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Using Pregabalin for Prevention of Post Anesthesia Shivering

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ABSTRACT

Background: post anesthesia shivering (PAS) is one of the most common complications after surgeries. There are two methods to reduce the shivering, including pharmacological and non-pharmacological methods.

Aim of the study: the present study compared the efficacy and safety of 150 mg oral pregabalin premedication on preventing PAS, perioperative core body temperature changes, hemodynamic stability and postoperative complications. **Patients and methods**: this prospective, observational study consisted of 200 adult patients scheduled for general, orthopedic or ENT surgery. The patients were randomized into two groups of 100 patients each. Group I received 150 mg of oral pregabalin, group II received an oral placebo 60-90 min before operation. All patients were assessed for perioperative hemodynamic changes, Core body temperature changes, PAS, amount of pethidine used and postoperative side effects. **Results**: regarding the efficacy of the preoperative administration of oral pregabalin, the current study reports valuable preventive effect on shivering for pregabalin group (8.1%) compared to control group (44.3%), and there was highly significant difference between both groups according to incidence and scoring of shivering. On the other hand we found no significant difference between groups according to heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP). However reduction in SBP and DBP was recorded in both groups after induction which became back up at the end of surgery. Also tympanic temperature reduction was recorded intraoperatively and came back up during recovery period with no statistically significant differences between groups. Postoperative nausea and vomiting were significantly lower with the administration of pregabalin compared with the placebo group. Additionally, pregabalin increased the incidence of dizziness, blurred vision and drowsiness.

Conclusion: oral pregabalin premedication adequately prevent PAS but could not affect its timing nor mean dose of pethidine used. Additionally, oral pregabalin reduced postoperative nausea and vomiting but increased significantly the incidence of dizziness, blurred vision and drowsiness.

Keywords: Pregabalin, Premedication, Post anesthesia shivering

INTRODUCTION

Postoperative shivering is one of the most common complications after surgeries, which is seen among 6.3-65% of patients and include involuntary movements of one or more groups of muscles. Shivering can cause many side effects such as increased oxygen consumption, carbon dioxide production, heart rate, and blood pressure, resulting in exacerbation of ischemic heart disease, as well as increased intracranial pressure, pain at the surgical site, and also a sense of discomfort to the patient [(1)]. General anesthesia facilitates redistribution of the temperature from the central tissues to the peripheral tissues. Due to anesthesia, core temperature regulation responses like the vasoconstriction threshold are controlled, and most anesthetic drugs cause peripheral vasodilatation [(2)].

Shivering could be the result of hypothermia readjustment of body core temperature during surgery, or because of fever and shivering, which could lead to activation of the inflammatory response and cytokine release [(3)]. There are two methods to reduce the shivering, including pharmacological and non-pharmacological methods. Non-pharmacological methods involve the use of moisturizers, preventing hypothermia using warm blankets, and warm and moist oxygen inhalation [(1)].

Pregabalin is a GABA analogue; it was introduced and approved by FDA in 2005 for clinical use. It has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. It reduces excitability of dorsal horn neurons after tissue damage. Pregabalin has been proven to improve various aspects of recovery after surgery. It has high oral bioavailability (90%), more rapid absorption (peak plasma level: 1 hr.) and linear increase in plasma concentration when its dose is increased. Pregabalin is associated with a significant reduction in pain scores at rest and during movement and also reduction in opioid consumption at 24 h of surgery compared with placebo. Patients receiving pregabalin have less postoperative nausea and vomiting and pruritus compared with placebo [(4)]. The use of Pregabalin in the perioperative setting has been evaluated in many studies. These studies report promising reductions in postoperative morphine consumption but none of these studies have used a comprehensive scoring system to assess impact on postoperative shivering [(5-7)]. Ozgencil ***et al***. [(8)] reported that although postoperative shivering was not part of their original study design, it was apparent in the course of the study that incidence of shivering differed among the groups, patients in the placebo group were found to experience more

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postoperative shivering than those in the pregabalin group.

AIM OF THE WORK

The aim of the study is to evaluate the efficacy of Pregabalin as an oral premedication drug in prevention of post anesthesia shivering.

- The primary outcome is the incidence of shivering.
- The secondary outcomes are:
  1. Shivering score.
  2. Duration of shivering.
  3. Timing of shivering.
  4. Incidence of complications.

PATIENTS AND METHODS

Approval was obtained from the local Ethics Committee, and written informed consent was obtained from each patient in this prospective, observational study consisting of 200 undergoing elective general, orthopedic and ENT surgeries with mild and moderate 3rd space under general anesthesia in AL-Azhar University Hospitals.

Inclusion criteria

1. ASA I and II patients.
2. Elective general, orthopedic and ENT surgeries with mild and moderate 3rd space under general anesthesia.
3. Patients of age 18-60 years, body mass index (BMI) ≤30, had no clinically significant cardiovascular, renal or central nervous system diseases.

Exclusion criteria

1. Known allergy to study drugs,
2. Contraindications of study drugs,
3. Patients with thyroid disorders,
4. Raynaud's syndrome,
5. Cardiopulmonary disorders,
6. Severe hemorrhages, blood transfusion during surgery,
7. Using large amount of irrigation fluids,
8. Neuromuscular diseases, and
9. Fever.

Total 200 patients, 5 of them were excluded from the study (2 patients required blood transfusion and other 3 patients exceeded two hours of anesthetic time). Finally, 195 patients were randomly divided into two groups:

- **Group I** - pregabalin Group (N=98) received 150mg oral pregabalin
- **Group II** - control Group (N=97) received placebo drug.

The placebo and pregabalin were administrated orally with sips of water approximately 60-90 min before operation.

On arrival to the operating room, monitors were attached. Baseline HR, SBP and DBP were recorded. After pre-oxygenation for 3 min with 100% oxygen, anesthesia was induced with Propofol at (2 mg/kg) or dose sufficient for the loss of verbal commands. The direct laryngoscopy and intubation was facilitated with atracurium at 0.5 mg/kg. Anesthesia was maintained with isoflurane in 40% air and 60% oxygen. The patients were mechanically ventilated to maintain normocapnia (ETCO2 between 35 and 40 mmHg). The supplemental neuromuscular blockade was achieved with atracurium at 0.1 mg/kg. After completion of the surgery, residual neuromuscular block was antagonized with appropriate doses of neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg), and extubation was performed when respiration was adequate.

Assessed parameters:

1. **Demographic data:** Regarding patients' age, sex, and BMI were all Recorded.
2. **Hemodynamic parameters:**

a) Heart rate (beats per minute) using lead II electrocardiogram (ECG) waves.

b) Systolic arterial blood pressure and diastolic arterial blood pressure were measured in (mmHg) and recorded at the following times:

- Premedication.
- After induction of general anesthesia.
- At the end of surgery,
- After the patient entrance to post anesthetic care unit (PACU),
- And before the patient exit from PACU.

3. **Anesthetic time:** defined as from the start of induction to the time when the anesthetic was discontinued.
4. **Recovery time (extubation time):** defined as from discontinuation of anesthetic till patient response to verbal stimuli.
5. **Core body temperature:** For all patients, the core temperature was measured and recorded through tympanic temperature using (QQcute IT-121 infrared thermometer) at the following time:

- Premedication (baseline),
- After induction of anesthesia,
- Then every 15 min interval till end of surgery,
- After the patient entrance to PACU,
- And before the patient exit from PACU.

6. **Post anesthesia shivering:**

The incidence and intensity of shivering: was carried out using (Bedside Shivering Assessment Score) (BSAS) [9] as follows:

(1) None, no shivering noted on palpation of the masseter, neck, or chest wall.
(2) Mild, shivering localized to the neck and/or thorax only.
(3) Moderate, shivering involves gross movement of the upper extremities (in addition to the neck and thorax).
(4) Severe, shivering involves gross movements of the trunk and upper and lower extremities.
In case with score 3-4 for more than 4 minutes duration, the prophylaxis was considered ineffective and intravenous bolus of pethidine 20 mg was administrated then titration as requirements.

- Timing of shivering: assessment of shivering was done at this intervals: just after extubation, after entrance to recovery room, then every 15 minutes till exit from recovery room.
- Duration of significant shivering which need treatment (score 3 and 4).

7. **Total amount and mean dose of pethidine.**
8. **Postoperative nausea and vomiting (PONV):** The severity of PONV was classified to three categories:

1. No nausea or vomiting.
2. Nausea only.
3. Severe nausea with vomiting. Rescue antiemetic ondansetron 4mg I.V. was given to all patients with PONV.

9. **Postoperative side effects:** Patients were observed for any side effects during the recovery period such as dizziness (including lightheadedness and vertigo), blurred vision, dyspnea, respiratory depression (respiratory rate ≤8 or peripheral oxygen saturation SPO_2 below 90%), headache, pruritis or drowsiness.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:
- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

Table (1): Comparison between groups according to demographic data.

Demographic Data	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t/x^2#	p-value
Age (years)				
Mean±SD	31.45±9.84	33.56±9.70	1.323	0.138
Range	18-54	19-59		
Sex				
Female	34 (34.7%)	51 (52.6%)	3.340#	0.092
Male	64 (65.3%)	46 (47.4%)		
BMI				
Mean±SD	24.87±1.45	24.98±1.48	0.254	0.615
Range	22.6-27.2	23-27.3		
ASA				
ASA I	73 (74.5%)	59 (60.8%)	1.162#	0.141
ASA II	25 (25.5%)	38 (39.2%)		

This table shows no statistically significant difference between groups according to demographic data.

Table (2): Comparison between groups according to anesthetic time (min).

Anesthetic time (min)	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Mean±SD	82.19±13.06	82.94±11.72	0.175	0.676
Range	65-115	70-115		

This table shows no statistically significant difference between groups according to anesthetic time (min).

Table (3): Comparison between groups according to intraoperative requirements of additional fentanyl.

Intraoperative requirements of additional fentanyl	Group I: Pregabalin (N=98)	Group II: Control (N=97)	x^2	p-value
No	94 (95.9%)	91 (93.8%)	0.444	0.505
Yes	4 (4.1%)	6 (6.2%)		

This table shows no statistically significant difference between groups according to intraoperative requirements of additional fentanyl.

Table (4): Comparison between groups according to tympanic temperature.

Tympanic temperature:	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Baseline Mean±SD	36.94±0.34	36.92±0.32	0.225	0.636
At induction Mean±SD	36.31±0.42	36.31±0.29	0.313	0.590
After 15 min. Mean±SD	35.88±0.31	36.07±0.29	1.271	0.187
After 30 min. Mean±SD	35.68±0.28	35.80±0.31	2.130	0.286
After 45 min. Mean±SD	35.46±0.31	35.62±0.27	1.221	0.132
After 60 min. Mean±SD	35.31±0.20	35.41±0.35	0.411	0.211
After 75 min. Mean±SD	35.29±0.15	35.22±0.37	1.772	0.186
After 90 min. Mean±SD	35.16±0.21	34.90±0.22	1.238	0.193
End of Surgery Mean±SD	35.30±0.26	35.17±0.32	1.720	0.121
Entrance to PACU Mean±SD	35.39±0.27	35.30±0.33	0.539	0.344
Exit from PACU Mean±SD	36.16±0.32	36.02±0.30	1.715	0.211

This table shows no statistically significant difference between groups according to tympanic temperature.

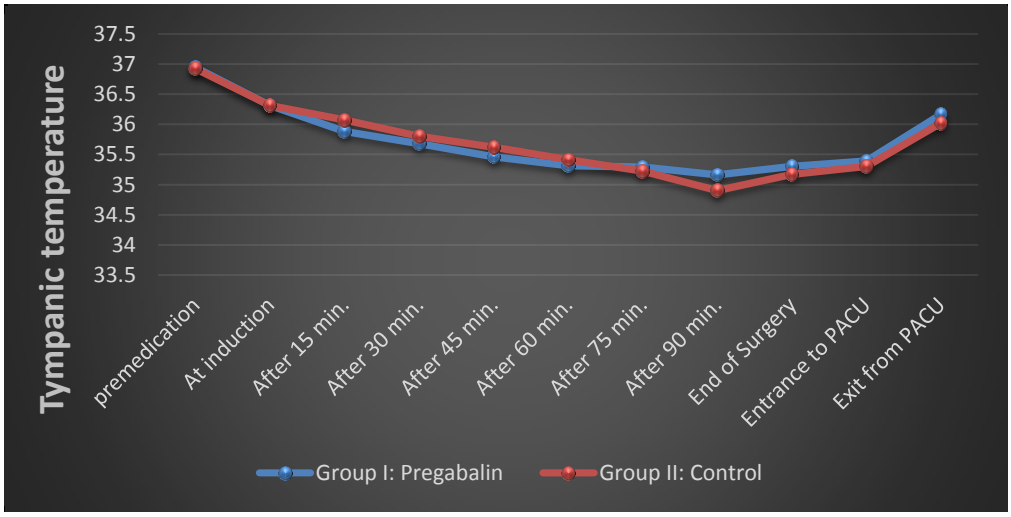

Fig. (1): Line chart between groups according to tympanic temperature.

Table (5): Comparison between groups according to systolic blood pressure.

Systolic Blood Pressure:	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Baseline				
Mean±SD	120.58±7.85	120.82±11.22	0.031	0.861
Range	109-135	100-135		
After induction				
Mean±SD	104.76±9.41	104.54±8.16	0.030	0.862
Range	90-130	90-117		
End of Surgery				
Mean±SD	118.18±6.69	117.99±7.34	0.037	0.847
Range	107-130	99-125		
Entrance to PACU				
Mean±SD	127.52±4.41	121.91±5.07	0.753	0.142
Range	115-135	105-130		
Exit from PACU				
Mean±SD	120.18±3.73	121.57±8.09	2.357	0.126
Range	110-125	110-135		

This table shows no statistically significant difference between groups according to systolic blood pressure.

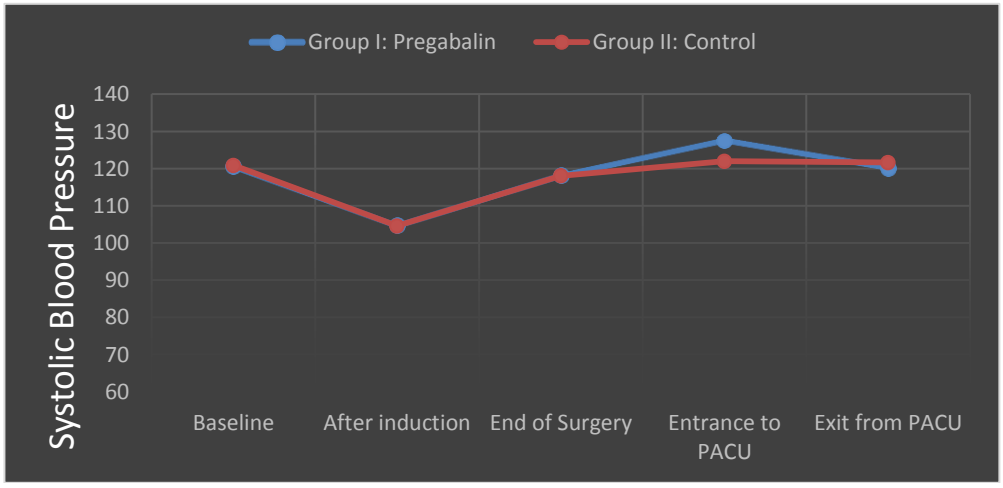

Fig. (2): Line chart between groups according to systolic blood pressure.

Table (6): Comparison between groups according to diastolic blood pressure

Diastolic Blood Pressure:	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Baseline				
Mean±SD	78.43±6.52	77.79±6.61	0.456	0.500
Range	69-90	65-88		
After induction				
Mean±SD	69.04±5.43	70.29±6.25	1.216	0.138
Range	60-80	60-80		
End of Surgery				
Mean±SD	77.36±6.51	77.23±4.52	0.026	0.871
Range	60-85	70-83		
Entrance to PACU				
Mean±SD	82.77±4.33	81.61±3.32	0.382	0.376
Range	75-90	75-85		
Exit from PACU				
Mean±SD	79.03±4.87	79.81±4.19	1.448	0.230
Range	70-85	70-85		

This table shows no statistically significant difference between groups according to diastolic blood pressure.

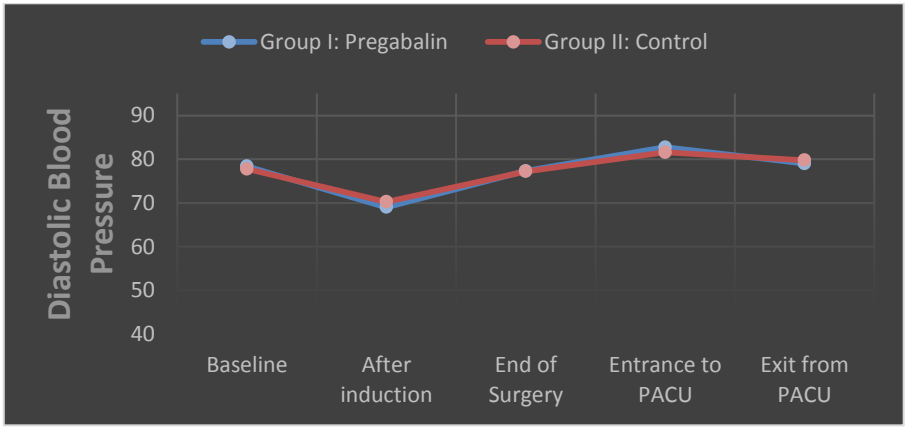

Fig. (3): Line chart between groups according to diastolic blood pressure.

Table (7): Comparison between groups according to heart rate.

Heart Rate:	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Baseline Mean±SD Range	 77.58±8.90 62-92	 75.62±6.76 63-87	1.006	0.085
After induction Mean±SD Range	 74.52±8.47 57-90	 73.34±7.26 58-87	1.090	0.298
End of Surgery Mean±SD Range	 79.71±6.95 69-96	 79.06±5.91 69-90	0.498	0.481
Entrance to PACU Mean±SD Range	 80.63±7.49 65-104	 79.92±4.80 70-85	0.618	0.587
Exit from PACU Mean±SD Range	 77.56±4.79 70-91	 77.87±3.79 67-87	0.242	0.623

This table shows no statistically significant difference between groups according to heart rate.

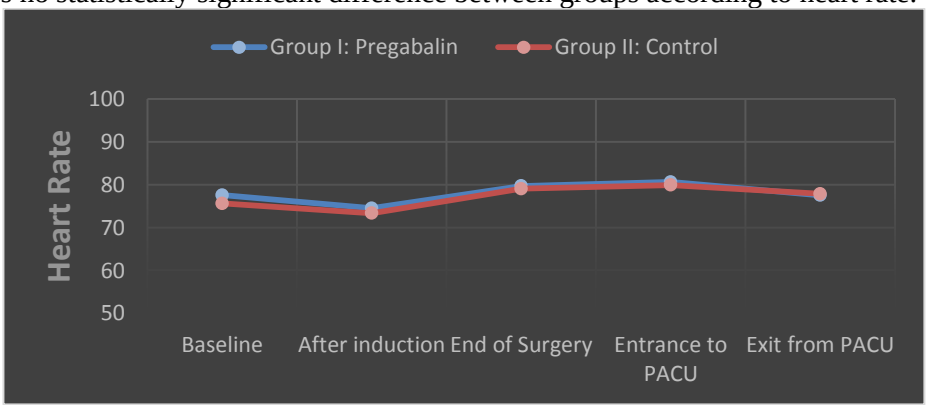

Fig. (4): Line chart between groups according to heart rate.

Table (8): Comparison between groups according to PONV.

PONV	Group I: Pregabalin (N=98)	Group II: Control (N=97)	x2	p-value
No Nausea or Vomiting	33 (33.7%)	23 (23.7%)	4.918	0.047
Nausea	48 (49.0%)	32 (33.0%)	5.152	0.023
Nausea and Vomiting	17 (17.3%)	42 (43.3%)	15.559	<0.001

This table shows statistically moderate significant difference between groups according to no nausea or vomiting and according to nausea only, but shows highly significant difference between groups according to nausea and vomiting.

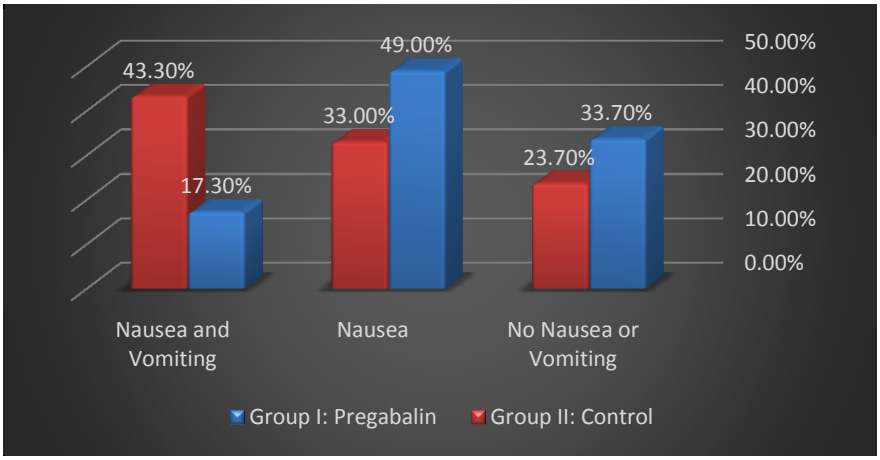

Fig. (5): Bar chart between groups according to nausea and vomiting.

Table (9): Comparison between groups according to side effects.

Side Effects	Group I: Pregabalin (N=98)	Group II: Control (N=97)	x2	p-value
Headache				
No	90 (91.8%)	92 (94.8%)	0.709	0.400
Yes	8 (8.2%)	5 (5.2%)		
Dizziness				
No	72 (73.5%)	86 (88.7%)	6.361	0.012
Yes	26 (26.5%)	11 (11.3%)		
Blurred vision				
No	71 (72.4%)	85 (87.6%)	6.104	0.014
Yes	27 (27.6%)	12 (12.4%)		
Drowsiness				
No	69 (70.4%)	79 (81.4%)	4.245	0.042
Yes	29 (29.6%)	18 (18.6%)		
Pruritus				
No	84 (85.7%)	75 (77.3%)	2.282	0.131
Yes	14 (14.3%)	22 (22.7%)		
Respiratory Depression				
No	90 (91.8%)	92 (94.8%)	0.709	0.400
Yes	8 (8.2%)	5 (5.2%)		

This table shows statistically significant difference between groups according to dizziness, blurred vision and drowsiness.

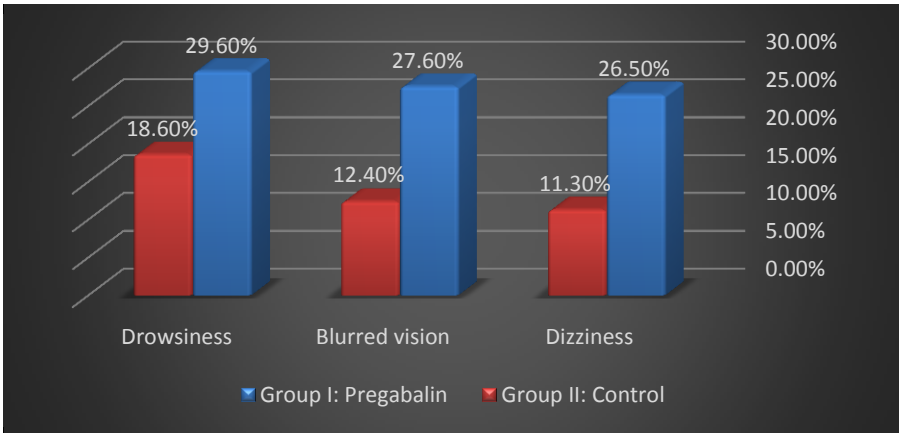

Fig. (6): Bar chart between groups according to side effects with statistically significant difference.

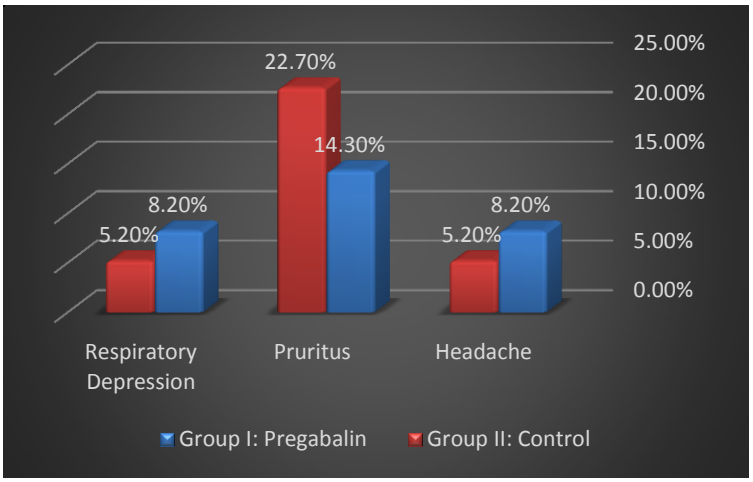

Fig. (7): Bar chart between groups according to side effects with no statistically significant difference**.**

Table (10): Comparison between groups according to mean recovery time.

Mean recovery time	Group I: Pregabalin (N=98)	Group II: Control (N=97)	t-test	p-value
Mean±SD	9.02±3.83	8.22±3.66	1.491	0.137
Range	6-14	5-12		

This table shows no statistically significant difference between groups according to recovery time.

Table (11): Comparison between groups according to shivering score.

Shivering score (BSAS score)	Group I: Pregabalin (N=98)	Group II: Control (N=97)	x2	p-value
1	90 (91.8%)	54 (55.7%)	33.052	<0.001
2	5 (5.1%)	28 (28.9%)		
3	1 (1.0%)	6 (6.2%)		
4	2 (2.0%)	9 (9.3%)		
Total number of shivered patients	8 (8.1%)	43 (44.3%)		

This table shows statistically highly significant difference between groups according to BASAS score.

Table (12): Comparison between groups according to timing of shivering

	Timing of shivering	Group I: Pregabalin (N=98)	Group II: Control (N=97)	x2	p-value
Just After Extubation (T1)	No	96 (98.0%)	85 (87.6%)	7.806	0.005
	Yes	2 (2.0%)	12 (12.4%)		
PACU (T2)	No	94 (95.9%)	77 (79.4%)	12.352	<0.001
	Yes	4 (4.1%)	20 (20.6%)		
After 15 Min. (T3)	No	97 (99.0%)	89 (91.8%)	5.784	0.016
	Yes	1 (1.0%)	8 (8.2%)		
After 30 Min. (T4)	No	97 (99.0%)	94 (96.9%)	1.042	0.307
	Yes	1 (1.0%)	3 (3.1%)		
After 45 Min. (T5)	No	98 (100.0%)	97 (100.0%)	0	1
	Yes	0 (0.0%)	0 (0.0%)		
At discharge (T6)	No	98 (100.0%)	97 (100.0%)	0	1
	Yes	0 (0.0%)	0 (0.0%)		

This table shows statistically significant difference between groups according to timing of shivering at these times: just after extubation (T1), PACU (T2) and after 15 min. (T3).

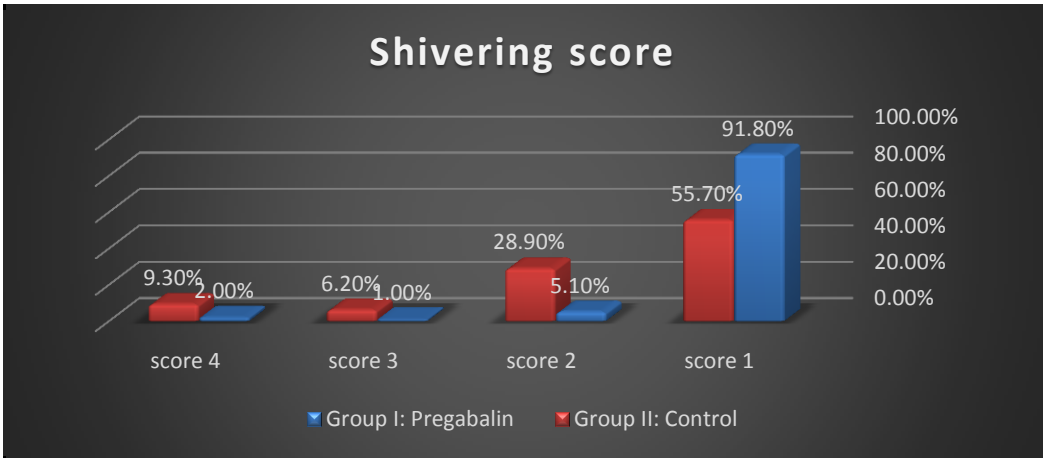

Fig. (8): Bar chart between groups according to shivering score.

Table (13): Comparison between groups according to mean duration of shivering which need treatment

Mean duration of shivering which need treatment	Group I: Pregabalin (N=3)	Group II: Control (N=15)	t-test	p-value
Total duration (min)	27 min	124 min	0.353	0.561
Mean±SD	9.00±1.73	8.27±1.98		
Range	8-11	6-12		

This table shows no statistically significant difference between groups according to mean duration of shivering which need treatment.

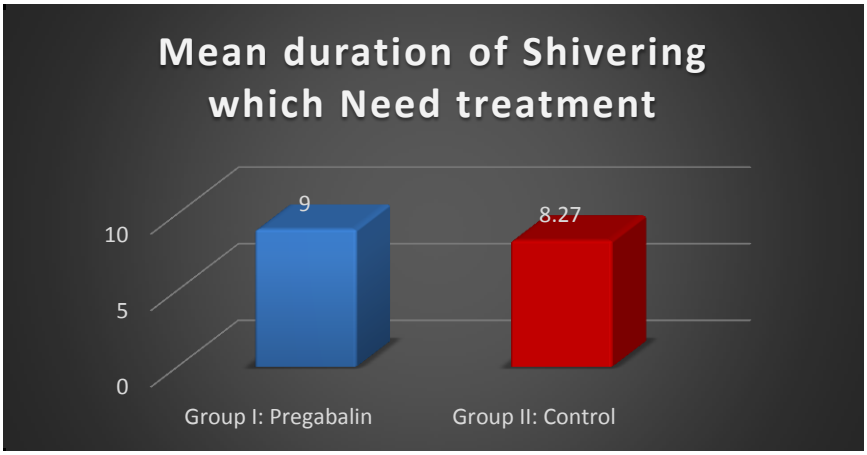

Fig. (9): Bar chart between groups according to duration of shivering which need.

Table (14): Comparison between groups according to mean dose of pethidine used for management of shivering score 3 and 4

Mean dose of Pethidine	Group I: Pregabalin (N=3)	Group II: Control (N=15)	t-test	p-value
Total dose of pethidine (mg)	70 mg	340 mg	0.049	0.827
Mean±SD	23.33±5.77	22.67±4.58		
Range	20-30 mg	20-30 mg		

This table shows no statistically significant difference between groups according to mean dose of pethidine used for management of shivering score 3 and 4 in both groups.

DISCUSSION

General anesthesia facilitates redistribution of the temperature from the central tissues to the peripheral tissues. Due to anesthesia, core temperature regulation responses like the vasoconstriction threshold are controlled, and most anesthetic drugs cause peripheral vasodilatation [(2)]. Shivering could be the result of hypothermia readjustment of body core temperature during surgery, or because of fever and shivering, which could lead to activation of the inflammatory response and cytokine release [(3)].

Pregabalin is a GABA analogue. It has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. It reduces excitability of dorsal horn neurons after tissue damage. Pregabalin has been proven to improve various aspects of recovery after surgery. It has high oral bioavailability (90%), more rapid absorption (peak plasma level: 1 hr.) and linear increase in plasma concentration when its dose is increased. The use of Pregabalin in the perioperative setting has been evaluated in many studies. These studies report promising reductions in postoperative morphine consumption [(5-7)]. To our knowledge no randomized controlled study has been done to evaluate the effect of pregabalin as an oral premedication on post anesthesia shivering.

In the present study there were no significant demographic differences between both groups according to age, sex, BMI, and ASA group.

As regard the anesthetic time there was no statistically significant difference between both groups. We also found no significant difference between groups according to intraoperative requirements of additional fentanyl dose. Meena ***et al***, [(10)] were against that as they found that the preoperative administration of oral pregabalin 300mg significantly reduces the intraoperative fentanyl requirements and end-tidal isoflurane concentrations required to maintain an adequate depth of anesthesia. Regarding the recovery time there was no statistically significant difference between both groups. However, mean recovery time was shorter (8.22±3.66) with control than with pregabalin (9.02±3.83).In our study regarding HR, SBP and DBP there was no significant difference between both groups. However, we found reduction in SBP and DBP in both groups after induction which became back up at the end of surgery. This was the same result reported by Gupta ***et al.*** [(11)] as they found that there was no statistically significant difference between pregabalin 150mg to placebo and no statistically significant attenuation of heart rate in pregabalin group.

The trend of tympanic temperature changes in the patients has been shown in (fig.1). We found that the tympanic temperature reduction was recorded intraoperatively and came back up during recovery period. Comparing two groups regarding tympanic temperature there was no statistically significant.

The current study reports valuable preventive effect on shivering for pregabalin group (8.1%) compared to control group (44.3%), and there was highly significant difference between both groups according to incidence and scoring of shivering as showed in (table 11). **Ozgencil *et al.*** [(8)] reported that although postoperative shivering was not part of their original study design, it was apparent in the course of the study that incidence of shivering differed among the groups, patients in the placebo group were found to experience more postoperative shivering than those in the pregabalin group.

According to timing of shivering we found that maximum number of patients with shivering in both groups was on arrival to PACU, and there was no shivered patient after 30 min of recovery in both groups. The same reported by **Zahedi** [(12)] as he found that the incidence of shivering is highest in the first 30 min of recovery. This was consistent with the findings of our study which showed that the maximum number of patients suffered from shivering on arrival in the PACU and in vast majority of patients, the PAS had disappeared within 30 min of arrival in the PACU.

In our study we recorded the total duration of significant shivering (grade 3 and 4 that need treatment) in both groups and pregabalin group showed greater reduction than control group, 27 min and 124 min respectively. However, there was no statistically significant difference between groups according to mean duration of shivering.

As deleterious effects of PAS are related to its severity, active treatment is indicated in more severe forms to minimize these effects. We recorded the severity of PAS with BSAS score 1 and 2 not requiring treatment, while score 3 and 4 significant and requiring treatment with pethidine intravenous bolus.Dose of pethidine required to treat significant PAS was comparable in both groups with control group (70 mg) greater than pregabalin group (340 mg) but this considered statistically insignificant difference between both groups as regarding to mean (mean±SD) dose of pethidine used for management of shivering score 3 and 4 and it was (23.33±5.77) in pregabalin and (22.67±4.58) placebo group.

About PONV in this study we found that there was mild significance difference between groups about no nausea or vomiting and with nausea. But

moderate significance difference between groups at nausea & vomiting. Similarly, in the meta-analysis of **Lam *et al.*** [13] the incidence of postoperative vomiting was significantly lower with the use of pregabalin. Also in the meta analysis of **Zhang *et al*.** [14] combined data showed that patients who received pregabalin were at a lower risk of vomiting. Regarding other side effects analyzed were dizziness, blurring of vision & drowsiness occurring in the 3 hours after surgery. There were statistically significant differences between two groups, as patients of pregabalin group developed dizziness, drowsiness and blurred vision more than placebo group with statistically significant differences.

We also recorded headache, pruritis, and respiratory depression, and there were no statistically significant differences between both groups. Although, pregabalin group showed more patients with headache and respiratory depression but less patients with pruritis. These results came in agreement of the previous study of **Paech *et al.*** [15] who found that a single preoperative dose of pregabalin 100 mg gave similar pain relief with increasing of side effects, such as confusion, dizziness and dry mouth than placebo in patients scheduled for day case gynecological surgery. Also **Griffin & Browen** [16] reported that dizziness, fatigue, and somnolence were among the most common adverse effects of pregabalin. And Park ***et al.*** [17] who found that perioperative administration of 600 mg pregabalin was associated with an increased incidence of dizziness, blurred vision, and headache.

CONCLUSION

Pre-operative administration of oral pregabalin adequately prevent post anesthesia shivering but could not affect its timing nor mean dose of pethidine used. Additionally, oral pregabalin reduced postoperative nausea and vomiting but increased significantly the incidence of dizziness, blurred vision and drowsiness.

RECOMMENDATIONS

1. The need for more clinical studies to justify the best appropriate dose and timing for pregabalin use in prevention of PAS to get maximum effect and least side effects.
2. Further studies should be promoted to compare the long-term effects of pregabalin on PAS and its complications as our study was limited to recovery period.
3. Further studies should be promoted on prolonged operations to compare intraoperative requirements of fentanyl.
4. Further studies should be promoted to evaluate the additive effect of different doses of pregabalin premedication to other drugs commonly used during anesthesia.

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