Hepatic Injury Secondary to Renal Ischemia-Reperfusion (I/R) Injury: Possible Role of Nitric Oxide

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Abstract

Renal I/R injury is a common clinical problem that encountered in many conditions such as transplantation, partial nephrectomy, and aortic cross clamping (1). Recent studies have suggested cross-talk between the liver and kidneys and found that any injury to either of them may affect the other. Liver injury is one of the distant-organ damages induced by kidney I/R (2). There remains continuing uncertainty about the role of NO in renal I/R injury with theoretical and experimental evidences offering support for both toxic (3) and protective roles (4).

Objectives

1. To declare the probability of liver affection consequent to renal I/R
2. To study the role of NO (toxic or protective) in the pathogenesis of this probable hepatic affection

Methods

48 Sprague-Dawley rats (250-300 g) divided randomly into 4 equal groups:
A. Group I (Sham-operated)
B. Group II (I/R injury)
C. Group III (I/R injury with administration of L-arginine; 300 mg/kg IV 20 min before ischemia)
D. Group IV (I/R injury with administration of N-omega-nitro-L-arginine methyl ester (L-NAME); 50 mg/kg in IV 20 min before ischemia).

Kidney functions tests (serum creatinine and BUN), liver enzymes (ALT, AST) were measured at 2 hrs after reperfusion.

Malondialdehyde (MDA), catalase, reduced glutathione (GSH) and NO were assessed at 2 hrs after reperfusion in liver tissues.

Histopathology (H&E stain) of the liver was also examined.

Results

I/R group showed significant elevation in liver enzymes (AST and ALT) and minimal histopathological damage of liver compared to sham group (p<0.001).

Administration of either L-arginine (NO precursor) or L-NAME (non-selective inhibitor of NOS) caused significant worsening of liver enzymes and pathology (p≤0.028) than I/R group.

NO concentration in liver tissues was significantly increased in L-arginine group and decreased in L-NAME group compared to control group (p<0.001).

<table>
<thead>
<tr>
<th>Table (1): Effects of 45 min bilateral renal ischemia on liver concentration of NO, MDA, GSH, and catalase</th>
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<tbody>
<tr>
<td>NAME group</td>
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<tr>
<td>NO (μmol/L)</td>
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<td>MDA (nmol/gm liver)</td>
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<td>GSH (gm/liver)</td>
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<td>Catalase (U/gm liver)</td>
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Conclusions

Endogenous NO has a protective effect against hepatic injury induced by renal I/R injury, while exogenous NO by L-arginine worsens the hepatic injury induced by renal I/R injury. This probably is due to increased formation of reactive oxygen species.

References