Original Article

Effect of Two Different Doses of Oral Pregabalin Premedication for Postoperative Pain Relief after Gynecological Surgeries: A Randomized Controlled Study

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ABSTRACT

Introduction: The introduction of minimally invasive surgical techniques is associated with earlier postoperative ambulation, but controlling the postoperative pain didn't achieve the level of full control. Pregabalin has been shown to have perioperative analgesic effects.

Aim of the work: Assessment and comparison between the effects of two different doses of oral pregabalin premedication in gynecological surgeries under spinal anesthesia regarding postoperative analgesia and side effects.

Patients and Methods: Ninety female patients scheduled for gynecological operations were randomized to receive the study drug one hour before the operation according to each group; one placebo capsule of vitamin C (group C), one capsule of pregabalin 150mg once (group P1) or one capsule of pregabalin 300mg once (group P2). The primary outcome was the analgesic effects of pregabalin using visual analogue scale (VAS).

Results: The VAS score was statistically significantly lower in group P1 and group P2 compared to group C at 4, 6 and 8 hours postoperative (p<0.001). The time to first analgesic recall was statistically significantly prolonged in both group P1 and group P2 as compared to group C (P<0.001), furthermore, it was statistically significantly prolonged in group P2 compared to group P1.

Conclusion: The current study reveals the analgesic efficacy of pregabalin when administered as a premedication in patients undergoing gynecological surgeries under spinal anesthesia with lower post-operative VAS scores, lower doses of rescue analgesics needed and Pregabalin 300mg had a better analgesic profile noticed by hastening the onset of sensory and motor block.

Key Words: Gynecological, Pregabalin, Spinal, Visual analogue scale.

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INTRODUCTION

Improperly treated acute post-operative pain is associated with post-operative complications and considered as a strong risk factor for the development of chronic pain[1]. Perioperative opioid consumption may produce undesirable side effects such as nausea, vomiting, constipation, urinary retention, increased length of hospital stay and opioid-induced respiratory depression (ORD) which is considered as a significant cause of brain damage and death in the postoperative period[2].

Opioid reduction strategies prove useful for reducing total opioid dose and include adjuvant non-opioid analgesics, local, regional or neuraxial anesthesia and if possible modification of surgical technique[3].

Pregabalin is a synthetic molecule and a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). It has analgesic, anxiolytic, anticonvulsant and sleep-modulating activities[4].

The current study was conducted to assess and compare the effects of two different doses of oral pregabalin premedication in gynecological surgeries under spinal anesthesia regarding postoperative analgesia (1ry outcome).

METHODS

Study design and population:

This prospective randomized double-blinded controlled clinical trial (both precipitants and clinical providers wasn't known type of tablets given) was conducted Anesthesiology Department from January 2021 to June 2022 after obtaining the patient's informed written consent

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and approval from our Institutional Review Board (6191-16-8-2020) and registration in Clinical Trials.gov (ID: NCT04708353) on 19/11/2020.

The included cases were 90 female patients who were scheduled for benign gynecological surgeries (abdominal hysterectomy, ovarian cystectomy or myomectomy) under spinal anesthesia with operative time not more than 3 hours. The included cases were in age between 21 and 60 years, with a BMI between 20 to 35kg/m^2 and of ASA class I or II.

The study excluded pregnant females, patients with known allergies to the used drugs, suspected coagulopathy or patients receiving anticoagulant therapy, patients with psychological or mental disorders, renal impairment or heart failure, patients on chronic alcohol, tranquilizer, opioid or sedative use, patients on anticonvulsant therapy, ACE inhibitors or any drug interacting with pregabalin and patients already on pregabalin or gabapentin therapy. The patient was withdrawn from the study if she had failed spinal anesthesia.

Using computer-generated randomization tables, the cases were randomly allocated into three equal groups (each of 30 patients); Group C or the control group (patients received one placebo capsule of vitamin C once, one hour before the operation), group P1 (patients received one capsule of pregabalin 150mg once, one hour before the operation) and group P2 (patients received one capsule of pregabalin 300mg, once, one hour before the operation)[5,6].

The preoperative evaluation included history taking, clinical examination and routine preoperative laboratory investigations. Patients were asked to fast for 6-8 hours before the operation.

All patients learned how to express their pain on the pain scale, a visual analogue scale (VAS), from 0 to 10, with 0 for no pain, and 10 for the maximum pain ever felt[7]. The study medication was given by mouth with a sip of water one hour before surgery.

On arrival to the operating room, standard monitoring was applied to the patients including five-lead electrocardiography (ECG), automated noninvasive blood pressure monitor (NIBP) and pulse oximetry, and the basal vital data [mean arterial blood pressure (MAP), heart rate (HR) and O_2 saturation (SPO_2) were recorded. The intravenous line (22G) was secured in a peripheral forearm vein, and patients were preloaded with lactated ringer solution (10ml/kg) over 15-20 minutes.

The patient was supported to be in the sitting position and the skin was sterilized using a povidone iodine solution. The L4/L5 intervertebral space was located using a hypodermic needle size 22G. The skin overlying the intervertebral space was anesthetized with 3mL of 2% lidocaine. A midline approach was performed for lumbar puncture using a Quincke 25G spinal needle and 3.5-4ml (17.5-20mg) of hyperbaric bupivacaine 0.5% was injected followed by putting the patient in the supine position.

Continuous monitoring and recording of patient hemodynamics including HR, MAP and SPO_2 were done. These parameters were recorded intraoperatively every 15 minutes to 90 minutes.

The level of sensory block was checked by alcohol swab at the mid-axillary line on both sides of the chest and it was performed every 1 minute until the maximum sensory blockade was achieved in the relevant body segment and subsequently every 15 minutes until recovery of sensation in the L2 segment. The time from the end of injection to T6 sensory block, peak sensory level achieved and time from the end of injection to the peak level were recorded. The degree of motor block was assessed via the modified Bromage scale[8]. Time from the end of injection to reach Bromage 1 (B1) was recorded.

1: Complete block (unable to move feet or knees).
2: Almost complete block (able to move feet only).
3: Partial block (just able to move knees).
4: Detectable weakness of hip flexion while supine (full flexion of knees).
5: No detectable weakness of hip flexion while supine.
6: Able to perform partial knee bend.

The surgeon started the operation when adequate sensory blockade at the T6 level and adequate motor blockade B1 were achieved.

If hypotension (MAP 20% lower than the basal) occurred, it was managed by fluid and/or a bolus dose of ephedrine 5 mg; if bradycardia (HR <60 beats/min) occurred, it was managed by atropine (0.01mg/kg I.V). The incidence of hypotension and bradycardia were recorded. Intraoperative nausea and vomiting were managed by 8mg ondansetron IV.

After the operation ended, the operative time was recorded, and the patients were transferred to the post-anesthesia care unit (PACU). The time of PACU admission was considered time 0 for postoperative data collection. All patients' data were recorded by another anesthesiologist, who was not aware of the drug given.

The patients were observed in PACU for one hour (for HR, MAP, level of sensory and motor block) before transfer to the ward. Both HR and MAP were recorded 30 minutes after admission to PACU. All patients received standard analgesia of 75mg diclofenac by intramuscular injection every 12h.

• Postoperative pain was assessed via VAS that was recorded at 2, 4, 6, 8, 12, 16 and 24 hours. If a patient reported a VAS of three or more, meperidine (pethidine) 50 mg intramuscular (as rescue analgesia) was commenced and repeated as necessary with a maximum daily dose of 400mg per day.

• The time to the first analgesic request (time from drug intake and first request of rescue analgesia).

• The total amount of rescue analgesia requirement during the 1st 24 hours was recorded.

• The level of sedation was assessed using the modified Ramsay Sedation Score[9] at the same intervals as the VAS assessment (2, 4, 6, 8, 12, 16 and 24 hours) postoperatively.

1= Awake and alert, minimal or no cognitive impairment.

2= Awake but tranquil, purposeful responses to verbal commands at conversation level.

3= Appears asleep, purposeful responses to verbal commands at conversation level.

4= Appears asleep, purposeful responses to verbal commands but at louder than usual conversational level or requiring light glabellar taps.

5= Asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap.

6= Asleep, sluggish purposeful responses only to painful stimuli.

7= Asleep, reflex withdrawal to painful stimuli only (no purposeful response).

8= Unresponsive to external stimuli, including pain.

• Effect of pregabalin on spinal anesthesia:

- Onset and duration of sensory block.
- Peak sensory level achieved and time to peak sensory level.
- Onset and duration of motor block.

• Incidence of pregabalin adverse effects (such as dizziness or blurring of vision) and opioid adverse effects (such as respiratory depression, nausea and vomiting) were also recorded.

Sample Size Calculation

Assuming that the mean±SD of VAS at 15 minutes among patients receiving pregabalin 150mg and those receiving pregabalin 300mg was (1.90±0.06 versus 1.96±0.1 respectively)[5] so the sample size is calculated by open EPI program to be 81 patients with a confidence level of 95% and power of test 80%. 10% will be added for dropout, so the total sample size will be 90 patients (30 patients in each group).

Statistical analysis

The data collected were coded, processed and analyzed with Statistical Package for Social Sciences (SPSS) version 26 for Windows® (IBM, SPSS Inc, Chicago, IL, USA). Qualitative data were shown as number (frequency) and percent. The Chi-Square test made the comparison between groups (Monte-Carlo test as a correction). The Kolmogorov-Smirnov test tested quantitative data for normality. Parametric data were expressed as mean±SD while non-parametric data were shown as median (range).

Normally distributed quantitative variables were analyzed using one-way ANOVA test to compare three groups, and the Kruskal Wallis test was used if the data were abnormally distributed. Post-hoc test was conducted by post-hoc Tukey or Bonferroni tests with ANOVA and Kruskal Wallis test respectively. For all tests, *P* values <0.05 are considered significant.

RESULTS

One hundred-nine females scheduled for benign gynecological surgeries under spinal anesthesia were aligned in this study. From them 19 patients were excluded (8 patients didn't meet inclusion criteria, 9 patients refused to participate and 2 patients were excluded due to operation cancellation; The remaining 90 patients were enrolled and randomized as shown in the flowchart (Figure 1).

There was no statistically significant difference between the three study groups regarding the mean age, BMI, ASA classification, indication for surgery and the operative time. Ovarian cystectomy was the most commonly performed surgery in the three study groups in 46.7%, 43.3% and 36.7% in group C, group P1 and group P2 respectively. Other indications included hysterectomy and myomectomy (Table 1).

The VAS score was statistically significantly lower in group P1 and group P2 as compared to group C at 4 hours, 6 hours and 8 hours postoperatively (*P*<0.001). However, there was no statistically significant difference between group P1 and group P2 along the duration of the follow up (Table 2).

The mean time to first rescue analgesia was 124.80±12.76 minutes, 480.53±14.43 minutes and 503.23±18.73 minutes in group C, group P1 and group P2 respectively. The time to first analgesic recall was statistically significantly prolonged in both group P1 and

group P2 as compared to group C (P<0.001). Meaning while the time to first analgesic recall was statistically significantly prolonged in group P2 compared to group P1 (Table 3).

The total dose of rescue analgesia (Pethidine) was statistically significantly lower in both groups P1 and P2 as compared to group C (P<0.001), with no significant difference between the different pregabalin groups (Table 3).

Ramsay sedation score was statistically significantly lower in the control group compared to the other two pregabalin groups at all follow-up times except at 24 hours, meaning while there was no significant difference between the P1 and P2 at all follow-up times except at 6 hours where P2 showed higher score than group P1 (Table 4).

Onset of sensory block, time to peak sensory block level and the onset of motor block were statistically significantly shorter in both group P1 and group P2 as compared to group C (P<0.001). Moreover, group P2 showed statistically significantly shorter times compared to group P1 (P<0.05) (Table 5).

The duration of sensory block and the duration of motor block were statistically significantly longer in both group P1 and group P2 as compared to group C (P<0.001), with no significant difference between the different pregabalin doses (Table 5).

There was no statistically significant difference between the three study groups regarding the basal, intraoperative and postoperative HR or MAP (Figure 2,3 respectively).

Regarding the postoperative complications (Table 6), no statistically significant difference was detected between the three study groups. Dizziness was reported in 3.3%, 20% and in group C, group P1 and group P2 respectively. The blurring of vision was reported in 6.7% and 13.3% in group P1 and group P2 respectively. Nausea and vomiting were reported in 16.7%, 16.7% and 13.3% in group C, group P1 and group P2 respectively. No cases showed respiratory depression within the three study groups.

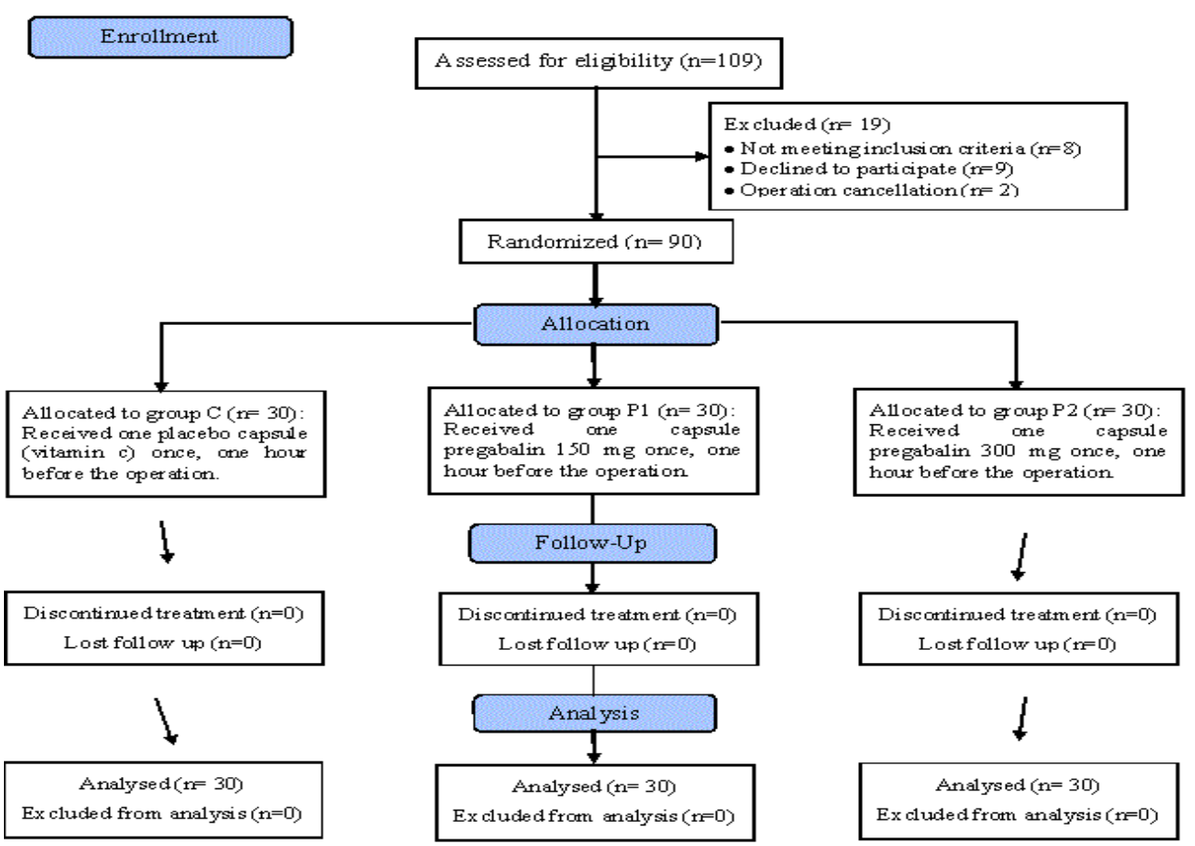

Figure 1: Consort flowchart of the cases in the study.

Table 1: Patients' characteristics and operative data:

Variables		Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
Age (years) mean±SD		43.37±10.16	41.60±7.13	42.77±6.20	0.143
BMI (Kg/m^2) mean±SD		28.17±3.75	29.10±3.45	30.12±2.76	0.084
ASA N (%)	ASA I ASA II	19(63.3%) 11(36.7%)	17(56.7%) 13(43.3%)	20(66.7%) 10(33.3%)	0.718
Indication of surgery N (%)	Hysterectomy	7(23.3%)	9(30%)	9(30%)	0.923
	Ovarian cystectomy	14(46.7%)	13(43.3%)	11(36.7%)	
	Myomectomy	9(30%)	8(26.7%)	10(33.3%)	
Operative time (min) mean±SD		108.33±9.68	111±10.46	106.83±9.05	0.250

Quantitative data were expressed as mean±SD/ Test of significance (One-way ANOVA test). Qualitative data were expressed as number (percentage)/ Test of significance chi-square test. Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg.

Table 2: Visual analogue scale in the study groups:

VAS score	Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
2 hours	1(0-1)^A	0(0-1)^A	0(0-1)^A	0.733
4 hours	3(2-3)^A	1(1-2)^B	1(1-2)^B	<0.001*
6 hours	3(3-4)^A	2(1-2)^B	1(1-2)^B	<0.001*
8 hours	4(3-5)^A	3(2-3)^B	2(2-3)^B	<0.001*
12 hours	4(3-5)^A	4(2-4)^A	3(2-4)^A	0.106
16 hours	3(2-5)^A	4(2-4)^A	3(3-4)^A	0.373
24 hours	4(3-5)^A	3(3-4)^A	3(2-4)^A	0.074

Quantitative data are expressed as median (Range)/ Test of significance (Kruskal Wallis test). Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg. *P* value <0.001 mean there was statistically significant difference. A, B: Different results indicate significant difference between the adjacent groups.

Table 3: Time to first rescue analgesia and total rescue analgesic dose:

Analgesic data	Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
Time to first rescue analgesic recall (min) mean±SD	124.80±12.76 ^{A}	14.43±14.43 B	503.23±18.73 C	<0.001*
Total dose of rescue analgesia (Pethidine mg) median (Range)	150(150–250) ^{A}	50(50–100) ^{B}	50(50–100) ^{B}	<0.001*

Data are expressed as mean±SD/ Test of significance (One-way ANOVA test). Data are expressed as median (Range)/ Test of significance (Kruskal Wallis test). Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg. *P* value <0.001 mean there was statistically significant difference. A, B, C: Different litters indicate significant difference between the adjacent groups.

Table 4: Modified Ramsay sedation scale in the study groups:

Ramsay sedation scale	Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
2 hours	1^A	3(2-3)^B	3(1-3)^B	<0.001*
4 hours	1^A	3(2-3)^B	3(2-3)^B	<0.001*
6 hours	1^A	2(1-3)^B	3(2-3)^C	<0.001*
8 hours	1^A	1(1-2)^B	1(1-2)^B	<0.001*
12 hours	1^A	1(1-2)^B	1(1-2)^B	0.001*
16 hours	1^A	1(1-2)^B	1(1-2)^B	0.013*
24 hours	1^A	1^A	1^A	1

Quantitative data are expressed as median (Range)/ Test of significance (Kruskal Wallis test). Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg. *P* value <0.001 mean there was statistically significant difference. A, B, C: Different results indicate significant difference between the adjacent groups.

Table 5: Sensory and motor block data in the study groups:

Sensory and motor block data		Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
Onset of sensory block (min) mean±SD		6.53±1.14[A]	4.43±0.50[B]	3.57±0.68[C]	<0.001*
Peak sensory level N (%)	T6	8(26.7%)	9(30%)	9(30%)	0.954
	T5	15(50%)	12(40%)	13(43.3%)	
	T4	7(23.3%)	9(30%)	8(26.7%)	
Time to peak sensory level (min) mean±SD		13.47±1.11[A]	10.60±0.89[B]	9.93±1.01[C]	<0.001*
Duration of sensory block (min) mean±SD		132.67±13.26[A]	223.87±10.78[B]	225.20±10.52[B]	<0.001*
Onset of motor block (B1) (min) mean±SD		9.83±1.23[A]	8.77±1.04[B]	7.27±0.83[C]	<0.001*
Duration of motor block (min) mean±SD		107.10±13.20[A]	198.83±10.96[B]	199±10.70[B]	<0.001*

Data are expressed as mean±SD/ Test of significance (One-way ANOVA test). Data are expressed as number (percentage)/ Test of significance chi-square test. Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg. *P* value <2 0.001 mean there was statistically significant difference. A, B, C: Different litters indicate significant difference between the adjacent groups.

Table 6: Side effects in the study groups:

Side effects	Group C (*n*= 30)	Group P1 (*n*= 30)	Group P2 (*n*= 30)	*P*
Dizziness N (%)	1(3.3%)	6(20%)	7(23.3%)	0.073
Blurring of vision N (%)	0(0%)	2(6.7%)	4(13.3%)	0.117
Nausea and vomiting N (%)	5(16.7%)	5(16.7%)	4(13.3%)	0.919
Respiratory depression N (%)	0(0%)	0(0%)	0(0%)	____

Qualitative data are expressed as number (percentage)/ Test of significance Monte-Carlo test. Group C: Received one placebo capsule (vitamin c). Group P1: Received one capsule of pregabalin 150mg. Group P2: Received one capsule of pregabalin 300mg.

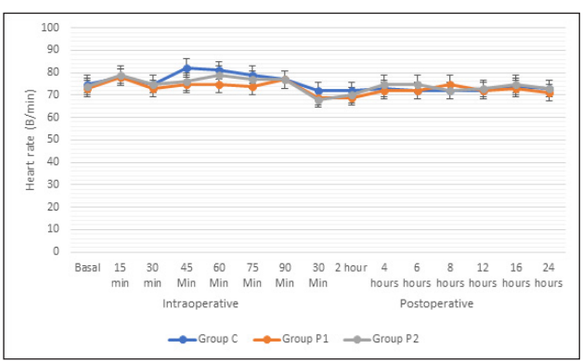

Figure 2: Heart rate in the study groups.

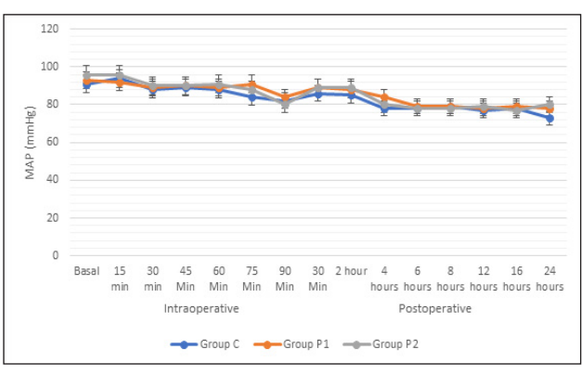

Figure 3: Mean arterial pressure in the study groups.

DISCUSSION

Adjuvants added to spinal anesthesia have the advantages of prolonging its action, delaying the onset of postoperative pain and subsequently reducing postoperative analgesic requirements[10].

A previous meta-analysis has stated that pregabalin reduces pain scores in the postoperative period with opioid-sparing effects at all doses and administration regimens[11].

For this, the current study was conducted to assess and compare the effects of two different doses of oral pregabalin premedication in gynecological surgeries regarding postoperative analgesia (1ry outcome) and the effect of pregabalin on spinal anesthesia.

In the current study, the VAS score was statistically significantly lower in group P1 and group P2 as compared to group C at 4, 6 and 8 hours postoperatively. However, there was no statistically significant difference between group P1 and group P2 along the duration of follow-up.

Our results came in accordance with Singh and his colleagues[12] who compared the efficacy of 150mg and 300mg of pregabalin for postoperative analgesia in laparoscopic cholecystectomy. The overall mean postoperative VAS score values in the two pregabalin-

receiving groups were significantly lower as compared to the control group. Amongst the two pregabalin-receiving groups, mean VAS values were high in the group that received 150mg pregabalin as compared to the group that received 300mg, though their difference was not statistically significant and this agree also with El-Hussiny *et al.,*[13] and with the same line with an earlier study by Jokela *et al.,*[14].

The current results agreed with Rajappa and associates[15] who conducted a randomized controlled trial on 135 patients who received spinal anesthesia for vaginal hysterectomy. The patients were divided into three groups: (group 0) received a placebo, (group 1) received 75mg of pregabalin and (group 2) received 150mg of pregabalin. The results showed that the pain score was lower for groups that received pregabalin as compared to the control group at all times. However, when comparing pregabalin groups, it was significantly higher in group 1 at all times except at 24 hours[15]. This was disagreed with our result may be due to the difference in doses used.

Ghadami *et al.,* conducted a randomized double-blind clinical trial studying the effect of oral pregabalin on reducing acute pain after abdominal hysterectomy. The pregabalin group received 300mg oral pregabalin, and the control group received a placebo. They observed that the VAS at 2, 4, 6, and 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. They explained the absence of difference in later times; as the half-life of pregabalin is 4.5–7 hours (mean 6.3 hours). The drug might have been eliminated leading to almost the same amount of pain in all the groups after 12 h in all groups[16].

In the current study, the time to first rescue analgesia was statistically significantly longer in both P1 and P2 groups compared to group C, with significant prolongation in group P2 compared to group P1. In the same context, the total dose of rescue analgesia (Pethidine) was statistically significantly lower in both P1 and P2 groups compared to group C, with no significant difference between the different pregabalin doses.

This agreed with Rajappa *et al.,* who showed that the mean times for the first rescue analgesia were 4.45 hours for the control group, 10.86 hours for group 1, and a maximum of 16.8 hours for group 2. The inter-group comparison revealed a significant difference in the first rescue analgesic time for each comparison[15]. Rescue analgesic consumption decreased significantly in pregabalin groups in this study.

This was in accordance with Ahmed et al. who showed that the time of the first analgesic requirement was significantly delayed in the pregabalin group compared to the control group[17].

The current results came in accordance with Hadavi *et al.,*[18]; who reported that morphine consumption at 1st 24h post-surgery was significantly lower in the pregabalin group than the control group. This is due to the lower pain score of the pregabalin group which was accompanied by lower opioid consumption.

On the contrary, our results disagreed with Sisa *et al.,*[19]; who evaluated the effects of preoperative pregabalin and multimodal anesthesia on postoperative opioid requirements on patients undergoing robot-assisted laparoscopic prostatectomy. There was no significant difference regarding intra-operative fentanyl consumption or opioid requirements in the first postoperative day between pregabalin and control groups. Different study designs may be a suitable explanation for this variation from our findings.

In the current study, there was a statistically significant difference between the three study groups regarding the modified Ramsay sedation scale along the duration of follow-up except at 24 hours where the groups P1 and P2 had higher Ramsay sedation scale compared to group C.

This came in agreement with Rajappa *et al.,* who compared the preoperative Ramsay sedation score (RSS) one hour after receiving premedication, they found that a majority of patients in the two groups who received pregabalin had a RSS score of ≥3 compared to the group who didn't receive[15].

Our results showed that onset of sensory block, time to peak sensory level and onset of motor block were statistically significantly shorter in both group P1 and group P2 as compared to group C. Moreover, there were statistically significantly shorter in group P2 as compared to group P1. Also, the the duration of motor block and duration of sensory block were statistically significantly longer in both group P1 and group P2 as compared to group C, with no significant difference between the different pregabalin doses.

The current result agrees with Ezema et al who found that the duration of sensory and motor blockades was significantly more prolonged in the group received 150mg pregabalin compared to the group received a placebo, both one hour preoperative[20].

The current results are supported also by the results of Omara and his colleagues who stated that oral pregabalin significantly shortened the time for the onset of sensory and motor block and significantly prolonged the time for two-segment regression of sensory block; the time required for regression of spinal block to L2 and the duration of motor block[21].

Moreover, Park *et al.,* evaluated the effect of oral pregabalin on the intrathecal block and they stated that

preoperative administration of 150mg oral pregabalin, 2 hrs before the operation improves the duration of sensory and motor block[22].

Pregabalin is an attractive adjuvant for perioperative analgesia in this regard as it is generally well-tolerated, can be taken on an empty stomach, does not lead to gastrointestinal bleeding, and with minor side effects[23].

Regarding the postoperative complications in our study, no statistically significant difference was detected between the three study groups.

According to the results reported by Park and his colleagues, the groups did not differ in terms of the occurrence of dizziness, pruritus, sedation, and dry mouth[22].

Dizziness has been considered the most common adverse effect after a single dose[24]. According to the study of Rajappa *et al.,* dizziness was found to be significantly higher in the study groups that received pregabalin, more so in higher doses[15].

Agarwal *et al.,* also reported significant nausea and vomiting in the pregabalin group, but none of the study groups in our study had such significance[25].

However, well-established adverse effects of pregabalin are dizziness, headache, and sedation, so pregabalin should be used with caution in an ambulatory setting[26].

Limitations of our study include a small sample size of only 30 patients in each group. Pain was evaluated during rest only and pain on mobilization and with deep breathing was not assessed. Further studies should be done to find the optimal dose of pregabalin for other various surgeries done under the neuraxial block.

CONCLUSION

The present study reveals the analgesic and sedative efficacy of pregabalin when given as a premedication in patients undergoing gynecological surgeries under spinal anesthesia. This was shown through the lower post-operative VAS scores, the longer time to first rescue analgesia and the decreased dose of rescue analgesics needed. Pregabalin 300mg had a better analgesic profile noticed by hastening the onset of sensory and motor block and prolongation of durations of analgesia.

LIST OF ABBREVIATIONS

VAS: Visual analogue scale.
GABA: γ-aminobutyric acid receptor
ERAS: Enhanced Recovery After Surgery
ORD: Opioid-induced respiratory depression
NMDA: N-methyl-D-aspartate
ASA: American Society of Anesthesia
BMI: Body mass index.
ACE: Angiotensin-converting enzyme
NIBP: Non-invasive blood pressure
ECG: Electrocardiograph.
MAP: Mean arterial pressure.
HR: Heart rate.
IV: Intravenous.
PACU: Post-anesthesia care unit
RSS: Ramsay sedation score.

DECLARATIONS

Ethics approval and consent to participate:

This prospective randomized controlled clinical study was carried out on female patients scheduled for gynecological surgeries at Zagazig University hospitals. The ethical approval from the institutional review board (The research ethical committee of Faculty of Medicine, Zagazig University) with the reference number (ZU-IRB#:6191-16-8-2020). This study was registered under clinicaltrials.gov (NCT04708353) the registration date 19/11/2020. Written informed consent was obtained from all participants after they understood the concept of this research. The study was carried out in accordance with the guidelines and regulations of the Helsinki Declarations.

AVAILABILITY OF DATA AND MATERIALS

The data used and analyzed during our study are available from the corresponding author on reasonable request.

AUTHORS' CONTRIBUTIONS

All authors reviewed the final manuscript and approved it. Asmaa M. Galal Eldin registered, collected, and analyzed the data, helped within the design of the study, and wrote the main manuscript text. Rehab A. Wahdan and ahmed awdallah prepared the tables and figures, writing review and editing, analyzed the data, and helped within the study design.

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CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Catro-Alves LJ, De Azevedo VL, De Freitas Braga TF, Goncalves AC, De Oliveira GS Jr. (2011). The effect of neuraxial versus general anesthesia techniques on postoperative quality of recovery and analgesia after abdominal hysterectomy: a prospective, randomized, controlled trial. Anesth Analg 113(6):1480-6. doi: 10.1213/ANE.0b013e3182334d8b.

2. Koepke EJ, Manning EL, Miller TE, Ganesh A, Williams DGA, Manning MW. (2013). The rising tide of opioid use and abuse: the role of the anesthesiologist. Perioper Med (Lond) 7:16. doi: 10.1186/s13741-018-0097-4.

3. Izrailtyan I, Qiu J, Overdyk FJ, Erslon M, Gan TJ. (2018). Risk factors for cardiopulmonary and respiratory arrest in medical and surgical hospital patients on opioid analgesics and sedatives. PLoS One 13(3): e0194553. doi: 10.1371/journal.pone.0194553.

4. Gupta P, Saxena A, Chaudhary L. (2017). Effect of Pregabalin Premedication on the Requirement of Anesthetic and Analgesic Drugs in Laparoscopic Cholecystectomy: Randomized Comparison of Two Doses. Anesth Essays Res. 11(2):330-333. doi: 10.4103/0259-1162.186862.

5. Balaban F, Yağar S, Özgök A, Koç M, Güllapoğlu H. (2012). A randomized, placebo-controlled study of pregabalin for postoperative pain intensity after laparoscopic cholecystectomy. J Clin Anesth 24(3):175-8. doi: 10.1016/j.jclinane.2011.06.027.

6. El Kenany S, El Tahan MR. (2016). Effect of preoperative pregabalin on post-caesarean delivery analgesia: a dose-response study. Int J Obstet Anesth 26:24-31. doi: 10.1016/j.ijoa.2015.11.001.

7. Katz J, Melzack R. (1999). Measurement of pain. Surg Clin North Am. 1999; 79(2):231-52. doi: 10.1016/s0039-6109(05)70381-9. PMID: 10352653.

8. Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. (1993). Epidural anesthesia for labor in an ambulatory patient. Anesth Analg 77(5):919-24. doi: 10.1213/00000539-199311000-00008.

9. Sheahan CG, Mathews DM. (2014). Monitoring and delivery of sedation. Br J Anaesth 113 Suppl 2:ii37-47. doi: 10.1093/bja/aeu378.

10. Panse, Neha & Adate, Kavita & Panchal, Sachin (2021). Comparative Evaluation of Two Different Doses of Pre-Emptive Oral Pregabalin on Duration of Spinal Anesthesia and Postoperative Pain. Arch Anesth & Crit Care 7(2):75-81. doi: 10.18502/aacc.v7i2.6300.

11. Mishriky BM, Waldron NH, Habib AS. (2015). Impact of pregabalin on acute and persistent postoperative pain: a systematic review and meta-analysis. Br J Anaesth 114(1):10-31. doi: 10.1093/bja/aeu293.

12. Singh T, Kathuria S, Jain R, Sood D, Gupta S. (2020). Premedication with pregabalin 150mg versus 300mg for postoperative pain relief after laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol 36(4):518-523. doi: 10.4103/joacp.JOACP_440_19. PMID: 33840934; PMCID: PMC8022042.

13. El-Hussiny H, Fahmy H, Eldemrdash AM. (2018). Preoperative sedation, hemodynamic stability during general anesthesia and improving postoperative pain: pregabalin is the answer. Open Journal of Anesthesiology 8(01):14-26. https://doi.org/10.4236/ojanes.2017.81002.

14. Jokela R, Ahonen J, Tallgren M, Haanpää M, Korttila K. (2008). Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynaecological laparoscopic surgery. Br J Anaesth 100(6):834-40. doi: 10.1093/bja/aen098.

15. Rajappa GC, Vig S, Bevanaguddaiah Y, Anadaswamy TC. (2016). Efficacy of Pregabalin as Premedication for Post-Operative Analgesia in Vaginal Hysterectomy. Anesth Pain Med 6(3): e34591. doi: 10.5812/aapm.34591. PMID: 27642577; PMCID: PMC5018136.

16. Ghadami N, Sarshivi F, Barzanji A. (2021). Nouri B, Mohammadi Z. Comparison of the effect of oral pregabalin with intravenous ketamine on reducing acute pain after abdominal hysterectomy: A randomized double-blind clinical trial. Caspian J Intern Med 12(2):217-222. doi: 10.22088/cjim.12.2.217. PMID: 34012541.

17. Ahmed MGE, Amr E, Hanaa A, Ahmed FK. (2023). The Effect of Pregabalin on Postoperative Pain in Patients Undergoing Abdominal Surgery under General Anesthesia. The Medical Journal of Cairo University 91(06):567-75. http://www.medicaljournalofcairouniversity.net/.

18. Hadavi SMR, Eghbal MH, Kaboodkhani R, Alizadeh N, Sahmeddini MA. (2022). Comparison of

pregabalin with magnesium sulfate in the prevention of remifentanil-induced hyperalgesia in patients undergoing rhinoplasty: A randomized clinical trial. Laryngoscope Investigative Otolaryngology 7(5):1360-6. DOI: 10.1002/lio2.905.

19. Sisa K, Huoponen S, Ettala O, Antila H, Saari TI, Uusalo P. (2021). Effects of pre-emptive pregabalin and multimodal anesthesia on postoperative opioid requirements in patients undergoing robot-assisted laparoscopic prostatectomy. BMC Urol. 21(1):14. doi: 10.1186/s12894-021-00785-9.

20. Ezema E, Ezema O, Nebuwa E, Oranusi I,Geofrey O, Okoro C, *et al.* (2020). Effects of preoperative pregabalin on outcome of spinal anaesthesia for patients undergoing open myomectomy. European Journal of Biomedical AND Pharmaceutical sciences 7(11): 202-8. http://www.ejbps.com/.

21. Omara AF, Ahmed SA, Abusabaa MM. (2019). The Effect of The Use of Pre-Emptive Oral Pregabalin On The Postoperative Spinal Analgesia In Patients Presented For Orthopedic Surgeries: Randomized Controlled Trial. J Pain Res 12:2807-2814. doi: 10.2147/JPR.S216184.

22. Park M, Lee H, Jeon Y. (2016). Preoperative pregabalin prolongs duration of spinal anesthesia and reduces early postoperative pain: A double-blind, randomized clinical CONSORT study. Medicine (Baltimore) 95(36):e4828. doi: 10.1097/MD.0000000000004828. PMID: 27603398; PMCID: PMC5023921.

23. Hindmarch I, Trick L, Ridout F. (2005). A double-blind, placebo- and positive-internal-controlled (alprazolam) investigation of the cognitive and psychomotor profile of pregabalin in healthy volunteers. Psychopharmacology (Berl) 183(2):133-43. doi: 10.1007/s00213-005-0172-7.

24. Rose MA, Kam PC. (2002). Gabapentin: pharmacology and its use in pain management. Anaesthesia 57(5):451-62. doi: 10.1046/j.0003-2409.2001.02399.x.

25. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. (2008). Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. Br J Anaesth 101(5):700-4. doi: 10.1093/bja/aen244.

26. Schug SA, Goddard C. (2014). Recent advances in the pharmacological management of acute and chronic pain. Ann Palliat Med 3(4):263-75. doi: 10.3978/j.issn.2224-5820.2014.10.02.