

## To Study the Effect of Pre-Emptive Dose of Pregabalin for Postoperative Analgesia in Patients Undergoing Surgery under General Anaesthesia

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### Original Research Article

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#### Article History

Received: 26.10.2018

Accepted: 03.11.2018

Published: 07.11.2018

#### DOI:

10.36347/sjams.2018.v06i11.038



**Abstract:** Successful recovery after surgery depends on complication free postoperative period. Pre-emptive use of analgesic agents reduces total analgesic consumption after surgery and increases patients comfort. Our hypothesis is that pre-emptively given oral pregabalin reduces postoperative pain in patients scheduled for surgery under general anaesthesia. This randomized control study was conducted on 60 patients of ASA grade 1 and 2 after taking ethics committee approval. Patients were divided into two groups. In Group P (n=30), patients who received 300 mg of Pregabalin orally one and half hours prior to surgery and in group C, patients received Placebo orally one and half hours prior to surgery. Diastolic, systolic and mean blood pressure, heart rate were measured throughout the procedure. Time of rescue analgesia and VAS score was recorded postoperatively. oral pregabalin given pre-emptively provides postoperative analgesia. Mean duration of first rescue analgesia in group P was that was  $58.69 \pm 25.21$  in comparison to group C  $38.40 \pm 24.61$ . Time of second rescue analgesia in group P was  $132.06 \pm 23.77$  and in group C was  $100.86 \pm 30.26$  showing better analgesia in group P when compared with group C ( $p < 0.05$ ). oral pregebalin given pre-emptively reduces postoperative pain in patients scheduled for surgery under general anaesthesia.

**Keywords:** Analgesia, General Anaesthesia, Pre-emptive analgesia, Pregabalin.

### INTRODUCTION

Patient going for surgery feared most about the pain associated with it. Also the most common complication after surgery and anaesthesia is pain [1] "Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [2]."

Successful recovery after surgery depends on complication free postoperative period. Postoperative pain, if not treated adequately may cause many physiological complications like hypertension, tachycardia, myocardial ischemia, angina, shallow breathing, cough suppression, retention of pulmonary secretion, gastric stasis and paralytic ileus, reduced mobility, muscle atrophy etc[3].

Many drugs are used to reduce post operative pain. These drugs are opioids e. g. morphine, meperidine, fentanyl, Non-steroidal anti-inflammatory drugs e.g. paracetamol, ibuprofen, cyclooxygenase-2-selective inhibitors like celecoxib, etoricoxib, rofecoxib, N-methyl-D-aspartate antagonists: ketamine, magnesium, Alpha-2-adrenergic agonists: clonidine, dexmedetomidine, local anaesthetic like bupivacaine, ropivacaine, levobupivacaine, Gabapentin and

Pregabalin etc. have been used as preemptive analgesics.

Pre-emptive analgesia is a treatment that is initiated before the surgical procedure in order to reduce sensitization. Pregabalin is a structural analogue of GABA with anticonvulsant, anxiolytic and sleep modulating properties. As a successor of Gabapentin, Pregabalin was shown to be effective in several models of neuropathic pain, incisional injury and inflammatory injury [4]. Pregabalin binds potently to the  $\alpha 2\delta$  subunit and modulates calcium influx at nerve terminals, and, thereby, reduces the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P [5]. Pregabalin is used in the treatment of peripheral neuropathic pain and as an adjunctive therapy for partial seizures in patients with epilepsy, neuropathic pain associated with diabetic

peripheral neuropathy (DPN) and postherpatic neuralgia (PHN), generalized anxiety disorder.

In the present clinical study, we have assessed the effect of Pregabalin on postoperative pain reduction by using it pre-emptively in patients scheduled for surgery under general anesthesia.

**MATERIALS AND METHODS**

After obtaining approval from the ethics committee, the present study was conducted on 60 patients of ASA grade I and II, age group 18 to 50 years of either sex, scheduled for elective surgery under general anaesthesia in the Department of

Anaesthesiology, J.A. Group of Hospitals of G.R. Medical College, Gwalior (M.P.) after getting written informed consent from the patients.

**Exclusion Criteria**

**Following patients are excluded from the study**

ASA grade III and above, known history of allergy or sensitivity or any other reaction to study drugs, patient with Psychiatric illness, history of neurological, hepatic, renal diseases, hypertension, peptic ulcer diseases, diabetes mellitus, bleeding or clotting disorders, patients on anti-depressants or calcium channel blockers, patients who received sedatives other than those determined by protocol.

**Patient’s grouping**

|                |  |
|----------------|--|
| Group P (n=30) | Patients who received 300 mg of Pregabalin orally one and half hours prior to surgery. |
| Group C (n=30) | Patients who received Placebo orally one and half hours prior to surgery.              |

**ANAESTHESIA TECHNIQUE**

**Premedication**

All patients were uniformly premedicated with inj.Glycopyrrolate 0.2 mg I.M. 30 minutes before operation.

**Preparation of patient**

After overnight fasting, patients were given either placebo or 300 mg of Pregabalin orally with a sip of water or two, 90 minutes before surgery.

Upon arrival of patient in the operation theatre securing an I.V. line with 18 G cannula and 500 ml of Ringer’s lactate solution was started. Various monitoring devices like NIBP, pulse oxymeter, 3 lead ECG were connected and basal reading like pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate were recorded.

Patients were premedicated with Inj. Pentazocine 0.5 mg/kg followed by preoxygenation with 100% oxygen for 3 minutes. After preoxygenation Inj.Thiopentone sodium 5 mg/kg body weight and Inj. Succinylcholine 1.5 mg/kg body weight were injected intravenously. IPPV was done with 100% oxygen for 1 minute.

Laryngoscopy done by Macintosh laryngoscope and tracheal intubation done with appropriate size of cuffed endotracheal tube, cuff was inflated and bilateral equal air entry checked on both side of chest and then tube was fixed.

Anaesthesia was maintained on oxygen (33%), nitrous oxide (67%) along with intermittent doses of inj. Atracurium Besylate 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.

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

**SEDATION SCORE**

**Sedation was assessed on the basis of Modified Ramsay sedation score [8]:**

| 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     |

**Assessment of postoperative pain**

Postoperative Pain was assessed using a visual 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.

**TRA-I** Time at which first request for analgesia is made by the patient

**TRA-II** Time at which second request for analgesia is made by patient.

Inj. Tramadol 2 mg/kg body weight I.V. was given as rescue analgesic whenever the subject requests for analgesia.

**STATISTICAL ANALYSIS**

The observations were recorded and subjected to statistical analysis using students "t" test by statistics calculator SPSS 17. Student 't'-test for inter group comparison was used. p-value >0.05 was taken to be statistically insignificant & p-value <0.05 was taken statistically significant and p-value <0.01 taken to be statistically highly significant.

**RESULTS**

Data obtained from the patients involved in the study were analyzed. The mean age, weight, sex, duration of anaesthesia and surgery and Ramsay sedation score after extubation were comparable in two groups as shown in table 1.

Preoperative heart rate, systolic, diastolic and mean blood pressures were comparable in both the groups.

**Table-1: Showing demographic variables of two groups**

| DEMOGRAPHIC DATA              | Group C     | Group P     |
|-------------------------------|-------------|-------------|
| Age                           | 37.06±10.63 | 37.90±10.20 |
| Weight (Kg)                   | 58.36±12.15 | 57.60±9.56  |
| Sex (Female)                  | 76.7%       | 86.7%       |
| Duration Of Anaesthesia (Min) | 97.16±17.05 | 98.00±20.82 |

**Table-2: Showing distribution of sedation score in two groups**

| SEDATION SCORE | GROUP-C |     | GROUP- P |       |
|----------------|---------|-----|----------|-------|
|                | (n)     | (%) | (n)      | (%)   |
| 1              | 30      | 100 | 11       | 36.66 |
| 2              | 0       | 0   | 3        | 10    |
| 3              | 0       | 0   | 6        | 20    |
| 4              | 0       | 0   | 10       | 33.33 |
| 5              | 0       | 0   | 0        | 0     |
| 6              | 0       | 0   | 0        | 0     |

Table 2 shows that in control group, none of the patients had sedation while in group P 33.33%

patients were not sedated at all but 10% had sedation score 2, 20% of 3 and 33.33% had sedation score of 4.

**Table-3: Time of rescue analgesia-1 (tra-1) in two study groups**

| TRA-1    | GROUP – C   | GROUP – P   |
|----------|-------------|-------------|
| Mean± SD | 38.40±24.61 | 58.69±25.21 |

Table-3 shows request for analgesia made for the first time in postoperative period in two groups.

Request was made significantly earlier in control group when compared with group G (p<0.05).

**Table-4: Time of rescue analgesia-2 (tra-2) in two study groups**

| TRA-2    | GROUP – C    | GROUP – P    |
|----------|--------------|--------------|
| Mean± SD | 100.86±30.26 | 132.06±23.77 |

Table-4 shows request for analgesia made for second time in postoperative period in two groups. Request was made significantly earlier in control group when compared with group G (p<0.05).

analgesia in patients undergoing surgery under general anaesthesia" was conducted on 60 patients of ASA grade I and II of either sex of age group 18 - 50 years scheduled for surgeries under general anesthesia who were randomly divided into two groups according to the drugs received as shown below:

**DISCUSSION**

The present study entitled "to study the effect of pre-emptive doses of pregabalin for postoperative

**Group C** (n=30) – received a placebo orally one and half hours prior to surgery.

**Group P** (n=30) – Patients who received 300 mg of Pregabalin orally one and half hours prior to surgery.

Successful recovery after surgery depends on complication free postoperative period. Postoperative pain, if not treated adequately may cause many physiological complications like hypertension, tachycardia, myocardial ischemia, angina, shallow breathing, cough suppression, retention of pulmonary secretion, gastric stasis and paralytic ileus, reduced mobility, muscle atrophy etc[3].

Many drugs are used to reduce post operative pain and thus complications associated with it like NSAIDS, opioids, alpha-2 agonists, ketamine, gabapentin, pregabalin etc. Pre-emptive analgesia is a treatment that is initiated before the surgical procedure in order to reduce sensitization.

Pregabalin is a structural analogue of GABA with anticonvulsant, anxiolytic and sleep modulating properties. As a successor of Gabapentin, Pregabalin was shown to be effective in several models of neuropathic pain, incisional injury and inflammatory injury [4]. Pregabalin binds potently to the  $\alpha 2\delta$  subunit and modulates calcium influx at nerve terminals, and, thereby, reduces the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P [5].

Selected groups were comparable for the demographic variables like age and weight parameters, type of surgery, sex and duration of anaesthesia as shown in table 1 with  $P > 0.05$ .

## ANALGESIA

Pain relief was assessed in both the groups by analyzing time of rescue analgesia 1 and 2 i.e. when patient complains of pain for the first and second time after extubation in postoperative period.

Pain control was better in group P when compared to group C as shown by TRA-1 as  $58.69 \pm 25.21$  in group P and in group C, it is  $38.40 \pm 24.61$ .

TRA-2 was  $132.06 \pm 23.77$  and  $100.86 \pm 30.26$  in group P and group C respectively showing better analgesia in pregabalin group.

Agarwal A. *et al.* [6] and Alieman *et al.* [7] who compared oral 150 mg Pregabalin and placebo administered 1 hour before surgery and observed that premedication with Pregabalin reduces postoperative pain scores and total analgesic consumption.

Alimian Mahzad *et al.* [8] used oral Pregabalin 300 mg one hour before surgery for postoperative pain in dacryocystorhinostomy surgery.

Eskandar A.M. *et al.* [9] also used oral premedication of Pregabalin 300 mg 12 hours and 1 hour prior to surgery on postoperative pain in patients undergoing shoulder arthroscopy.

Soltanzadeh M *et al.* [10] observed similar results as our study i.e. reduction in postoperative pain with use of gabapentin during preoperative preparation.

Pandey CK *et al.* [11] from their study concluded that pre-emptive use of Gabapentin significantly decreases postoperative pain and rescue analgesic requirement in laproscopic cholecystectomy.

Mardani-Kivi M. *et al.* [12] also used oral Gabapentin 600 mg two hours prior of surgery to evaluate the effect of Gabapentin on pain management after arthroscopic anterior cruciate ligament reconstruction.

Chiu TW *et al.* [13] and Jadeja C.A. *et al.* [14] in their respective studies observed that oral 1200 mg of Gabapentin when given 2 hours preoperatively, reduces the postoperative pain and analgesic requirement in tongue reconstruction and upper abdominal surgeries.

Marashi Seyed M. *et al.* [15] supports our study by observing the effect of premedication with oral Gabapentin 900 mg on 66 patients (22 each), and found a significant decrease in postoperative VAS for pain.

Parikh H.G. *et al.* [16] conducted a study concluding that a single oral dose of Gabapentin 600 mg given pre-operatively decreased the postoperative pain, enhanced the analgesic effect of tramadol and it also reduced the requirement of rescue analgesia with diclofenac when compared with placebo.

For post-tonsillectomy pain control Park Soo Seog *et al.* [17] used oral 150 mg Pregabalin night before and 1 hour before surgery (total 300 mg before surgery).

Similar results were found by Akhavanakbari G *et al.* [18] and Mansor Mardhiah S.H. *et al.* [19] and these results are in accordance with our findings.

## CONCLUSION

This study was carried out to study the effect of pre-emptive doses of pregabalin for postoperative analgesia in patients undergoing surgery under general anaesthesia. We found that oral pregabalin 300mg when given pre-emptively 1.5 hours before surgery reduces postoperative pain, increases time of first and second

rescue analgesia and also decreases total analgesic consumption in postoperative period.

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