Furosemide inhibits Na+-K+-Cl- cotransporter and alleviates coagulopathy in endotoxin-induced disseminated intravascular coagulation

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Disseminated intravascular coagulation (DIC) is a common complication of sepsis and leads to multiple organ failure and death. A considerable body of recent evidence suggests that oxidant stress and inflammation response play a major role in DIC. A growing body of evidence shows that furosemide is a powerful anti-oxidant and anti-inflammatory reagent in addition to its diuretic effect. Thus, we tried to evaluate effects of furosemide on lipopolysaccharide (LPS)-induced DIC in Wistar rats. Rats were divided into four groups: (1) sham operation (SOP), (2) SOP + furosemide (3 mg/kg for 10 min i.v. infusion), (3) LPS (10 mg/kg for 40 min i.v. infusion) and (4) LPS + furosemide (3 mg/kg for 10 min i.v. infusion at 1 hr after LPS). Whole blood sample was collected at 0, 1, 2, 4 and 6 h. The changes of hemodynamics, blood glucose, fibrinogen (FIB), prothrombin time (PT), platelet, lactate dehydrogenase (LDH), hepatic (ALT) function, renal (BUN and CRE) function, and survival rate were monitored over 6 h. The vital organs including lung, liver and kidney were harvested at 6 hr after LPS challenge to perform Western blot and histo-pathological studies. The survival rate in each group was calculated at the end of studies. Our results showed that the LPS group matched the diagnostic criteria of the ISTH for overt-DIC. The administration of furosemide increased the concentration of FIB and platelet count, decreased the level of plasma LDH, ALT, BUN and CRE, improved prolongation of the PT and the LPS-induced delayed hypotension, and increased survival rate in LPS-induced DIC rats. In addition, furosemide not only attenuated the inducible nitric oxide synthase (iNOS) expression in the lung and liver but also attenuated the superoxide in the lung and kidney. Thus, our results suggest that furosemide has benefit effects on the LPS-induced consumptive coagulopathy occurred in late endotoxemia.