Does Early Low-Dose Ketorolac Modulate Cytokine Levels Following Polytrauma?

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Purpose: The posttraumatic inflammatory response is a complex process associated with many clinical complications affecting outcomes in trauma patients. Dampening the inflammatory response during hospitalization may improve outcomes in polytrauma patients. The goal of this study was to determine if early administration of a low-dose, low-duration nonsteroidal anti-inflammatory drug (NSAID, ketorolac) can modulate inflammatory cytokines following polytrauma. The authors hypothesized that the treatment will reduce cytokine and prostaglandin (PGE2) levels during the inpatient stay, improving patient's inflammatory response to trauma.

Methods: Patients between 18 and 70 years of age; with a New Injury Severity Score (NISS) greater than 9, and without a contraindication to the NSAID were recruited from a Level I trauma center. Patients were randomized to the ketorolac or placebo group with the ketorolac group receiving 15 mg of IV ketorolac every 6 hours during their inpatient for up to 5 days and the placebo group receiving 2 mL of IV saline in a similar fashion. At enrollment and every 24 hours, blood samples were taken and assessed using sandwich ELISA (enzyme-linked immunosorbent assay) to determine cytokine serum concentrations of PGE2, interleuken (IL)-1A, IL-1B, IL-6, and IL-10. Repeated-measures analysis of variance model was used to estimate differences across groups over time.

Results: In total, 43 participants were included with 22 randomized to the ketorolac group and 21 to the placebo group. Demographics and NISS were evenly distributed between both groups (age, P = 0.330; NISS, P = 0.756; body mass index [BMI], P = 0.931). Inflammatory cytokines IL-1A, IL-10, and PGE 2 showed an appreciable but nonsignificant decrease in the treatment group compared to the control (P = 0.318, 0.096, and 0.339, respectively). Inflammatory cytokine IL-6 was not significantly different between groups (P = 0.313) with higher overall values in the treatment group after adjusting for age, NISS, and BMI. IL-1B achieved statistical significance (P = 0.0042), with the treatment group demonstrating a higher trend over the 5-day period.

Conclusion: Early, consistent, low-dose ketorolac does not appear to reduce proinflammatory cytokines, although a trend was observed in IL-10. There appears to be a mixed response to the administration of ketorolac, with IL-1B demonstrating a significant increase in concentration. Early results from our ongoing study cannot attest to the effects a consistent low-dose, low-duration NSAID plays in dampening the inflammatory response, highlighting the extensive interplay between cytokines and the inflammatory cascade following trauma.

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