A Randomized Clinical Trial: Does Scheduled Low-Dose Short-Term NSAID (Ketorolac) Modulate Cytokine Levels Following Orthopaedic Polytrauma?

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Purpose: The posttraumatic inflammatory response after orthopaedic injury is a complex process that can lead to posttraumatic complications. A double-blinded, randomized controlled trial was conducted at a single Level I trauma center to determine whether scheduled low-dose, short-term IV ketorolac modulates various cytokine concentrations in orthopaedic polytrauma patients.

Methods: From August 2018 to October 2022, 70 orthopaedic polytrauma patients between 18-75 years with a New Injury Severity Score greater than 9 were enrolled. 35 participants were randomized to the ketorolac group, receiving 15 mg of IV ketorolac every 6 hours for up to 5 inpatient days, and 35 patients were randomized to the placebo group, receiving 2 mL of IV saline in a similar fashion. The primary outcome was daily concentrations of prostaglandin E2 (PGE2), interleukin (IL)-1a, IL-1b, IL-6, and IL-10. Secondary outcomes included length of stay (LOS), pulmonary complications, acute kidney injury (AKI), and mortality. Group-level summary statistics were calculated for demographic and clinical variables. Time and group comparisons were made using linear mixed models and covariate analyses.

Results: IL-10 was significantly reduced in the ketorolac group and over time ($P = 0.043$). IL-6 was not significantly different between groups but showed a significant time effect, with patients experiencing an estimated 65.8% higher IL-6 at enrollment than on Day 3 ($P<0.001$). There was no significant treatment effect for PGE2, IL-1a, or IL-1b. There were no significant differences in secondary outcomes between groups.

Conclusion: Scheduled low-dose, short-term IV ketorolac was associated with significantly reduced IL-10 concentrations in orthopaedic polytrauma patients without any impact on LOS, pulmonary complications, AKI, and mortality in this pilot study. Future larger studies are needed to further characterize whether this medication- induced cytokine modulation impacts clinical outcomes following polytrauma.

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