

## Oral Gabapentin versus Pregabalin for Postoperative Pain Relief in Elective Cesarean Section Patients under Spinal Anesthesia

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### ABSTRACT

**Background:** Pain after Cesarean delivery is the main postoperative complain in parturients, pregabalin and gabapentin have been shown to decrease acute postoperative pain in parturient. **Objective:** The aim of the study was to compare gabapentin and pregabalin as oral premedication in patients for elective cesarean section under spinal anesthesia for postoperative pain relief and the need to rescue analgesia.

**Methods:** This study was carried out at Obstetric Operating Rooms, Zagazig University Surgical Hospitals. The study included 54 consenting women aging 20–40 yrs old with uncomplicated pregnancies that were scheduled to undergo elective Cesarean section delivery under spinal anesthesia. They were randomly allocated into three equal groups. Group (P) received 300 mg pregabalin, group (G) received 900 mg gabapentin, and control group (C). The study medication given orally one hour before the anticipated time of the surgical incision, and data measured included visual analogue scale (VAS), the total doses of analgesia, the incidence of post-operative nausea and vomiting (PONV) and the level of sedation. **Results:** The VAS was comparatively low in patients of group P as compared to G and C groups (P value < 0.05). Total analgesic requirement of pethidine in first 24 h was significantly lower in groups P as compared to groups G & C (P value < 0.001). We found that there was statistically significant increase in the sedation scores of the patients in P group as compared to G & C groups.

**Conclusion:** Pregabalin 300 mg was more effective than gabapentin 300 mg in reducing post Cesarean section pain, opioid consumption, nausea, and vomiting.

**Keywords:** Cesarean section, Postoperative pain, Pregabalin, Gabapentin.

### INTRODUCTION

The relief of postoperative pain is a subject, which has been receiving an increasing amount of attention in the past few years specifically obstetric surgeries <sup>(1)</sup>. Pain relief of good quality after cesarean section (CS) results in early mobilization and good early mother–child interaction <sup>(2)</sup>. Patient-controlled analgesia (PCA), with systemic opioids, gives a very high level of patient satisfaction. However, opioids have well documented side-effects i.e. sedation, nausea and respiratory depression <sup>(3)</sup>.

Gabapentin and pregabalin are structural analogues of gamma amino butyric acid that were introduced as antiepileptic drugs and have been extensively used to treat painful neuropathies. Their mechanism of action is likely mediated by binding to the presynaptic voltage-gated calcium channels, inhibiting calcium influx via these channels, and subsequently inhibiting the release of excitatory neurotransmitters from the primary afferent nerve fibers in the pain pathway <sup>(4)</sup>.

Several clinical trials studying perioperative use of gabapentin and pregabalin, with a variety of surgical procedures producing visceral and somatic injury, have found significant reduction in postoperative analgesic requirements and others a reduction in early and late postoperative pain <sup>(5)</sup>.

### AIM OF THE WORK

To compare gabapentin and pregabalin when given as oral premedication in patients for elective cesarean

section under spinal anesthesia regarding postoperative pain relief and the need to rescue analgesia.

### Ethical approval and written informed consent :

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

### PATIENTS AND METHODS

#### I. Technical Design:

##### a. Site of study:

This study was carried out in Obstetric Operating Rooms, Zagazig University Surgical Hospitals.

##### b. Sample size

Assuming that percent of three doses of postoperative analgesic requirements in gabapentin group is 20% verse 65% in control group so total sample size will be 54 (18 in each group) using open EPI, power 80% ,CI 95%<sup>(6)</sup>.

##### \*Inclusion criteria:

1. Age: 21-40 years old.
2. Gender: females
3. Physical status: ASA II.
4. BMI < 35 & > 20 kg/m<sup>2</sup>.
5. Written informed consent from the patient.



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6. Elective uncomplicated cesarean section under spinal anesthesia

**\*Exclusion criteria:**

1. Patient refusal.
2. Patients with known history of allergy to study drugs.
3. Advanced hepatic, renal and respiratory diseases.
4. Psychological and mental disorders.
5. Patient with reduced level of consciousness.
6. Hypertensive, cardiac and diabetic patients.
7. Patients receiving anticoagulants therapy or suspected coagulopathy.

**II. Operational Design:**

**a. Type of study:**

Prospective comparative randomized controlled clinical study.

**b. Study design:**

The patients was divided randomly using computer generated randomization table into three groups (18 for each group)

- **Group C** (n = 18): control group will receive three placebo capsules once one hour before the surgical incision.
- **Group G** (n= 18): gabapentin group will receive three capsules of gabapentin 300 mg once one hour before the surgical incision <sup>(7)</sup>.
- **Group P** (n= 18): pregabalin group will receive three capsules of pregabalin 100 mg once one hour before the surgical incision <sup>(8)</sup>.

❖ **Preoperative**

- Preoperative evaluation for all patients were included; a detailed history, physical examination and investigations (complete blood content (CBC), random blood glucose, kidney function, liver function tests, prothrombin time (PT) and international normalized ratio (INR)).
- Recording baseline measurement of patient hemodynamic state: mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR) and peripheral oxygen saturation (SPO<sub>2</sub>).
- The study medication was given by mouth with a sip of water one hour before the anticipated time of the surgery.
- No other premedication will be given at this time.
- Intravenous line (18G) was secured and patients were preloaded with (10 ml/kg) ringer lactate solution over 15-20 minutes.

❖ **Intraoperative**

- On arrival to the operating room all patients were continually monitored by automated noninvasive blood pressure monitor (NIBP), pulse oximetry and 5 leads electrocardiography (ECG) for monitoring of mean arterial blood pressure (MAP), HR, RR and peripheral oxygen saturation
- The parturient was supported to be in the sitting position for preparation for the administration of the spinal anesthesia. Complete aseptic precautions including

sterilization with povidone iodine and draping was performed. The L4/L5 intervertebral space was located.

- Using a size 22 G hypodermic needle, the skin overlying the intervertebral space was identified and anesthetized by 3 mL of 2% lidocaine. Lumbar puncture was performed through a midline approach using a 25G spinal needle and 2.5-3 ml of hyperbaric bupivacaine 0.5% with 25 (µg) fentanyl was administered intrathecal, then the patient was positioned supine with (15) degree left lateral tilt.
  - When satisfactory spinal anesthesia (adequate motor blockade and adequate sensory blockade at T10 level) was achieved, surgeon was allowed to start.
  - Continuous monitoring of patient hemodynamics, if hypotension (mean arterial blood pressure 20% lower than the basal) occurred, it was treated by fluid and ephedrine (5mg I.V), bradycardia (HR< 60 beats/min) was treated by atropine (0.5 mg I.V)
  - At the end of surgery, all patients were transferred to post anesthesia care unit (PACU).

❖ **Postoperative**

All patients' data were recorded for the following:

- Hemodynamics of patients (mean arterial blood pressure (MAP), HR, RR and peripheral oxygen saturation) every hour for first 4h and every 4h until 24h postoperative.
- The time to first postoperative rescue analgesic request was recorded (defined as time elapsed from the onset of spinal anesthesia to time of first call for analgesics). It was assessed by a visual analogue scale (VAS)<sup>(9)</sup> a scoring system used by the patient. The patient put a mark on a horizontal line which reads "no pain at all" at one end at 0, and "worst pain imaginable" at the other end at 10 and recorded initially every 2 h for the first 12 h and then every 4 h till 24 hrs.
- Baseline analgesia with 75 mg diclofinac Na was given IM/12h started postoperative.
- If VAS score  $\geq$  4 intravenous meperidine (pethidine) 1 mg/ kg will be given as rescue analgesia (repeated if needed during the first 24 h postoperatively), the number of doses and total analgesic dose will be recorded in the first 24 hrs postoperatively.
- The incidence of postoperative nausea and vomiting (PONV) and nausea severity for each patient was assessed by the simplified PONV impact scale <sup>(10)</sup>. When PONV impact scale scor was  $>$  5, Ondansteron (Zofran), 4 mg and Ranitidine (zantac), 50 mg was administered to the patient.

**Q1. Have you vomited or had dry retching?**

0. No
1. Once
2. Twice
3. Three or more times

**Q2. Have you experienced a feeling of nausea (an unsettled feeling in the stomach and slight urge to vomit)?**  
If yes, has your feeling of nausea interfered with activities

of daily living, such as being able to get out of bed, being able to move about freely in bed, being able to walk normally or eating and drinking?

0. Not at all
1. Sometimes
2. Often or most of the time
3. All of the time

To calculate the PONV impact scale score, sum the numerical responses to questions 1 and 2. A PONV impact scale score of  $\geq 5$  defines clinically important PONV.

- The level of sedation was assessed at 2 h intervals for the first 12 h and then every 4 h for the next 12 h postoperative by using the modified Ramsay Sedation Score.

#### **Modified Ramsay sedation score<sup>(11)</sup>:**

- 1 Patient is anxious and agitated or restless or both.
- 2 Patient is cooperative, oriented and tranquil.
- 3 Patient responds to commands only.
- 4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
- 5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
- 6 Patient exhibits no response.

- Neonatal APGAR score<sup>(12)</sup> at 1 and 5 min were recorded, which is a quick test performed at 1 and 5 min after birth to determine the physical condition of the newborn.

The test is generally done at 1 and 5 minutes after birth and may be repeated later if the score is low. Scores of 7 and above are generally normal, 4 to 6 are fairly low and 3 and below are generally regarded as critically low and cause for immediate resuscitative effort

- Recording of other postoperative complications such as itching, hypotension, respiratory depression, bradycardia and shivering after exclusion of surgical cause.

#### **Statistical Analysis**

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ( $\chi^2$ ) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation). One way ANOVA test supplied with post hoc (LDS) test was used to compare between more than two dependent groups of normally distributed variables. All statistical comparisons were two tailed with significance level of P-value  $\leq 0.05$  indicates significant,  $p < 0.001$  indicates highly significant difference while,  $P > 0.05$  indicates Non-significant difference.

#### **RESULTS**

54 female patients aged from 21 to 40 years old, with ASA physical status II were scheduled for elective cesarean section under spinal anesthesia. 18 cases (group C), each patient of them received placebo capsules, 18

cases (group G) each patient of them received 900 mg gabapentin and 18 cases (group P) each patient of them received 300 mg pregabalin. All drugs were received 1 hour preoperative. 10 cases were recorded as failed cases and excluded from the study 3 of them because of pain felt at skin incision indicating block failure, 3 cases due to complicated and prolonged surgery more than 3.5 hours requiring initiation of general anesthesia and 2 cases in control group (group C) lost in follow up. 1 case lost in follow up in gabapentin group (group G), 1 case lost in follow up in pregabalin group (group P) and these excluded cases were replaced by equal number of cases (Fig 1). Demographic characteristics in all three groups did not show any statistically significant difference [(P value  $> 0.05$ ) (Table 1)]. Comparing the outcome of the three groups, all patients in the three groups remained hemodynamically stable with no statistically significant difference.

As regards postoperative VAS, it was significantly higher in group C compared to group G & P in all time intervals except at 1 hr postoperative where there was no significant difference between the three groups. Meanwhile, group G found to be significantly higher in VAS compared to group P in all time intervals except at 16 and 24 hours postoperative where there was no significant difference between G & P [(P-value 0.300 & 0.477) (Table 2, Fig 2)].

As regards group C, it was found that the lowest value of VAS was at 1, 20 and 24 hours postoperative and the highest value was at 4 and 6 hours postoperative. As regards group G, the result showed that the lowest value of VAS was at 2 and 24 hours postoperative and the highest value was at 6 and 8 hours postoperative but still less than the control group. As regards group P, it was found that the lowest value of VAS was at 2 and 24 hours postoperative and the highest value was at 4 and 16 hours postoperative but still less than the control group.

**As regards PONV**, there was significant high incidence of nausea & vomiting in group C compared to group G & P in all time intervals except at 24 hour postoperative there was no significant difference between group C & G (p-value 0.880). Meanwhile group G showed a significant high incidence of nausea & vomiting compared to group P in all time intervals. As regard group C the table showed that the lowest value of PONV was at 24 hours postoperative ( $1.72 \pm 1.447$ ) and the highest value was at 4 hours postoperative ( $4 \pm 1.33$ ).

Concerning group G, the table showed that the lowest value of PONV was at 16 hours postoperative ( $1.22 \pm 1.166$ ) and the highest value was at 4 hours postoperative ( $1.89 \pm 0.676$ ). As regards group P, the table showed that the lowest value of PONV was at 10 hours postoperative (0) and the highest value was at 6 hours postoperative ( $0.5 \pm 0.618$ ) (Table 3, Fig 3).

As regards to the frequency of pethidine doses administration in first 24 h as an analgesic, the result of this study found that the control group needed about 59 pethidine doses (1350 mg) given to the 18 patients. 13 patients needed three doses and 5 patients needed four doses of pethidine to cover the rest of 24 h of

the study. While in group (G), they needed 40 pethidine doses (650 mg) distributed in the form of 14 patients asked for two consecutive doses while only 4 patients asked for three doses, to cover the study time.

However, group (p) needed only 29 doses of pethidine (350 mg) where 7 patients from 18 asked for an extra one dose while the other 11 patients asked for extra two doses in the study time (Table 4).

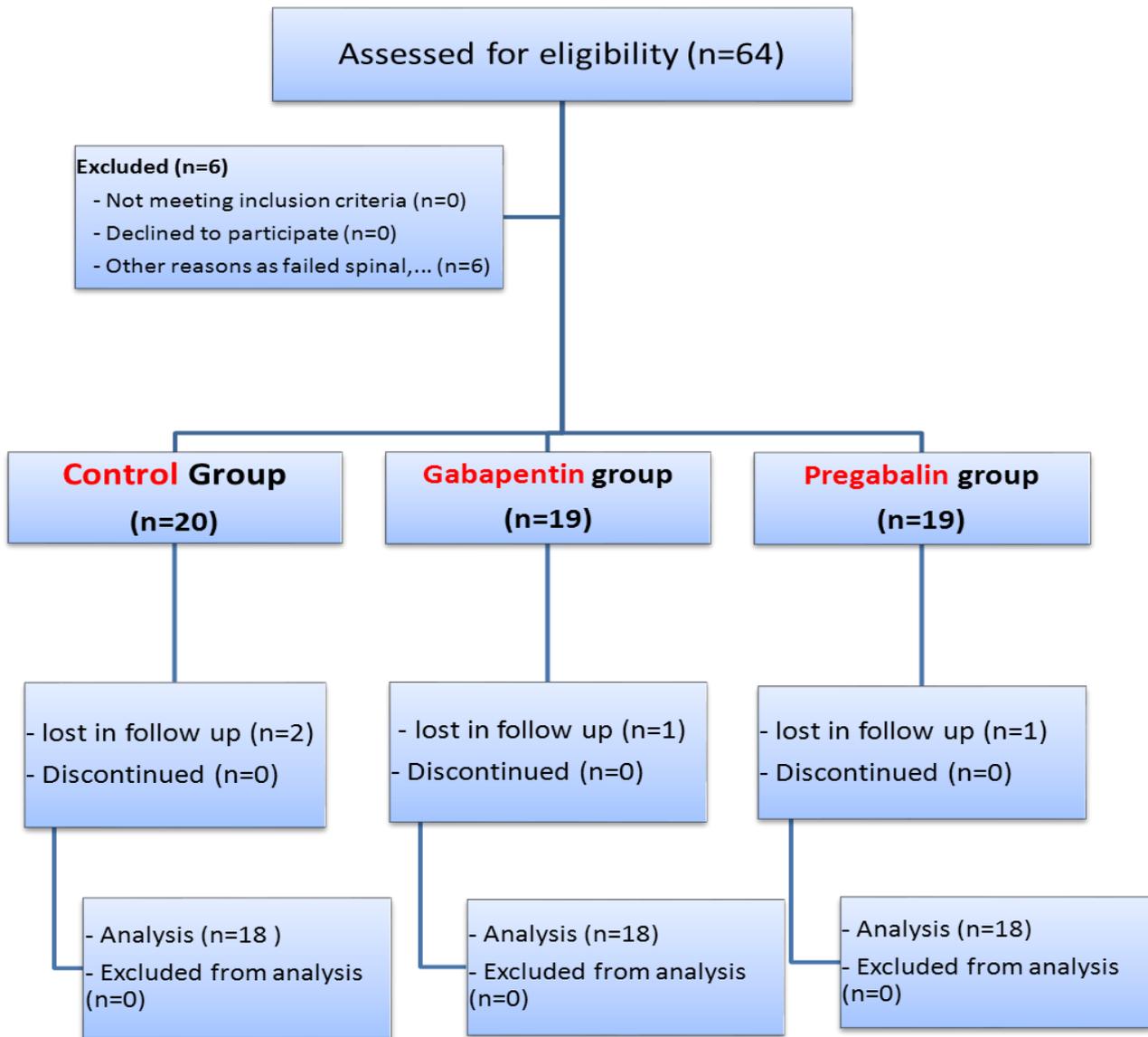


Figure (1): Flow chart of patients in the study

Table (1): Patients characteristics of the three studied groups.

Variable	Group C (N=18)	Group G (N=18)	Group P (N=18)	F	P
Age (years) Mean ± SD	27.67 ± 3.395	27.83 ± 3.666	27 ± 4.459	0.234	0.792
BMI (kg/m <sup>2</sup> ) Mean ± SD	29.56 ± 2.357	28.44 ± 2.307	29.11 ± 1.906	1.164	0.320

Data presented as mean ± SD P-value >0.05 was considered non-significant F: ANOVA test BMI: Body Mass Index (C): Control group (G): Gabapentin group (P): Pregabalin group

**Table (2):** VAS (Visual Analogue Scale) score of the three studied groups postoperatively.

<b>Group</b> <i>Time</i>	<b>Group C</b> (N=18)	<b>Group G</b> (N=18)	<b>Group P</b> (N=18)	<b>F</b>	<b>P</b>	<b>LSD</b>
<b>1hr</b> <i>Mean ± SD</i>	1.2(1,2)	1.5(1,2)	1(1,2)	0.464	0.137	0.211 0.194 0.264
<b>2hr</b> <i>Mean ± SD</i>	4(4,5)*^	2(2,3)^#	1(1,2)	<b>68.0</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.007</b>
<b>4hr</b> <i>Mean ± SD</i>	4(4,5)*^	3(2,3)^#	2(2,4)	<b>77.612</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.002</b>
<b>6hr</b> <i>Mean ± SD</i>	4.5(4,5)*^	4(3,4)^#	2(2,2)	<b>43.325</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>8hr</b> <i>Mean ± SD</i>	4.5 (4,5)*^	3(3,4)^#	2(1,2)	<b>48.453</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>10hr</b> <i>Mean ± SD</i>	4(4,5)*^	3(2,3.75)^#	2(1,2)	<b>33.933</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>12hr</b> <i>Mean ± SD</i>	4(4,5)*^	3(2,4)^#	1.5(1,2)	<b>38.360</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>16hr</b> <i>Mean ± SD</i>	4 (3,5)*^	3(2,4)	2.5(2,3)	<b>8.090</b>	<b>0.001</b>	<b>1* 0.006</b> <b>2^ &lt;0.001</b> <b>3# 0.300</b>
<b>20hr</b> <i>Mean ± SD</i>	4(3,4)*^	3(2.25,4)^#	2(1,2)	<b>14.919</b>	<b>&lt;0.001</b>	<b>1* 0.024</b> <b>2^ &lt;0.001</b> <b>3# 0.003</b>
<b>24hr</b> <i>Mean ± SD</i>	4(2,4)*^	2(1,2)	1(1,2)	<b>20.832</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.477</b>

Postoperative (started by 1hr after the end of surgery) Data presented as median (range)

P-value <0.05 was considered significant and <0.001 considered highly significant

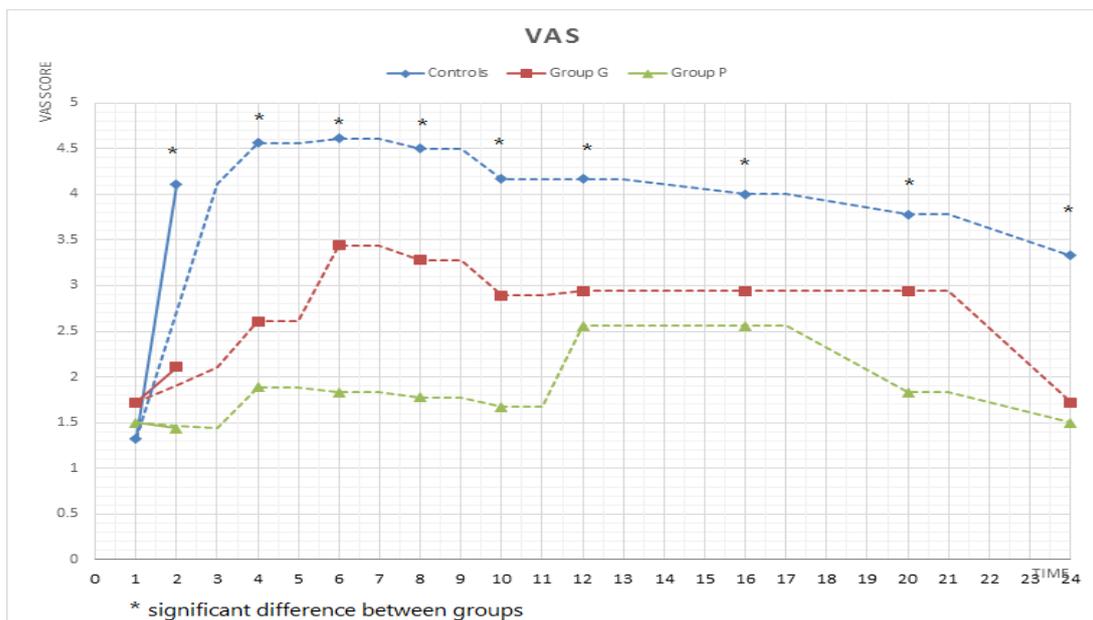
1: C & G. 2: C & P. 3: G & P

\* a significant difference between C and G group ^ a significant difference

between C and P group # a significant difference between P & G group

LSD: least significant difference test

(C): Control group, (G): Gabapentin group, (P): Pregabalin group.



**Figure (2):** VAS of the three studied groups postoperatively

**Table (3):** PONV impact scale of the three studied groups

<i>Group Time</i>	<i>Group C (N=18)</i>	<i>Group G (N=18)</i>	<i>Group P (N=18)</i>	<i>F</i>	<i>P</i>	<i>LSD</i>
<b>2hr</b> <i>Mean ± SD</i>	3.11 ± 1.45* <sup>^</sup>	1.83 ± 1.2 <sup>#</sup>	0.17 ± 0.383	<b>31.879</b>	<b>&lt;0.001</b>	<b>1* 0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>4hr</b> <i>Mean ± SD</i>	4 ± 1.33* <sup>^</sup>	1.89 ± 0.676 <sup>#</sup>	0.17 ± 0.514	<b>80.041</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>6hr</b> <i>Mean ± SD</i>	3.72 ± 1.526* <sup>^</sup>	1.39 ± 1.092 <sup>#</sup>	0.5 ± 0.618	<b>38.296</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.023</b>
<b>8hr</b> <i>Mean ± SD</i>	3.39 ± 1.092* <sup>^</sup>	1.78 ± 1.215 <sup>#</sup>	0.11 ± 0.471	<b>50.155</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>10hr</b> <i>Mean ± SD</i>	3.33 ± 1.188* <sup>^</sup>	1.56 ± 1.149 <sup>#</sup>	0	<b>54.986</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>12hr</b> <i>Mean ± SD</i>	3.83 ± 1.383* <sup>^</sup>	1.56 ± 1.381 <sup>#</sup>	0.5 ± 0.707	<b>36.276</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>
<b>16hr</b> <i>Mean ± SD</i>	3.72 ± 1.565* <sup>^</sup>	1.22 ± 1.166 <sup>#</sup>	0.17 ± 0.514	<b>44.219</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.009</b>
<b>20hr</b> <i>Mean ± SD</i>	3.56 ± 1.423* <sup>^</sup>	1.72 ± 1.32 <sup>#</sup>	0.28 ± 0.669	<b>34.567</b>	<b>&lt;0.001</b>	<b>1* &lt;0.001</b> <b>2^ &lt;0.001</b> <b>3# 0.001</b>
<b>24hr</b> <i>Mean ± SD</i>	1.72 ± 1.447 <sup>^</sup>	1.78 ± 1.166 <sup>#</sup>	0.17 ± 0.383	<b>12.542</b>	<b>&lt;0.001</b>	<b>1 0.880</b> <b>2^ &lt;0.001</b> <b>3# &lt;0.001</b>

PONV: postoperative nausea and vomiting

Data presented as mean ± SD

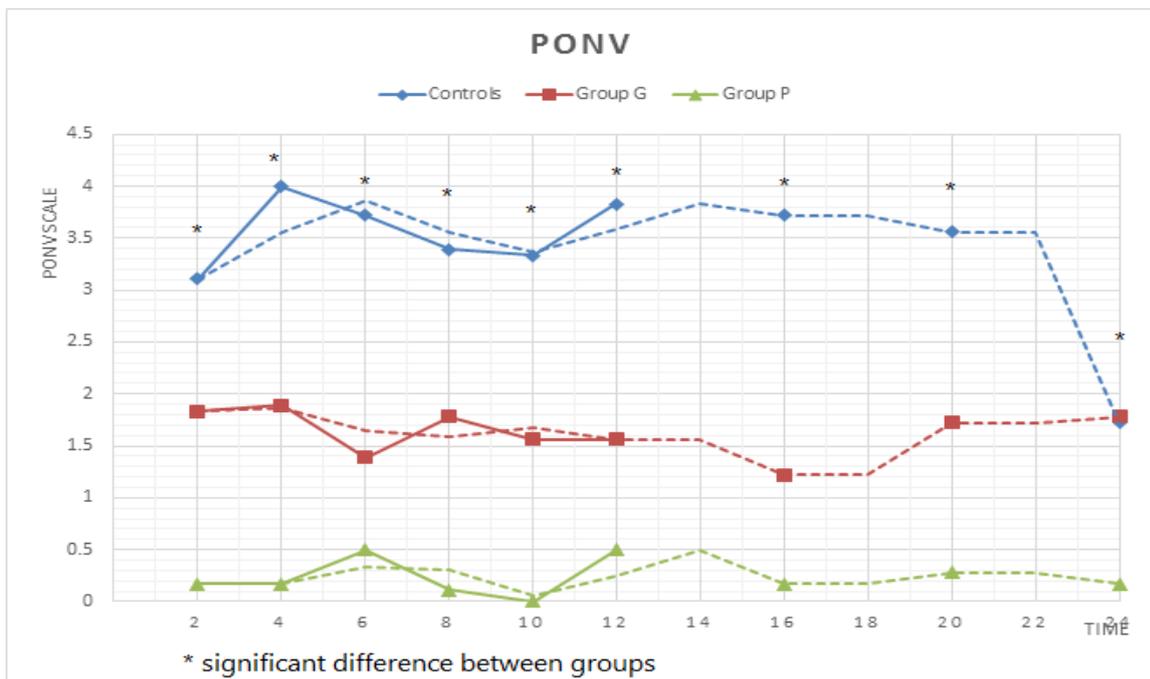
P-value < 0.001 was considered highly significant. 1: C & G. 2: C & P. 3: G & P

\* a significant difference between C and G group

<sup>^</sup> a significant difference between C and P group

<sup>#</sup> a significant difference between P & G group

(C): Control group, (G): Gabapentin group, (P): Pregabalin group



**Figure (3):** PONV impact scale of the three studied groups.

**Table (4):** Mean Postoperative opioid (Pethidine, mg) consumption in study groups

Group	Group C (N=18)	Group G (N=18)	Group P (N=18)	P-value
<b>Analgesic requirements</b>				
One dose	--	--	7 (38.9%)	<b>&lt;0.001</b>
Two doses	--	14 (77.8%)	11 (61.1%)	
Three doses	13 (72.2%)	4 (22.2%)	--	
Four doses	5 (27.8%)	--	--	
Total no. of pethidine doses	59	40	29	
Total doses of pethidine in mg	1350	650	350	<b>&lt;0.001</b>

Numerical data were presented as no. (%).

P-value <0.05 was considered significant

\* a significant difference between C and (P & G) groups

(C): control group

(G): Gabapentin group (P): Pregabalin group

**DISCUSSION**

Relief of postoperative pain is a subject, which has been receiving an increasing attention in the past few years. Pre-emptive analgesia aims to decrease acute pain after tissue injury and to inhibit the persistence of post-operative pain and the development of chronic pain<sup>(13)</sup>.

Gabapentin and pregabalin are structural analogues of gamma amino butyric acid that were introduced as antiepileptic drugs and have been extensively used to treat painful neuropathies. Recently, they have been studied as pre-emptive analgesics with a variety of surgical procedures to reduce postoperative pain and analgesic requirements<sup>(14)</sup>.

In agreement with the result of this study, **Bafna and colleagues**<sup>(15)</sup> had studied preemptive gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. In their study, patients received a single dose of identical placebo capsule (group A), gabapentin 600 mg (group B) or pregabalin 150 mg (group C). A significantly longer mean duration of effective analgesia in group C was observed compared to other groups (P < 0.001). Also, the current study match with another study conducted by **Bekawi et al.**<sup>(16)</sup> to evaluate pregabalin efficacy and tolerability for pain management in 90 patients undergoing elective laparoscopic cholecystectomy under general anesthesia. Pregabalin group (P), received 150 mg pregabalin capsules 2 hours preoperatively, 12 hours postoperatively, and twice daily for 2 days. Gabapentin group (G), received 1200 mg gabapentin capsules (400 mg x3) 2 hours preoperatively, 12 hours postoperatively, and 400 mg three times daily for 2 days. Control group (C), received placebo capsules. It was found that the 24-hour pethidine consumption was significantly lower (P < 0.001) in both pregabalin and gabapentin groups versus control. Both groups had significantly less (P < 0.001) patients with postoperative nausea, vomiting, sedation, and dizziness versus control. Overall, patient satisfaction with pain management was significantly higher (P < 0.001) in pregabalin group versus gabapentin or control groups. This is consistent with the results of the present study, where it was found that pregabalin administered preoperatively had considerable postoperative opioid-sparing effect, as the number of meperidine doses required in the first 24 hours postoperatively was

significantly reduced in the pregabalin groups when compared to the gabapentin group and the placebo group (P-value < 0.001).

In the present study, pregabalin administered preoperatively was found to decrease the intensity of post-operative pain as indicated by reduced VAS scores when compared to those with the gabapentin group and the control group. However, there was no difference between the three groups regarding the immediately postoperative VAS score, which can be easily explained by the residual effect of spinal anesthesia. Although, the VAS score had gradually decreased overtime in the three groups postoperative, to reach its minimal measured values at 24 hour postoperative. However, it remained significantly lower in both gabapentin and pregabalin groups compared to the placebo group, with its being slightly lower in the pregabalin group than in the gabapentin group. This finding included also the VAS score at time of regaining full muscle power (which indicates the end of any analgesic effect due to the regional anesthesia).

On other hand, the study conducted by **Short and his colleagues**<sup>(17)</sup>, could not reach the same conclusion as the previous studies and could not even replicate the positive results from a previous study from their own group evaluating the analgesic benefits of gabapentin 600 mg given orally preoperatively to women undergoing elective cesarean delivery. They did not observe an improvement in pain scores with either 300 or 600 mg gabapentin and concluded that a single preoperative dose of 300 mg or 600 mg gabapentin did not improve post-cesarean pain management or maternal satisfaction in the context of a multimodal analgesic regimen inclusive of intrathecal morphine. These differences in results can be attributed to their using intrathecal morphine, which prolongs the analgesic effect of spinal anesthesia in all groups. The regular use of both diclofenac and paracetamol with the on demand use of systemic morphine for post-operative analgesia, and the fact of their using lower doses of gabapentin (300 mg and 600 mg) than the dose used in the current study (900 mg). It was however reassuring that they did not observe any significant maternal sedation or neonatal side effects with these doses of gabapentin. Unexpectedly, this is in contrast to the results reported by **Moore and colleagues**<sup>(18)</sup> in a previous study conducted on 46 women

undergoing scheduled cesarean delivery under spinal anesthesia who were randomized to receive preoperative gabapentin 600 mg, or placebo. The results of their study suggested that even in the context of a multimodal regimen that included intrathecal fentanyl and morphine, oral acetaminophen and diclofenac, and systemic opioids for breakthrough pain, a single dose of gabapentin 600 mg given 1 hour before cesarean delivery significantly improved pain scores in the first 48 hours postpartum and increases patient satisfaction. They referred that the reason for their observed greater-than-expected improvement in pain scores to the possible synergistic effect of gabapentin with intrathecal morphine. The combination of morphine and gabapentin has been shown to enhance analgesia in humans. Since the proposed site of action of gabapentin and intrathecal opioids is at receptors in the dorsal horn of the spinal cord, their interaction at this site may be synergistic. The differences in the incidence of nausea, vomiting, pruritus, persistent pain, and persistent abnormal wound sensation at 3 months were not different between the groups. Gabapentin in that dosage increased maternal sedation; however, it didn't adversely affect the neonate. Severe sedation did not last more than 24 hours and did not seem to affect the outcome of the patients. No patients in the study had respiratory depression or oxygen desaturation.

## CONCLUSION

Under the present study design, preemptive administration of a single dose pregabalin in female patients undergoing elective cesarean section under spinal anesthesia was effective more than a single dose of gabapentin in decreasing the intensity of acute postoperative pain and decreased meperidine requirements during the first 24 hours postoperative without serious side effects. Further studies are still required to identify the most appropriate doses of preemptive gabapentin and pregabalin that will yield the best outcome regarding acute postoperative pain modification with the least adverse effects.

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