EFFECT OF MPLA TREATMENT ON IMMUNE RESPONSES TO A BURN WOUND INFECTION

J. Bohannon, C. Romero, E. Sherwood

University of Texas Medical Branch

As a result of loss of the protective barrier of the skin combined with numerous injury-induced immunological alterations that decrease the ability to clear and control infections, severely burned patients are highly susceptible to opportunistic infections. Infection remains the leading cause of death in patients that survive the initial burn injury. Lipopolysaccharide (LPS) and monophosphoryl lipid A (MPLA) have been shown to have strong immunomodulatory properties. Prior sensitization with low doses of LPS or MPLA is known to induce a state of tolerance to subsequent LPS challenge, which is associated with an enhanced ability to clear bacteria following systemic challenge with *Pseudomonas aeruginosa*. Whereas LPS has numerous undesirable side effects, MPL is relatively innocuous and would therefore be more suited for clinical usage to enhance immune responses to infection. Previous studies have shown that treatment of mice with MPLA greatly enhances bacterial clearance, leading to increased survival, in a cecal ligation and puncture sepsis model, and this clearance is mediated, in part, by increased numbers of phagocytic myeloid cells. The current study was designed to determine if MPLA treatment of severely burned mice would similarly alter immune functions, leading to improved bacterial clearance and survival following a burn wound infection. Mice underwent a severe burn injury to approximately 35% of their total body surface area. Mice received treatment with either MPLA or lactated ringers (LR) as a control for two days following the injury. Wounds were then topically inoculated with *Pseudomonas aeruginosa* and mice were monitored for survival and bacterial clearance, and various immune cell populations were characterized. MPLA-treated mice showed improved survival, as well as decreased local and systemic dissemination of bacteria. MPLA treatment increased numbers of various innate immune cells responsible for clearing infection. This evidence suggests that MPLA provides protective immune-modulating potential against deadly burn wound infections.