Hemodynamic and antifibrotic effects of a selective liver nitric oxide donor V-PYRRO/NO in bile duct ligated rats.

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AIM: To assess whether a liver specific nitric oxide (NO) donor (V-PYRRO/NO) would prevent the development of portal hypertension and liver fibrosis in rats with bile duct ligation (BDL).

METHODS: Treatment (placebo or V-PYRRO/NO 0.53 micromol/kg per hour) was administered i.v. to rats 2 d before BDL (D-2) and maintained until the day of hemodynamic measurement (D26). Intra-hepatic NO level was estimated by measuring liver cGMP level. Effects of V-PYRRO/NO on liver fibrosis and lipid peroxidation were also assessed.

RESULTS: Compared to placebo treatment, V-PYRRO/NO improved splanchnic hemodynamics in BDL rats: portal pressure was significantly reduced by 27% (P<0.0001) and collateral circulation development was almost completely blocked (splenorenal shunt blood flow by 74%, P=0.007). Moreover, V-PYRRO/NO significantly prevented liver fibrosis development in BDL rats (by 30% in hepatic hydroxyproline content and 31% in the area of fibrosis, P<0.0001 respectively), this effect being probably due to a decrease in lipid peroxidation by 44% in the hepatic malondialdehyde level (P=0.007). Interestingly, we observed a significant and expected increase in liver cGMP, without any systemic hemodynamic effects (mean arterial pressure, vascular systemic resistance and cardiac output) in both sham-operated and BDL rats treated with V-PYRRO/NO. This result is in accordance with studies on V-PYRRO/NO metabolism showing a specific release of NO in the liver.

CONCLUSION: Continuous administrations of V-PYRRO/NO in BDL rats improved liver fibrosis and splanchnic hemodynamics without any noxious systemic hemodynamic effects.

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