Abstract

During ischemia reperfusion (IR) injury, high mobility group box 1 (HMGB1), a chromatin binding protein, is released from necrotic cells and triggers inflammatory responses. We assessed the therapeutic effect of a neutralizing anti-HMGB1 monoclonal antibody (mAb) on lung IR injury. A murine hilar clamp model of IR was used, where mice were divided into sham and IR groups with intravenous administration of anti-HMGB 1 mAb or control mAb. We analyzed the effect of anti-HMGB1 mAb against IR injury by assessing lung oxygenation, lung injury score, neutrophil infiltration, expression of proinflammatory cytokines and chemokines, levels of mitogen-activated protein kinase (MAPK) signaling, and measurement of apoptotic cells. Anti-HMGB1 mAb significantly decreased the plasma level of HMGB1 elevated by IR. The severity of IR injury represented by oxygenation capacity, lung injury score, and neutrophil infiltration was significantly improved by anti-HMGB1 mAb treatment. The expression of proinflammatory factors, including IL-1β, IL-6, IL-12, TNF-α, CXCL-1, and CXCL-2, and phosphorylation of p38 MAPK were both significantly reduced by anti-HMGB1 mAb treatment. Furthermore, anti-HMGB1 mAb treatment suppressed apoptosis, as determined through TUNEL assays. Overall, anti-HMGB1 mAb ameliorated lung IR injury by reducing inflammatory responses and apoptosis. Our findings indicate that anti-HMGB1 mAb has potential for use as a therapeutic to improve IR injury symptoms during lung transplantation.