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Preemptive Analgesia for Attenuation of Postoperative Pain in Patients Undergoing Hip Surgery under Spinal Anesthesia: A Comparative Study between Pregabalin and Gabapentin

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Abstract: *Pain is a sensation which makes most of the patients to move to a hospital. One of the biggest concerns for the patients undergoing surgery as well as for the anaesthetists going to anaesthetize them. The duty of an anaesthetist giving spinal anesthesia to a patient is to make the patient pain free postoperatively when effect of spinal anesthesia disappears. Many methods are being used to give analgesia postoperatively. Pre-emptive analgesia is one of them in which drugs are given before giving an incision in order to provide analgesia postoperatively. Pregabalin and Gabapentin both are effective as pre-emptive analgesia but neither of the drugs provided long term pain relief. Long term pain relief through pre-emptive analgesia will be a boon for patients if achieved. Search is still on for the pharmacological agents which can be used pre-emptively to provide adequate analgesia postoperatively.*

Keywords: *analgesia, Gabapentin, Hip Surgery, Preemptive, Pregabalin*

I. Introduction

Pre-emptive Analgesia has been defined as treatment that starts before surgery, prevents the establishment of central sensitization caused by incisional injury (covers only the period of surgery), and prevents the establishment of central sensitization caused by incisional and inflammatory injuries (covers the period of surgery and the initial postoperative period).[1] It is an antinociceptive treatment that prevents the establishment of altered central processing, which amplifies postoperative pain.

Various studies and meta-analysis have explored the use of Gabapentin in the field of pre-emptive analgesia. The number of studies using Pregabalin is comparatively less. The number of studies comparing the two drugs is fewer still. It has been seen that not only do both the drugs provide postoperative pain relief, they also reduce the requirements of other analgesics.[2,3,4,5,6]

Gabapentin and Pregabalin, are structural analogues of the inhibitory neurotransmitter Gamma-Amino Butyric acid (GABA), but are functionally not related to it. Both drugs were introduced in the treatment of epilepsy, Gabapentin in 1993-94 and Pregabalin in 2004. Anecdotal reports were followed by randomized controlled trials proving these drugs to be useful in treating neuropathic pain like that of diabetic neuropathy, trigeminal neuralgias, post herpetic neuralgia and reflex sympathetic dystrophy. The mechanism of action of Pregabalin is probably the same as Gabapentin but it has a superior pharmacokinetic profile.[1,4]

II. Objectives

Primary purpose

To evaluate post-operative analgesic benefits in patients receiving gabapentin or pregabalin pre-emptively, posted for elective hip surgery under spinal anesthesia and to compare their post-operative efficacy with respect to

- Increase in duration of postoperative analgesia.
- Reduction in total postoperative requirement of analgesics.

Secondary purpose

To compare gabapentin and pregabalin regarding:

- Hemodynamic changes intra-operatively and post-operatively.
- Sedative effects.
- Intra-operative and post-operative complications.
- Side effects, if any.

This study was a randomized, prospective, double blinded, controlled study.

III. Sample Selection

120 patients of ASA grade I and II between 30 – 60 years of age of either sex admitted in BGH, Bokaro Steel City (Jharkhand), scheduled for hip surgeries were included in the study. The study protocol was approved by institutional ethical and scientific committee and written informed consent was obtained from all patients.

Inclusion criteria:

- ASA Grade I and II
- Age between 30-60 years
- Either sex
- Scheduled for elective hip surgery under spinal anesthesia
- Who gave their free consent for participation in the study

Exclusion criteria:

- Patient's refusal
- ASA Grade III and IV
- Age < 30 years or > 60 years
- Patients with central nervous system disorders
- Patients with coagulation abnormalities and bleeding disorders
- Patients having cardiac diseases
- Patients with h/o of chronic pain using regular analgesics, sedatives and anticonvulsants
- Patients with hypersensitivity to these drugs
- Patients with impaired renal function

The sample group of 120 was randomly divided into three groups of 40 patients each (group P, group G and group C) using computerized randomization prior to commencement of the study.

- **Group G**: Patients in this group received, Oral Gabapentin, 900mg, 1 hour prior to surgery, with a sip of water.
- **Group P**: Patients in this group received, Oral Pregabalin, 300mg, 1 hour prior to surgery, with a sip of water.
- **Group C**: Patients in this group received, Oral Placebo capsule, 1 hour prior to surgery, with a sip of water.

IV. Methodology

A methodical pre-anesthetic check up and assessment was performed which included – detailed history, general, systemic and airway examinations and relevant baseline investigations.
All patients were kept fasting overnight (6-8 hrs) prior to surgery.

All patients were premedicated with tab ranitidine 150mg per oral night before the surgery and tab ranitidine 150mg and tab metoclopramide 10mg per oral in the morning 1 hr prior to surgery. All doses of Gabapentin, Pregabalin and placebo were given per oral one hour prior to the administration of spinal anesthesia.

In the pre-operative hold patients were monitored for basal heart rate (HR), respiratory rate (RR), non invasive blood pressure (NIBP), mean arterial pressure (MAP) and peripheral oxygen saturation (SpO2). Intravenous access was obtained on the forearm with 18 Gauge IV cannula and patient was preloaded with an i.v. infusion of one litre of ringer lactate solution in preoperative area.

On arrival in operating room each patient was identified and then placed on a tilting operation table. Spinal anesthesia was performed with the patient in sitting position. After positioning puncture site was infiltrated with 2% Lignocaine. SAB was performed under strict aseptic and antiseptic measures using a 25-gauge Quincke's needle at L_3-L_4 or L_4-L_5 intervertebral space through midline approach. 3ml of hyperbaric bupivacaine(0.5%) was administered over 15-20 secs. A sterile pack was applied at the puncture site after removal of the spinal needle and the patient was placed gently in supine position. After the spinal block HR, RR, NIBP, MAP and SpO2 were measured every 5 mins. intraoperatively and then every 15 mins. in postoperative period.

Hypotension was defined as 20% decrease in blood pressure from baseline values, and was treated with fluid replacement and incremental i.v. boluses of Ephedrine 5–10 mg. Bradycardia was defined as heart rate less than 50bpm and treated with i.v. atropine.

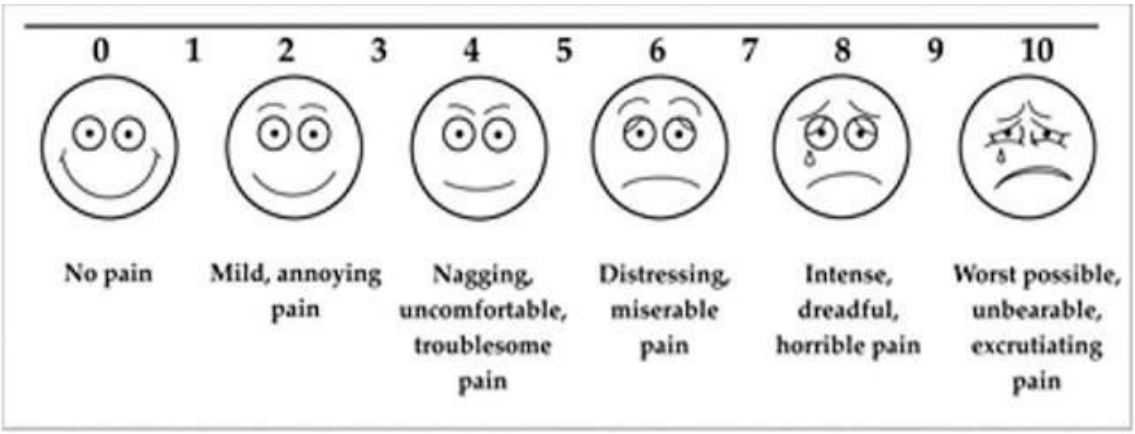
The maximum height of sensory block was assessed by pin prick method using sterilized needle. Time to first complaint of pain and request for rescue analgesia was recorded. Patient's pain was assessed immediate postoperatively and then at 2, 4, 6, 12 and24 hours by visual analogue Scale (VAS) and dose of rescue analgesic

drug was measured during these intervals of time. Sedation score was assessed by Ramsay sedation score[62]immediate postoperatively then at 2, 4, 6, 12 and 24 hours.

V. Ramsay Scale For Rating Sedation

SCORE	INDICATION
1	Anxious**,** agitated or restless
2	Co-operative, oriented & tranquil
3	Sedated, but responds to commands
4	Asleep, brisk glabellar reflex or response to loud noise
5	Asleep, sluggish glabellar reflex or response to loud noise
6	Asleep with no response to painful stimulus

VI. Visual Analogue Scale For Pain Assessment



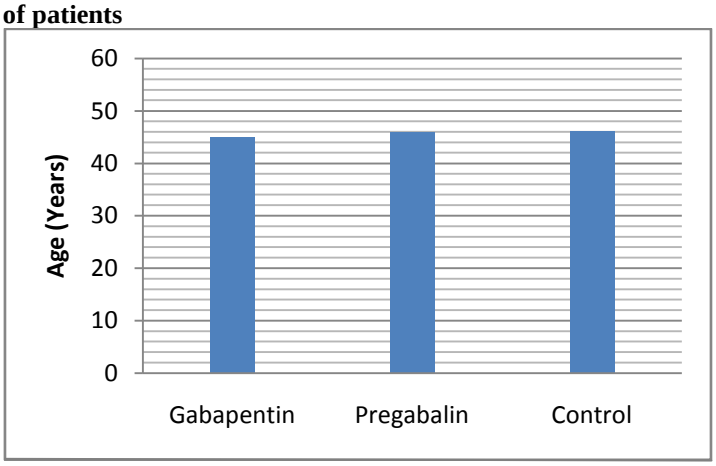
VII. Results

- Proper template was generated for data entry in Ms Excel. Data analysis was performed using SPSS (Statistical Package for Social Sciences) software version 13.0 for windows
- Chi-square test was utilized to compare discrete variables (A test of association between two events in binomial samples)
- ANOVA Was used to compare different parameters like means of BP, HR, RR, SpO_2, VAS score and sedation score along time between groups.
- Irrespective of methods used, differences between various parameters among different groups or sub-groups were considered significant if the p-value was <0.05. If p-value was > 0.05 then the differences were considered statistically insignificant.

Age wise distribution of patients

Age in years	Group G	Group P	Group C
	n = 40	n = 40	n = 40
30 - 40	14	11	12
41 - 50	15	18	14
51 - 60	11	11	14
Total	40	40	40
Mean ± SD	44.90±7.79	45.97±7.20	46.12±7.60
P-value	0.839		

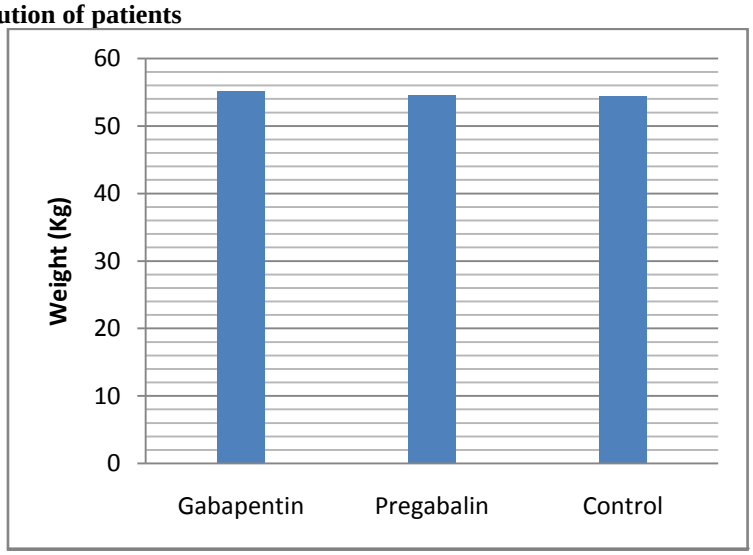
Age wise distribution of patients



Weight wise distribution of patients

Weight in (kg)	Group G	Group P	Group C
	n=40	n=40	n=40
40 – 50	19	14	17
51 - 60	13	19	16
61 - 70	5	6	7
71 - 80	3	1	0
Total	40	40	40
Mean ± SD	55.10±8.76	54.62±7.18	54.42±6.47
P-value	0.455		

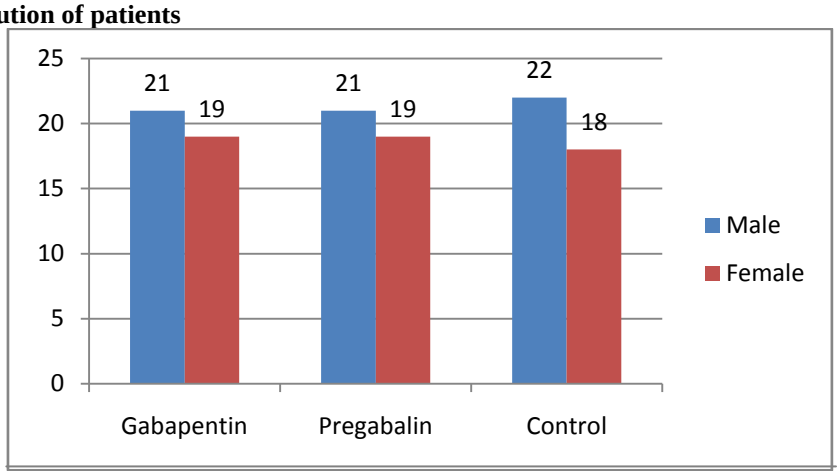
Weight wise distribution of patients



Sex wise distribution of patients

Sex	Group G	Group P	Group C
	n=40	n=40	n=40
Male	21	21	22
Female	19	19	18

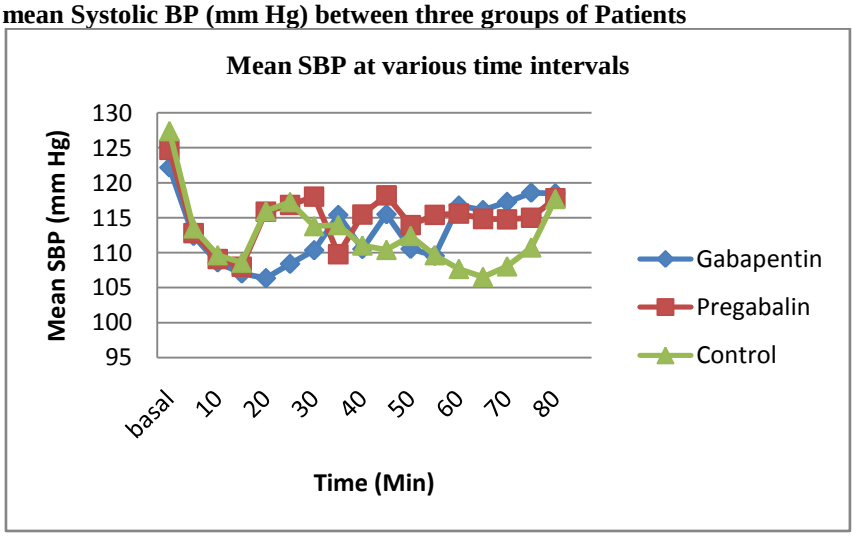
Sex wise distribution of patients



Comparison of mean Systolic BP (mm Hg) between three groups of Patients

SBP (mm Hg)	Group G	Group P	Group C	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Basal	122.20±8.60	124.72±6.34	127.40±5.11	0.004
5 min	112.40±8.23	112.80±5.92	113.50±5.47	0.756
10 min	108.60±7.52	109.10±6.23	109.67±6.35	0.777
15 min	107.02±8.20	108.00±6.61	108.60±6.29	0.603
20 min	106.35±5.69	115.87±6.23	115.97±6.11	0.000
25 min	108.40±6.08	116.85±5.52	117.27±4.68	0.000
30 min	110.35±6.84	118.02±6.95	113.82±4.88	0.000
35 min	115.40±6.89	109.77±7.47	113.97±7.62	0.002
40 min	110.52±7.67	115.47±7.41	111.05±8.04	0.008
45 min	115.50±6.33	118.20±8.07	110.42±7.47	0.000
50 min	110.55±7.65	113.95±8.91	112.42±4.90	0.121
55 min	109.55±5.98	115.42±9.08	109.67±8.03	0.001
60 min	116.75±6.39	115.60±8.63	107.70±8.08	0.000
65 min	116.10±6.57	114.85±7.20	106.55±5.41	0.000
70 min	117.27± 5.03	114.77±7.20	108.07± 6.19	0.000
75 min	118.60± 6.65	115.00 ± 7.26	110.77± 6.94	0.000
80 min	118.50 ±6.17	117.80±5.67	117.70±4.77	0.783

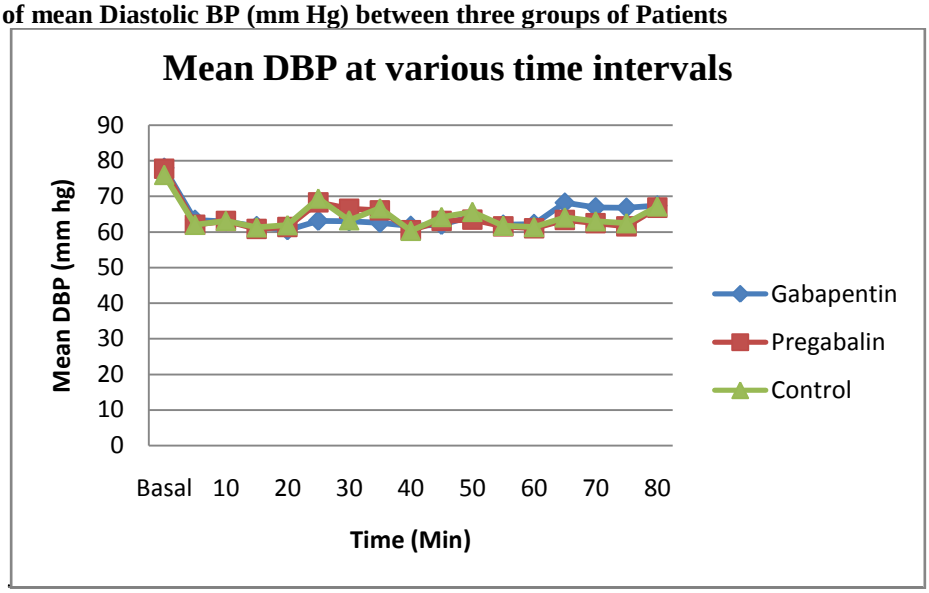
Comparison of mean Systolic BP (mm Hg) between three groups of Patients



Comparison of mean Diastolic BP (mm Hg) between three groups of Patients

DBP (mm Hg)	Group G	Group P	Group C	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Basal	77.97 ± 7.84	77.77 ± 8.87	76.02 ± 5.55	0.448
5 min	63.35 ± 10.01	62.02 ± 6.23	61.97 ± 5.66	0.652
10 min	62.90 ± 7.28	63.05 ± 7.37	63.07 ± 7.33	0.994
15 min	61.57± 9.59	60.80 ± 7.37	61.27 ± 7.47	0.914
20 min	60.45 ± 7.47	61.37 ± 6.98	61.87 ± 6.92	0.666
25 min	63.10 ± 7.51	68.30 ± 8.14	69.37 ± 8.28	0.001
30 min	62.95 ± 9.54	66.52 ± 6.83	63.25 ± 7.25	0.089
35 min	62.52 ± 9.55	66.02 ± 6.29	66.62 ± 6.15	0.034
40 min	61.65 ± 9.94	60.47 ± 9.18	60.27 ± 8.86	0.775
45 min	61.95 ± 7.98	63.07 ± 10.25	64.17 ± 9.61	0.569
50 min	64.40 ± 8.28	63.45 ± 7.39	65.60 ± 4.42	0.380
55 min	61.97 ± 7.71	61.52 ± 9.75	61.70 ± 10.61	0.977
60 min	62.17 ± 8.01	61.00 ± 7.80	61.35 ± 7.82	0.793
65 min	68.17 ± 7.84	63.37 ± 7.82	64.05 ± 8.07	0.016
70 min	66.87 ± 6.60	62.45 ± 9.33	62.97 ± 9.54	0.046
75 min	66.75 ± 7.25	61.57 ± 9.29	62.42 ± 9.34	0.019
80 min	67.35 ± 7.42	66.82 ± 8.32	67.15 ± 5.90	0.947

Comparison of mean Diastolic BP (mm Hg) between three groups of Patients

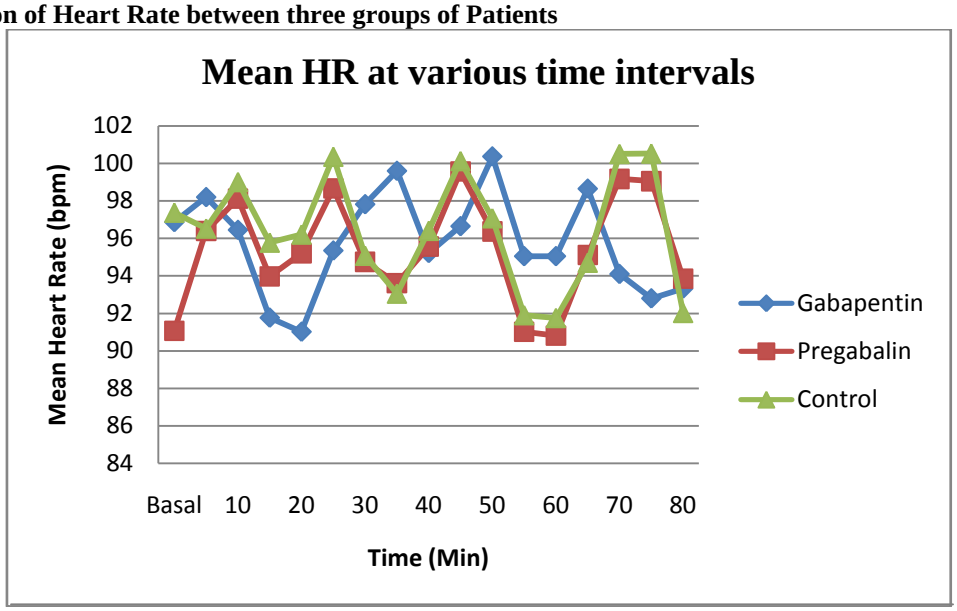


Comparison of Heart Rate between three groups of Patients

Time (min)	Group G	Group P	Group C	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Basal	96.87±12.49	91.07±13.87	97.37±10.87	0.046
5 min	98.20±16.14	96.40±15.50	96.52±14.17	0.841
10 min	96.45±10.88	98.12±13.99	99.00±13.34	0.665
15 min	91.77±13.87	93.97±13.40	95.77±11.58	0.389
20 min	91.02±15.41	95.20±12.94	96.20±11.60	0.191
25 min	95.35±14.08	98.67±9.48	100.35±9.39	0.131
30 min	97.82±14.94	94.75±11.59	95.07±12.10	0.509
35 min	99.60±15.06	93.62±10.98	93.05±11.03	0.038
40 min	95.22±12.52	95.57±12.53	96.40±13.62	0.916

45 min	96.65±16.13	99.57±16.64	100.12±15.79	0.590
50 min	100.37±14.68	96.37±10.88	97.07±10.63	0.297
55 min	95.05±12.91	91.02±14.72	91.90±13.35	0.386
60 min	95.05±11.54	90.82±15.66	91.75±15.45	0.386
65 min	98.65±9.71	95.12±15.30	94.70±15.15	0.367
70 min	94.10±11.95	99.17±14.72	100.50±13.91	0.089
75 min	92.80±12.02	99.05±15.57	100.52±15.03	0.041
80 min	93.32±10.20	93.85±10.26	92.02±7.48	0.670

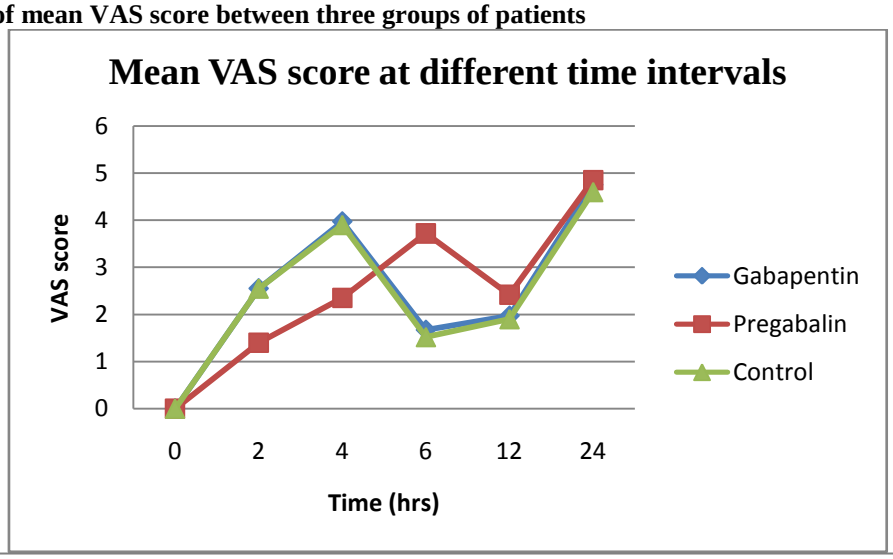
Comparison of Heart Rate between three groups of Patients



Comparison of mean VAS score between three groups of patients

VAS (Hrs)	Group G	Group P	Group C	P value
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	
0	0	0	0	0.000
2	2.55 ± 0.63	1.40±0.49	2.55±0.50	0.000
4	3.97±0.83	2.35±0.57	3.90±0.81	0.000
6	1.67±0.61	3.72±0.84	1.52±0.59	0.000
12	1.97±0.76	2.42±0.59	1.90±0.70	0.002
24	4.75±1.23	4.85±1.02	4.60±1.12	0.608

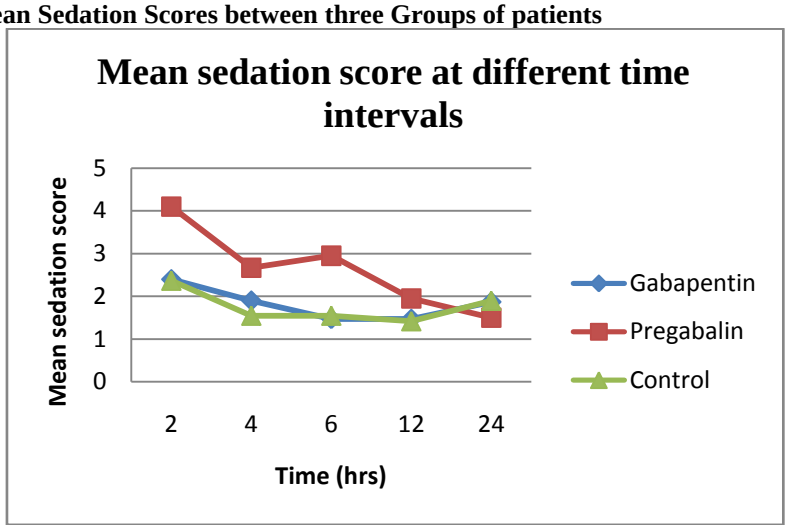
Comparison of mean VAS score between three groups of patients



Comparison of mean Sedation Scores between three Groups of patients

Sedation score (Hrs)	Group G *Mean ± SD*	Group P *Mean ± SD*	Group C *Mean ± SD*	P-value
2	2.40±0.54	4.10±0.81	2.37±0.49	0.000
4	1.90±0.77	2.67±0.65	1.55±0.50	0.000
6	1.47±0.50	2.95±0.71	1.55±0.50	0.000
12	1.47±0.50	1.95±0.81	1.42±0.50	0.000
24	1.87±0.51	1.50±0.50	1.90±0.54	0.001

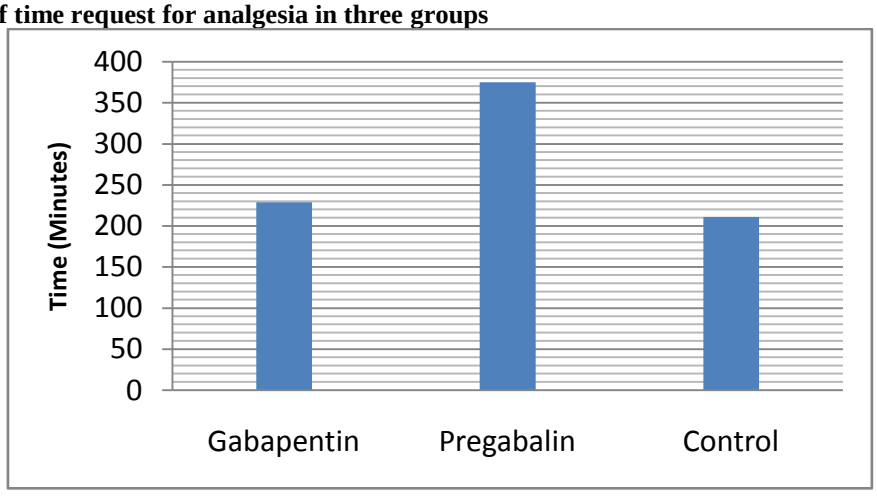
Comparison of mean Sedation Scores between three Groups of patients



Comparison of time request for analgesia in three groups

Time in (min)	*Group G*	*Group P*	*Group C*
100 – 200	*12*	*0*	*17*
201- 300	*28*	*6*	*23*
301 – 400	*0*	*25*	*0*
401 - 500	*0*	*9*	*0*
Mean ± SD	229.00±51.97	375.00±47.23	211.00±28.89
P-value	*0.000*		

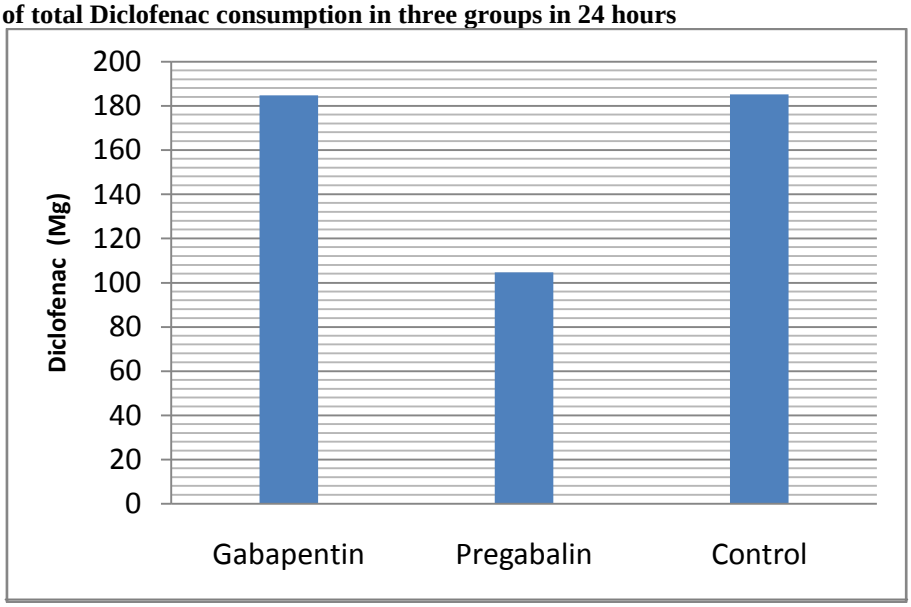
Comparison of time request for analgesia in three groups



Comparison of total Diclofenac consumption in three groups in 24 hours

Diclofenac *(mg)*	*Group G*	*Group P*	*Group C*
50- 100	*0*	*23*	*0*
110- 200	*29*	*17*	*34*
210 – 300	*11*	*0*	*6*
Mean ± SD	184.75±42.25	104.75±18.53	185.25±34.56
P value	*0.000*		

Comparison of total Diclofenac consumption in three groups in 24 hours



Incidence of side effects in three groups G, P & C

Groups	Total	Side effects no. (%)		
		Sedation	PONV	Other Side Effects
Group G	40	9 (22.5%)	5 (12.5%)	-
Group P	40	14 (35%)	-	-
Group C	40	-	-	-

VIII. Conclusions

- As compared to the control the study drugs (Gabapentin and Pregabalin) did not have any pre-operative anxiolytic effect in the doses used for the study.
- Giving Gabapentin or Pregabalin to the patients pre-emptively did not alter the hemodynamic status of patients intraoperatively as compared to the control group.
- It was observed that analgesic requirement was more in the Control group, suggesting thereby the possible analgesic sparing effect of Gabapentin and Pregabalin.
- Gabapentin and Pregabalin can be considered as effective pre-emptive analgesics but in the doses used neither drug provided long term pain relief.
- Pregabalin has superior efficacy in respect to quality and duration of analgesia as compared to gabapentin.
- The major side effect noted was sedation in the immediate post-operative period with both study drugs. The sedation observed was not disabling. Gabapentin caused an increase in PONV.
- We conclude that both Gabapentin (900mg) and Pregabalin (300mg) are effective pre-emptive analgesics for short duration surgeries. Further studies using higher or divided doses can be suggested to increase quality and duration of analgesia.

References

[1]. Kissin I. Preemptive analgesia. Anesthesiology. 2000;93:1138– 43.
[2]. Gottschalk A, Smith DS. New concepts in acute pain therapy. Preemptive analgesia. Am Fam Physician 2001;63:1979-84,1985-6.
[3]. Tiippana EM, Hamunen K, Kontinen VK, Kalso E. Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. AnesthAnalg 2007; 104:1545-56.
[4]. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty D. A randomized placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery; Anesth Analg 2007;105:1449-53.
[5]. Peng PWH, Wijeysundera DN, Li CCF. Use of gabapentin for perioperative pain control - A meta- analysis. Pain Res Manage. 2007;12(2):85-92.
[6]. Mathiesen O, Moiniche S, Dahl JB. Gabapentin and postoperative pain: a qualitative and quantitative systematic review, with focus on procedure. BMC Anesthesiology. 2007;7:6.
[7]. Jokela R, Ahonen J, Tallgren M, Haanpa M, Korttila K. Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynecological laparoscopic surgery. Br J Anaesth. 2008;100: 834-40.