Association between endotoxemia and blood no in the portal circulation of cirrhotic patients: results of a pilot study

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Abstract

Pathophysiology of portal vein thrombosis (PVT) in cirrhosis is still not entirely understood. Elevated levels of lipopolysaccharides (LPS) in portal circulation are significantly associated with hypercoagulation, increased platelet activation and endothelial dysfunction. The aim of the study was to investigate if LPS was associated with reduced portal venous flow, the third component of Virchow's triad, and the underlying mechanism. Serum nitrite/nitrate, as a marker of nitric oxide (NO) generation, and LPS were measured in the portal and systemic circulation of 20 patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedure; portal venous flow velocity (PVV) was also measured in each patient and correlated with NO and LPS levels. Serum nitrite/nitrate and LPS were significantly higher in the portal compared to systemic circulation; a significant correlation was found between LPS and serum nitrite/nitrate ($R = 0.421$; $p < 0.01$). Median PVV before and after TIPS was 15 cm/s (6-40) and 31 cm/s (14-79), respectively. Correlation analysis of PVV with NO and LPS showed a statistically significant negative correlation of PVV with portal venous NO concentration ($R = - 0.576$; $p = 0.020$), but not with LPS. In vitro study with endothelial cells showed that LPS enhanced endothelial NO biosynthesis, which was inhibited by L-NAME, an inhibitor of NO synthase, or TAK-242, an inhibitor of TLR4, the LPS receptor; this effect was accomplished by up-regulation of eNOS and iNOS. The study shows that in cirrhosis, endotoxemia may be responsible for reduced portal venous flow via overgeneration of NO and, therefore, contribute to the development of PVT.