ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS: Pre-emptive analgesia, Pregabalin, gabapentin, lower limb surgeries.

A COMPARATIVE STUDY OF ORAL PREGABALIN VERSUS GABAPENTIN FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES UNDER SPINAL ANAESTHESIA.

Dr. J. Vasanthy MDDA, Senior Assistant Professor, Thanjavur Medical College, Thanjavur.

Dr. Sandeep* M.D.(anaes), Intensivist, vijaya hospital, Chennai. *Corresponding Author

ABSTRACT

BACKGROUND AND AIM: Postoperative pain could be attributed to inflammation resulting from tissue trauma due to surgical incision, tissue injury. This study was done to evaluate and compare the preemptive analgesia efficacy of oral gabapentin vs oral Pregabalin for postoperative analgesia and to assess the adverse effect of the drugs.

METHODS: This study is a randomized single blinded prospective study conducted at the tertiary hospital on patients undergoing lower limb surgeries under spinal anaesthesia 90 ASA grade 1 and grade2 patients were allocated into 3 groups, group P-30, group G-30 and group C 30(placebo). The visual analogue scale,Ramsay sedation score and side effects *were analyzed using anova , t test and chi-square test.*

RESULTS: Pre-emptive pregabalin and gabapentin provide good postoperative analgesia.

CONCLUSION: Pregabalin (300mg) provides prolonged pain relief compared to gabapentin(900mg)in the postoperative period. Both drugs have minimal adverse effects.

INTRODUCTION:

Postoperative pain could be attributed to inflammation resulting from tissue trauma due to surgical incision, cauterization, direct nerve injury stretching or compression .pro inflammatory mediators released during injury contribute to nociceptor sensitization. Inadequately treated postoperative patients may have various implications on the patient such as tachycardia. hypertension, increased blood glucose, delayed wound healing and anxiety. Anxiety leads to stress response and hemodynamic instability. Therefore the relationship between anxiety and pain is well established.

Depression, psychological stress and late recovery are related to chronic postsurgical pain, hence adequate pain relief must be an integral part of anaesthesia. This is achieved by multimodal approach regarding the management of postoperative pain,this study was designed to compare the pre-emptive analgesic efficacy of oral gabapentin versus pregabalin in patients undergoing lower limb surgeries under spinal anaesthesia.

Preemptive analgesia is an anti-nociceptive treatment that prevents establishment of altered processing of afferent which amplifies postoperative pain. Effective pre-emptive analgesia uses multiple agents to reduce nociceptor activation either by blocking or decreasing receptor activation. It is started before the onset of pain stimulus.

AIM OF THE STUDY

To evaluate and compare the preemptive analgesic efficacy of oral gabapentin vs oral pregabalin for postoperative analgesia in patients undergoing elective orthopaedic lower limb surgeries under spinal anaesthesia and to assess the incidence of adverse effects of gabapentin and pregabalin

MATERIALS AND METHODS

This study was a randomized, single blinded, prospective study conducted at the Department of Anaesthesiology, Thanjavur Medical College in association with the Department of Orthopaedics,Thanjavur Medical College.

INCLUSION CRITERIA:

Patients undergoing elective lower limb surgeries under department of orthopaedics

ASA I and II patients with Age group 18 to 60 yrs including male and female.

EXCLUSION CRITERIA:

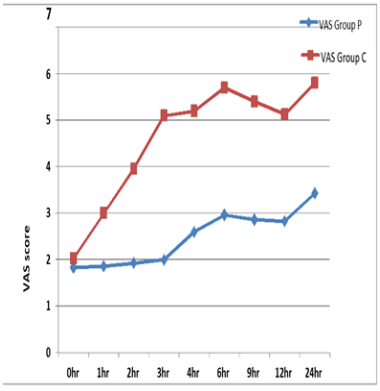
Patient refusal .H/o of allergy to gabapentin and pregabalin & H/o of drug and /or alcohol abuse. Patients who have been prescribed pregabalin or gabapentin for other indications .H/o of epilepsy and other neurological disorders .Pregnancy and breast feeding mothers & pts with Liver or renal disease were excluded.

Written informed consent was obtained from all patients. Patients satisfying inclusion criteria were randomly allocated into group P received 300mg of pregabalin orally. Group G,received gabapentin group and group C placebo .They were informed preoperatively about the visual analogue scale. The capsules given with sips of water, two hours before surgery inside the operating room,monitors were connected.(ECG,NIBP, pulse oximeter).Bladder was catheterized to monitor urine output. IV access established with18g cannula. All patients were preloaded with 10ml/kg of ringer lactate solution under aseptic precautions.3ml of hyperbaric bupivacaine with 25mcg of Inj. Fentanyl was given in sub arachnoid space using 25g Quinckes needle.

At the end of surgery,patients were shifted to ward. VAS scores were assessed at 1,2,3,4,6,9,12 and 24 hours postoperatively. Patients were given Inj. Tramadol 2mg/kg IM .when the vas score was4 or greater dosage did not exceed 250mgat one time and 600mg per day. Time since S.A to first requirement of analgesia (t1),total analgesia requirement in first 24 hours,vas scores, Ramsay sedation score,side effects of the drug taken dizziness, confusion,nausea,vomiting were recorded. Data collected were analyzed using oneway analysis of variance(anova),t-test and chi square test. The results are expressed in terms of mean and standard deviation .p value of less than 0.05 is considered to be statistically significant.

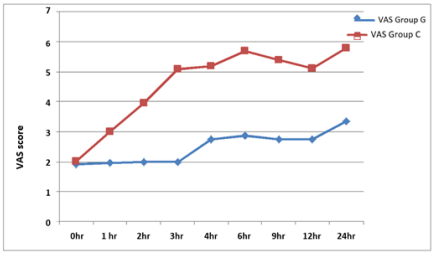
STATISTICS AND RESULTS

FIGURE 1 VAS SCORE BETWEEN GROUP P AND C



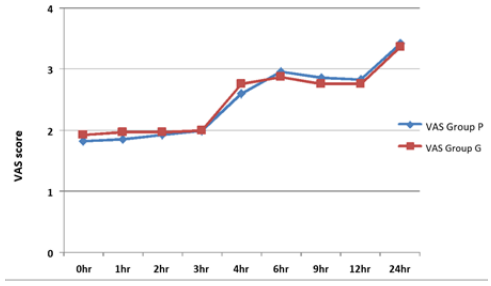
All patients were monitored for VAS scores at rest in the immediate postoperative period (0 hr), at 1, 2, 4, 6, 9 12, and 24 hours postoperatively. In the immediate postoperative period (0 hr), the mean VAS score was found to be 1.83 in Group P and 2.03 in Group C with no statistically significant difference between the groups. This may be due to the effect of spinal anaesthesia.

Figure 2: Visual analogue scale (VAS) score of Group G vs Group C



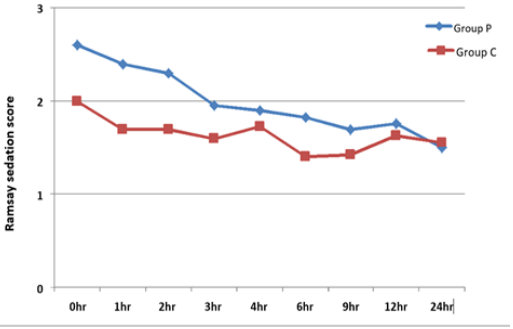
In the immediate postoperative period (0 hr), the mean vas score was found to be 1.93 in group g and 2.03 in group c with no statistically significant difference between the groups. In all these time intervals, the p value was less than 0.05 which is highly significant. This shows that there is a significant reduction in the mean vas scores in patients receiving gabapentin premedication compared to control in the first 24 hours after surgery.

Figure 3: Visual analogue scale (VAS) score of Group P vs Group G



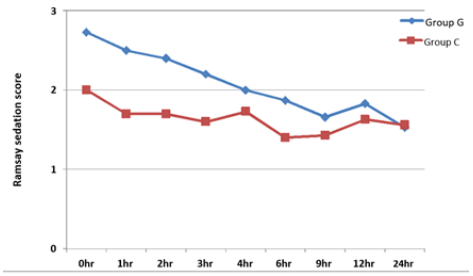
The mean VAS scores during postoperative period of 0, 1, 2, 4, 6, 9, 12 and 24 hours in group P patients were 1.83, 1.86, 1.93, 2, 2.6, 3.36, 3, 2.83 and 3.43 respectively .In Group G patients the mean VAS scores were 1.93, 1.97, 1.97, 2, 2.76, 2.87, 2.76, 2.76 and 3.26 respectively . As the P value at all these time intervals was > 0.05 which was not statistically significant and so No significant difference between the analgesic properties of pregabalin and gabapentin

Figure 4: Ramsay sedation score. Group P vs Group C



Postoperatively all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 9,12, and 24 hours. However, the scores at 9,12 and 24 hrs were not statistically significant among the 2 groups. This shows that the sedation effect of pregabalin is not significant beyond 6 hrs postoperatively .

Figure 5: Ramsay sedation score. Group G vs Group C



Postoperatively all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 9,12, and 24 hours. The mean sedation scores at 0, 1, 2,3, 4, 6 hours of postoperative period in group P were 2.6, 2.4, 2.3, 1.96, 1.9, 1.83.In Group C, the scores were2, 1.7, 1.7, 1.6, 1.73 and 1.4 respectively. The P value at all time intervals upto6 hrs was less than 0.05 which was highly significant.This shows that the level of sedation was significantly higher in group P patients compared to Group C upto 6 hours in the postoperative periodHowever, the scores at 9,12 and 24 hrs were not statistically significant among the 2 groups. This shows that the sedation effect of pregabalin is not significant beyond 6 hrs postoperatively

Table 1: Time of rescue analgesic (T1)

Duration in minutes from the end of surgery	Group P	Group G	Group C	P value
Mean	502.3	382.6	137.8	**0.000**
SD	101.087	119.162	44.483	
Range	220-550	220-570	60-205	

Postoperatively all patients were monitored for VAS scores periodically. When the VAS score at rest is 4 or greater, patients were given Tramadol 2mg/kg intravenously as initial dose. So T1 is the time interval between providing spinal anaesthesia and administration of first dose of tramadol. The P value was found to be 0.00, which is considered significant. This indicates that T1 score was significantly greater in group C compared to group P and Group G. Hence Pregabalin provides more prolonged pain relief compared to gabapentin

Table 2: Total dose of Tramadol administered in 24 hours post surgery

Dose in mg	Group P	GroupG	Group C	
Mean(SD)	170 (46.609)	176.7 (50.401)	286.7 (34.575)	**P.000<0.05 Significant**
Range	100-200	100-300	100-300	

Postoperative analgesia was provided with tramadol at a dose of 2 mg/kg when the VAS score was 4 or more, or on patients demand. The P value was found to be 0.000 which is highly significant.. Hence it was found that total tramadol consumption was significantly lower in group P and group G patients compared to group C.

Table 3: Incidence of adverse effects

Adverse Effects	Group P(n=30)	Group G (n=30)	Group C(n=30)
Nausea	0	2	5(16%)
Vomiting	0	0	3(10%)
Giddiness	4(13%)	3 (10%)	0

These values in table 3 were not statistically significant .This implies that Pregabalin and gabapentin has no significant side effects. In group C, 5 patients had nausea and 3 patients had vomiting due to increased doses of tramadol in the placebo group.

DISCUSSION:

The concept of preemptive analgesia introduced by Crile and further developed by wall and Woolf revolutionized postoperative pain relief.Kehlet and dahl developed the concept of multimodal analgesia to reduce the dosage of opioids and its side effects.Gabapentinoids are very effective and this was the basis of this study.This study of 90 patients undergoing lower limb surgeries under spinal anaesthesia were randomly allocated into3 groups –group p received oral pregabalin 300mg,group g received gabapentin 900mg and group c placebo. Similar study conducted by Rajendran et al with similar dosage of drugs. Higher dose were more clinically significant in reducing postoperative pain than lower doses.

The drugs were given preoperatively 1hour before surgery similar to study conducted by elinor ben menachene,who reported the maximal plasma concentration of pregabalin was one hour and gabapentin 2 hours.in all patients standard anaesthesia technique was followed. The men duration of surgery was 129-130minutes.the patients were educated about the visual analoguescoring. As scores were measured at 0hrs,1hr,2hrs,3hrs,4hrs,6hrs,9hrs,12hrsand 24 hours after surgery. The mean score were compared and were significantly less in both group p and group g than group cthis was similar to study conducted by rajendran et al. All patients were assessed for the level of sedation using Ramsay sedation score periodically at 0,1,2,4,6,9,12,24hours. The level of sedation were higher in group p and group g than group c.

The time of first rescue analgesia 137.8minutes in control group,502.3 minutes in pregabalin group p value was found to be 0.001 which is significant.Tramadol 2mg/kg intravenously was given as rescue analgesia as initial dose. This concurs with the findings of the study conducted by tiipana et almetaanalysis.The incidence of side effects were negligible in both group p and group g similar to the conducted by dirks et al.

CONCLUSION:

Pre-emptive pregabalin and gabapentin provide good postoperative analgesia compared to placebo in patients undergoing lower limb surgeries under spinal anaesthesia. Pregabalin(300mg)provides prolonged pain relief compared to gabapentin. These drugs reduce the postoperative opioid requirement in the first 24 hrs. Both drugs have minimal side effects.

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