

Effects of nitric oxide synthesis inhibitor in long-term treatment on hyperdynamic circulatory state in cirrhotic rats

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Abstract

AIM: To investigate the effects of low dosage of nitric oxide synthesis (NOS) inhibitor NG-nitro-L-arginine methyl ester (L-NAME) in long-term treatment on hyperdynamic circulatory state in rats with cirrhosis.

METHODS: Cirrhosis model was induced in male SD rats by injection of 60% CCl₄ oily solution subcutaneously. Cirrhotic rats were treated with L-NAME (0.5 mg·kg⁻¹·d⁻¹) by gavage for two weeks. Mean arterial pressure (MAP), cardiac output (CO), cardiac index (CI), splanchnic vascular resistance (SVR), splanchnic blood flow (SBF) and serum NO levels were determined in L-NAME-

treated, L-NAME-untreated cirrhotic rats and controls by using 57 Co Labeled microsphere technique and a fluorometric assay, respectively.

RESULTS: Untreated cirrhotic rats had significantly lower MAP, SVR and higher PP, CO, CI, SBF and NO concentration than controls (14.42 ± 0.47 kPa vs 17.05 ± 0.34 kPa, 2.974 ± 0.186 kPa·mL⁻¹·min⁻¹ vs 4.234 ± 0.118 kPa·mL⁻¹·min⁻¹, 1.665 ± 0.067 kPa vs 1.123 ± 0.096 kPa, 189.99 ± 9.26 mL/min vs 135.5 ± 3.55 mL/min, 55.89 ± 1.82 mL⁻¹·mL⁻¹·100 g⁻¹ BW vs 39.68 ± 1.64 mL⁻¹·mL⁻¹·100 g⁻¹ BW, 4.60 ± 1.25 μmol/L vs 0.53 ± 0.26 μmol/L, $P < 0.01$, respectively). In treated cirrhotic rats, L-NAME significantly attenuated the increase of CO, CI, SBF, NO concentration and the decrease of MAP and SVR. In treated cirrhotic rats, L-NAME induced a marked decrement of NO concentration than untreated cirrhotic rats (1.471 ± 0.907 μmol/L vs 4.204 ± 1.253 μmol/L, $P < 0.01$).

CONCLUSION: The endogenous NO may play an important role in the changes of hemodynamics pattern in cirrhosis, and hyperdynamic circulatory state in rats with cirrhosis can be ameliorated by long term low dose L-NAME treatment.

Key words: Nitric oxide synthase; Hemodynamics; Fibrosis; Microsphere; Fluorometry; Rats

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