Complement System Targets and Models

Early Inhibition of Complement C5 Significantly Reduces Mortality and Protects Against Multi-Organ Failure in a Clinically Relevant Model of Blast Injury and Severe Hemorrhage

Trauma-induced hemorrhagic shock is a leading cause of death for military casualties and civilian trauma patients. Researchers at U.S. Army Institute of Surgical Research (USAISR; Fort Sam Houston, TX) previously demonstrated that early complement terminal pathway activation was present in rats exposed to blast overpressure (BOP) and correlated with clinical outcomes in Service members with blast-related trauma. They have also recently evaluated the efficacy of a complement C5 inhibitor, Coversin, on survival and multi-organ damage in an animal model of blast injury and severe hemorrhagic shock.

Early treatment with Coversin led to full complement inhibition within 10 hours and sustained inhibition for up to 24 hours (Figure 1). Animals treated with Coversin had significantly lower mortality, less metabolic acidosis, and better response to fluid resuscitation than untreated controls (Figure 2). In addition, Coversin significantly mitigated damage to brain, lung, and liver tissue.

These data demonstrate that complement C5 inhibition during the acute phase of injury could be an important therapeutic approach to protect against multi-organ failure and improve survival after blast-related trauma. Using a C5 inhibitor in the pre-hospital setting may lead to a significant reduction in morbidity and mortality of Service members and civilians who suffer traumatic hemorrhage.

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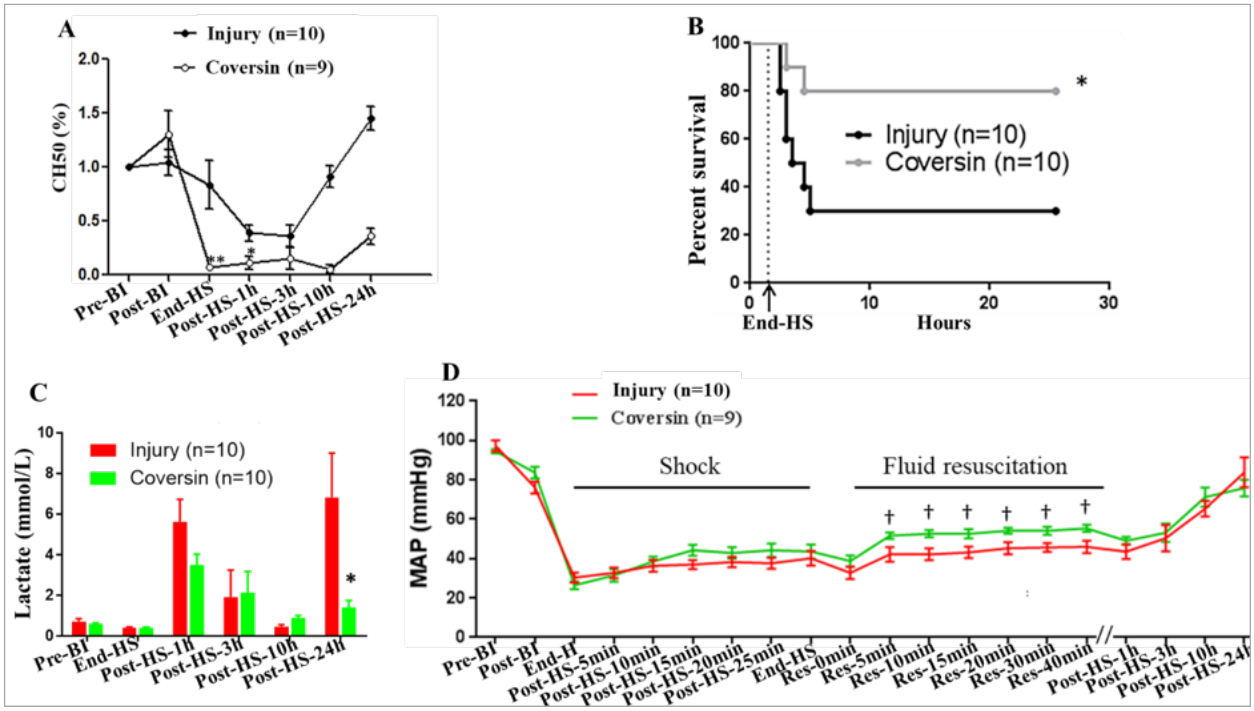

FIGURE 1: Complement C5 inhibitor (Coversin) treatment significantly inhibits complement activation (A), increased survival (B), reduced acidosis (C), and elevated blood pressure (D).

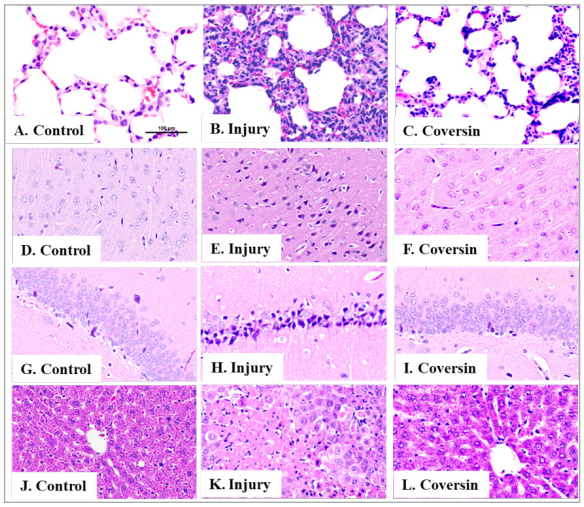

FIGURE 2: Effect of Coversin on lung injury (A-C), brain cortex (D-F), brain hippocampal injury (G-I), and liver injury (J-L), in a rat model of blast Injury and hemorrhage. Tissues were collected and fixed in 10% formalin solution. Tissue damages were evaluated by H&E staining.