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Acute Kidney Injury

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The Characteristics of Chemokine Regulation 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. So, we aimed to determine the role of caspases/calpain on chemokine regulation in LPS-treated endothelial cells.

Methods: Human umbilical vein endothelial cells (HUVECs) were exposed to 10 – 10,000 ng/ml LPS. The changes of MCP-1, IL-8, CX3CL1 expression and cell viability test was compared in Control, LPS-(100 ng/ml), IL-1α-(10 ng/ml), IL-1β-(10 ng/ml), LPS+IL-1α-, LPS+IL-1β-, LPS+ IL-1α+IL-1β-treated HUVECs. The changes of MCP-1, IL-8, CX3CL1 expression and cell viability test was compared with 50 μM inhibitors of pancaspase, caspase-1, caspase-3, caspase-9, calpain in LPS-treated HUVECs.

Results: 1) There was a dose-dependent increase in MCP-1, IL-8, CX3CL1 expression but cell viability was decreased in dose-dependent manner in LPS-treated HUVECs. 2) The expression of MCP-1, IL-8, CX3CL1 was the highest in IL-1β-treated HUVECs compared to Control, LPS-, IL-1α-, LPS+IL-1α-, LPS+IL-1β-, LPS+IL-1α+IL-1β-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 MCP-1, IL-8, CX3CL1 was extremely inhibited with calpain inhibitors.

Conclusion: In conclusion, there was no significant difference between inhibitors of pancaspase, caspase-1, caspase-3, caspase-9, calpain in restoring cell viability in LPS-treated HUVECs. But a calpain inhibitor extremely protects against MCP-1, IL-8, CX3CL1 expression in LPS-treated HUVECs.

Keywords: sepsis, endothelial cell, chemokine, cytokine