Establishment of Canine Endotoxemia Model by Continuous Infusion of Low Dose of Lipopolysaccharide

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Purpose: Sepsis is still one of the most common causes of death in humans and animals in intensive care units. Activated immune responses can lead to parenchymal injury and multiple organ dysfunction syndrome (MODS) through neutrophil-endothelial interaction or "cytokine storm" in this situation. Many experiments have been performed in bolus infusions of lethal doses of lipopolysaccharide (LPS), but use of that technique does not simulate the conditions of clinical sepsis. Therefore, we selected a continuous low dose infusion for 24 hours comparable to the clinical situation of septic shock. MODS and hyper-activated immune responses were also evaluated.

Materials and methods: A total of twelve healthy adult beagles received a continuous IV infusion (10 ?g/kg/h, IV) of a low dose of LPS (Escherichia coli serotype 0111:B4; Sigma) dissolved in physiologic saline solution (total volume, 10ml/kg/h). Neutrophil activation was evaluated by complete blood cell counts (CBC) and cell surface expression of CD11b by use of the flow cytometry. Plasma cytokine level was determined using commercially available matched antibody pairs for sandwich enzyme linked immunosorbent assays (ELISA). Assessment of organ injury was performed by serum biochemical analysis. This study was approved by the Committee on Bioethics of Chonbuk National University (CBU2008?021).

Results: After 15~30min of LPS infusion, typical signs of canine endotoxemia including fever, vomiting, bloody diarrhea were shown. Severe leucopenia observed 0.5 h after endotoxin results mainly from migration and sequestration of circulating leukocytes. The expression of cell surface molecules of CD11b was increased after 3~6h of LPS administration. Typical time course of cytokine level was showed that early increase of TNF-α at hour 3, IL-6 at hour 6 and IL-10 at hour 6. Enzyme levels of ALT, ALP, LDH, CPK were markedly increased during 24 hours.

Conclusion: Canine endotoxemia model and MODS were successfully established by continuous infusion of low dose of LPS. Hyper-cytokinemia and activated neutrophils may contribute MODS in canine model.

Keywords: lipopolysaccharide, canine endotoxemia, multiple organ dysfunction syndrome

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