

Gut-derived endotoxemia: One of the factors leading to production of cytokines in liver diseases

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Abstract

AIM: To understand the relationship between levels of endotoxin and cytokines in serum and to clarify the cause of cytokines change in liver diseases.

METHODS: Serum endotoxin level was determined by quantitative limulus amoebocyte lysate chromogenic assay in 89 cases of acute and chronic liver diseases. Cytokines (TNF- α , IL-2, IL-6, IL-8, G-CSF) were assayed by ELISA. Patients were divided into two groups based on oral administration of lactulose or not. Mean concentration of endotoxin and cytokines was compared before and 20 d after lactulose treatment.

RESULTS: The highest serum level of endotoxin was found in patients with cirrhosis (69.3 ± 23.6 pg/mL) and the lowest in patients

with chronic hepatitis (28.4 ± 7.9 pg/mL), the moderate in patients with acute hepatitis (44.6 ± 14.3 pg/mL) ($P < 0.01$). Serum levels of TNF- α , IL-2, IL-6, IL-8, G-CSF were higher in patients with acute hepatitis than those with chronic hepatitis ($P < 0.05$). No difference was noted between chronic hepatitis and cirrhosis ($P > 0.05$). In all cases, serum levels of endotoxin were positively correlated with the concentration of TNF- α ($r = 0.555$, $P < 0.05$), IL-6 ($r = 0.531$, $P < 0.01$), IL-8 ($r = 0.440$, $P < 0.05$) and G-CSF ($r = 0.440$, $P < 0.05$), but not with IL-2 ($r = 0.101$, $P < 0.05$). The decrease of serum levels of endotoxin was greater in patients taking lactulose than controls (25.6 ± 14.4 pg/mL, $n = 49$ cases vs 10.9 ± 9.5 pg/mL, $n = 40$ cases, $P < 0.01$), the recovery from endotoxemia was higher in group with lactulose treatment than in controls (94.7%, $n = 19$ vs 36.4%, $n = 22$, $P < 0.01$). The decrease of endotoxin resulted in decreases of TNF- α , IL-6, IL-8, G-CSF, ALT, AST and TB.

CONCLUSION: Endotoxemia is common in liver diseases, which could induce production and release of cytokine from monocytes and macrophages and has harmful effects on hepatocytes. Treatment with lactulose could decrease serum levels of endotoxin and cytokines, suggesting that lactulose could protect liver cells from injury by reducing the absorption of endotoxin in intestine.

Key words: Endotoxins; Cytokines; Liver diseases; Serology; Lactulose

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