

## Original Research

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### KEYWORDS:

Opioid consumption, Pain intensity, Pre-emptive analgesia, Rescue analgesic.

## Impact of Pre-Emptive Analgesia and Opioid use on Postoperative Pain in Patients undergoing Major Orthopaedic Surgeries

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### ABSTRACT:

**Background:** Postoperative pain is a common and serious issue affecting patient recovery. Pre-emptive analgesia, which blocks pain signals before surgery, can significantly reduce postoperative pain.

**Objective:** This study evaluated pre-emptive analgesia using oral pregabalin (150mg) and intravenous paracetamol (1gm) in reducing postoperative pain intensity using the Visual Analogue Scale. It compared pain scores at various time points between both the groups, total opioid consumption and its related side effects post-operatively and the time for first rescue analgesic.

**Methods:** This Prospective Cohort Study was performed on 82 patients undergoing major orthopaedic surgeries. Patients were randomly allocated to Group A receiving pre-emptive analgesia, while group B received only standard post-operative treatment, in both the groups pain intensity at 1,6,8,12,24 and 48 hours postoperatively, cumulative amount of opioid consumption, time for first rescue analgesia, PONV and sedation were compared.

**Results:** Group A had significantly lower pain scores at 6 ( $p < 0.001$ ), 8 ( $p = 0.008$ ), and 12 hours ( $p = 0.012$ ). Time to first rescue analgesia was longer in Group A ( $p < 0.001$ ). Opioid use was reduced by 69%, with fentanyl required only in Group B ( $p < 0.001$ ). Sedation scores at 2 and 6 hours, and PONV at 12 hours, were also significantly lower in

Group A ( $p < 0.05$ ).

**Conclusion:** Pre-emptive oral pregabalin and intravenous paracetamol significantly improved postoperative analgesia and reduced opioid consumption post-operatively in major orthopaedic surgeries. Pain scores were consistently lower, with delayed rescue analgesia and fewer opioid-related side effects.

## INTRODUCTION

Post-operative pain is a major challenge in patient's recovery, and if not managed properly, it can lead to discomfort, delayed healing and various other issues such as hypertension, tachycardia and prolonged hospital stay.<sup>[1]</sup> On the other hand, proper pain management can increase patient's satisfaction, result in rapid recovery of patient, shorten the length of hospital stay and can lower the risk of developing deep vein thrombosis.<sup>[2][3]</sup> A widely accepted method of providing analgesia for post-operative pain is with the use of opioids, which can lead to potential side effects and long-term risk leading to opioid crisis. So one of the non-opioid alternatives for the management of post-operative pain is use of pre-emptive analgesia.<sup>[2]</sup> Pre-emptive analgesia is an approach in which analgesics are administered before the onset of a noxious stimulus, with the objective of inhibiting the transmission of pain signals at both peripheral and central levels of the nervous system.<sup>[4][5]</sup> Paracetamol is the most widely used and well-tolerated drug. It inhibits COX-1 and COX-2 enzymes and potentiates pain-suppressing serotonergic pathways.<sup>[2]</sup> Pregabalin is a synthetic analogue of the neurotransmitter gamma-aminobutyric acid (GABA). Pregabalin binds to the  $\alpha 2\text{-}\delta$  subunit of voltage-gated calcium channels. It reduces entry of calcium into nerve cells, thereby restricting release of excitatory neurotransmitters such as glutamate and substance P, thus decreasing pain sensitivity.<sup>[6][7][8][9][14]</sup>

This study aimed at evaluating the efficacy of intravenous Paracetamol and oral Pregabalin as pre-emptive analgesia in reducing post-operative pain and opioid consumption. The specific objectives were to assess effectiveness of pre-emptive analgesia in reducing pain intensity using Visual Analogue scale (VAS), to compare score at each time point between the groups, to compare total opioid consumption between both the groups, to evaluate the incidence of opioid related side-effects and to determine the time for first rescue analgesia administration.

### Methodology: -

This prospective cohort study was conducted over a period of 6 months, and included 82 patients aged 20-80, American Society of Anaesthesiologists (ASA) I, II, III with no history of chronic opioid use were scheduled for major orthopaedic surgeries after providing informed consent. Participants excluded from the study were -Patients with renal and hepatic insufficiency, known allergy or hypersensitivity to the drugs used in the study, Patients with a history of analgesic use within 48 hours prior to surgery, substance abuse, psychiatric and neurological disorders, Patients who were pregnant and lactating, Patients on abductor canal or femoral nerve blocks. Patients were randomly divided into two groups, either to group A receiving oral pregabalin 150mg and IV paracetamol 1g 2 hours before anaesthetic induction, or to group B receiving standard postoperative treatment, by the staff nurse who was not involved in the study and no other premedication was given. In this primary outcomes were to assess the efficacy of pre-emptive drugs in reducing post-operative pain intensity and total post-operative opioid consumption. Secondary outcomes were to assess incidence of opioid related side effects and to the time required for first rescue analgesia. Assessment of pain was done using visual Analogue scale (VAS-0-no pain to 10-worst pain), pain was assessed at 1, 6, 12, 24 and 48 hours post-operatively. For sedation Ramsay sedation scale was used (1-awake levels were: -anxious, agitated, or restless, 2- cooperative, oriented, and tranquil, 3- responds to command; asleep levels were dependent on patient's response to a light glabellar tap or loud auditory stimulus, 4- brisk response, 5- a sluggish response, 6- no response). For nausea & vomiting PONV grading scale was used (0-without PONV, I-Nausea without vomiting, II-Nausea with vomiting (<3 times/day), III-Vomiting > 3 times /day). Statistical analysis was conducted using SPSS (Version 25.0). The Independent t-test was utilized to assess and compare post-operative pain scores at different time intervals, as well as the time to the first request for rescue analgesia. The Chi-square test was applied to compare ASA grades,  $P < 0.05$  was considered to be significant.

## Ethical Consideration:

Ethical approval was obtained from the Institutional Ethics Committee of Udai Omni Hospital, Abids, Hyderabad. (Reg. No: 42671/P1/2025).

## RESULTS

**Table 1:** Association of Demographics of patients

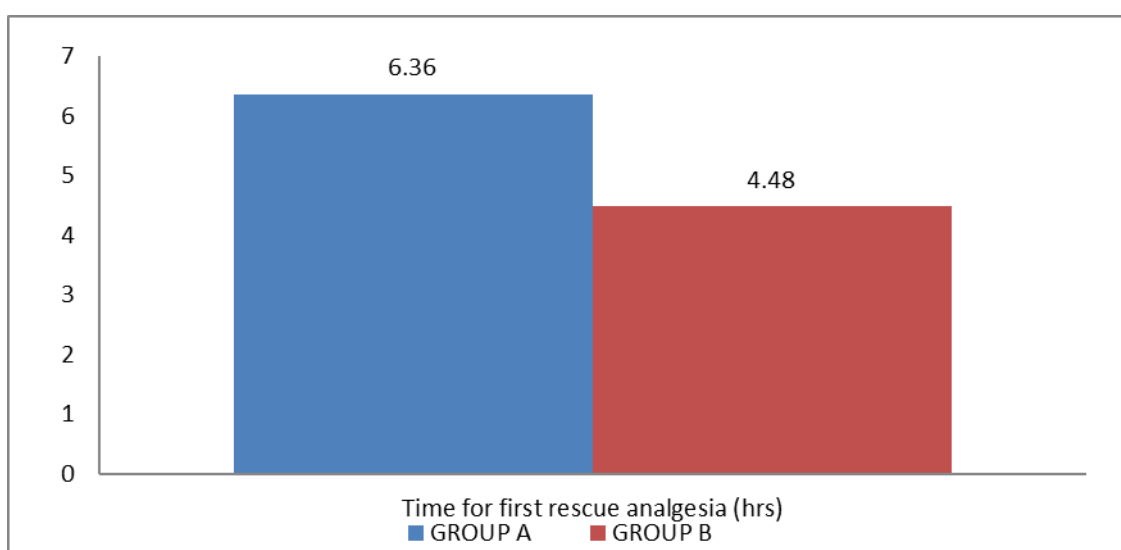
| Parameter            | Group A (Mean $\pm$ SD) | Group B (Mean $\pm$ SD) | p-value |
|----------------------|-------------------------|-------------------------|---------|
| Age (years)          | 46.63 $\pm$ 18.00       | 52.24 $\pm$ 18.70       | 0.145   |
| Gender (M/F)         | 26 / 15                 | 20 / 21                 | 0.182   |
| ASA Grade (I/II/III) | 17 / 18 / 6             | 9 / 27 / 5              | 0.113   |

There was no substantial difference among groups with regard to age, gender, ASA grade. (\* $p > 0.05$ )

**Table 2:** Postoperative Visual Analogue Score (VAS) at different time intervals

| Time Post-op | Group-A         | Group-B         | p-value |
|--------------|-----------------|-----------------|---------|
| 1 hour       | 0.00 $\pm$ 0.00 | 0.00 $\pm$ 0.00 | -       |
| 6 hours      | 1.71 $\pm$ 1.40 | 3.63 $\pm$ 2.36 | 0.002   |
| 8 hours      | 3.22 $\pm$ 1.31 | 4.68 $\pm$ 2.29 | 0.001   |
| 12 hours     | 3.93 $\pm$ 1.42 | 4.90 $\pm$ 2.14 | 0.002   |
| 24 hours     | 3.85 $\pm$ 1.44 | 4.49 $\pm$ 2.12 | 0.006   |
| 48 hours     | 2.95 $\pm$ 1.32 | 3.83 $\pm$ 2.22 | 0.001   |

VAS scores were significantly lower in group A compared with group B at 6,8,12-, 24-, and 48-hours following surgery, indicating superior postoperative pain control in group A. The observed differences were statistically significant ( $P = < 0.002$ , 0.001, 0.006, respectively).



**Figure 1:** Time for first rescue analgesia

From the above figure it was observed that the time for request of first rescue analgesia was significantly longer in the group A compared to the group B, indicating better initial pain control in group A. ( $P = 0.001$ )

**Table 3:** Assessment of total Opioid Consumption

| Opioids             | Group-A           | Group-B           | p-value |
|---------------------|-------------------|-------------------|---------|
| Tramadol (MME)      | $19.51 \pm 29.49$ | $27.07 \pm 25.91$ | 0.107   |
| Inj. Fentanyl (MME) | $0.30 \pm 1.95$   | $1.95 \pm 6.41$   | 0.077   |
| Patch Buprenorphine | $0.00 \pm 0.00$   | $5.12 \pm 32.80$  | 0.314   |
| Patch Fentanyl      | $0.00 \pm 0.00$   | $36.58 \pm 99.39$ | 0.006   |

Although, there was no considerable difference between both groups in postoperative opioid use, tramadol was the most commonly administered opioid in both groups. However, its usage was significantly higher in Group B (68.29%) compared to Group A (19.51%) ( $P = 0.017$ ). Injectable Fentanyl was used infrequently, with 1.22% in Group A and 9.76% in Group B ( $P = 0.077$ ). Notably, opioid patch formulations—Buprenorphine and Fentanyl—were utilized exclusively in Group B, at rates of 2.44% and 17.07% respectively, with no reported use in Group A. ( $P = 0.314$ ,  $P = 0.666$ ).

**Table 4:** Incidence of side effects

| Parameter    | Group A (n %) | Group B (n %) | p-value |
|--------------|---------------|---------------|---------|
| PONV 2h      | 2 (4.9%)      | 5 (12.2%)     | 0.066   |
| PONV 6h      | 3 (7.3%)      | 6 (14.6%)     | 0.474   |
| PONV 12h     | 1 (2.4%)      | 4 (9.8%)      | 0.033   |
| Sedation 2h  | 4 (9.8%)      | 7 (17.1%)     | 0.005   |
| Sedation 6h  | 3 (7.3%)      | 6 (14.6%)     | 0.004   |
| Sedation 12h | 2 (4.9%)      | 5 (12.2%)     | 0.649   |

Postoperative adverse events were generally less frequent in group A than in group B. Although the incidence of PONV was lower in group A at all assessed time points, a statistically significant difference was observed only at 12 hours postoperatively ( $P = 0.032$ ). Similarly, sedation was significantly lower at 2 and 6 hours ( $P = 0.005$  and  $P = 0.004$ , respectively). No significant differences were observed in PONV at 2 and 6 hours or sedation at 12 hours.

## DISCUSSION

In this prospective Cohort study, we observed that pre-emptive use of oral Pregabalin (150 mg) and IV Paracetamol (1 gm) was effective in reducing post-operative pain and opioid consumption in patients undergoing major orthopaedic surgeries, it also demonstrated that pre-emptive was effective in significantly delaying the need for first rescue analgesia, and produced notable opioid sparing effects without increasing the adverse effects.

These findings were consistent with prior randomized controlled trials assessing the benefits of pregabalin and paracetamol as pre-emptive agents<sup>[10]</sup> Reported that a single dose of pregabalin 150 mg before arthroscopic shoulder surgery significantly reduced opioid use, pain intensity, and the need for rescue analgesia over 48 hours without an increase in adverse effects. Similarly, <sup>[11]</sup> show that pregabalin reduced postoperative pain scores and opioid requirement. Similar results were also observed by <sup>[12]</sup>, which imply that preoperative pregabalin was helpful reducing the postoperative pain and fentanyl requirements following laparoscopic cholecystectomy. In our cohort, the mean time to first rescue analgesia was significantly prolonged in the pre-emptive group ( $6.37 \pm 1.56$  h) compared to the control group ( $4.49 \pm 1.33$  h;  $p < 0.001$ ). These results correspond with <sup>[11]</sup>, who found the time to first rescue analgesia prolonged to 164 minutes in patients receiving pregabalin 150 mg versus 27.5 minutes with paracetamol alone. Our study results were also similar with the findings of <sup>[7]</sup>, who observed reduced pethidine use and lower the pain scores in patient undergoing orthopaedic surgery, receiving pre-operative pregabalin

150 mg. moreover,<sup>[11,7]</sup> reported a notable opioid-sparing effects, prolonged analgesia, and reduced incidence of PONV with pregabalin, these findings were also consistent with <sup>[16,7]</sup> and further it was supported by <sup>[14]</sup>, in a meta-analysis, indicated that pregabalin significantly reduces opioid consumption and related side effects such as nausea and vomiting. Other studies that were conducted by <sup>[15,16]</sup> consistently reported no increase in the incidence of adverse events with a notable decline in Morphine and Fentanyl consumption after the administration of pre-emptive IV paracetamol. Likewise, <sup>[2]</sup> also found that when IV paracetamol given as a pre-emptive was effective in reducing fentanyl consumption after head and neck surgeries. These outcomes were in support with results of our study that IV paracetamol in combination with pregabalin can effectively enhance analgesia while minimizing incidences of opioid-related complications. Our study demonstrated 69% reduction in total opioid use in patients receiving pre-emptive analgesia. These results are consistent with the studies of <sup>[17,18]</sup>, who also observed that pregabalin can reduce the opioids need following hip arthroplasty and chronic neuropathic pain conditions.

## CONCLUSION

This prospective study affirmed that the administration of Intravenous paracetamol and oral pregabalin as a pre-emptive can improve post-operative pain as patients receiving this regimen reported a lower pain score at various time interval and it can also reduce opioid consumption in patient undergoing major orthopaedic surgeries, total opioid requirement—including tramadol and fentanyl—was markedly reduced, reflecting a substantial opioid-sparing effect of approximately 69% and patients also experienced a delayed need for first rescue analgesia. Additionally the incidence of side-effects, such as sedation and PONV was also lower in the patients receiving pre-emptive analgesia. All these findings highlight the efficacy and safety of using paracetamol and pregabalin as a pre-emptive.

## CONFLICTS OF INTEREST

The Author declares no conflict of interest.

## AUTHOR CONTRIBUTION:

P.A.K.J.T, A.M, SIS contributed to the study design, assisted in data interpretation, and critically reviewed the manuscript. M.A., B.U.A.H., contributed in Study design, Data collection, Data entry and Manuscript preparation. A.S, SIS, MMK participated in Literature review, Data analysis, Interpretation of results along with critical evaluation of manuscript.

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