Complement System Targets and Models

HMGB1 Release is Associated with Clinical Outcomes After Blast Injury

High mobility group box 1 (HMGB1) is a key damage-associated molecular pattern that mediates inflammation and contributes to multi-organ failure after injury. In this study, researchers at U.S. Army Institute of Surgical Research (USAISR; Fort Sam Houston, TX) investigated HMGB1 levels and determined their correlation with mortality in Service members and rats with blast-related trauma (Figure 1).

Levels of HMGB1 in Service members with blast-related trauma (n = 54) were significantly higher than levels in healthy controls (n = 10) at admission and 8 hours later, but the difference was no longer significant at 24 hours. Levels of HMGB1 were significantly correlated with clinical variables including injury severity score; Glasgow Coma Scale; systemic inflammatory response syndrome; infusion of RBC, crystalloids, and FFP; and levels of complement factors C3a, C5a, and Bb. In a rat model of blast exposure (116 kPa) and subsequent 50 percent hemorrhage (n = 10), levels of HMBG1 were significantly higher 3 hours after injury than at baseline but returned to pre-injury levels by 10 hours after injury. Levels of HMBG1 were significantly higher in non-surviving than surviving rats at the 3-hour time point (n = 7 and 3, respectively).

These results demonstrate that HMGB1 is expressed in the acute phases of blast injury and HMGB1 levels correlated with clinical outcomes. Thus, HMGB1 may be a promising diagnostic and therapeutic target in trauma patients.

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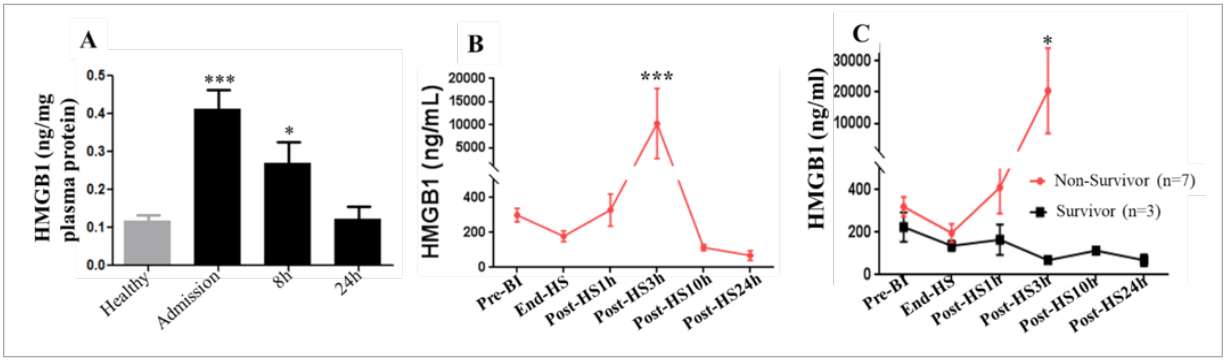

FIGURE 1: (A) early HMGB1 release in Service members with blast injury. * $p < 0.05$, and *** $p < 0.001$ vs. healthy controls. Increased blood levels of HMGB1 (B) were associated with mortality in rats subjected to blast injury and 50% hemorrhage (C). * $p < 0.05$ vs. non-survivor.