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Comparison between Oral Gabapentin and Pregabalinfor PostoperativePain Relief In Elective Cesarean Section Patients Under Spinal Anesthesia at Zagazig University Hospital

[1]Neveen Mahmoud Alaasar, [2]Dalal El-sayed Mohammed soud, [3]Asmaa Mohammed Galal El-Deen, [*4]Ahmad Ibraheem Ahmad AbdElfattah

ABSTRACT:

Background*: Pain relief of good quality after cesarean section (CS) results in early mobilization and good early mother–child interaction. The aim was to assess gabapentin and pregabalin as oral premedication in patients for elective cesarean section under spinal anesthesia regarding postoperative pain relief.* ***Methods****: This study included 54 consenting women had old ASA II, with uncomplicated pregnancies scheduled to undergo elective CS delivery under spinal anesthesia were. This study classified into 3 groups: pregabalingroup (P), gabapentin group (G), and control group (C). The study medication given orally one hour before the anticipated time of the surgical incision, and data measured include, visual analogue scale(VAS), the total doses of analgesia.* ***Results:*** *The VAS was 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 group G&C (P value <0.001) and wefound that there was statistically significant increase in the sedation scores of the patients in the P group as compared to G&C group.* ***Conclusion:*** *Pregabalinhad more effective than gabapentin300 mg in reducing post CS pain, opioid consumption.*

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

I. INTRODUCTION:

Postoperative pain, nausea and vomiting continue to be the most common and unpleasant complications after surgery especially obstetric surgeries[1]. The traditional pain treatment with opioids alone is not adequate any

[1] *Professor of Anesthesia and Surgical Intensive care, Faculty of Medicine – Zagazig University.*
[2] *Professor of Anesthesia and Surgical Intensive care, Faculty of Medicine – Zagazig University.*
[3] *Lecturer of Anesthesia and Surgical Intensive care, Faculty of Medicine – ZagazigUniversity.*
[4] *MBBCH Faculty of Medicine-al azhar University.*

more. To optimize pain treatment and postoperative outcome, new analgesics and new combination of already existing analgesics are searched for[2].

Pain relief of good quality after cesarean section (CS) results in early mobilization and good early mother–child interaction[3]. 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[4].

Opioid reduction strategies prove useful for decreasing total opioid dose and, in turn, their associated adverse effects. Such strategies may include adjuvant non opioid analgesics such as α-2 agonists, gabapentinoids, and N-methyl-D-aspartate receptor agonists as well as local, regional, or neuroaxial anesthesia and modification of surgical technique where possible for operative patients[5].

Gabapentinoids inhibit Ca2+ currents via high-voltage-activated channels containing the (α2δ-1) alpha 2 delta one subunit, reducing neurotransmitter release and attenuating the postsynaptic excitability. They are antiepileptic drugs successfully used also for the chronic pain treatment. A large number of clinical trials indicate that gabapentinoids could be effective as postoperative analgesics [6].

Pregabalin is a new synthetic molecule and a structural derivative of the inhibitory neurotransmitter gamma-amino butyric acid. It is an (α2δ-1) ligand that has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. Pregabalin binds potently to the α_2–δ subunit of calcium channels, resulting in a reduction in the release of several neurotransmitters including glutamate, noradrenaline, serotonin, dopamine, and substance P [7].

Recent meta-analysis demonstrated that pregabalin reduce the postoperative 24 hours cumulative opioid consumption and opioid-related adverse effects namely, vomiting and visual disturbances after surgery[8].

The efficacy and safety of preoperative oral Gabapentin on pain and opioids consumption were studied in patients undergoing a variety of surgical procedures as total abdominal hysterectomy , vaginal hysterectomy , thoracotomy , and spine surgeries but conclusions about optimal dose and duration of treatment cannot be made because of heterogeneity of the trials[9]. Gabapentin seems to prevent acute nociceptive and inflammatory pain and might reduce postoperative pain[10].

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.

II. PATIENTS AND METHODS:

I. Technical Design:

This study was carried out in obstetric operating rooms of Zagazig University surgical hospitals.

a. Sample size

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

***Inclusion criteria:**

1. Age: 21-40 years old.
2. Gender: females
3. Physical status: ASA II.
4. BMI < 35&>20 kg/m2.
5. Written informed consent from the patient.
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. Psycological 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
- **Group P** (n= 18): pregabalin group will receive three capsules of pregabalin 100 mg once one hour before the surgical incision**.**

❖ **Preoperative**

- Recording baseline measurement of patient hemodynamic state: mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR) and peripheral oxygen saturation (SPO2).
- 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 (10ml/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 identified was anesthetized with 3 mL of 2% lidocaine. Lumbar puncture was performed through a midline approach using a 25G spinal needle and 2.5-3ml of hyperbaric bupivacaine 0.5% with 25 (µg) fentanyl was administered intrathecally; 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) achieved surgeon was allowed to start.
- Continuous monitoring of patient hemodynamics, if hypotension(mean arterial blood pressure 20% lower than the basal) occured, it was treated by fluid and ephedrine (5mg I.V), bradycardia (HR<60 beats/min) was treated by atropine (0.5mg I.V)
- At the end of surgery all patients were transferred to post anesthesia care unit (PACU) .

❖ **Postoperative**

All patients data was 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 till 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), which was assessed by a visual analoge scale (VAS)[9] 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 75mg diclofinac Na was given IM/12h started postoperative.
- If VAS score ≥ 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 24hrs postoperativly.

Modified Ramsay sedation score

1Patient is anxious and agitated or restless, or both.

2Patient is cooperative, oriented and tranquil.

3Patient responds to commands only.

4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.

5Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.

6 Patient exhibits no response.

- Neonatal APGAR score[12] at 1 and 5 min: will be 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 and remains low. Scores of 7 and above are generally normal, 4 to 6, 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 ± 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 ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference.

III. RESULTS:

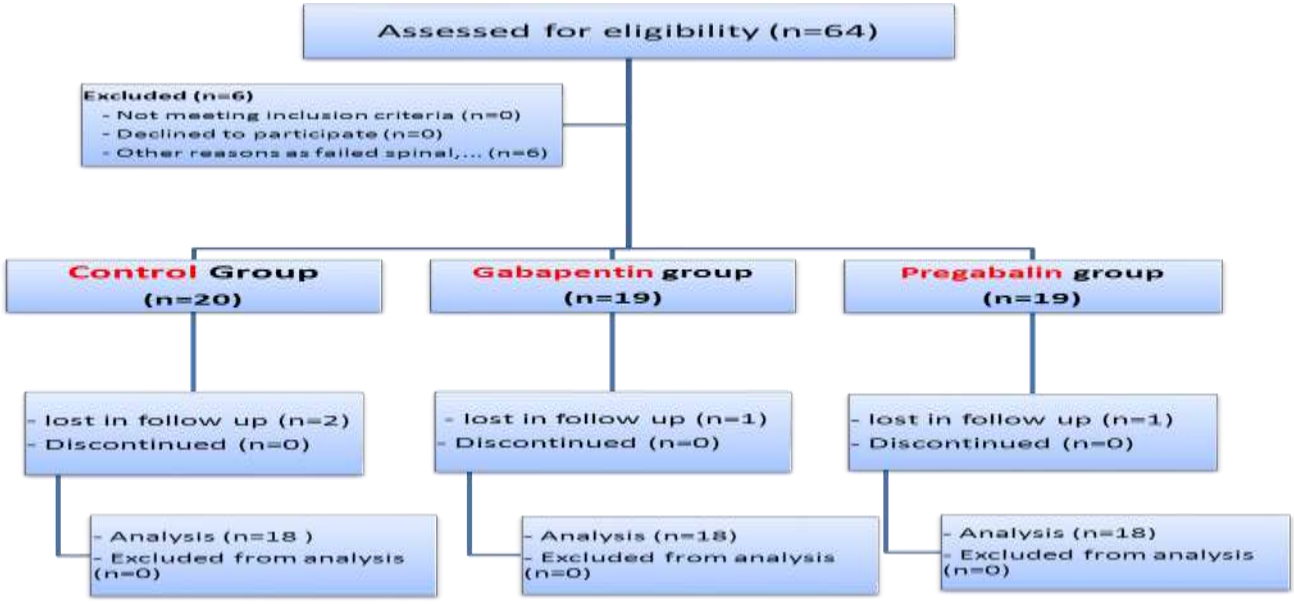

Figure (6): Flow chart of patients in the study

Among 54 female patients aged from 21 to 40 years old, with ASA physical status II, 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 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,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. 6).

Table (2): Patients characteristics of the three studied groups.

Group / ***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^2)* *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*

This table shows:

There is no significant difference between the three studied groups regarding age and BMI

Table (3): MAP (Mean Arterial blood Pressure) changes between the three studied groups basal & postoperatively.

Group / ***Time***	***Group C*** *(N=18)*	***Group G*** *(N=18)*	***Group P*** *(N=18)*	***F***	***P***	**LSD**
Baseline *Mean ± SD*	85.17 ± 4.79	84.94 ± 6.36	84.5 ± 2.43	1.432	0.979	1 0.456 2 0.521 3 0.732
1hr *Mean ± SD*	75.44 ± 9.26	73.61 ± 5.99	74.94 ± 4.32	0.346	0.709	1 0.425 2 0.827 3 0.561
2hr *Mean ± SD*	90.72 ± 5.62*	73.61 ± 3.22	85.83 ± 3.35	**9.041**	**0.001**	**1* 0.001** 2 0.099 3 0.124
3hr *Mean ± SD*	80.1 ± 2.59*^	75.83 ± 3.34	73.61 ± 3.22	**9.714**	**0.001**	**1* 0.032** **2^ 0.001** 3 0.351

4hr *Mean ± SD*	89.4 ± 4.41^	83.72 ± 3.2	79.17 ± 3.17	**12.89**	**0.001**	1 0.116 **2^ 0.001** 3 0.072
8hr *Mean ± SD*	90.43 ± 2.21^	84.39 ± 4.85	82.44 ± 3.2	**9.167**	**0.001**	1 0.221 **2^ 0.011** 3 0.617
12hr *Mean ± SD*	89.33 ± 3.58	86.89 ± 4.32	88.59 ± 3.46	0.236	0.813	1 0.488 2 0.611 3 0.556
16hr *Mean ± SD*	88.89 ± 3.63	87 ± 2.49	88.83 ± 2.01	0.297	0.764	1 0.376 2 0.505 3 0.654
20hr *Mean ± SD*	85.83 ± 5.16	86.61 ± 4.05	84.4 ± 1.24	0.891	0.431	1 0.833 2 0.534 3 0.489
24hr *Mean ± SD*	86.17 ± 4.79	82.94 ± 6.26	84.2 ± 2.44	1.432	0.179	1 0.189 2 0.313 3 0.280

Baseline (MAP before spinal anesthesia) ,Postoperative (started by 1hr after the end of surgery)

*Data presented as mean ±SD *P-value <0.05 was considered 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

F : ANOVA test LSD: least significant difference test

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

Regarding to the basal (MAP) of three studied groups before spinal anesthesia there was no significant difference in (MAP) between the three studied groups.

Regarding to (MAP) changes of three studied groups postoperatively there was a significant difference in (MAP) between group C & G at 2, 3 hours, where (MAP) significantly higher in group C compared to group G, meanwhile group C found to be significantly higher in (MAP) compared to group P, at 3, 4, 8 hours, meanwhile there is no significant difference in (MAP) between group G and P at 2, 3,4,8 hours postoperative

And there is no significant difference in (MAP) between the three studied groups in the remaining studied intervals postoperative.

Table (4): HR (Heart Rate) changes of the three studied groups basal & postoperatively.

Group / ***Time***	***Group C*** *(N=18)*	***Group G*** *(N=18)*	***Group P*** *(N=18)*	***F***	***P***	**LSD**
Baseline *Mean ± SD*	96.89 ± 4.75	94.32 ± 5.11	95.19 ± 3.12	2.497	0.071	1 0.546 2 0.451 3 0.672
1hr *Mean ± SD*	106.28 ± 2.82*****	85.72 ± 5.6	84.89 ± 3.05^	**6.364**	**0.001**	**1* 0.001** **2^ 0.001** 3 0.641
2hr *Mean ± SD*	102.62 ± 4.31*****	85.78 ± 5.52	81.44 ± 10.55^	**7.612**	**0.001**	**1* 0.001** **2^ 0.001** 3 0.106
3hr *Mean ± SD*	98.66 ± 3.64*****	86.47 ± 4.65#	82.89 ± 8.14^	**3.261**	**0.004**	**1* 0.009** **2^ 0.001** **3# 0.001**
4hr *Mean ± SD*	103.72 ± 5.23*****	84.83 ± 3.43^	83.78 ± 3.04^	**6.932**	**0.001**	**1* 0.001** **2^ 0.001** 3 0.712
8hr	96.89 ± 4.76*	88.32 ± 5.16	85.19 ± 3.12^	**5.621**	**0.003**	**1* 0.021**

Mean ± SD						**2^ 0.001** 3 0.267
12hr *Mean ± SD*	93.27 ± 4.37	85.91 ± 4.53	83.63 ± 2.74^	**4.798**	**0.006**	1 0.071 **2^ 0.001** 3 0.426
16hr *Mean ± SD*	89.11 ± 4.19	84.63 ± 3.64	81.36 ± 3.17	2.312	0.061	1 0.236 2 0.091 3 0.654
20hr *Mean ± SD*	89.89 ± 3.84	85.36 ± 2.15	79.93 ± 2.98	1.981	0.053	1 0.383 2 0.064 3 0.096
24hr *Mean ± SD*	88.72 ± 4.42	83.78 ± 3.61	81.35 ± 2.11	2.497	0.071	1 0.102 2 0.154 3 0.223

Baseline (HR before spinal anesthesia), Postoperative (started by 1hr after the end of surgery)

Data presented as mean ±SD

1 C&G, 2 C&P, 3 G&P

**P-value <0.05 was considered significant,*

** 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

F : ANOVA test

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

Regarding to the basal (HR) of three studied groups before spinal anesthesia there was no significant difference in (HR) between the three studied groups.

There was a significant difference in HR between group(C&G) and (C&P) at 1, 2, 3, 4, 8 hours, where HR significantly higher in group C compared to group G &P . meanwhile there was a significant difference in HR between group G&P at 3 hr where HR significant higher in group G compared to P

And there was a significant difference in HR between group C&P at 12 hr where HR significant higher in group G compared to P

And there was no significant difference in HR between the three studied groups at 16,20,24 hours postoperative.

Table (5): Changes in RR (Respiratory Rate) between the three studied groups basal & postoperatively.

Group / ***Time***	***Group C*** *(N=18)*	***Group G*** *(N=18)*	***Group P*** *(N=18)*	***F***	***P***	***LSD***
Baseline	12.21 ± 0.315	12.13 ± 0.255	12.19 ± 0.298	0.294	0.780	1 0.546 2 0.451 3 0.672
1hr *Mean ± SD*	14.83 ± 0.924*****	12.92 ± 0.611	12.31 ± 0.412^	**2.612**	**0.042**	**1* 0.001** **2^ 0.001** 3 0.641
2hr *Mean ± SD*	14.95 ± 0.641*****	12.64 ± 0.554	12.42 ± 0.503^	**2.781**	**0.037**	**1* 0.001** **2^ 0.001** 3 0.106
3hr *Mean ± SD*	13.64 ± 0.512*****	12.62 ± 0.365#	12.22 ± 0.541^	0.364	0.239	**1* 0.009** **2^ 0.001** **3# 0.001**
4hr *Mean ± SD*	13.92 ± 0.467*****	12.31 ± 0.416	12.02 ± 0.315^	0.661	0.244	**1* 0.001** **2^ 0.001** 3 0.712

8hr *Mean ± SD*	12.83 ± 0.462	12.62 ± 0.211	12.36 ± 0.164^	0.261	0.623	**1*** **0.021** **2^** **0.001** 3 0.267
12hr *Mean ± SD*	12.46 ± 0.343	12.32 ± 0.351	12.31 ± 0.454^	0.364	0.561	1 0.071 **2^** **0.001** 3 0.426
16hr *Mean ± SD*	12.26 ± 0.346	12.15 ± 0.321	12.34 ± 0.452	0.492	0.692	1 0.236 2 0.091 3 0.654
20hr *Mean ± SD*	12.34 ± 0.236	12.06 ± 0.312	12.11 ± 0.299	0.426	0.656	1 0.383 2 0.064 3 0.096
24hr *Mean ± SD*	12.24 ± 0.315	12.13 ± 0.255	12.19 ± 0.298	0.294	0.782	1 0.102 2 0.154 3 0.223

Baseline (HR before spinal anesthesia), Postoperative (started by 1hr after the end of surgery)

Data presented as mean ±SD P-value <0.05 was considered significant

1 C&G, 2 C&P, 3 G&P

**P-value <0.05 was considered significant,*

** 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 F : ANOVA test

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

Regarding to the basal (RR) of three studied groups before spinal anesthesia there was no significant difference in (RR) between the three studied groups.

There was a significant difference in RR between group(C&G) and (C&P) at 1, 2, 3, 4, 8 hours, where RR significantly higher in group C compared to group G &P. meanwhile there was a significant difference in RR between group G&P at 3 hr where RR significant higher in group G compared to P

And there was a significant difference in RR between group C&P at 12 hr where RR significant higher in group G compared to P

And there was no significant difference in RR between the three studied groups in the remaining studied intervals.

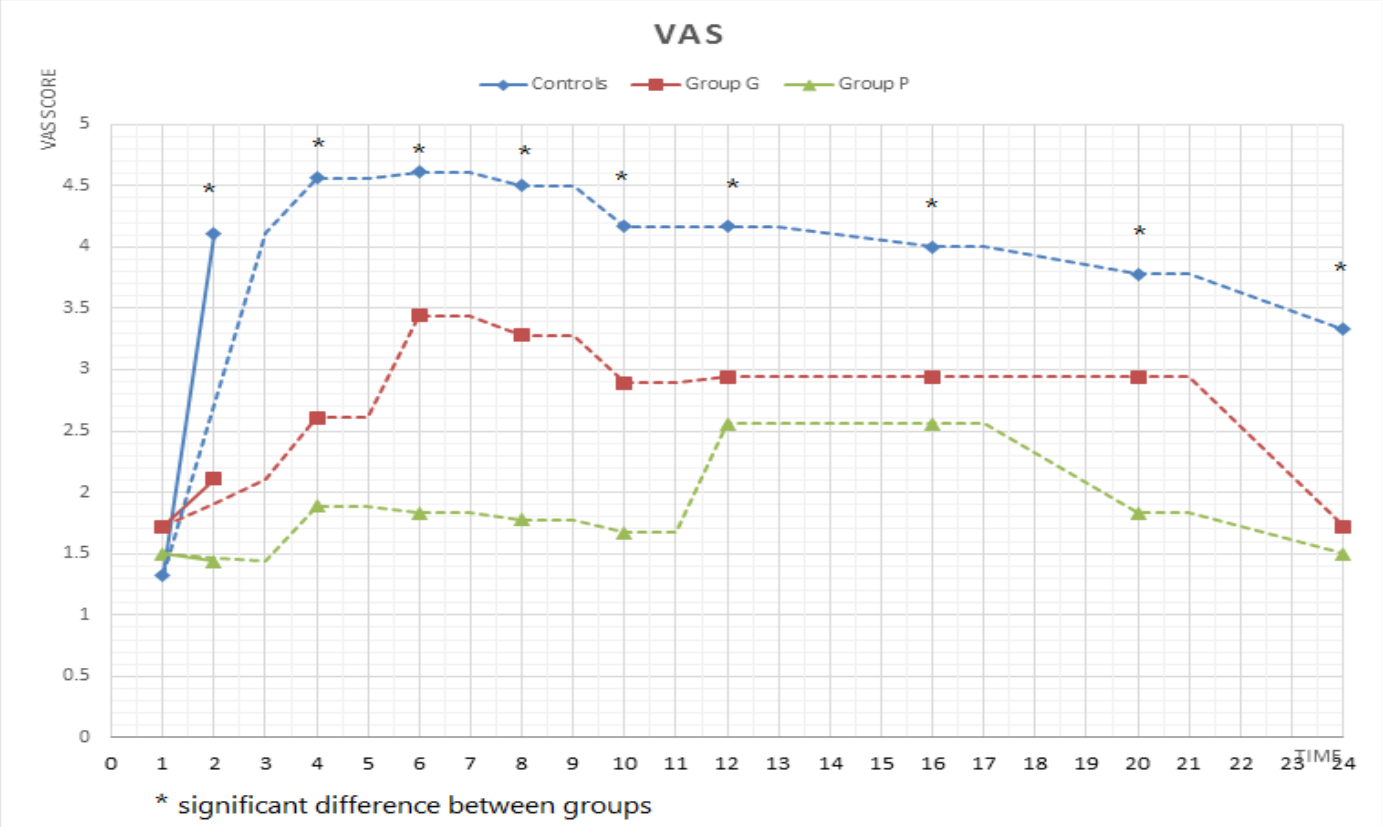

Figure (7):VAS of the three studied groups postoperatively

figure(7) showed that VAS found to be 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 interval except at 16 and 24 hours postoperative where there was no significant difference between G&P (P-value 0.300 &0.477)

As regard group C, it was found that the lowest value of VAS was at 1, 20 and 24 hours postoperativeand the highest value was at 4 and 6 hours postoperative

As regard 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 regard 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.

Table (8): Ramsy sedation score of the three studied groups.

Group / ***Time***	***Group C*** *(N=18)*	***Group G*** *(N=18)*	***Group P*** *(N=18)*	***F***	***P***	***LSD***
2hr *Mean ± SD*	1.17 ± 0.383*^	2.83 ± 1.2#	4.44 ± 1.042	**54.263**	**<0.001**	**1* <0.001** **2^ <0.001** **3# <0.001**
4hr *Mean ± SD*	1.78 ± 0.428*^	2.44 ± 0.705#	4.56 ± 0.705	**96.522**	**<0.001**	**1* 0.002** **2^ <0.001** **3# <0.001**
6hr *Mean ± SD*	1.94 ± 0.725*^	4 ± 0.594	4.28 ± 0.752	**60.731**	**<0.001**	**1* <0.001** **2^ <0.001** **3** 0.235
8hr *Mean ± SD*	2.28 ± 0.752^	2.17 ± 0.924#	4.17 ± 0.924	**30.037**	**<0.001**	**1** 0.703 **2^ <0.001** **3# <0.001**
10hr *Mean ± SD*	1.44 ± 0.511*^	2.89 ± 0.583#	4.5 ± 0.707	**14.56**	**<0.001**	**1* <0.001** **2^ <0.001** **3# <0.001**
12hr *Mean ± SD*	1.72 ± 0.575*^	2.39 ± 0.778#	4.61 ± 0.979	**65.299**	**<0.001**	**1* 0.015** **2^ <0.001**

						3$^{\#}$<0.001
16hr *Mean ± SD*	1.56 ± 0.511*^	2.5 ± 1.15$^{\#}$	4 ± 0.840	**35.819**	**<0.001**	**1* 0.002** **2^ <0.001** **3# 0.009**
20hr *Mean ± SD*	1.83 ± 0.618*^	3.72 ± 1.179	3.44 ± 1.097	**18.887**	**<0.001**	**1* <0.001** **2^ <0.001** **3** 0.407
24hr *Mean ± SD*	1.72 ± 0.461*^	4.44 ± 1.042	4.67 ± 1.328	**47.408**	**<0.001**	**1* <0.001** **2^ <0.001** **3** 0.512

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*

^ a significant difference between C and P group

$^{\#}$ a significant difference between P & G group

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

The table(8) showed that Ramsy sedation score was found to be significantly lower in group C compared to group G & P in all time intervals, except at 8 hours postoperative there was no significant difference between group C& G (p-value 0.703). Meanwhile group P found to be significantly higher in Ramsy sedation score compared to group G in all time intervals, except at 6,20 and 24 hours postoperative where there was no significant difference between G&P (P-value 0.235, 0.407&0.512)

As regard group C the table showed that the lowest value of Ramsy sedation score was at 2 hours postoperative (1.17 ± 0.383) and the highest value was at 8 hours postoperative (2.28 ± 0.752)

As regard group G the table showed that the lowest value of Ramsy sedation score was at 8 hours postoperative(2.17 ± 0.924) and the highest value was at 24 hours postoperative(4.44 ± 1.042)

As regard group P the table showed that the lowest value of Ramsy sedation score was at 20 hours postoperative(3.44 ± 1.097) and the highest value was at 24 hours postoperative(4.67 ± 1.328)

Table (10): Mean Postoperative Opioid (Pethidine, mg) Consumption in Study Groups

Group / ***Analgesic requirments***	***Group C (N=18)***	***Group G (N=18)***	***Group P (N=18)***	***P-value***
One dose	--	--	*7 (38.9%)*	***<0.001***
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*	***<0.001***

Numerical data were presented as no. (%).

(C): Control group *(G): gabapentin group* *(P): pregabalin group*

There was significant reduction in number of doses of pethidine as postoperative analgesia in group (P) compared to group (G) and group (C).

As regard 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(1350mg) given to the 18 patients as 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(650mg) 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(350mg) as 7 patients from 18 asked for an extra one dose while the other 11patients asked for extra two doses in the study time.

Table (11) : Complications of the used drugs among the three studied groups.

Group / ***Complication***	***Group C*** *(N=18)*	***Group G*** *(N=18)*	***Group P*** *(N=18)*	P
Drowsiness	3 (16.7%)*	--	--	**0.042**
Dizziness or unsteadiness	4 (22.2%)	2 (11.1%)	1 (5.6%)	0.317
Sweating or flushing	2 (11.1%)	--	--	0.125
Constipation	9 (50%)*	3 (16.7%)	2 (11.1%)	**0.016**
Hallucination	1 (5.6%)	--	--	0.361

Numerical data were presented as no. (%).

P-value <0.05 was considered significant

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

(C): control group

(G): Gabapentin group

(P): Pregabalin group

There was significant difference between group(C) and (G) &(P) regarding to drowsiness, and constipation where there was increase in the incidence in the control group, while there was no difference between group (G) & (P).

IV. DISCUSSION:

In the present study, there was no statistically significant differences between the three groups regarding the demographic data (age, BMI and ASA status).

Pre-incisional analgesia has been shown to be more effective in control of post-operative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia and increased pain. Gabapentin and pregabalin have antiallodynic and antihyperalgesic properties useful for treating neuropathic pain and therefore may be beneficial in acute post-operative pain management [11].

In agreement with the result of this study**, Bafna and colleagues** [12] 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 600mg (group B) or pregabalin 150 mg (group C). A significantly longer mean duration of effective analgesia in group C was observed compared with other groups ($P<$ 0.001).

In the present study also, pregablin administered preoperatively were 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, but 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 VASscore at time of regaining full muscle power (which indicates the end of any analgesic effect due to the regional anesthesia).

Also the result of this study matched with the another study conducted by **Srivastava and his colleagues**[13], who demonstrated that preoperative administration of gabapentin was more effective than the placebo in reducing the VAS scores of pain both at rest and those evoked by movement during first 24 h. It nearly resulted in 33% reduction in consumption of postoperative tramadol. This tramadol sparing effect was associated with a significant reduction in incidence of postoperative nausea and vomiting (PONV) also. However, pain scores and consumption of tramadol were comparable on second postoperative day in the two groups. Gabapentin did not have any effect on intraoperative hemodynamics. Sedation was observed in 23% of patients given gabapentin, but sedation occurred only in early postoperative hours and thus did not delay recovery and discharge from the post-anesthesia care unit (PACU).

Similar results were obtained by **Kohli and colleagues**[14]**,** Their randomized, double-blind, placebo-controlled trial was conducted in 150 patients undergoing hysterectomy under spinal anesthesia, who were divided into three groups, group I control group, group II received 150 mg pregabalin 1 hour before surgery and group III received 300 mg pregabalin 1 hour before surgery. In their study they observed that the pregabalin group showed reduced anxiety scores which showed no difference between pregabalin 150mg and pregabalin 300mg groups. The time of rescue analgesia required by the patients was increased in pregabalin groups, with more effective prolongation of analgesia after spinal anesthesia in the pregabalin 300mg group. This prolongation in the analgesia was correlating well with the half life of pregabalin which is 4.6 to 6.8 hours, and was not associated with any hemodynamic instability. On comparing the complications like sedation, dizziness, nausea and vomiting, the incidences of dizziness was more in patients receiving pregabalin 300mg. Incidence of nausea and vomiting showed no significant difference between the groups. Patient satisfaction was better with pregabalin 300mg group than 150mg group and much better than with the control group. The reduction in mean blood pressure and heart rate was seen in all groups, mostly due to the effect of spinal anesthesia. In their study they concluded that preemptive administration of pregabalin before hysterectomy under spinal anesthesia will prolong the neuroaxial block, help in

immediate postoperative analgesia and reduce the rescue analgesia requirements, with 150mg being the optimal dose.

On other hand, the study conducted by **Short and his colleagues [15]**, couldn't reach the same conclusion as the previous studies and couldn't 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 postcesarean 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 morpine for post-operative analgesia, and the fact of their using lower doses of gabapentin (300mg and 600mg) than the dose used in the current study (900mg). It was however reassuring that they did not observe any significant maternal sedation or neonatal side effects with these doses of gabapentin.

In the current study regarding the incidence of complications, few episodes of intraoperative hypotension and bradycardia occurred almost equally in the three groups which might be attributed to the effect of spinal anesthesia. Also, there was no statistically significant difference between the three groups regarding the occurrence of shivering. However, there was a highly significant reduction in the incidence of PONV in both the gabapentin and the pregabalin groups compared to the control group. A possible explanation for this finding was the fact that a part of this nausea and vomiting occurred as an adverse effect of the opioids given as rescue analgesia postoperative, and since the gabapentin and pregabalin were shown to have an opioid-sparing effect, consequently they decreased the opioid related adverse effects.

In 2009, Şen and his colleagues[16] had studied the effects of gabapentin on acute and chronic pain after inguinal herniorrhaphy. In their study, sixty male patients – aged 20 to 40 years – who were scheduled for unilateral inguinal herniorrhaphy under spinal anesthesia were randomly allocated to two groups: the gabapentin group received a single dose of 1200 mg oral gabapentin 1 hour before surgery, and the placebo group received a placebo capsule instead. All operations were performed by the same surgeon with the same technique. Postoperative pain was assessed at 1, 3 and 6 months. In their study, they observed that, preoperative single dose of gabapentin decreased the intensity of acute postoperative pain, the amount of tramadol consumption and the incidence and intensity of pain in the first 6 months after surgery. The impact of pain on daily activities was not found to be different between the groups.

Different results were obtained by **Lunn and his colleagues[17]**, who had found that, gabapentin might have a limited if any role in acute postoperative pain management of opioid-naive patients and should not be recommended as a standard of care. They had studied the analgesic and sedative effects of perioperative gabapentin in total knee arthroplasty performed under spinal anesthesia with optional propofol, in a randomized, double-blind, placebo-controlled dose-finding study. In their study, 300 opioid-naive patients scheduled for total knee arthroplasty were randomized to 3 groups. Group A: Gabapentin “high dose” group received gabapentin 1300 mg/d: 900 mg

preoperatively and 400 mg at 10:00 PM on the day of surgery, thereafter 400 mg at 8:00 AM and 900 mg at 10:00 PM. Group B: Gabapentin "low dose" group received gabapentin 900 mg/d: 600 mg preoperatively and 300 mg at 10:00 PM, thereafter 300 mg at 8:00 AM and 600 mg at 10:00 PM. Group C: Placebo group received placebo at all time points. In addition to a standardized multimodal analgesic regime consisting of oral slow release 2 gm acetaminophen and 200 mg celecoxib, administered preoperatively together with the study drug then regularly at 8 AM and 10 PM up to postoperative day 6. Rescue analgesics consisted of intravenous sufentanil in the post anesthesia care unit, and oral morphine thereafter. The researchers didn't observe any differences between groups in overall pain, and no opioid-sparing effect were observed with either doses of gabapentin in the first 48 hours and from days 2-6. This could be again attributed to the use of two non-opioid analgesics on regular basis for post-operative analgesia beside the rescue morphine doses, the practice that could significantly reduce post-operative pain in the control group as well. More adverse reactions related to sedation or confusion were observed in the "high-dose" gabapentin group, of which 5 were characterized as severe due to prolonged hospitalization or readmission. Furthermore, dizziness was more pronounced in both gabapentin groups. And this could be explained by the prolonged use of high dose gabapentin (for 6 days post-operative) including day time doses. The only benefit observed with gabapentin in this study was a finding of improved sleep the first to second postoperative nights.

In the present study, the possible sedative effect of gabapentin and pregabalin was assessed by estimating Ramsay score at 2,4,6,8,10,12,16,20 and 24 hours postoperatively and comparing it with that estimated in the placebo group. As expected the incidence of postoperative sedation was significantly higher in both gabapentin and pregabalin groups, but fortunately these sedative effects were not reported as being so severe as the Ramsay score didn't exceed 4 (brisk response to stimulus) at any time during the first 24 hours postoperative, and also didn't affect the duration of hospital stay because in all cases it had completely resolved by the end of first day postoperative (Ramsay score at 24 hours postoperative didn't exceed 2 in the 3 groups).

This study showed that pregabalin administered in a single dose preoperatively in patients for elective cesarean section under spinal anesthesia, has significantly prolonged the duration of effective analgesia, decreased the rescue analgesia requirements and decreased the opioid associated side effects more than a single dose of gabapentin. These benefits were not associated with intra or postoperative hemodynamic unstability.

V. Conclusion

Under the present study design, preemptive administration of a single dose pregabalin in female patients undergoing elective cesarean section under spinal anesthesia was effectivemore 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 pre-emptive gabapentin and pregabalin that will yield the best outcome regarding acute postoperative pain modification with the least adverse effects.

REFERENCES:

[1]Cardinale, J. P., Gillespie, N., &Germond, L. (2019). Complications of General Anesthesia. In Catastrophic Perioperative Complications and Management (pp. 95-103).

[2] Zaccagnino, M. P., Badr, A.M., Sang, C. N., &Correl, D. J.(2017): The Perioperative Surgical Home: A New Role for the Acute Pain service. Anesthesia & Analgesia, 125(4),1394-1402

[3] Lavand' homme, P . (2018). Postoperative cesarean pain: real but is it preventable? : Current Opinion in Anesthesiology, 31(3), 62-267

[4] Nelson, G., Altman, A. D., Nick, A., Meyer, L. A., Ramirez, P. T., Achtari, C., ... & Acheson, N. (2016): Guidelines for postoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations—Part II. Gynecologic oncology, 140(2), 323.

[5] Kaye, A. D., Cornett, E. M., Helander, E., Menard, B., Hsu, E., Hart, B., &Brunk, A. (2017): An update on nonopioids: intravenous or oral analgesics for perioperative pain management. Anesthesiologyclinics, 35(2), e55-e71.

[6] Patel, R., &Dickenson, A. H. (2016). Mechanisms of thegabapentinoids and α2δ-1 calciumchannelsubunit in neuropathicpain. Pharmacologyresearch&perspectives, 4(2).

[7] 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. Anesthesia, essays and researches, 11(2), 330.

[8] Fabritius, M, L., Storm, C., Koyuncu, S., Jaegaer, P., Petersen, P. L., Geisler, A... &Mathiesen, O. (2017): Benefit and harm of pregabalin in acute pain treatment: a systematic review with meta-analyses and trial sequential analyses BJA: British Journal of Anaesthesia, 119(4), 775-791.

[9] Dauri M, Faria S, Gatti A et al.(2009):Gabapentin and pregabalin for the acute post-operative painmanagement. A systematic-narrative review of the recent clinicalevidences. Curr Drug Targets,10:716–733

[10] Reddi, D . (2016). Preventing chronic postoperative pain Anaesthesia 71,64-71

[11] Tiippana EM, Hamunen K, Kontinen VK et al. (2007): Do surgical patients benefit from perioperative gabapentin/pregabalin? asystematic review of efficacy and safety.Anesth Analg,;104:1545–1556.

[12] Bafna U, Rajarajeshwaran K, Khandelwal M et al. (2014): A comparison of effect of preemptive use of oral gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. J AnaesthesiolClinPharmacol,; 30(3): 373–377.

[13] Srivastava U, Kumar A, Saxena S et al. (2010): Effect of preoperative gabapentin on postoperative pain andtramadol consumption after minilap open cholecystectomy:a randomized double-blind, placebo-controlled trial. Eur J Anaesthesiol ;27:331–335.

[14] Kohli M, Murali T, Gupta R et al. (2011): Optimization of Subarachanoid Block by Oral Pregabalin for Hysterectomy. J AnaesthClinPharmacol,; 27(1): 101-105.

[15] Short J, Downey K, Bernstein P et al. (2012): A single preoperative dose of gabapentin does not improve postcesarean delivery pain management: a randomized, double-blind, placebo-controlled dose-finding trial. AnesthAnalg ;115:1336–1342.

[16] Şen H, Sızlan A, Yanarateş O et al. (2009): The effects of gabapentin on acute and chronic pain after inguinal herniorrhaphy.Eur J Anaesthesiol,; 26:772–776.

[17] Lunn TH, Husted H, Laursen MB et al. (2015): Analgesic and sedative effects of perioperativegabapentin in total knee arthroplasty:a randomized, double-blind, placebo-controlleddose-finding study.PAIN,; 156: 2438–244.