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Pre-Emptive Use of Pregabalin for PostOperative Relief of Pain in Patients Scheduled For Surgery under General Anaesthesia

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Original Research Article

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Abstract: The aim of this original study was to evaluate the pre-emptive effect of Pregabalin on postoperative pain in patients scheduled for surgery under general anaesthesia. Post-operative ward and OT Department of anesthesia J. A. Hospital, G. R. Medical College, Gwalior MP. This was double-blind, randomised, prospective clinical study. Total 60 patients of ASA grade I and II posted for elective surgeries under general anaesthesia were randomised into 2 groups (Group A and Group B of 30 patients each). One and half hour before surgery, the drug selected for the study was given blindly with a sip of water. Group A received 300mg Pregabalin capsule; Group B received identical placebo capsule. Pain (Visual analogue score) and side effects assessment were performed immediately and then at 15mins. 30mins 45mins. 60mins, 90mins, 120mins, and 180mins, postoperatively. The mean (±SD) of VAS score was 5.86 ± 0.34 in Group B and 4.96 ± 1.03 in Group A. VAS score was significantly lower in Group A as compared to Group B. With oral pregabalin time required for rescue analgesia is delayed as compared to control group. The mean (±SD) TRA-1 was 38.40±24.61 in Group B and 58.69±25.21 in Group A. Pregabalin also causes sedation. No significant difference was observed among the two groups regarding side effects during the study period. This clinical study demonstrated that pre-emptive oral Pregabalin 300 mg significantly decreases the severity of pain postoperatively as compared to placebo in patients posted for surgery under general anaesthesia. Time for analgesic requirement is more with oral Pregabalin. The VAS score was lower in Pregabalin group. Oral Pregabalin produces higher degree of sedation than the placebo group.
Keywords: Pregabalin, General Anaethesia, postoperative pain, pre-emptive.

INTRODUCTION

The most common and distressing symptom, which follows anaesthesia and surgery is pain [1]. The postoperative pain management is important for decreasing patient morbidity and pain related clinical complication[2].

Because of the multiplicity of the mechanisms involved in postoperative pain, multimodal analgesia regimen combination of opioid and non-opioid analgesic drugs is often used to enhance analgesic efficacy and reduce opioid requirements and side effects. In this context Pregabalin has been used as pre-emptive analgesic [3].

The transmission of pain signals evoked by tissue damage leads to sensitization of peripheral and central pain pathways. Pre-emptive analgesia is a treatment initiated before a surgical procedure that reduces this sensitization thus decreasing pain severity and duration. Pre-emptive analgesia was first introduced by Woolf in 1983.

Pregabalin is chemically 3–amino methyl–5–methyl hexanoicacid and is structurally related to the naturally occurring amino acids L – leucine and gamma aminobutyricacid(GABA). Pregabalin decreases central neuronal excitability by binding to an auxiliary subunit (α2–δ protein) of a voltage – gated calcium channel on neurons in the central nervous system. Pregabalin reduces the release of several neurotransmitters include glutamate, norepinephrine, serotonine, dopamine and Substance P[4].

Pregabalin has good analgesic efficacy in patients with spinal cord injury, postherpetic neuralgia, dental surgery, gynecological surgery, lumbar laminectomy, discectomy [5], epilepsy, neuropathic pain and generalized anxiety disorder [6].

The aim of this study was to compare the effect of Pregabalin with the control group on the postoperative pain in patients scheduled for surgery under general anaesthesia.

MATERIALS AND METHODS

After Ethical committee approval and written informed consent this double-blind, randomised, prospective clinical study was carried out in 60 patients of ASA grade I or II of either sex, aged 18-50 years scheduled for elective surgeries under general anaesthesia J. A. Hospital G.R. Medical College Gwalior M.P. Exclusion criteria included known allergy or sensitivity to the drug, phychiatric illness, history of neurological, hepatic, renal, cardiovascular, respiratory diseases, hypertension, peptic ulcer diseases, diabetes mellitus, bleeding or clotting disorders. Menstruating, pregnant or lactating females were also excluded from this study. Sixty patients who fulfilled the eligibility criteria were chosen, explained about the procedure and written consent was taken. Patients were subsequently randomized into two groups of 30 each. Group B (n=30) – received a placebo orally one and a half hours prior to surgery and Group A (n=30) – received Pregabalin 300mg orally one and a half hours prior to surgery.

One and a half hours before surgery vital parameters including pulse rate, Blood Pressure (BP) and Electrocadiography (ECG) of all the patients were recorded in pre-anaesthetic room and then the drug selected for the study was given with a sip of water. Anaesthesia technique was standardised in all the groups. In the operative room Intravenous (IV) line was secured by using 18-gauge cannula and preoperative vitals (pulse, BP, respiratory rate, Sp02) were recorded. The patients were premedicated with Inj. Glycopyrrolate 0.02mg/kg I/M 30 minutes before surgery and Inj. Pentazocine 0.5 mg/kg IV on OT table.

After pre-oxygenation for three minutes, anaesthesia was induced with Inj. Thaiopentone sodium 5mg/kg IV and Inj. Succinylcholine 1.5mg/kg IV. Intubation was done with appropriate size endotracheal tube and anaesthesia was maintained on oxygen (33%), nitrous oxide (67%) along with intermittent doses of Inj. Atracuriumbesylate 0.5 mg/kg body weight ,initially followed by increments of 0.1 mg/kg body weight and halothane (0.75%) under controlled ventilation.

After completion of the surgery, neuromuscular blockade was reversed with Inj. Glycopyrrolate 0.4 mg/kg + inj. Neostigmine 0.08 mg/kg body weight i.v. and once adequate reversal was obtained the patient was shifted to postoperative ward for further monitoring.

Postoperative

Pulse rate, blood pressure, respiratory rate and severity of pain on VAS scale was noted immediate postoperatively and then at 15mins, 30mins. 45mins. 60mins.90mins. 120mins.and at 180mins.

Assessment of Postoperative Pain

Postoperative pain was assessed using analogue score scale, which consisted of a 10 cm horizontal scale with gradations marked as ‘0’ means no pain at all and ‘10’ means unbearable pain Inj. Tramadol 2 mg/kg body weight IV was given as rescue analgesic whenever the subject requests for analgesia.

Sedation Score Sedation was assessed on the basis of Modified Ramsay Sedation Score[7].

Indication	Score
Anxious, agitated, restless	1
Awake, cooperative, oriented, tranquil	2
Semiasleep but responds to commands	3
Asleep but responds briskly to glabellar tap or loud auditory stimulus	4
Asleep with sluggish or decreased response to glabellar tap or loud auditory stimulus	5
No response can be elicited	6

The occurrence of side effects such as nausea and vomiting, respiratory depression, dizziness, sedation, headache and shivering were recorded.

All data were collected and analysed with the SPSS version 17.0 for Windows Statistical Software Package (SPSS Inc., Chicago, IL, USA). Quantitative data were analysed by student t-test. P-value < 0.05 was considered statistically significant.

RESULTS

A total of 60 patients were recruited and studied. The two groups were comparable with respect to age, sex, weight and duration of surgery (Table 1).

On haemodynamic parameters, there was no significant changes (P value) were present in pulse rate, systolic blood pressure, diastolic blood pressure and respiratory rate among two groups (P>0.05).

The mean (±SD) of VAS score was 5.86 ± 0.34 in Group B and 4.96 ± 1.03 in Group A. VAS score was highly significantly lower (p<0.001) in Group A as compared to Group B and this is a highly significant difference in Group A as compared to Group B at all points of observations(Table 2).

The mean (±SD) TRA-1 was 38.40±24.61 in Group B and 58.69±25.21 in Group A. TRA-I in group A was lower in highly significant values ($p<0.01$) as compared to group B at all the points of observations(Table 3).

In group B none of the patients had sedation and in group A 6.66% patients had sedation score 2, 16.66% patients had sedation score 3, 43.33% patients had sedation score 4. Thus it was found that Pregabalin causes sedation (Table 4). None of the patients in both the groups had respiratory depression.

Table-1: Baseline data of study group

Characteristic	Group 'B'	Group 'A'
Age (Years)	34.20 (±8.80)	34.60 (±9.33)
Sex (M:F)	10:20	13:17
Weight (Kgs)	56.10 (±6.65)	58.3 (±4.11)
Duration of Procedure (Minutes)	105.83 (±45.45)	110 (±40.95)

Table-2: Statistical Analysis of Visual Analog

Sl.No.	Time in Min.	Group- B (Mean±SD)	Group-A (Mean±SD)
1	PO_i	5.86±0.34	4.96±1.03
2	PO_{15}	5.60±0.49	4.93±1.14
3	PO_{30}	5.20±0.48	4.63±1.09
4	PO_{45}	5.03±0.66	4.43±1.04
5	PO_{60}	4.90±0.40	4.03±1.03
6	PO_{90}	4.70±1.02	3.56±1.43
7	PO_{120}	4.86±1.07	3.50±1.52
8	PO_{180}	4.86±0.97	3.36±1.49

Score in Two Study Groups

Table-3: Comparison between Tramadol –I of the Groups

	Group – B	Group – A
Mean	38.40	58.69
± SD	24.61	25.21

Table-4: Showing Distribution of Sedation Score among Two Groups

Sedation Score	Group-B		Group-A	
	(n)	(%)	(n)	(%)
1	30	100	10	33.33
2	0	0	2	6.66
3	0	0	5	16.66
4	0	0	13	43.33
5	0	0	0	0
6	0	0	0	0

DISCUSSION

The findings of this study indicate that pre-emptive oral Pregabalin 300 mg significantly decreases the severity of pain postoperatively as compared to placebo in patients posted for surgery under general anaesthesia. We also observed that time for analgesic requirement is more with oral Pregabalin. We used Pregabalin in a dose of 300 mg, one and a half hours prior to surgery. The doses were chosen after careful consideration of the oral bioavailability of the drug as well as a few previous trials done on similar lines. In comparison to the control group, patients in the Pregabalin group had significantly lower VAS scores in all time intervals during the study period. The mean (±SD) TRA-I was 38.40±24.61 in group B, and 58.69±25.21 in group A. Time for rescue analgesia is more with oral Pregabalin than control group. Pregabalin is gamma-aminobutyric acid and binds to α2δ subunit of presynaptic voltage dependent calcium channels and reduces the calcium influx at nerve terminals and decrease the release of their neurotransmitters and produces analgesia and their synergistic effect with opioid reduces the analgesic requirement.

Eskandar A. M. *et al.* [8] found that oral 300 mg pregabalin decreases VAS score significantly and total consumption of nalbuphine also decreased.

Alimian M *et al*. [9] and Alimian M *et al*. [10] in their respective studies also observed that postoperative pain intensity level were lower in patients who received oral 300 mg Pregabalin an hour before surgery. Opioid consumption were also lower in the Pregabalin group than the placebo group. Similar conclusions have been reported from other studies[11,12,13].

Table 4 shows that in group B none of the patients had sedation, in group A 6.66% patients had sedation score 2, 16.66% patients had sedation score 3, 43.33% patients had sedation score 4. Thus, it was found that Pregabalin causes sedation. Similar results were obtained from other studies [12,14].

CONCLUSION

This clinical study demonstrated that pre-emptive oral Pregabalin 300 mg significantly decreases the severity of pain postoperatively as compared to placebo in patients posted for surgery under general anaesthesia. Time for analgesic requirement is more with oral Pregabalin. The VAS score was lower in Pregabalin group. Oral Pregabalin produces higher degree of sedation than the placebo group.

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