TOLL-LIKE RECEPTOR INDUCED RESPONSES BY CIRCULATING LEUKOCYTES ARE SUPPRESSED IN TRAUMA ICU PATIENTS

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Blunt traumatic injury often is associated with profound inflammation and activation of the innate immune system, which may involve alterations in Toll-like receptor (TLR)-mediated responses. To study this, a prospective observational study was designed. Following IRB approval, 14 severely injured (ISS = 16-41) and mechanically-ventilated trauma ICU patients were enrolled along with 6 healthy normal volunteers that served as controls. Heparinized whole blood was collected at 2-12 days after ICU admission and incubated for 3 hrs in the presence of media alone (baseline), zymosan (TLR2 agonist) or LPS (TLR4 agonist). Inflammatory cytokine levels (IL-1β, -6, -10, TNF-α) in the supernatants were measured by Luminex multiplex assay. Whole blood cultures from both healthy volunteers and subjects were responsive to TLR2 and TLR4-mediated activation with elevated cytokines levels over that observed at baseline. Subject cultures with media alone (baseline) had significantly elevated levels of TNF-α, IL-6, and IL-10, as compared to healthy volunteers. In sharp contrast, healthy volunteer cultures stimulated with zymosan (TLR2 agonist) or LPS (TLR4 agonist) had 2-3-fold greater levels of IL-6, and TNFα than those of subjects. IL-1β and IL-10 levels did not differ significantly between healthy volunteers and subjects. In conclusion, these findings show that TLR-mediated activation of circulating leukocytes from trauma ICU patients is markedly suppressed, which may play a role in the development of subsequent infectious complications.