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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 also was 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).

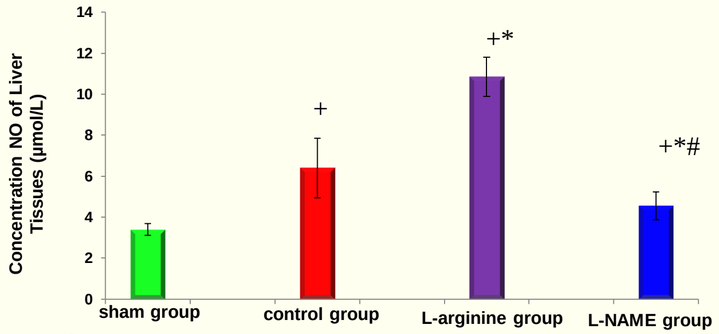

Figure (1)

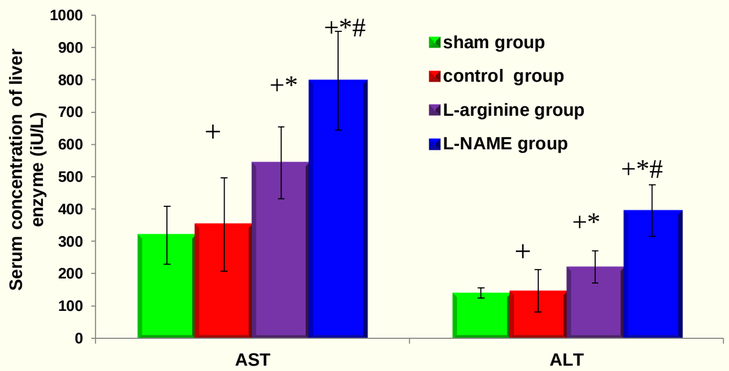

Figure (2) + Significant Vs. sham group, * significant vs. I/R group, # significant vs. L-arginine group

There were significant increase in **MDA** (marker of lipid peroxidation) and **GSH and catalase** (antioxidants) concentrations in liver tissue in I/R group (p< 0.001) .Moreover, further significant increase in **MDA** and significant decrease in **GSH and catalase** concentrations in liver was shown in L-NAME and L-arginine groups compared to I/R group (p< 0.001)

Table (1): Effects of 45 min bilateral renal ischemia on liver concentration of NO, MDA, GSH, and catalase

	Sham group	Control group	L-arginine group	L-NAME group
NO (umol/L)	3.4 ± 0.29	6.4 ± 1.46	10.85 ± 0.95	4.55 ± 0.68
MDA (nmol/gm liver)	10.34 ± 1.45	15.43 ± 2.27	19.85 ± 1.97	20.189 ± 1.148
GSH (mg/gm liver)	146.65 ± 29.22	197.9 ± 44.215	85.75 ± 5.29	121.75 ± 17.82
Catalase (U/gm liver)	0.25 ± 0.07	0.33 ± 0.02	0.19 ± 0.05	0.20 ± 0.07

Fig. (A): Specimens of liver tissues.= normally appeared liver architecture (H&E X200) (sham group); **Fig. (B):** Normal liver with the characteristic pattern of the hepatocytes trabeculae between central veins and portal areas (H&E X200) (control group); **Fig. (C):** Liver with focal degenerative changes in the form of hyperchromatic large nuclei and frequent mitosis (white arrows) (H&E X400) (L-arginine group); **Fig. (D):** liver with focal ischemic changes mainly in zone 3 with areas of haemorrhage (H&E X200) (L-NAME group).

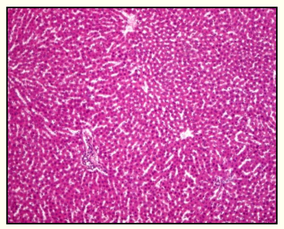

Fig. 3.A

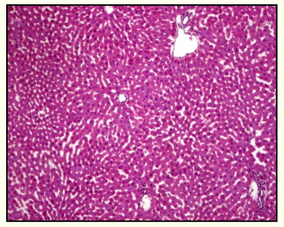

Fig. 3.B

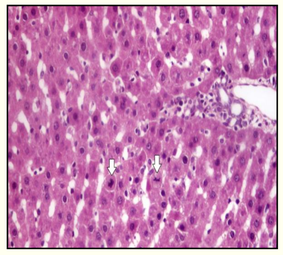

Fig. 3.C

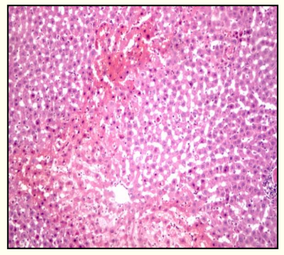

Fig. 3.D

Figure (3)

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

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