesia [10,11].

Preemptive analgesia is successful in reducing postoperative pain following lumbar spine surgeries, as demonstrated by Zhang et al. in their meta-analysis [12]. A study by Mishra et al. found that preoperative administration of melatonin and pregabalin significantly reduces perioperative anxiety, postoperative pain, and rescue analgesic requirement, with pregabalin outperforming melatonin in providing postoperative analgesia [13].

Due to the lack of evidence in the current literature regarding combining more than one type of surgery in one study, especially comparing the administration of preoperative pregabalin versus oxycodone for controlling postoperative pain, this research will be dedicated to filling these gaps.

The findings of this research can contribute to the enhancement and advancement of strategies for managing post-operative pain, leading to a positive impact on the practical approach to reducing post-surgery pain, opioid use, and associated side effects. As a result, it can facilitate faster recovery after surgery and ultimately improve health-related quality of life. However, it shows the effectiveness of preemptive analgesia in postoperative pain relief in adults undergoing surgical procedures. Furthermore, it compares the effect of a single oral preemptive dose of pregabalin versus oxycodone on postoperative pain relief, minimizing opioid use, their side effects, sedation levels, and using rescue analgesia (timing and dose) and rescue antiemetics (timing and dose), and on changes in vital signs.

METHODOLOGY

The study was performed in parallel groups in a three-arm, double-blinded, randomized controlled trial (RCT). It was conducted from August 2021 to July 2022 in Nablus-Westbank-Palestine at the An-Najah National University Hospital (NNUH) surgery department. We enrolled reliable adult patients (who can give history by him/herself) and were scheduled to undergo laparoscopic cholecystectomy, submucosal resection, breast lumpectomy, or median laparotomy under general anesthesia. All participants were screened to confirm having the 2022 American Society of Anesthesiology grades 1 or 2 [14].

We excluded patients who were currently pregnant or breastfeeding, those with a history of consistent analgesic use, defined as regular consumption of pain-relief medications for the majority of days within the preceding three months, due to the risk of developing dependence and heightened dosage needs, and those who had taken analgesics within the last 24 hours. Additionally, patients were excluded if they had allergies to any medications used in the study, a recent history of smoking or hookah (Nargila) use within 24 hours prior to surgery and until discharge, a history of psychiatric medication or disorders, known liver or kidney impairment, or a history of alcohol or illicit drug use.

Moreover, we excluded any patient who had complications during surgery leading to changes in the study protocol, was discharged from the hospital within 6 hours after surgery, or was transferred from the ward to the ICU or other wards. The Oxycodone, Pregabalin, and multivitamins were in table form. They were prepacked in envelopes identical in appearance and consecutively numbered for each patient according to a randomization schedule. Simple randomization was performed according to a computer-generated random number list prepared by an investigator with no clinical involvement in the trial to group A (oxycodone 20 mg), group B (pregabalin 150 mg), or group C (multivitamins pill). According to the list, the nonclinical investigator prepared and filled a nonopaque plastic container with the designed envelopes. We gave every patient a code; this code was the file number of the participant and the previously enveloped pill. Patients, surgeons, and the staff responsible for administering drugs preoperatively and perioperatively and evaluation postoperatively were blinded.

After arrival at the hospital, the anesthesiology resident informed the participant about the study, explained the protocol, and invited him/her to participate. After signing the informed consent, each participant underwent standard care that included general examination, vital signs recording, a brief history to ensure that the participant met all the inclusion and none of the exclusion criteria of the study, cannula insertion for required procedures, and teaching him/her to use the numeric rating scale (NRS) for pain.

Thirty minutes before surgery, an anesthesiology resident gave the participant a closed envelope with a code similar to the participant's file code and ensured the participant ingested the pill with a sip of water and got rid of the envelope immediately. The participant was then transferred to the preparation room before surgery, and the induction of anesthesia began. The anesthetic protocol was standardized as follows: induction by 30 mic/kg midazolam, 1.5 mic/kg fentanyl, 2 mg/kg propofol, 0.6 mg/kg rocuronium, and 2% sevoflurane, and anesthesia was maintained by fentanyl and sevoflurane. Postoperative pain treatment was with patient-controlled IV morphine 3 mg bolus (rescue analgesia), and postoperative nausea and vomiting were treated with 4 mg IV ondansetron (rescue antiemetic).

The primary outcome of the study was the pain score, which was measured using a pain numeric rating scale (NRS), on which patients rate their current pain intensity from 0 (no pain) to 10 (worst possible pain). Secondary outcomes included vital signs (heart rate, blood pressure, temperature, respiratory rate, and oxygen saturation) and sedation score, which were measured using the Modified Ramsay Sedation Score (MRSS) [15). Pain score, sedation score, and vital signs were reported 30 minutes preoperatively and at 0, 1, 4, and 8 hours postoperatively. Moreover, side effects (constipation, respiratory depression, diarrhea, headache, dyspepsia, itching, urinary retention, and pruritus), time to first use of rescue analgesia (which is 3 mg IV morphine), total analgesic consumption, time to first use of antiemetic (which is 4 mg IV ondansetron), and total antiemetic consumption were also reported 30 minutes preoperatively and at 0, 1, 4, and 8 hours postoperatively.

Statistical Analysis

SPSS statistical software version 20 was used to enter and evaluate the data. Intention-to-treat analysis was used. Continuous variables were summed and provided as mean and standard deviation, while categorical variables were presented in frequencies and percentages. The Shapiro–Wilk test was used to investigate data for normality. The results with P values greater than 0.05 were considered normally distributed, while those with P values less than 0.05 were considered not normally distributed. The chi-square test compared the intervention and control groups for categorical data. Continuous data, on the other hand, were compared using ANOVA when the variable data were normally distributed and the Kruskal–Wallis H test when they were not, while the Wilcoxon signed-rank test was also used for nonnormally distributed two related samples. The significance level was set as a P value less than 0.05.

RESULTS

The study flow chart is shown in Figure (1). A total of 257 patients planned for the four elective surgeries were screened; nine refused to participate, and 80 were excluded for not meeting the inclusion criteria (a detailed description is provided in Figure (1). A total of 168 patients were randomized to the control group, i.e., multivitamins (n=56), or to intervention groups (n=112), distributed as oxycodone (n=55) and pregabalin (n=57). However, ten patients were excluded due to smoking postoperatively or refusal to continue. Therefore, 158 participants were enrolled in the study for analysis.

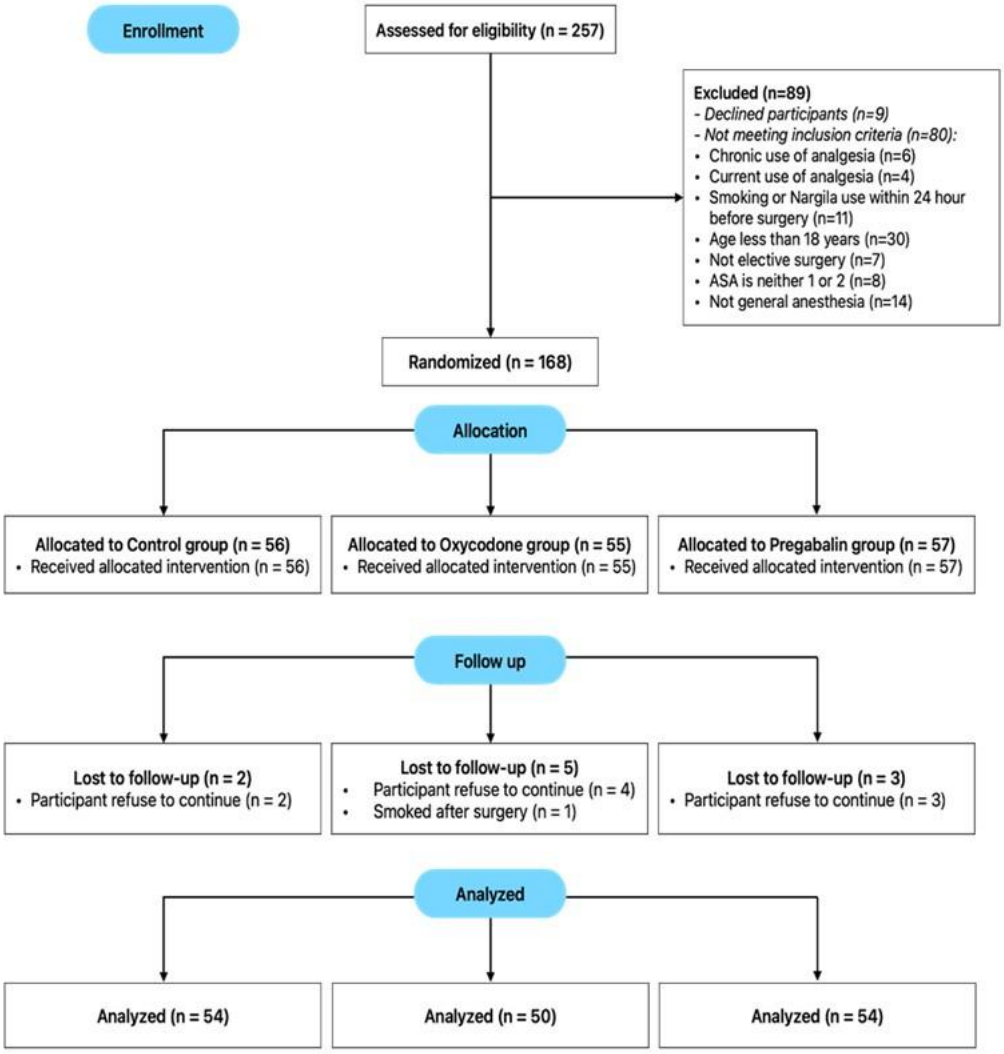

Figure (1): CONSORT flow chart of the study participants.

Table (1) shows the distribution of clinical and sociodemographic variables between the three groups. The groups were almost equal in terms of gender, age, and BMI (all of the patients were older than 18 years with a mean age of 35±14 years, BMI 26±5 kg/m^2, and 47% of them were males). Moreover, the results in Table (1) showed no statistically significant association between the three groups regarding chronic illnesses, previous surgeries, and smoking, which were 32%, 40%, and 35%, respectively.

Table (1): Distribution of clinical and sociodemographic between interventions and control groups.

	Oxycodone (n=50)	**Pregabalin** (n=54)	**Multivitamins** (n=54)	**P-Value***
Age (mean ± SD)	38±16	35±12	33±13	0.140
Gender				
Male n (%)	29(58.0%)	24(44.4%)	26(48.1%)	0.364
Employment,				
Yes n (%)	15(30.0%)	17(31.5%)	24(44.4%)	0.231
Social Status				
Married n (%)	33(66.0%)	34(63.0%)	33(61.1%)	0.873
Residency				
Urban n (%)	19(38.0%)	26(48.1%)	24(44.4%)	0.522
Rural n (%)	31(62.0%)	28(51.9%)	30(55.6%)	
Education level				
School n (%)	19 (38.0%)	15(27.8%)	22(40.7%)	0.183
University n (%)	28 (56.0%)	38(70.4%)	30(59.3%)	
Chronic Illness (%)	19(38.0%)	17(31.5%)	17(31.5%)	0.722
Previous surgeries n (%)	23(46.0%)	23(42.6%)	22(40.7%)	0.861
Smoking n (%)	18(36.0%)	20(37.0%)	20(37.0%)	0.992
BMI (mean±SD)	27±5	26±4	26±5	0.471

**Chi-square test and *ANOVA Test*.

Table (2) represents the vital signs of the patients both preoperatively and postoperatively. Regarding the O_2 saturation and temperature, there were no statistically significant differences between the preoperative and postoperative readings throughout all three groups. However, while heart rate readings showed a statistically significant decrease postoperatively (p=0.008, p=0.036, and p=0.027 for Oxycodone, Pregabalin, and Multivitamin groups, respectively), respiratory rate readings showed a statistically significant increase throughout the intervention and control groups (p=0.000, p=0.014, and p=0.002 for Oxycodone, Pregabalin, and Multivitamin groups, respectively).

Table (2): Effect of Oxycodone, Pregabalin, and multivitamins on vital signs preoperatively and at 0, 1, 4, 8 hours postoperatively.

Characteristic	**Oxycodone**		**Pregabalin**		**Multivitamin**	
	(Mean ± SD)	***P-value***	*(Mean ± SD)*	***P-value***	*(Mean ± SD)*	***P-value***
Heart Rate						
Preoperative	78.2±10.8	0.008	82.3±9.7	0.036	80.8±10.5	0.027
Postoperative	77.2±9.5		78.3±7.8		78.3±8.9	

Characteristic	Oxycodone		Pregabalin		Multivitamin	
	(Mean ± SD)	***P-value***	*(Mean ± SD)*	***P-value***	*(Mean ± SD)*	***P-value***
SBP						
Preoperative	123.0±10.9	0.056	122.3±10.9	0.159	127.6±14.6	0.009
Postoperative	120.9±9.7		119.8±10.0		124±11.2	
DBP						
Preoperative	89.8±88.6	0.223	77.5±8.3	0.022	77.6±8.5	0.034
Postoperative	73.2±6.8		75.0±6.7		74.9±7.8	
SPO2						
Preoperative	96.6±4.7	0.246	97.2±2.9	0.600	97.3±1.3	0.455
Postoperative	96.9±1.4		97.2±1.2		97.1±1.2	
Respiratory Rate						
Preoperative	15.5±2.2	0.000	15.2±2.8	0.014	14.6±2.2	0.002
Postoperative	15.7±2.0		15.6±1.9		15.4±1.9	
Temperature						
Preoperative	36.5±0.5	0.156	36.5±0.5	0.449	36.5±0.5	0.566
Postoperative	36.4±0.3		36.4±0.4		36.4±0.4	

** Paired samples T Test*

Moreover, there were only statistically significant differences between the preoperative and postoperative systolic blood pressure in the multivitamin group, which decreased significantly postoperatively compared to preoperative measurements (p=0.009), and between the preoperative and postoperative diastolic blood pressure in the pregabalin and multivitamin groups (p=0.022, 0.034 consecutively). Table (3) and Figure (2) demonstrate the pain score at 0, 1, 4, and 8 hours postoperatively. At 0 hours and 1 hour postoperatively, the mean pain scores were the lowest in the pregabalin group (2.7±1.6 and 1.7±1.5, respectively) and the highest in the multivitamins group, i.e., the control group (3.2±1.7 and 1.9±1.2, respectively). At 4 hours postoperatively, the mean pain score was the lowest in the multivitamins group (1.31±0.98) and the highest in the pregabalin group (1.37±1.2). At 8 hours postoperatively, the mean pain score was the lowest in the pregabalin group (0.98±0.47) and the highest in the oxycodone group (1.17±0.60). However, all the results were not statistically significant (p=0.270, 0.568, 0.961, 0.233, consecutively).

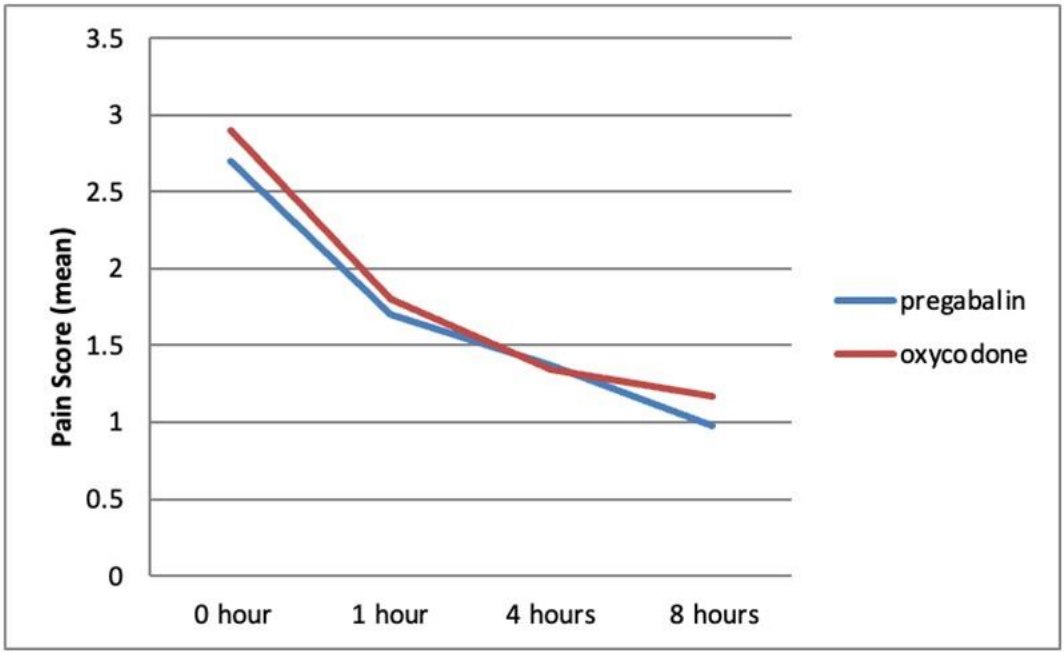

Figure (2): Effect of oxycodone and pregabalin on the pain score at 0,1,4,8 hours.

Participants who needed rescue analgesia were almost equal in people who took oxycodone and pregabalin (22.0% and 18.9%, respectively), while it was higher in people who took multivitamins (27.8%). Moreover, participants who needed rescue antiemetics varied in the three groups, as it was the highest in people who took multivitamins (22.2%) and the lowest in people who took pregabalin (11.1%). However, rescue analgesia and antiemetics had no statistically significant differences between interventional and control groups (p=0.539 and p=0.205, respectively).

Table (3): Effect of preemptive analgesia (Oxycodone and Pregabalin) on the pain score at 0,1,4,8 hours.

	Intervention 1 (Oxycodone)	**Intervention 2 (Pregabalin)**	**Control (Multivitamins)**	**P value***
Pain Score (NRS) at 0 hour *(mean ± SD)*	2.9±1.4	2.7±1.6	3.2±1.7	0.270
Pain Score (NRS) at 1 hour *(mean ± SD)*	1.8±1.1	1.7±1.5	1.9±1.2	0.568
Pain Score (NRS) at 4 hours *(mean ± SD)*	1.34±0.8	1.37±1.2	1.31±0.98	0.961
Pain Score (NRS) at 8hour *(mean ± SD)*	1.17±0.60	0.98±0.47	1.15±0.58	0.233
Rescue Analgesia *n (%)*	11 (22.0%)	10 (18.9%)	15 (27.8%)	0.539
Rescue Anti-emetic *n (%)*	6 (12.0%)	6 (11.1%)	12 (22.2%)	0.205

**ANOVA Test.*

Table (4) reports the incidence of the side effects postoperatively during the study (8 hours postoperatively). It was clear that hypotension, constipation, headache, urinary retention, and visual disturbances were found in the three groups. In contrast, dyspepsia and bradycardia occurred only in the oxycodone and multivitamin groups. Nonetheless, pruritus was found only in the oxycodone group, and diarrhea occurred only in the multivitamin group. None of the side effects showed statistically significant differences between the groups.

Table (4): Incidence of postoperative side effects among the intervention and control groups.

Side effect	**Oxycodone** n (%)	**Pregabalin** n (%)	**Multivitamins** n (%)	**P-Value***
Hypotension	4(8)	2(4)	2(4)	0.519
Headache	3(6)	9(17)	7(13)	0.239
Urinary Retention	3(6)	4(7)	3(6)	0.919
Visual Disturbances	3(6)	7(13)	5(9)	0.479
Pruritus	2(4)	0(0)	0(0)	0.107
Dyspepsia	2(4)	0 (0)	1(2)	0.328
Bradycardia	2(4)	0(0)	1(2)	0.328
Constipation	1(2)	3(6)	3(6)	0.6
Diarrhea	0(0)	0(0)	1(2)	0.379
Respiratory Depression	0(0)	0(0)	0(0)	-

**Chi-square Test*

Table (5) declared no statistically significant differences between the three groups regarding the sedation score, which was taken at 0, 1, 4, and 8 hours postoperatively. (p=0.459, p=0.503, p=0.342, and p=0.406, respectively).

Table (5): Sedation score between 3 groups at 0, 1, 4 and 8 hours.

	Oxycodone n(%)	**Pregabalin** n(%)	**Multivitamins** n(%)	**P value***
Sedation Score at 0 hour (Mean±SD)	2.42±0.8	2.33±0.6	2.26±0.6	0.459
Sedation Score at 1 hour (Mean±SD)	1.28±0.5	1.28±0.5	1.19±0.4	0.503
Sedation Score at 4 hours (Mean±SD)	0.98±0.14	1.00±0.0	1.00±0.0	0.342
Sedation Score at 8 hours (Mean±SD)	1.00±0.0	0.98±0.15	1.00±0.0	0.406

**ANNOVA Test.*

DISCUSSION

Some literature data regarding the pain reduction efficacy of oxycodone and pregabalin in the preoperative period are conflicting. Although many studies reported that preemptive use of these drugs achieves significant postoperative analgesia, some researchers contradict these results. In the case of Pregabalin, the findings of our study align with and expand upon some studies in several key aspects, where the results showed insignificant effects of preemptive analgesia on pain levels. For instance, Myhre et al. reported no pain reduction during the first 48 hours in the pregabalin group who underwent laparoscopic nephrectomy[16]. Similarly, Gurunathan et al. revealed that the addition of pregabalin offered no clinical analgesia benefit in laparoscopic cholecystectomy surgery patients [17].

Furthermore, Hang et al. showed that pregabalin does not reduce post-laparoscopic cholecystectomy pain[18]. On the other hand, numerous studies have reported that preemptive analgesia can significantly reduce postoperative pain[19,20]. For example, a systematic review included 74 studies found that pregabalin decreased pain levels in different surgical categories in the first 2 hours [20].

This current study found that pregabalin and oxycodone exhibited potential in alleviating postoperative pain, although the trends favored pregabalin, particularly at the early postoperative time points (0, 1, and 8 hours). These findings are consistent with those reported in previous research, where pregabalin was effective in reducing postoperative pain after various surgical procedures [19–22]. However, it's important to note that the current study did not demonstrate statistically significant differences between the groups, which could be attributed to the limited sample size or inter-individual variability.

Current clinical data regarding the efficacy and adverse effects of these drugs are controversial and nonhomogeneous when the dosing and the operation type are differentiated. In our study, headache was the most common side effect recorded in 44% of patients receiving intervention, with 21% of them receiving pregabalin. Since pregabalin side effects are dose-dependent, this could be a result of the higher pregabalin dose that was used as premedication (150 mg). It seems that low pregabalin doses have a limited analgesic role, whereas higher doses are associated with an increased incidence of side effects [20–23].

In general, the safety profile of pregabalin and oxycodone due to this study is in line with the existing literature. Both medications were well-tolerated, with side effects that are typical for these drugs [17,24]. The absence of statistically significant differences in side effects between the groups aligns with the general safety of preemptive analgesia with these medications. This consistency with prior research emphasizes that preemptive analgesia can be administered without introducing significant risks to patients' well-being. However, the concept of opioid-sparing and shorter hospital stays as a result of preemptive analgesia is well-established in the literature. Many previous studies have shown that preemptive analgesia can minimize opioid consumption and lead to a faster

recovery, which was one of the objectives of this research [19–22]. We observed significantly lower postoperative morphine consumption in the active groups at all-time endpoints with no statistical significance. We can hypothesize that higher opioid consumption is necessary to achieve similar pain control in the placebo group compared to the active groups. A systematic review concluded that pregabalin reduces the consumption of morphine in the first 24 hours after different surgical categories [20].

Rescue antiemetics it represents an objective way of measuring postoperative antiemetic requirements. We observed a significantly lower postoperative antiemetic consumption in the active groups at all-time endpoints with no statistical significance, though. Another study concluded that nausea and vomiting could be caused by surgery or even associated with extubation [25]. The study results regarding sedation levels, satisfaction scores, and vital signs are in accordance with the literature. Preemptive analgesia with pregabalin and oxycodone did not lead to substantial alterations in sedation, satisfaction, or vital signs. These findings are consistent with the concept that preemptive analgesia can improve postoperative pain management without causing excessive sedation or dissatisfaction among patients [17,24]. The heterogeneity of surgical procedures in this study, a characteristic also found in the literature [19–22], is a limitation that may introduce variability in postoperative pain experiences. Future research could benefit from standardizing surgical procedures to assess the impact of preemptive analgesia more rigorously.

Nevertheless, it's important to acknowledge the limitations of our study, which include a relatively small sample size, a common issue found in existing literature where research often involves a restricted number of participants [19–22]. Additionally, the COVID-19 pandemic introduced constraints by reducing the number of elective surgeries, impacting our data collection and consequently limiting the sample size. Moreover, our study was conducted at a single center. The lack of statistically significant differences in particular outcomes, such as opioid consumption and hospital stay, might be attributed to the limited sample size. Expanding the study population in future research may help to establish these outcomes more definitively.

CONCLUSION

The current RCT is meant to examine the impact of preoperative oxycodone and pregabalin administration on postoperative analgesia in patients submitted to laparoscopic cholecystectomy, submucosal resection, breast lumpectomy, or median laparotomy. At the end of the experiment, the study findings show that the preoperative use of oxycodone and pregabalin is efficient in decreasing the consumption of postoperative opioids; however, it does not have a significant impact on postoperative pain scores. The results also indicate that preoperative use of oxycodone or pregabalin, compared to placebo, does not significantly reduce early postoperative pain levels and/or opioid consumption postoperatively. The researchers recommend that pregabalin be administered to the patient before undergoing any surgical operation, as it helps reduce pain not only immediately after the surgery but also after some time (e.g., 4 hours or 8 hours). irrespective of the patient's age, gender, etc. Despite the time, place, and sample constraints, the researchers have managed to ensure the efficacy of these medications. It might be significant to investigate the effect of these analgesics on a larger sample of patients who undergo surgeries in different medical facilities in Palestine.

Ethics approval and consent to participate

Approval was obtained from the Institutional Review Board (IRB) An-Najah National University (Reference #: Med March. 2021/24). Any serious or unexpected events used to be reported to the IRB. Additionally, confidentiality was maintained, and participants' names were never mentioned in the data collection forms, except for the patients who took oxycodone, which the head of the anesthesia department had to prescribe because the Ministry of Health restricted its use. However, all of the study data were saved in files kept in a locked office. All participants signed an informed written consent form obtained from eligible patients while maintaining privacy and following our

institutional guidelines. Eligible patients had to make their own decision to participate without any force.

Registration

This was a randomized controlled clinical trial that is registered at clinicaltrials.gov, with the number NCT05389813 (Comparison between Oxycodone and Pregabalin as Preemptive Analgesia).

Consent for publication

Not applicable

Availability of data and materials

The datasets supporting the conclusions of this article are available from the corresponding authors upon reasonable request. within the article and its additional files.

Author's contribution

Wael Sadaqa: conceptualization, writing-original draft, data curation, investigation, resources, software, supervision, validation, visualization, and writing review & editing. ***Carmel Khalil***: writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Thaer Alhroob***: writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Mohammad Shakhshir***: writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Shaden Jabali***: writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Jihad Zuhd***: data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Sudqi Assi***: data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Taqwa Qubaja***: data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Reem Yaseen***: data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. ***Zaher Nazzal***: conceptualization, formal analysis, methodology, project administration, resources, software, supervision, validation, visualization, and writing review & editing.

The research draws from the undergraduate graduation project of the student Mai Abu Al- *Carmel Khalil, Shaden Jabali,* and *Mohammad Shakhshir* entitled: Comparison between Oxycodone and Pregabalin as preemptive analgesia for postoperative pain control, RCT-2021.

Competing interest

The authors declared that there is no competing interest in this research

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REFERENCES

1] Ozgencil E, Yalcin S, Tuna H, Yorukoglu D, Kecik Y. Perioperative administration of gabapentin 1,200 mg day-1 and pregabalin 300 mg day-1 for pain following lumbar laminectomy and discectomy: a randomised, double-blinded, placebo-controlled study. Singapore Med J. 2011 Dec;52(12):883–9.

2] Richebé P, Capdevila X, Rivat C. Persistent Postsurgical Pain: Pathophysiology and Preventative Pharmacologic Considerations. Anesthesiology. 2018 Sep;129(3):590–607.

3] Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. J Pain Res. 2017;10:2287–98.

4] Dueñas M, Ojeda B, Salazar A, Mico JA, Failde I. A review of chronic pain impact on patients, their social environment and the health care system. J Pain Res. 2016;9:457–67.

5] Long JB, Bevil K, Giles DL. Preemptive Analgesia in Minimally Invasive Gynecologic Surgery. J Minim Invasive Gynecol. 2019 Feb;26(2):198–218.

6] Altiparmak B, Güzel Ç, Gümüş Demirbilek S. Comparison of Preoperative Administration of Pregabalin and Duloxetine on Cognitive Functions and Pain Management After Spinal Surgery: A Randomized, Double-blind, Placebo-controlled Study. Clin J Pain [Internet]. 2018;34(12). Available from: https://journals.lww.com/clinicalpain/fulltext/2018/12000/comparison_of_preoperative_administration_of.4.aspx

7] Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. Anesth Analg. 2007 Nov;105(5):1449–53, table of contents.

8] Karaca O, Pınar HU, Turk E, Dogan R, Ahiskalioglu A, Solak SK. Effects of Single-Dose Preemptive Pregabalin and Intravenous Ibuprofen on Postoperative Opioid Consumption and Acute Pain after Laparoscopic Cholecystectomy. J Investig Surg Off J Acad Surg Res. 2019 Apr;32(3):189–95.

9] Abdelfattah AAM, Rizk F, Hawash N, Hanafy A, El-Kalla F, Abd-Elsalam S. Randomized trial of preoperative administration of oral pregabalin for postoperative analgesia in patients scheduled for radiofrequency ablation of focal lesions in the liver. Int J Hyperth Off J Eur Soc Hyperthermic Oncol North Am Hyperth Gr. 2018 Dec;34(8):1367–71.

10] Konstantatos AH, Kavnoudias H, Stegeman JR, Boyd D, Street M, Bailey M, et al. A randomized, double-blind, placebo-controlled study of preemptive oral oxycodone with morphine patient-controlled anesthesia for postoperative pain management in patients undergoing uterine artery embolization for symptomatic uterine fibroids. Cardiovasc Intervent Radiol. 2014 Oct;37(5):1191–7.

11] Park IJ, Kim G, Ko G, Lee YJ, Hwang SH. Does preoperative administration of gabapentin/pregabalin improve postoperative nasal surgery pain? Laryngoscope. 2016 Oct;126(10):2232–41.

12] Zhang LK, Li Q, Quan RF, Liu JS. Is preemptive analgesia a good choice for postoperative pain relief in lumbar spine surgeries?: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2021 Apr;100(13):e25319.

13] Mishra A, Srivastava VK, Prakash R, Mishra NK, Agarwal J, Kabi S. Perioperative Anxiolysis and Analgesic Effect after Premedication with Melatonin and Pregabalin in Total Hip Arthroplasty under Spinal Anaesthesia: A Prospective Comparative Trial. Adv Biomed Res. 2023;12:185.

14] Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. Anesthesiology. 2022 Jan;136(1):31–81.

15] De Jonghe B, Cook D, Appere-De-Vecchi C, Guyatt G, Meade M, Outin H. Using and understanding sedation scoring systems: a systematic review. Intensive Care Med. 2000 Mar;26(3):275–85.

16] Myhre M, Romundstad L, Stubhaug A. Pregabalin reduces opioid consumption and hyperalgesia but not pain intensity after laparoscopic donor nephrectomy. Acta Anaesthesiol Scand. 2017 Nov;61(10):1314–24.

17] Gurunathan U, Rapchuk IL, King G, Barnett AG, Fraser JF. The effect of pregabalin and celecoxib on the analgesic requirements after laparoscopic cholecystectomy: a randomized controlled trial. J Anesth. 2016 Feb;30(1):64–71.

18] Chang SH, Lee HW, Kim HK, Kim SH,

Kim DK. An evaluation of perioperative pregabalin for prevention and attenuation of postoperative shoulder pain after laparoscopic cholecystectomy. Anesth Analg. 2009 Oct;109(4):1284–6.

19] Asgari Z, Rouholamin S, Nataj M, Sepidarkish M, Hosseini R, Razavi M. Dose ranging effects of pregabalin on pain in patients undergoing laparoscopic hysterectomy: A randomized, double blinded, placebo controlled, clinical trial. J Clin Anesth. 2017 May;38:13–7.

20] Lam DMH, Choi SW, Wong SSC, Irwin MG, Cheung CW. Efficacy of Pregabalin in Acute Postoperative Pain Under Different Surgical Categories: A Meta-Analysis. Medicine (Baltimore). 2015 Nov;94(46):e1944.

21] Xiang X, Yuan X, Lian Y, Fang J, Wu Y. Effect of oxycodone hydrochloride combined with flurbiprofen axetil for intravenous patient-controlled analgesia in lower abdominal patients: A randomized trial. Medicine (Baltimore). 2018 Feb;97(7):e9911.

22] Zhang Y, Wang Y, Zhang X. Effect of pre-emptive pregabalin on pain management in patients undergoing laparoscopic cholecystectomy: A systematic review and meta-analysis. Int J Surg. 2017 Aug;44:122–7.

23] Engelman E, Cateloy F. Efficacy and safety of perioperative pregabalin for post-operative pain: a meta-analysis of randomized-controlled trials. Acta Anaesthesiol Scand. 2011 Sep;55(8):927–43.

24] Stubhaug A, Breivik H, Eide PK, Kreunen M, Foss A. Mapping of punctuate hyperalgesia around a surgical incision demonstrates that ketamine is a powerful suppressor of central sensitization to pain following surgery. Acta Anaesthesiol Scand. 1997 Oct;41(9):1124–32.

25] Wu J, Gui Q, Wang J, Ye J, Xia Z, Wang S, et al. Oxycodone preemptive analgesia after endoscopic plasma total adenotonsillectomy in children: A randomized controlled trial. Medicine (Baltimore). 2020 Feb;99(6):e19004.