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The Effect of Pregabalin on Postoperative Pain in Patients Undergoing Abdominal Surgery under General Anesthesia

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Abstract

Background: Acute postoperative pain and side effects can be serious problems, due to either insufficient or excessive treatment. If analgesic treatment is begun after a painful stimulus, treating postoperative pain can be challenging because of the possibility of peripheral hypersensitivity and central nervous system hyperexcitability. Pre-emptive analgesia focuses on reducing postoperative opioid consumption and pain levels, decreasing the incidence of adverse events and improving patient satisfaction. Several pre-emptive analgesic regimens have been tried in the perioperative period, including opioids, nonsteroidal anti-inflammatory drugs, and so on.

Aim of Study: To evaluate the effects of oral pregabalin, before abdominal surgery, on postoperative pain intensity and analgesic requirements (primary outcome), and the incidence of post-operative nausea and vomiting (secondary outcome).

Patients and Methods: This randomized controlled trial was conducted on 60 adult healthy patients aged 21-50 years of both sex, ASA physical status I and II undergoing elective abdominal surgery (open or laparoscopic). Patients were equally randomized to: Group A: Received pregabalin 300mg/12hrs 24 hrs before surgery. Group B: Did not receive pregabalin.

Results: Time of first analgesic requirement was significantly delayed in group A compared to group B (*p*-value <0.001). Total pethidine consumption was significantly lower in group A compared to group B (*p*-value <0.001). Incidence of PONV was 5 (16.67%) patients in group A and 13 (43.33%) in group B. Incidence of dizziness was 20 (66.67%) patients in group A and 4 (13.33%) in group B. Incidence of PONV was significantly lower in group A compared to group B (*p* -value=0.024). Incidence of dizziness was significantly higher in group A compared to group B (*p*-value <0.001). Respiratory depression and hypotension were insignificantly different between both groups.

Conclusion: Preoperative administration of 300mg/12hrs 24hrs of pregabalin resulted in a significant reduction pain score, intraoperative fentanyl consumption, total pethidine consumption and incidence of PONV following elective abdominal surgery but with higher incidence of dizziness.

Key Words: *General anesthesia – Pregabalin.*

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Introduction

ACUTE postoperative pain and side effects can be serious problems, due to either insufficient or excessive treatment. Side effects and complications include: An increase in myocardial ischemia or infarction risk; an increase in thromboembolic and pulmonary complications; alterations in the immune system; an increase in persistent postoperative pain incidence; defective rehabilitation; increased hospital stay time or recurrent hospital admittance; impaired quality of life; and excessive sedation due to opioid usage **[1]**.

In such cases, if analgesic treatment is begun after a painful stimulus, treating postoperative pain can be challenging because of the possibility of peripheral hypersensitivity and central nervous system hyperexcitability **[2]**.

Since pre-emptive preoperative analgesia was first proposed by Wall in 1988, over the years it has been gradually regarded as an intervention given before incision, facilitating advance mobilization and functional rehabilitation after surgery **[3]**.

Pre-emptive analgesia focuses on reducing postoperative opioid consumption and pain levels, decreasing the incidence of adverse events and improving patient satisfaction. Several pre-emptive analgesic regimens have been tried in the perioperative period, including opioids, nonsteroidal anti-inflammatory drugs, and so on **[4]**.

If analgesic treatment begins after the onset of pain because of the possibility of peripheral hypersensitivity and central nervous system hyperexcitability, coping with the postoperative pain becomes difficult. Central sensitization, hyperalgesia, and allodynia can be reduced by a preemptive applica-

tion. Study has supported the effectiveness of preemptive analgesia, although various studies point out that preoperative analgesia timing is unconsiderable in terms of postoperative pain and opioid consumption [5].

Pregabalin is an anticonvulsant drug that reduces calcium entry to the nerve terminals of the central nervous system and lowers substance P, glutamate and noradrenaline levels, which plays a role in creating a sense of pain [6].

Pregabalin is also utilized in the reduction of neuropathic and even inflammatory pain, tissue irritation and fibromyalgia. Initial findings suggest that pregabalin can be effective in controlling acute post-operative pain, including major operations (abdominal, hysterectomy and orthopedic surgery). Pregabalin can considerably reduce pain intensity after an operation and lower the required dose of opioids. However, some studies point out that pregabalin lacks the necessary effectiveness in major operations and its effect is limited to minor operations [7].

Studies also suggest that gabapentin has a satisfactory effect in alleviating post-operative pain [8,9]. Pregabalin has been introduced with a higher efficacy and more desirable pharmacological profile than gabapentin. Therefore, it seems that pregabalin could be a better choice in alleviating post-operative pain than gabapentin.

Aim of the work:

To evaluate the effects of oral pregabalin, before abdominal surgery, on postoperative pain intensity and analgesic requirements (primary outcome), and the incidence of post-operative nausea and vomiting (secondary outcome).

Patients and Methods

This randomized controlled trial was conductedat Surgery Department, Ain Shams University Hospital during 2021 on 60 adult healthy patients aged 21-50 years of both sex, ASA physical status I and II undergoing elective abdominal surgery (open or laparoscopic). Patients were equally randomized to: Group A: Received pregabalin 300mg/ 12hrs 24hrs before surgery. Group B: Did not receive pregabalin. 6 months as enrollment, data management, and manuscript writing.

The inclusion criteria were: Patients undergoing elective abdominal surgery (open or laparoscopic) under general anesthesia, ASA class I or II, Patients aged (21-50 yrs.) and Patients willing to take part in the study. While the exclusion criteria were: Patients with impaired kidney or liver functions, Patients with history of hypersensitivity to pregabalin or a derivative, Patients with history of drug or alcohol abuse, chronic pain or daily intake of analgesics, uncontrolled medical disease (diabetes mellitus or hypertension), Patients with history of intake of non-steroidal anti-inflammatory drugs within 24h before surgery and Patients with history of moderate to severe respiratory disorder.

Using STATA program, setting alpha level at 5% and power at 80%. Results from previous study [10] showed that the mean pain score for pregabalin group at 24 hours was (0.6±0.8) compared to (1.6±1.5) for control group. Based on this, the needed sample is 30 cases per group, giving into account a 20% dropout.

All patients were subjected to the followings:

Preoperative: Patients were fasting 8 hours preoperatively. Routine preoperative investigations were done to all patients including laboratory investigations as (Complete blood picture, Bleeding Time, prothrombin time and partial thromboplastin time), age, weight, and sex were recorded. Patients were randomly divided into two groups using simple randomization (flipping a coin) for an example, where the side of the coin (i.e., heads - control group, tails-treatment group) determines the assignment of each subject. Group A: Received pregabalin 300mg/12hrs 24hrs before surgery, Group B: Did not receive pregabalin.

Inside the operating room, intravenous access was obtained: Anesthesia technique was standardized in both groups. An i.v infusion was placed before starting the induction. Monitor was connected and pulse oximetry (SPO_2), baseline noninvasive blood pressure (NIBP), heart rate (HR) and electrocardiography (ECG) were obtained, Anesthesia was induced with fentanyl 2µg/kg i.v and propofol 2mg/kg i.v; orotracheal intubation was facilitated by 0.5mg/kg atracurium i.v, Anesthesia was maintained with 100% oxygen and isoflurane with a MAC value of 1 and During surgery, 0.1mg/kg atracurium injections were repeated once every half an hour and 50µ fentanyl was also repeated once an hour to keep blood pressure and heart rate within 20% standard limits.

Postoperative:

After surgery vital data were monitored in the recovery room: All patients were closely monitored regarding the level of consciousness, occurrence of hypothermia and shivering, respiratory depression and hypotension and Pain was assessed using the visual analogue scale (VAS) every 15 minutes

during the first hour after regaining consciousness and every four hours in the first 24 hours after being transferred to the ward. The VAS is a 10cm line with the 0cm end representing no pain and 10cm representing the worst imaginable pain.

The occurrence of nausea/vomiting were recorded, Patients with (VAS < or = 3) did not receive further analgesia, but patients with (VAS > 3) were given pethidine 50mg i.v and pain was assessed after 30 minutes, if the pain score (VAS) is still >3, increments of pethidine 25mg i.v were given every 15 minutes interval till VAS become < or = 3, In case of respiratory depression, opioids were discontinued, and 100% oxygen was administered by mask, and in case of hypotension (systolic blood pressure <90 mmHg), 500cc of normal saline was infused over half an hour and The occurrence of nausea/vomiting during recovery and until 24 hours after surgery was recorded and an antiemetic (Granisetron 1mg/1ml i.v) was given if necessary.

Ethical considerations:

The study was approved by the Ethics Committee of Faculty of Medicine, Ain Shams University. There are adequate provisions to maintain privacy of participants and confidentiality of the data are as follows: Patients, before entering the trial, received all information regarding the scope, the methods, the possible benefits, and the potential risks, Their participation was voluntary, and they could withdraw their permission at any time, The informed consent was signed by the patient assisted by a physician or a relative, We put code number to each participant with the name and address kept in a special file and We used the results of the study only in a scientific manner and not to use it in any other aims.

Statistical analysis:

Data were entered and analyzed, using the statistical package for social sciences, SPSS version 24 (SPSS Inc., Chicago, Illinois, USA).

Shapiro-Wilks normality test and histograms were used to test the distribution of quantitative variables to select accordingly the type of statistical testing: parametric or nonparametric.

Parametric variables (e.g., age) were expressed as mean and standard deviation (SD) and were compared using F test among the three groups with post hoc (Tukey) test to compare each two groups. Comparison between two variables within the same group was compared by paired *t*-test.

Non-parametric variables (e.g., VAS) were expressed as median and interquartile range (IQR) and were analyzed using Kruskal-Wallis test; further analysis was performed by Mann-Whitney (U) test to compare each two groups. Comparison between two variables within the same group was compared by Wilcoxon test.

Categorial variables (e.g., sex) were expressed as frequency and percentage and were statistically analyzed by Chi-square test. A two-tailed *p*-value 0.05 was considered statistically significant.

Statistical analysis was done by SPSS v27 (IBM©, Chicago, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analysed by unpaired student *t*-test. Quantitative non-parametric data were presented as median and interquartile range (IQR) and were analysed by Mann Whitney-test. Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed *p*-value <0.05 was considered statistically significant.

Results

In this randomized controlled trial, 98 patients were assessed for eligibility, 26 patients did not meet the criteria and 12 patients refused to participate in the study. The remaining 60 patients were randomly allocated into two groups (30 patients in each). All 60 patients were followed-up and analyzed statistically.

Table (1): Baseline characteristics of the studied groups.

	Group A (n=30)	Group B (n=30)	*p*-value
Age (years):			
Mean ± SD	33.43±9.77	36.7±7.3	0.148
Range	21-48	22-47	
Weight (kg):			
Mean ± SD	77.43±17.81	80.8±17.95	0.469
Range	51-107	52-111	
Sex:			
Male	18 (60%)	17 (56.67%)	0.793
Female	12 (40%)	13 (43.33%)	
ASA physical status:			
ASA I	19 (63.33%)	16 (53.33%)	0.432
ASA II	11 (36.67%)	14 (46.67%)	
Duration of surgery (min):			
Mean ± SD	80.83±27.2	83.83±28.15	0.676
Range	45-140	40-150	

ASA: American Society of Anaesthesiologists.

Baseline characteristics (age, weight, sex, ASA physical status, duration of surgery) were insignificantly different between both groups.

Table (2): VAS score of the studied groups.

	Group A		Group B		*p*-value
	Median	IQR	Median	IQR	
15 min	2	(1-2)	2	(2-3)	0.006*
30 min	2	(1.25-3)	3	(2-3)	0.026*
45 min	2	(2-3)	3	(2-3)	0.050*
1 h	2	(1.25-2.75)	3	(2-5)	0.003*
5 h	2.5	(1-4)	4	(2.25-5)	0.007*
9 h	3	(2-4)	5	(3-6)	<0.001*
13 h	3	(2-4)	3.5	(2-6)	0.041*
17 h	3	(2.25-4.75)	4	(3-5)	0.138
21 h	3	(2-3.75)	4	(3-5)	0.084
25 h	4	(3-5)	4	(2.25-5)	0.786

IQR: Interquartile range.
VAS: Visual analog scale.
*: Significant as *p*-value 0.05

VAS score was significantly lower in group A compared to group B at 15, 30, 45 min, 1, 5, 9 and 13h (*p*-value <0.05) and was insignificantly different at 17, 21 and 25h between both groups.

Table (3): Intraoperative fentanyl consumption of the studied groups.

	Group A (n=30)	Group B (n=30)	*p*-value
Intraoperative fentanyl consumption (µg):			
Mean ± SD	165.67±43.92	228±48.59	<0.001*
Range	100-260	150-320	

*: Significant as *p*-value 0.05

Intraoperative fentanyl consumption was significantly lower in group A compared to group B (*p*-value <0.001).

Table (4): Time of first analgesic requirement of the studied groups.

	Group A (n=30)	Group B (n=30)	*p*-value
Time of first analgesic requirement (h):			
Mean ± SD	8.4±3.38	0.68±0.29	<0.001*
Range	4-12	0.25-1	

*: Significant as *p*-value 0.05

Time of first analgesic requirement was significantly delayed in group A compared to group B (*p*-value <0.001).

Table (5): Total pethidine consumption of the studied groups.

	Group A (n=30)	Group B (n=30)	*p*-value
Total pethidine consumption (mg):			
Mean ± SD	113.33±29.16	233.33±47.95	<0.001*
Range	50-150	150-300	

*: Significant as *p*-value 0.05

Total pethidine consumption was significantly lower in group A compared to group B (*p*-value <0.001).

Table (6): Side effects of the studied groups.

	Group A (n=30)	Group B (n=30)	*p*-value
PONV	5 (16.67%)	13 (43.33%)	<0.001*
Dizziness	20 (66.67%)	4 (13.33%)	
Headache	3 (10%)	3 (10%)	
Respiratory depression	0 (0%)	3 (10%)	
Hypothermia	0 (0%)	0 (0%)	
Hypotension	3 (10%)	2 (6.67%)	

PONV: Postoperative nausea and vomiting.
* : Significant as *p*-value 0.05.

Incidence of PONV was 5 (16.67%) patients in group A and 13 (43.33%) in group B. Incidence of dizziness was 20 (66.67%) patients in group A and 4 (13.33%) in group B.

Incidence of PONV was significantly lower in group A compared to group B (*p*-value=0.024). Incidence of dizziness was significantly higher in group A compared to group B (*p*-value <0.001). Respiratory depression and hypotension were insignificantly different between both groups.

Discussion

Acute postoperative pain management is a challenging clinical problem and if inadequate, may result in increased morbidity, mortality and affects patient's quality of life **[11]**. Traditionally, opioid analgesics have been the mainstay of treatment of postoperative pain **[12]**. However, opioid analgesics are not devoid of their share of side effects such as respiratory depression, bradycardia, hypotension, nausea and vomiting **[13]**. Hence, a multimodal approach is used to manage postoperative pain and reduce opioid related side effects **[14]**.

Pregabalin is a structural analogue of gamma-aminobutyric acid that acts as a potent ligand for alpha 2-delta subunits of the voltage-gated calcium channels in the nervous system. Such action results

in a reduction in the depolarization-induced influx of calcium, hence a reduction in the release of excitatory neurotransmitters including glutamate, noradrenaline, dopamine, and serotonin **[15]**.

Pregabalin is an attractive adjuvant for perioperative analgesia in this regard as it can be taken on an empty stomach, does not lead to gastrointestinal bleeding, and is generally well tolerated **[16]**. The efficacy of pregabalin in treating acute postsurgical pain has been demonstrated in numerous studies **[17,18,19]**. A meta-analysis has suggested that pregabalin, at all doses and administration regimens, has opioid-sparing effects and reduces pain scores in the postsurgical setting, **[20]** at the expense of increased sedation and visual disturbances; however, the efficacy of pregabalin in providing such in various surgical categories remains uncertain, and it is not known whether the risk: Benefit ratio is greater for certain surgical categories.

Also, there are lack of studies evaluating the effect of preemptive pregabalin in management of pain in patients undergoing abdominal surgery.

Therefore, the aim of this study was to evaluate the effects of oral pregabalin, before abdominal surgery, on postoperative pain intensity and analgesic requirements and the incidence of postoperative nausea and vomiting.

This randomized controlled trial was conducted on 60 adult healthy patients aged 21-50 years of both sex, ASA physical status I and II undergoing elective abdominal surgery (open or laparoscopic). Patients were equally randomized to: Group A: received pregabalin 300mg/12hrs 24 hrs before surgery. Group B: Did not receive pregabalin.

Our results showed that VAS score was significantly lower in pregabalin group compared to control group at 15, 30, 45min, 1, 5, 9 and 13h (p-value <0.05) and was insignificantly different at 17, 21 and 25h between both groups. Typically, postoperative pain is characteristically nociceptive which implicates the peripheral mechanoreceptor stimulation; besides, it is established that inflammatory, visceral, and neurogenic components also shears to the acute pain symptoms. It has been proposed that postoperative pain can be combined with a reversible brief variety of neuropathic pain **[21]**. It was confirmed that mechanical hyperalgesia around the wound postoperatively contribute to the general mechanism involving central neuronal sensitization **[22]**. This could explain the analgesic effect of pregabalin as it blocks both hyperalgesia and central sensitization **[23]**.

In agreement with our findings, Hadavi et al. **[17]** carried out a prospective, randomized, double-blinded placebo-controlled trial evaluating the effectiveness of pregabalin in postoperative remifentanil-induced hyperalgesia prevention. Patients who are candidates for rhinoplasty under general anaesthesia (G/A) were enrolled. Pregabalin group received 300mg pregabalin before anesthesia. They reported that the VAS in placebo group was significantly higher compared to the pregabalin group in the 1^{st} hour post-surgery (p<0.001). Also, the VAS from the 2nd hour to 24hrs post-surgery was significantly higher in placebo groups compared to the pregabalin group (p<.001) **[17]**.

Our results are supported by Krishna et al. **[24]** who conducted a prospective, double-blinded, randomized controlled trial evaluating acute postoperative pain management of pre-emptive gabapentin versus pregabalin in head and neck surgeries under G/A. 100 patients of either gender in ASA I or II were randomly allocated to one of the two groups of fifty each. Patients in group G received single dose of gabapentin 1200mg while in group P received pregabalin 300mg, 1 hour before induction of anesthesia. They observed that the VAS score was significantly reduced in pregabalin group when compared to gabapentin group in the postoperative period (p<0.05). This indicates pregabalin (300mg) provided better postoperative pain relief when compared to gabapentin (1200mg) **[24]**.

Also, Ghadami et al. **[25]** conducted a randomized double-blind clinical trial studying the effect of oral pregabalin on reducing acute pain after abdominal hysterectomy. Pregabalin group received 300mg oral pregabalin, and placebo group received the placebo and saline. They observed that compared to placebo group the VAS at 2, 4, 6, 12 hours was significantly lower in the pregabalin group, but at 18 and 24 hours after surgery there was no significant difference between the two groups **[25]**.

Moreover, El-Hussiny et al. **[26]** compared the efficacy and safety of two different doses (150mg and 300mg) of oral pregabalin premedication on attenuation of the hemodynamic pressor response to airway instrumentation, perioperative hemodynamic stability, preoperative sedation, and postoperative pain reduction. Their prospective, observational study consisted of 60 adult patients scheduled for laparoscopic cholecystectomy. The patients were randomized into three groups of 20 patients each. Group I (P0) received an oral placebo, group II (P150) received 150mg of oral pregabalin, and group III (P300) received 300mg of oral pregabalin

1h prior to induction. Comparison of static and dynamic postoperative pain showed significantly reduction in the pregabalin groups (p<0.001) compared with the placebo group from recovery to 24h [26].

In agreement to our findings, Barman et al. [18] evaluated preemptive analgesia of oral pregabalin during the postoperative period of gynaecological operation under spinal anaesthesia. Their randomized, placebo-controlled study enrolled 80 women with ASA I and II and were divided into two groups (n=40). One hour before anaesthesia, group P received pregabalin 75mg and group C received placebo, both in the form of identical gelatinous capsules. He reported that pregabalin group had a significantly lower VAS in the first 48 hrs in comparison to the control group. Number of patients having VAS 4 at 6, 24 and 48 hrs was lower in pregabalin group than in control group. However, number of patients having VAS 4 was higher at 12 hr in pregabalin group than in control group [18].

In contrast to our findings, Mazy et al. [23] evaluated pregabalin effects on hypotensive anesthesia during spine surgery. Their prospective, randomized, controlled, double-blinded study included two groups of adult patients, the pregabalin group (n=53): Received oral pregabalin capsule 150mg 1h before general anesthesia and the control group (n=53): Received oral placebo capsule. There was no statistical difference in VAS for pain except early at recovery where VAS score was significantly lower in the pregabalin than the control group. Lower dose of pregabalin may be an appropriate justification for this difference from our findings [23].

In the present study, intraoperative fentanyl consumption was significantly lower in pregabalin group compared to control group (p-value <0.001).

In the same line with our findings, El-Hussiny et al. [26] reporteda significant increase (p<0.05) in intraoperative fentanyl consumption was observed in the placebo group compared to both 150 and 300mg pregabalin groups [26].

Our results disagreed with,Sisa et al. [27] who evaluated the effects of pre-emptive pregabalin and multimodal anesthesia on postoperative opioid requirements in patients undergoing robot-assisted laparoscopic prostatectomy. Patients with ASA status 1-3, age between 30 and 80 years and treated with standard multimodal anesthesia were included in the study. Pregabalin group received 150mg of oral pregabalin as premedication before anesthesia induction, while the control group was treated conventionally. They included 245 patients in the pregabalin group and 103 in the control group. There was insignificant difference regarding intraoperative fentanyl consumption (p=0.06) or opioid requirements on first postoperative day between pregabalin and control groups. Different dosage of pregabalin, type of surgery and study design may be a suitable explanation for this variation from our findings [27].

In the current study, time of first analgesic requirement was significantly delayed in pregabalin group compared to control group (p-value <0.001).

In agreement with our findings, Barman and his colleagues [18] observed thatin pregabalin group, the number of patients with VAS 4 at 6, 24 and 48 hours postoperatively was lower than in the control group. At 12 hours postoperative, however, the number of patients with a VAS 4 was higher in pregabalin group than in control group [18].

Our results supported by Krishna et al. [24] who reported that the timing of first rescue analgesic postoperatively was 522±121.974 minutes in group gabapentin (n=50) while it was 623.41±114.534 minutes in group pregabalin (n=41), which was highly significant (p-value <0.0001). This indicates that pregabalin provides longer pain relief when compared to gabapentin [24].

In the present study,total pethidine consumption was significantly lower in pregabalin group compared to control group (p-value <0.001).

In agreement with our findings, Barman et al. [18] observed that the cumulative dose of injection diclofenac (mg) was 280±26.34 and 350±35.32 in pregabalin and control groups, respectively with significant lower value in pregabalin than in group control (p=0.0136) [18].

Also, Hadavi et al. [17] reported that morphine consumption at 1 st-h post-surgery and from 2 nd-h till 24-h post-surgery were significantly lower in pregabalingroup than control group (p<0.001). This is due to lower pain score of pregabalin group that was accompanied with lower opioid consumption [17].

Similar to our findings, Ghadami et al. [25] reported that there was a significant increase in postoperative ketorolac consumption in placebo compared with pregabalin group. Additionally, there was a highly significant increase in postoperative morphine consumption in placebo group compared with pregabalin group. Post-operative

analgesic consumption was effectively reduced by pregabalin in a dose-dependent manner **[25]**.

Similar to our findings, Krishna et al. **[24]** reported that pregabalingroup consumed less tramadol (109.14±27.814mg) when compared to gabapentin group (147±33.746mg) and the difference between both the groups was highly significant (p-value <0.0001) **[24]**.

In the same line with our findings, Mazy and Abo-Zeid **[23]** reported that the consumption of morphine in the first postoperative 24h was significantly lower in the pregabalin group (6.2±2.4mg) compared with the control group (7.4±2.8mg) (p=0.027) **[23]**.

In contrast to our findings, Sisa et al. **[27]** reported insignificant difference regarding postoperative opioid consumption in PACU, 0-12h, 0-24h and number of patients required postoperative opioid on first postoperative day between pregabalin and control groups. This is explained as there were insignificant difference between those groups regarding pain score which is associated with non-significant difference in post-operative opioid consumption **[27]**.

In this study, incidence of PONV was 5 (16.67%) patients in pregabalin group and 13 (43.33%) patients in control group. Incidence of dizziness was 20 (66.67%) patients in pregabalin group and 4 (13.33%) patients in control group. Incidence of PONV was significantly lower in pregabalin group compared to placebo group (p-value=0.024). Incidence of dizziness was significantly higher in pregabalin group compared to placebo group (p-value <0.001). Respiratory depression and hypotension were insignificantly different between both groups.

Our results are in harmony with Hadavi et al. **[17]** who reported, the incidence of the PONV is 33.30% in the placebo group, and 0.00% in the pregabalin group during different times of the study. Therefore, there were significant differences between the two groups regarding PONV (p=0.015) **[17]**.

Similar to our findings, Ghadami et al. **[25]** reported that the incidence of nausea and vomiting was higher in the pregabalin group (8 patients) compared to the placebo group (14 patients) **[25]**.

The incidence of adverse events was also reported by Krishna et al. **[24]** as they documented that nausea occurred in 1 (2%), 4 (8%) and dizziness occurred in 3 (6%), 1 (2%) patients in pregabalin and gabapentin groups respectively, however, there was no statistically significant difference between the two groups **[24]**.

In the same context, Mazy et al., (2020) reported that PONV occurred in 4 (7.5%), 9 (17%) and dizziness occurred in 7 (13.2%), 3 (5.7%) patients in pregabalin and control groups respectively, however, the difference was insignificant **[23]**.

Also, El-Hussiny et al. **[26]** documented that postoperative nausea and vomiting were significantly lower with the administration of pregabalin compared with the placebo group (p<0.008). Additionally, pregabalin increased the incidence of dizziness and visual disturbances in a dose-dependent manner **[26]**.

Our results did not agree with Barman et al. **[18]** who documented that there was a statistically significant difference in complications such as nausea, vomiting, and dizziness within 24hrs in both groups. 5 (12.5%) patients experienced post-operative side effects within 24hrs in pregabalin group whereas no patients experienced side effects in placebo group (p-value <0.001) **[18]**.

In contrast to our findings, Sisa et al. **[27]** reported that PONV occurred in 19 (7.6%) patients in pregabalin group and in 7 (6.6%) patients in control group and the difference was insignificant (p=0.34). This is explained as Sisa and his colleagues reported insignificant difference regarding post-operative opioid consumption which is associated with insignificant difference in PONV **[27]**.

Conclusion:

Preoperative administration of 300mg/12hrs 24hrs of pregabalin resulted in a significant reduction pain score, intraoperative fentanyl consumption, total pethidine consumption and incidence of PONV following elective abdominal surgery but with higher incidence of dizziness.

Recommendations:

Further clinical studies are needed with multicenter cooperation and on larger scale to validate our findings. Future studies comparing different doses of pregabalin are required to identify the optimum dose. Further studies are required studying preemptive effect of pregabalin in different types of surgeries. Future studies are recommended to compare pregabalin with other agents (magnesium sulphate, ketamine or gabapentin). We recommend administration of 300mg/12hrs 24 hrs of pregabalin oral pre-operatively as an adjuvant for multimodal analgesia in post-surgical pain.

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تأثير البريجابالين على آلام ما بعد الجراحة والغثيان والقئ في المرضى الذين يخضعون لجراحات البطن تحت التخدير الكلى

المقدمة والهدف من البحث : يعد الألم الحاد بعد الجراحة والآثار الجانبية من المشاكل الخطيرة، إما بسبب العلاج غير الكافى أو المفرط. إذا بدأ العلاج التسكينى بعد منبه مؤلم، فإن علاج ألم ما بعد الجراحة يمكن أن يكون صعباً بسبب احتمال فرط الحساسية المحيطية والاستثارة المفرطة للجهاز العصبى المركزى.

يركز المسكن الوقائى على تقليل استهلاك المواد الأفيونية بعد الجراحة ومستويات الألم، وتقليل حدوث الأحداث العكسية وتحسين رضا المريض. تم تجربة العديد من أنظمة المسكنات الوقائية فى الفترة المحيطة بالجراحة، بما فى ذلك المواد الأفيونية والأدوية غير الستيرويدية المضادة للالتهابات وما إلى ذلك.

المرضى والطرق : أجريت هذه الدراسة على ٦٠ مريضاً بالغاً يتمتعون بصحة جيدة تتراوح أعمارهم بين ٢١–٥٠ عاماً من كلا الجنسين، ولهم تقييم الحالة الجسدية واحد واثنين وفقاً للجمعية الأمريكية لأطباء التخدير ويخضعون لجراحة البطن الاختيارية (مفتوحة أو بالمنظار).

النتائج : حدث الغثيان والقئ بعد العملية الجراحية فى ٥ (١٦.٦٧٪) مرضى فى المجموعة أ وفى ١٣ (٤٣.٣٣٪) مريض فى المجموعة ب. وحدث الدوار فى ٢٠ (٦٦.٦٧٪) مريض فى المجموعة أ و ٤ (١٣.٣٣٪) مرض فى المجموعة ب. كانت نسبة حدوث الغثيان والقئ بعد العملية الجراحية أقل بشكل مهم إحصائياً فى أ مقارنة بالمجموعة ب كان معدل حدوث الدوخة أعلى بشكل مهم إحصائياً فى المجموعة أ مقارنة بالمجموعة ب كان تثبيط الجهاز التنفسى وانخفاض ضغط الدم مختلفين بشكل غير مهم إحصائياً بين المجموعتين

الاستنتاج : أدى تناول ٣٠٠ مجم / ١٢ ساعة على مدار ساعة من البريجابالين قبل الجراحة إلى انخفاض مهم إحصائياً فى درجة الألم، واستهلاك الفنتائيل أثناء العملية، وإجمالى استهلاك البيثيدين، وحدوث الغثيان والقئ ما بعد العملية الجراحية بعد جراحة البطن الاختيارية ولكن مع ارتفاع معدل الإصابة بالدوار.