Increased intestinal permeability in rats with portal hypertension-associated right heart failure

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Background: Right heart failure (RHF) is a major cause of mortality in pulmonary arterial hypertension and highly associated with portal hypertension (PH). PH is known to lead increased intestinal permeability, but its pharmacokinetic impact is unclear. The aim of this study was to evaluate the effect of RHF on the rat intestinal permeability.

Methods: RHF was induced by monocrotaline (MCT) treatment. Water-soluble probes (polyethylene glycols [PEG] 400 and 600) were administered at a dose of 3.38 g/kg into the duodenum and the time course of plasma PEG concentrations was measured to evaluate the intestinal permeability.

Results: Increased brain natriuretic peptide and right ventricle hypertrophy were observed in MCT treated rats, confirming that RHF is successfully induced. The plasma concentration of PEG 400 in the portal vein at 150 min after administration in MCT rats was 1.50-fold higher than control rats ($p < 0.05$), but there was marginal difference in that of PEG 600, suggesting that RHF leads to changes of intestinal barrier function. In addition, the morphological differences in the villi were clearly observed between control and MCT rats, and the relative mRNA expression of claudin-1 in the duodenum rats were decreased by 70% in MCT rats as compared to control rats ($p < 0.05$).

Conclusions: These findings suggest that RHF decreases intestinal barrier function and integrity by causing the disassembly of the claudin-1 from the tight junction complex.

Keywords: portal hypertension; right heart failure; drug absorption; monocrotaline; polyethylene glycol; tight junction; claudin-1