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Acute Kidney Injury

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Role of Caspases and Calpain in Proinflammatory Cytokines Expression in LPS-treated Endothelial cells.

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Background: Sepsis continues to be a major cause of morbidity and mortality world-wide. Preclinical and clinical sepsis studies have shown that the acute systemic inflammatory and procoagulant response results in structural and functional alterations in the endothelium, which may lead to organ failure and ultimately, death. Multiple pro-inflammatory cytokines, chemokines and adhesion molecules have been proven important mediators in orchestrating this process. We aimed to determine the role of caspases and calpain in proinflammatory cytokines expression in LPS-treated endothelial cells.

Methods: Human umbilical vein endothelial cells (HUVECs) were exposed to 10 - 10,000 ng/ml LPS. The changes of IL-1 α , IL-1 β , TNF- α , IL-6 expression and cell viability test was compared in Control, LPS-(100 ng/ml), IL-1 α - (10 ng/ml), IL-1 β -(10 ng/ml), LPS+IL-1 α -, LPS+IL-1 β -, LPS+ IL-1 α +IL-1 β -treated HUVECs. The changes of IL-1 α , IL-1 β , TNF- α , IL-6 expression and cell viability test was compared with 50 μ M inhibitors of pancaspase, caspase-1, caspase-3, caspase-9, calpain in LPS-treated HUVECs.

Results: 1) There was a dose-dependent increase in IL-1 α , IL-1 β , TNF- α , IL-6 expression but cell viability was decreased in dose-dependent manner in LPS-treated HUVECs. 2) The expression of IL-1 α , IL-1 β , TNF- α , IL-6 was the highest in IL-1 β -treated HUVECs compared to Control, LPS-, IL-1 α -, LPS+IL-1 α -, LPS+IL-1 β -, LPS+IL-1 α +IL-1 β -treated HUVECs. 3) Cell viability was significantly restored with inhibitors of pancaspase, caspase-1, caspase-3, caspase-9, calpain in LPS-treated HUVECs. 4) The expression of TNF- α , IL-6 was not decreased with a calpain inhibitor and the expression of IL-1 β was not reduced with caspase-1 inhibition 5) The expression of IL-1 α was significantly augmented with a calpain inhibitor.

Conclusion: In conclusion, there were no effects on TNF- α , IL-6 expression with a calpain inhibitor and the expression of IL-1 β was not reduced with caspase-1 inhibition whereas The expression of IL-1 α was significantly augmented with a calpain inhibitor.

Keywords: sepsis, cytokine, endothelial cell, caspase, calpain