

## **Is there Any Synergistic Effect of Perioperative Use of Pregabalin in Addition to Naproxen in Ankle Fractures? A Prospective, Randomized, Multicenter Study**

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### **INTRODUCTION:**

Opioid-centric pain management strategies have created an epidemic of prescription opioid abuse in the United States. Multimodal opioid-sparing analgesic regimens have spotlighted as alternatives to decrease postoperative pain. However there has been little study of the synergistic effect between naproxen and pregabalin. We aimed to compare the analgesic efficacy, adverse effects, and long-term functional outcomes between perioperative uses of naproxen only and naproxen with pregabalin.

**METHODS:** This study was designed in 70 patients belonging to the 19 to 65 age group indicated for operative fixation of a rotatory ankle fracture under general anesthesia in 3 different hospitals. Group A received naproxen 500mg only, Group B received naproxen 500mg with pregabalin 75mg 2 hour before surgery and 12 hourly for 3 days thereafter. Minimal clinically important difference of visual analog scale (VAS) for pain was set 13 mm out of 100 mm. VAS for pain, opioid consumption, time for first use of escape injection, and any adverse effect were recorded at 6-, 12-, 24-, 48-, and 72-hour postoperatively. VAS for pain was checked at 2-, 6-week, 3-, and 6-month afterward and functional outcomes including Olerud and Molander score and ankle-fracture outcome of rehabilitation measure (A-FORM) were measured at 3-month and 6-month postoperatively.

### **RESULTS:**

Sixty-two patients (33 in Group A and 29 in Group B) completed follow up until 6 months. Demographic data were similar between the 2 groups. VAS for pain scale was not significantly different between 2 groups at each timepoint until 6 months ( $P \geq 0.520$ ). Ninety-five percent confidential interval (CI) were within 13 mm at every time point except for at 6- and 12-hour postoperatively (95% CI -1.6 – 0.8, -1.4 – 1.0, each). There were no significant differences in opioid consumption, time for first use of escape injection, and functional outcomes between groups ( $P \geq 0.163$ ). Any adverse event at 48-hour postoperatively was significantly higher in Group B ( $P = 0.017$ ).

### **DISCUSSION AND CONCLUSION:**

There was no clinically significant effect of perioperative use of pregabalin in addition to naproxen to reduce pain after operative fixation of rotatory ankle fractures. Rather it significantly raised adverse events after 48-hour postoperatively. Therefore additional use of perioperative pregabalin should be cautiously decided.