ORIGINAL RESEARCH PAPER

Anaesthesiology

PRE-EMPTIVE ANALGESIA WITH ORAL GABAPENTIN 300MG GIVEN IN THE MORNING OF SURGERY AND AMOUNT OF POST OPERATIVE ANALGESIC REQUIREMENT

KEY WORDS: gabapentin, pain, analgesia

Dr. Prem Chandar. L. K – Post-graduate, Department of Anaesthesiology and Pain medicine, Saveetha Medical College and Hospital, Thandalam, Chennai.

Dr. Nikila Devarayasamudram Gopal – Assistant Professor, Department of Anaesthesiology and Pain medicine, Saveetha Medical College and Hospital, Thandalam, Chennai.

Dr. Vivekanand P – Post-graduate, Department of Anaesthesiology and Pain medicine, Saveetha Medical College and Hospital, Thandalam, Chennai.

Dr. Sagarika* – Under-graduate, Department of Anaesthesiology and Pain medicine, Saveetha Medical College and Hospital, Thandalam, Chennai*Corresponding Author

Dr. Lakshmi Ramakrishnan – Head of the Department of Anaesthesiology and Pain medicine, Saveetha Medical College and Hospital, Thandalam, Chennai.

ABSTRACT

The study was done to evaluate postoperative benefit in patients administered tablet gabapentin as premedication with primary outcome determining the total analgesic requirements. The duration of analgesia and postoperative sedation scores were secondary outcomes. The study was a prospective randomised observational study in 120 patients undergoing spinal anaesthesia. Patients were randomly assigned into two groups. Group G (n=60) patients received tablet gabapentin 300mg and Group P (n=60) patients received a placebo orally 2 hours before surgery. Postoperative pain was managed with IV Tramadol 2 mg/kg. Postoperative monitoring included pain assessment with NRS and sedation score every 2 hours till 12 hours and then at 24 hours. On comparison, the total opioid requirement was not significant (p value 0.250) between the two groups but the duration of analgesia was significant (0.03) with group G. Sedation scores were higher in Group G at 2 and 4 hours postoperatively. Single dose of 300mg Gabapentin has no effect in reducing the postoperative opioid consumption but has prolonged the duration of analgesia.

INTRODUCTION

Postoperative pain is an unpleasant experience for patient. Pain has both emotional and psychological components. Uncontrolled postoperative pain invokes several physical effects and psychological effects that could be a major factor for immune suppression, delayed wound healing, myocardial ischemia.

Several methods have been developed to treat postoperative pain that includes systemic opioids, NSAIDs, regional analgesia and other techniques. Preemptive analgesia essentially means administration of an analgesic before the onset of noxious stimuli. Surgical pain leads to sensitization of nervous system which predisposes the patient for hyperalgesia and allodynia.

Gabapentin is a drug that acts on peripheral sodium channels, voltage dependant calcium channels and decreases glutaminergic transmission in spinal cord. Hence it is an ideal drug to be used as preemptive analgesic. This study was conducted to evaluate the efficacy of preemptive administration of gabapentin (300 mg) on the duration of postop analgesia in patients undergoing spinal anaesthesia.

METHODOLOGY:

Study design – Prospective randomized double blinded Placebo Controlled trial

Study area – Saveetha medical college Hospital
Study population – Patients requiring lower limb orthopaedic surgeries aged 18 to 65 years

Inclusion criteria – Patients aged between 20 to 60 years belonging to American society of anaesthesiologists physical status 1 and 2 undergoing lowerlimb orthopaedic procedures.

Exclusion criteria – Patients unwilling to participate. Patients with known hypersensitivity to gabapentin. Patients who were receiving analgesics 24 hour before surgery. Patients suffering from epilepsy, liver disease, renal disease or chronic pain syndrome.

Study period – 8 months (from March 15 2022 to Nov 15 2022)

Sample size – 120. Two Means - Hypothesis testing for two means (equal variances) According to the study done by Roshan et al, considering the mean requirement of tramadol in post operative period, 123.3mg in Gabapentin grp and 140mg in placebo grp, and Standard deviation of total tramadol requirement in Gabapentin group is 34.07. Standard deviation of total tramadol requirement in placebo grp = 20.34

Mean difference = 16.67
Effect size = 0.612755008270539
Alpha Error(%) = 5
Power(%)= 90
sided = 2
Required sample size per group = 60

Once the institutional ethics committee has approved, each patient provided their written, fully informed consent. The patient, anaesthesiologist and surgeon were all blinded to the provided treatment as part of double-blinding. Patients gave written informed permission after being fully briefed about the study's protocol. The patients were explained the Numeric Rating Scale (NRS) of pain, which is a 10 cm horizontal line with the extreme right end marked as "10" denoting the worst imaginable pain and the extreme left end marked as "0" as no

pain. Patients were asked to rate their pain on the scale of ten. Using computer-generated random numbers, patients were divided into two equal groups. Each patient was randomly allocated using sealed envelope in either of two groups – Group G (gabapentin 300mg) and Group P (placebo).

A staff nurse who was not engaged in the study administered the study drug orally, with small sips of water, two hours before surgery. Patients in study Group-P (placebo) received matching placebo of calcium tablet while those in study Group-A (gabapentin) received 300mg tabs of the medication. In the operating room, routine monitoring with pulse oximetry, NIBP, ECG, temperature, and urine output with an indwelling catheter was started. Intravenous cannulation was established with 18G cannula and Ringers lactate infusion was started.

With a 25G Quicke babcock needle, 3ml of 0.5% hyperbaric bupivacaine was used to administer neuraxial anaesthesia at L3-L4 interspace. Hypotension, if occurred, was treated with 6mg IV ephedrine boluses. The total duration of surgery was noted.

Postoperatively, IV Paracetamol 1g was administered 8th hourly in the first postoperative day. The duration of analgesia which is the time taken from the transfer of patient to PACU till the first administration of analgesic on demand was noted. Rescue analgesia of IV Tramadol 50 mg was given when the patient demands for analgesic. Repeat injection of IV Tramadol 25 mg was given if there is no pain relief after 10 minutes.

Patients are assessed for their overall opioid use in the first 24 hours. Sedation level for the first 12 hours following surgery was assessed during 2, 4, 8 and 12th hour after surgery using Ramsay sedation score. The Numerical Rating Scale was utilised as the grading method for pain. The patient is required to rate their level of pain using a numerical rating scale (NRS). NRS was assessed during 2, 4, 8, 12 and 24 hours postoperatively.

STATISTICAL ANALYSIS

Data was entered in Microsoft excel and statistical analysis was done using SPSS Software (Statistical analysis for Social Sciences) version 20.0.Descriptive analysis was done using charts and graphs. Independent T-test was done to compare the difference in the duration of analgesia, opioid requirement, duration of surgery. age and weight.

Chi-square test was done to compare the association of demographic variables like age , Gender, ASA status, Sedation score and NRS core at different time intervals between the groups. P-value is considered significant if $P<0.05$

RESULTS

The demographic profiles were comparable between the two groups, justifying proper randomization. The mean duration of surgery were also comparable [Table 1].

Table 1 Demographic variables

Variables	Group G Gabapentin (n=60)	Group P Placebo(n=60)	P value
Age (years) mean±SD	40.13 ± 11.35	39.63 ± 11.84	0.814
Sex ratio (male/female)	28/32	28/32	1.00
Weight (kg), mean±SD	69.42 ± 8.26	67.93 ± 9.29	0.357
ASA I/II	28/32	31/29	0.584
Duration of surgery (min)	94.98 ± 8.65	94.87 ± 8.625	0.914

Outcome variables :

Table 2 Duration of analgesia

Groups	Mean ± SD	P-value
Gabapentin	272.20 ± 26.4	0.00(S)
Placebo	223.83 ± 14.239	

Table 3 Total tramadol requirement

Group	Mean	P-value
Gabapentin	141.6 ± 21.4	0.250(NS)
Placebo	145.8 ± 17.9	

Figure 1 Bar diagram showing the mean duration of analgesia

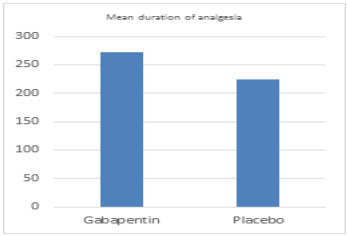

Figure 2 Bar diagram showing the total tramadol requirement

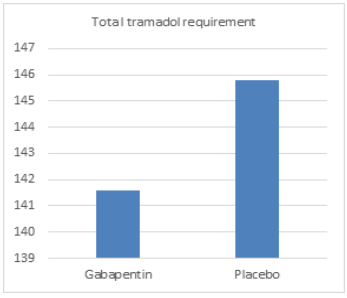

Table 4 Mean pain (NRS) scores

Groups	Mean ± SD	P value
Gabapentin	2.12 ± 0.50	0.00 (S)
Placebo	2.76 ± 0.74	

Figure 3 Bar diagram representing Numerical Rating Scale at various time intervals

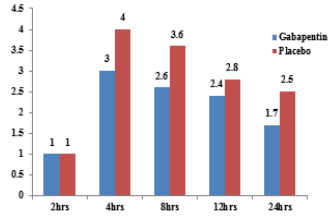

Figure 4 Bar diagram representing Ramsay sedation score at various time intervals

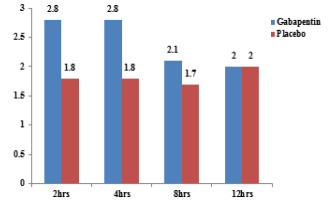

Table 5 Sedation scores

Time	Groups	N	Mean	Std. Deviation	P-value
2hrs	G	60	2.80	.403	.000(S)
	P	60	1.83	.376	
4hrs	G	60	2.78	.415	.000(S)
	P	60	1.83	.376	

8hrs	G	60	2.08	.279	.000(S)
	P	60	1.70	.462	
12hrs	G	60	2.00	.000	-
	P	60	2.00	.000	

Comparing the total tramadol requirement, Group G patients required 141.6 ± 21.4 mg whereas Group P patients required 145.8 ± 17.9 mg which is not statistically significant [Table 3]. When the total duration of analgesia in minutes was compared, Group G patients required first rescue analgesia at 272.20 ± 26.4 minutes whereas in Group P patients duration of analgesia lasted only till 223.83 ± 14.239 minutes with p = 0.0001 which is significant [Table 2].

Sedation scores were significantly higher in Group G at 2 h, 4 h and 8 h post operatively [Table 5]. Overall mean sedation scores of Group G when compared to Group P were significant. Cumulative pain scores when added after 24 hours was significantly lower in Group G when compared with Group P [Table 4]. Postoperatively none of the study patients had adverse effects other than sedation.

DISCUSSION:

For acute postoperative patient well-being effective pain relief is mandatory. Studies have indicated such negative clinical outcomes to include decreases in vital capacity and alveolar ventilation, pneumonia, tachycardia, hypertension, myocardial ischemia, myocardial infarction, transition to chronic pain, poor wound healing, and insomnia.

Gabapentin is a structural analogue of the neurotransmitter - aminobutyric acid. The absorption of gabapentin is dose-dependent due to a saturable l-amino acid transport mechanism in the intestine. Voltage gated calcium channel is the most likely anti-nociceptive target of gabapentin. The proposed consequence of gabapentin binding to the 2 subunit is a reduction in neurotransmitter release and hence a decrease in neuronal hyperexcitability.

Anil Verma et al., observed that 300 mg of gabapentin taken 2 h before surgery resulted in marked reduction in pain and requirement of the epidural boluses in patients undergoing total abdominal hysterectomy[1]. Eckhardt et al., showed a 600 mg single dose of gabapentin increases the adverse effects when these drugs were used concomitantly[2]. Keeping in mind, this study demonstrates the efficacy of gabapentin at a lower dose 300mg taken 2 hours before surgery.

The mean (SD) total dose of opioid (tramadol) consumed was not significant between both groups but the duration of analgesia was prolonged. This indicates that gabapentin potentiates the action of tramadol. Fabritius et al., in a meta-analysis showed that firm evidence for use of gabapentin is lacking as clinically relevant beneficial effect of gabapentin may be absent and harm is imminent, especially when added to multi- modal analgesia[3]. Paul, J. E et al., concluded in his study that gabapentin does not improve multimodal analgesia outcomes for total knee arthroplasty[6].

PengPW et al., observed higher incidence of sedation in gabapentin group which is corresponding to the present study[4].

Limitations of the study includes involving diverse surgeries in the study. Hence the extent of tissue handling will be a confounder for pain score assessment. Another limitation is the duration of block height regression after spinal anaesthesia being a confounder in pain score assessment.

CONCLUSION:

The study proves that preemptive analgesia with single dose of gabapentin (300 mg) orally 2 hours before surgery provides better duration of pain relief as compared to placebo. The total analgesic requirement was not reduced during the postoperative period compared to placebo.

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