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Original Article

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A Study of Preemptive Analgesia Caused By Oral Gabapentin and Oral Clonidine under Spinal Anaesthesia for Lower Limb and Abdomino-Pelvic Surgeries

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ABSTRACT

Study Objective: To compare the post-operative analgesic efficacy, pre-operative sedation and perioperative anxiety reduction of oral Gabapentin and oral Clonidine in abdomino-pelvic and lower limb surgeries done under spinal anaesthesia.

Design: Prospective randomized comparative study.

Materials and Methods: 60 patients belonging to ASA physical status I and II of both sexes (each group 30 patients) were randomly selected for the study.Group G patients received 300 mg Gabapentin orally and Group C patients received 100 microgram Clonidine orally 120 minutes before surgery. Preoperative sedation, post operative analgesia, perioperative anxiety and adverse effects were compared in both the groups.

Results: Group G showed better VAS readings of 2.33±0.92 in comparison to 5.7±1.29 of Group C at the 6th hour postoperatively. The p value was 0.0001 which is considered significant. Rescue analgesia was more associated with Group C (2.16±0.91) when compared to Group G (1.4±0.49) showing a p value of 0.0002, which is considered significant. The Ramsay sedation score which was used in this study showed a better sedative effect by Gabapentin than Clonidine in the preoperative period. Gabapentin group showed significant sedation at 120 minutes with a p value of 0.0001.

Hospital anxiety and depression score which was used in this study was significantly less in group G patients than group C patients. And remained less upto 24 hours post surgery with a value of 0.0001

Side effects like nausea and vomiting were more associated to Group C as compared to Group G but dizziness was more associated with patients receiving Gabapentin than Clonidine.

Conclusion: Our study shows that Gabapentin is a better adjuvant for providing preemptive analgesia than Clonidine. Gabapentin also showed lesser incidence of side effects.

Key Words: *Post operative analgesia ; spinal anaesthesia ; Gabapentin Clonidine*

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INTRODUCTION

"Pain is perfect miserie, the worst of evils; and, excessive, overturns all patience"- John Miller (Paradise Lost) The International Association for the Study of Pain has proposed a working definition: Pain is "an unpleasant sensory and emotional experience associated with either actual or potential tissue damage, or described in terms of such damage"[1].

Anaesthesia as a subject by itself originated in an endeavor to offer pain relief to the patient during surgical procedures. Most pain resolves once the noxious stimulus is removed and the body has healed, but it may persist despite removal of the stimulus and apparent healing of the body [2].

Acute pain following surgery has been managed inadequately because of wide variety of myths and fears. The incidence of post operative pain has been found to be between 25%-76%. This uncontrolled pain in postoperative period has some adverse physiologic responses and effects like delayed recovery and chronic pain.

In the earlier periods analgesia was restricted to surgical and postoperative period. However this was associated with lots of morbidity to the patient in terms of surgical stress and increased requirements for analgesics in the postoperative period which were associated with various adverse effects.

The concept of preemptive analgesia is administering an analgesic drug prior to a noxious stimulus such as surgical

skin incision. Various drugs like opioids, NSAIDs, antiepileptic drugs are being used for purpose of preemptive analgesia. Anxiety is an unpleasant emotion and may cause patients to avoid planned operation. It may also adversely influence anaesthetic induction and patient recovery. Controlling anxiety being a modifiable aspect, can be considered as a part of treatment of pain.

Gabapentin is a GABA analogue which was introduced as an anti-epileptic and later proved to be effective in neuropathic pain. More recently, it has been studied to treat acute post operative pain. it was observed that it attenuates pre-operative anxiety and stress response to intubation.

Clonidine is a selective central α2 agonist and is a antihypertensive drug. Clonidine premedication is known to produce sedation and reduce the requirement of postoperative analgesics.

Hence present study was designed to study and compare the effects of oral Gabapentin and oral Clonidine on pre-operative sedation, anxiolysis and post operative analgesia when used along with central neuraxial blockade.

MATERIALS AND METHODS

Ethical clearance It was obtained from institutional Ethical Committee of Govt Medical College, Kota. Study was carried out from 1st June, 2021 to 31st October, 2022.

Study Design: A prospective randomized comparative study.
Sample size: 60 patients, 30 patients in Group C (Clonidine) and 30 patients in Group G (Gabapentin) .

Sample population of study: Adult patients scheduled to undergo elective surgical procedures for lower limb and abdomino-pelvic surgeries under spinal anaesthesia in attached Hospitals of Govt. Medical College, Kota. Patients taken into study were posted for Surgical, Orthopedic, Gynaecological procedures under spinal anaesthesia or sub arachnoid block.

Inclusion criteria: ASA grade I and II, 18-60 years of age. Patients who consented, Patients scheduled to undergo elective surgical procedures under spinal anaesthesia. Patients from both sex.

Exclusion criteria: Pregnant, lactating and menstruating females.

Patients with chronic pain, psychiatric disease, peripheral vascular disease. Patients with severe renal or hepatic disease. Patients refusal for spinal anaesthesia. Local infection at injection site, neurological deficit, neuropathic pain,coagulopathy,Chronic hypertensive taking study medication as a treatment. Patient known to be sensitive or allergic to Clonidine & Gabapentin

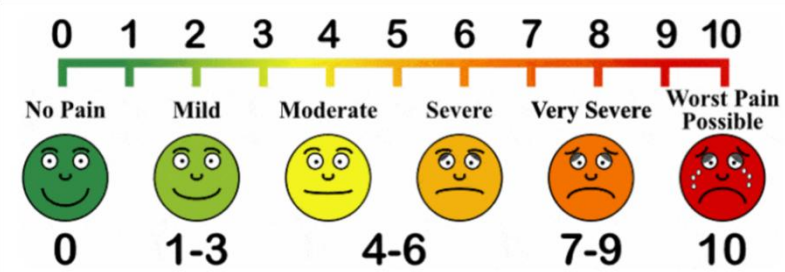
Consent: Written informed consent was taken from all the patients.

Methods: All 60 patients were assessed the day before surgery.

1) Tablet of Gabapentin (300 milligrams) was given for Group G patients. 1 Tablet of Clonidine (100 micrograms) was given for Group C patients. The tablets were given to the patient by the attending anaesthesiologist with sips of water 120 minutes before spinal anaesthesia in the preoperative ward. The identity of the tablet was not revealed to the patient. No other premedication was given other than the study drugs.

Visual analogue score (0= no pain, 10= worst imaginable pain) was explained to them. Upon arrival in the operating room, firstly baseline reading of all vital parameters were taken. Monitoring of non invasive blood pressure (NIBP), heart rate, electrocardiogram and arterial oxygen saturation was carried out. Anaesthesia was achieved by spinal anaesthesia technique with Quincke spinal needle.

Parameters observed were:



Visual analog scale

I	Anxious, agitated, restless.

II	Cooperative, oriented, tranquil.
III	Responds to commands only.
IV	Brisk response to light glabellar tap or loud noise.
V	Sluggish response to light glabellar tap or loud noise.
VI	No response.

Modified Ramsay sedation scale:

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) _____ Anxiety (A) _____
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

- HADS anxiety scores, heart rate and baseline mean blood pressure, orientation level of the patient before giving the drug orally in the ward on the morning of surgery.
- Heart rate, mean BP ,sedation after one hour of taking the drug
- HADS anxiety scores, heart rate, mean BP and sedation level just before taking the patient to OT or after two hours of taking the test drug.
- Heart rate, mean BP, throughtout the duration of operation procedure at 30 minutes interval upto 120 min.
- Occurence of side effects of Gabapentin and Clonidine like dizziness, nausea and vomiting were recorded if any.
- Post-operatively, patient's pain will be assessed using Visual Analogue Score at just after OT, 2, 4, 6 hours after surgery.
- The number of rescue analgesic medications the patient received in 24 Hours after surgery were noted.

STATISTICAL ANALYSIS [3, 4, 5 & 6]

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max). Student t test (two tailed, independent) has been used to find the significance of study parameters between two groups.

Significant figures
+ Suggestive significance (P value: 0.05< P<0.10)
* Moderately significant (P value: 0.01< P<0.05)
** Strongly significant (P value: P<0.01)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Table no 1: Age, Weight, Sex and ASA wise distribution of patients

Variables	Group G (n=30)	Group C (n=30)
Age (years)	43.56±12.67	42.16±13.41
ASA I/II	18/12	15/15
Sex(Male/Female)	18/12	14/16

The two groups were comparable with respect to demographic profile including mean age, sex, and ASA physical status.

Table no 2: Post operative pain assessment using VAS

VAS	Group G	Group C	P value
	Mean ±SD	Mean ±SD	
Just after Surgery	0.36±0.49	0.9±0.71	0.0013
2 hrs	0.96±0.80	3.5±1.30	0.0001
4 hrs	1.53±1.0	4.33±1.34	0.0001
6 hrs	2.33±0.92	5.7±1.29	0.0001

Table no 2: Showing post operative pain assessment after surgery using vas scale. after 6 hours Gabapentin group patients showing significantly less vas score than group Clonidine patients with a p value of 0.0001

Graphical representation of Post operative pain assessment using VAS

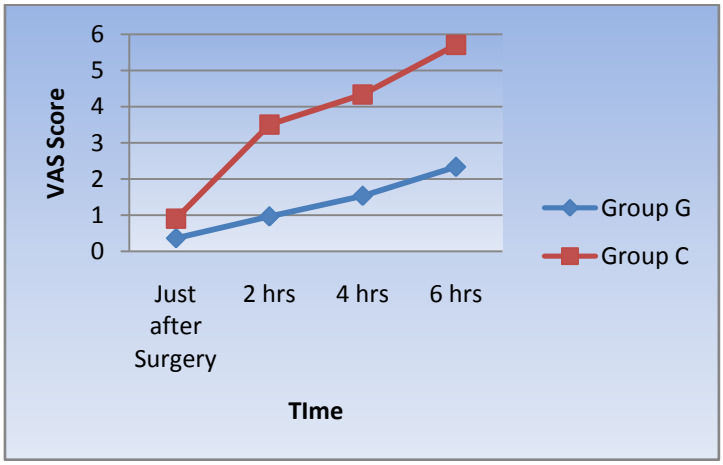


Table no 3: Rescue Analgesia

	Group G	Group C	P value
	Mean ±SD	Mean ±SD	
Rescue Analgesia	1.4±0.49	2.16±0.91	0.0002

Table no 3: showing need for rescue analgesia after surgery which was significantly lower in Gabapentin group patients as compared to Clonidine group patients with a p value of 0.0002 upto 24 hours post operatively

Table No 4: Observation of changes in sedation with Modified Ramsay Sedation Scale

Modified Ramsay Sedation Scale	Group G	Group C	P value
	Mean ±SD	Mean ±SD	
Baseline	1.7±0.46	1.56±0.50	0.2918
1 hr before	3.1±1.09	1.73±1.04	0.0001
Just before OT	3.2±0.88	1.53±0.68	0.0001

Table No. 4 showing Comparison of two groups with Modified Ramsay Sedation Scale at baseline, after 1 hour and just before OT after drug administration. Study depicted better sedative effect in Gabapentin Group patients as compare

to Clonidine Group patients after 1 hour and 2 hour of drug administration with a p value of 0.0001

Line graph comparison of Sedation score in two groups of patients studied.

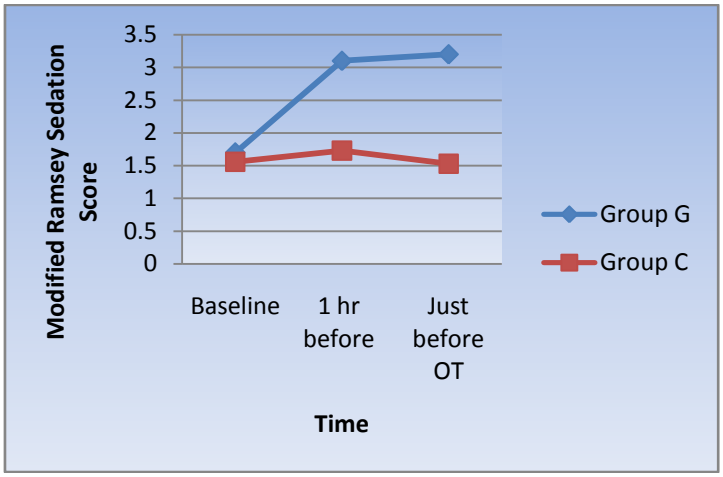


Table No 5: Observation of changes in Anxiety with Hospital Anxiety and Depression Scale (HADS)

HADS	Group G	Group C	P value
	Mean ±SD	Mean ±SD	
Baseline	8.93±1.59	9.4±1.47	0.2445
Just before OT	6.86±1.27	9.23±1.65	0.0001
Post operative			
Just after OT	8.33±1.29	10.73±1.66	0.0001
6 hrs	7.56±0.67	11.43±2.48	0.0001
24 hrs	6.66±0.80	11.1±2.17	0.0001

Table No.5 Showing Comparison of two groups with respect to Anxiety with Hospital Anxiety and Depression Scale, which was decrease in Group G as compared to Group C after 2 hours of drug administration, and remained decreased for post operative period upto 24 hours in group G than group C with p value of 0.0001

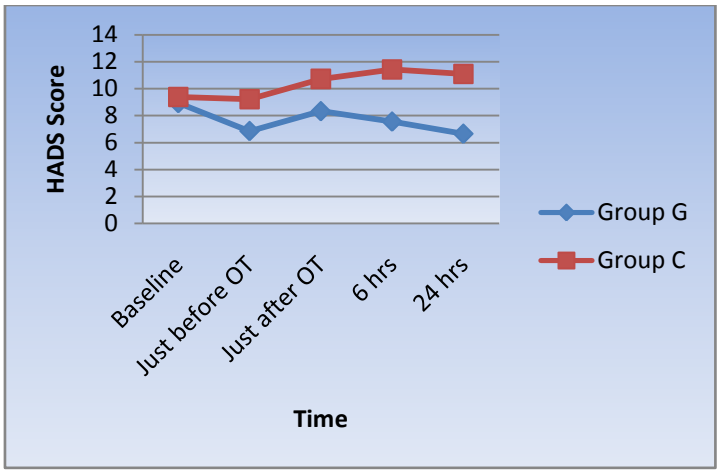


Table no 6: Adverse/Side effects

Side affect	Group G	Group C
Nausea		
Yes	8	17
No	22	13
Vomiting		
Yes	7	15
No	23	15
Dizziness		
Yes	12	7

No	18	23

Table No. 6 Showing adverse effects in both group G and group C patients which are comparable. Gabapentin Group patients showed less side effect as compared to Clonidine group patients in terms of nausea and vomiting but dizziness is more in patients receiving Gabapetin. So Gabapentin Group patients showed more dizziness as compare to Clonidine group patients.

DISCUSSION

This study was designed with aims of comparing the post-operative analgesic efficacy of oral Gabapentin and oral Clonidine in abdomino-pelvic and lower limb surgeries being done under spinal anaesthesia. Also to compare the pre-operative sedation and perioperative anxiety reduction produced by oral Gabapentin and oral Clonidine using scale like Modified Ramsay Sedation Scale and HADS.

Gabapentin and Clonidine have been employed orally in various doses for exerting their effect in management of postoperative pain. Oral Gabapentin is used in the range of 300mg-1600mg in both single and multiple doses. Oral Clonidine is used in the range of 100µg-300µg.We used '300mg' Gabapentin and '100µg' Clonidine because this was the dose used by many authors who have studied these drugs [7, 8].

The modified Ramsay sedation score which was used in this study showed a better sedative effect by Gabapentin than Clonidine in the preoperative period. At 60 minutes following administration of either Gabapentin or Clonidine the difference in sedation levels became significant (p=0.001) At 120 minutes there was a significant difference in the sedation scores (p=0.001).

Hospital anxiety and depression scale was used for anxiety assessment in our study. Patients showed less anxiety HADS score taking Gabapentin than patients taking Clonidine preoperatively as well as post operatively (p=.0001)

Gogna R et al. [9] have used oral Gabapentin for premedication in the dose of 600 mg 120min before spinal anaesthesia these authors observed good anxiolysis and sedation with the said doses of oral Gabapentine. We used 300mg oral Gabapentine and found effective pre-operative anxiolysis and sedation than Clonidine group patients.

Hidalgo et al. [10] conducted a study on 61 patients undergoing abdominal hysterectomy of ASA status I & II, were randomly assigned to receive either oral Clonidine 100 µg or placebo before surgery and 24 h after surgery. They concluded that Clonidine should be a good therapeutic alternative to other preoperative sedatives and further studies are necessary to compare its effects with those of different anxiolytics on postoperative outcomes over time.

In our study Clonidine also showed anxiolysis and analgesia but with comparison to Gabapentin, gabapentin is superior as anxiolytic and pre-emptive analgesic than Clonidine.

Zuleyha Kazak et al. [11] conducted a study to see the effectiveness of single dose of Gabapentin (600 mg) for intraoperative sedative effects and perioperative analgesic requirment. Gabapentin groups patients showed significant sedation score as compared to placebo group patients. Gabapentin group patients had significantly lower intraoperative VAS scores at all points ($p<0.05$) anxiety score is also lower at all Points ($p <0.05$) postoperative pain scores were lower in gabapentin group patients than placebo group patients.

In our study postoperative pain assessment was done using VAS for the first 6 hours following surgery. Patients who were premedicated with Gabapentin showed decreased requirement of rescue analgesics as compared to Clonidine group patients (p=0.0002).

In a similar study done by Mohd Hossein Ghafari et al. [12] on effects of preoperative Gabapentin or Clonidne in decreasing postoperative pain in patients who have undergone abdominal hysterectomy, they administered 300 mg of Gabapentin or 100 micrograms of Clonidine to the patients on the night prior to sugery and again an hour before surgery. The patients were monitored for 48 hours following surgery. At 8th postoperative hour, Gabapentin showed better postoperative analgesia than Clonidine group. Morphine consumption in both Gabapentin and Clonidine group were significantly lesser than the placebo group. In our study, patients who were premedicated with Gabapentin showed lesser VAS scores as compared to those who were given Clonidine. At 6th postoperative hour, mean VAS scores of Gabapentin group (2.33±0.92) was lesser than Clonidine group (5.7±1.29) The comparison was considered significant.

Hajare A et al. [13] in their study concluded that Oral Gabapentin 300mg given before 90 min as preemptive analgesic was more effective in reducing postoperative pain and morphine consumption also providing better anxiolysis in patients undergoing abdomino-pelvic surgeries under spinal anaesthesia compared to oral clonidine 100µg same as our study.

Baghel H et al. [14] conducted a study To compare single dose pre-emptive Gabapentin vs. Clonidine for post

operative pain relief in lower limb surgeries under spinal anaesthesia. They give orally Gabapentin 300mg and Clonidine 100mcg 1 hour prior to the administration of spinal anaesthesia. They concluded that patients who were premedicated with Clonidine showed better pain tolerance compared to Gabapentin. Clonidine group patients showed lesser need for rescue analgesia compared to those in gabapentin group. But in our study patients pre-medicated with oral Gabapentin showed better pain tolerance compared to Clonidine group.VAS score was significantly less in patients receiving oral Gabapentin prior to the spinal anaesthesia and need for rescue analgesia was also less in Gabapentin group compared to Clonidine group.

CONCLUSION

The primary goal of our research was to compare the post-operative analgesic efficacy of oral Gabapentin and oral Clonidine in abdominopelvic and lower limb surgeries being done under spinal anaesthesia. In a trial of 60 cases in which our research was applied, patients who were premedicated with Gabapentin showed better pain tolerance compared to those who were given Clonidine. Rescue analgesia was more associated with Clonidine Group patients (2.16±0.91) when compared to Gabapentin Group patients (1.4±0.49) with p value= 0.0002. Thus we conclude that Gabapentin is an better adjuvant.

Our second goal was to compare the pre-operative sedation and perioperative anxiety reduction by oral Gabapentin and oral Clonidine. The Ramsay sedation score which was used in this study showed a better sedative effect by Gabapentin than Clonidine in the preoperative period. Gabapentin group showed significant sedation at 120 minutes.

Hospital anxiety and depression score which was used in this study was significantly less in group G patients than group C patients upto 24 hours post surgery

Also in additional comparison of side effects, there was increased incidence of nausea and vomiting in Clonidine group patients and Gabapentin group patients showed an higher incidence of dizziness.

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