Effects of transjugular intrahepatic porto-systemic shunt on the insulin-like growth factor system, insulin sensitivity, and macrophage activation in patients with liver cirrhosis

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ABSTRACT

The studies were conducted at Department of Medicine V (Hepatology and Gastroenterology), Aarhus University Hospital.

Malnutrition is common in patients with liver cirrhosis and independently related to increased mortality. It is therefore remarkable that insertion of a transjugular porto-systemic shunt, which alleviates portal hypertension, results in a marked and favorable gain in body cell mass. It follows that identification of the responsible mechanisms has potential for the treatment of malnourished patients with liver cirrhosis.

We hypothesized that this anabolic situation was initiated by the shunting of insulin-rich portal blood to the systemic circulation and would involve increased activity of the insulin-like growth factor (IGF) system, especially IGF-I and improvement in insulin sensitivity. Furthermore, a transjugular intrahepatic porto-systemic shunt (TIPS) would prevent catabolic events such as variceal bleeding.

We examined 28 patients with liver cirrhosis before and after TIPS procedure. Seventeen were followed for one year during which changes to the IGF-system and body composition were recorded. Eleven were examined by a two step hyperinsulinemic euglycemic clamp before and 26 weeks after TIPS insertion. To elucidate the effects of a catabolic event we also examined 59 patients with liver cirrhosis either before TIPS insertion (n = 36) or before large volume paracentesis (n = 23) and determined macrophage activation with the use of a specific serum-marker (Soluble CD163).

Patients gained 10-15% in body cell mass. The gain was positively associated with liver function at baseline. Elements of the IGF-system did not change after TIPS. Peripheral insulin levels increased and glucose tolerance deteriorated, probably as a consequence of blunted suppression of hepatic glucose production since neither hepatic nor peripheral insulin sensitivity changed. Neither of these findings supported our hypotheses. We found, that macrophage activation predicted the portal venous pressure gradient and was sustained at a high level after TIPS. Large volume paracentesis was associated with an even higher level of macrophage activation.

We concluded that the circulating IGF-system was not implicated in the body cell mass gain.

Neither hepatic nor peripheral insulin sensitivity changed after TIPS. Even so, it appears that glucose tolerance deteriorates, probably due to blunted suppression of hepatic or endogenous glucose production, but further studies are warranted.

Although a sustained high level of macrophage activation persists after TIPS, indicating that the responsible pathological process persists, it is likely that TIPS prevents bouts of catabolic macrophage activation as seen in relation to tense ascites.

Macrophage activation predicted portal venous pressure gradient probably by increasing dynamic non-structural hepatic vascular resistance.