

Abstract

There is no clear relation between portal systemic shunting, reduced hepatic insulin extraction leading to an increased systemic delivery of insulin, and, resultant peripheral hyperinsulinemia and insulin resistance. Extrahepatic portal vein obstruction is a natural human model of portal systemic shunting with essentially normal liver function. To investigate the role of portal systemic shunting of insulin in creating systemic hyperinsulinemia and insulin resistance, we studied nine subjects with portal systemic shunting and nine controls matched for age (± 2 years), body weight (± 2 kg) and height (± 5 cm). We carried out an oral glucose tolerance test and hyperinsulinemic euglycemic clamp study at insulin infusion rate of 40 mU/m²/min. Comparable ($p = 0.61$) basal insulin concentrations in the two groups (Mean (SE): 21.0 (3.98) vs. 24.1 (4.28) mU/L) demonstrated a lack of hyperinsulinemia in the presence of portal systemic shunting. The lower ($p = 0.03$) insulin area under curve on oral glucose tolerance test in presence of portal systemic shunting (7.40 (0.95) vs. 10.83 (1.15) U/L-min) indicated that lower extraction of insulin by the liver leads to a lower requirements in the periphery. The coefficient of variation for plasma glucose between 60 and 120 min of the clamps was 4.44 (0.55)%. Comparable ($p = 0.82$) M-values (6.21 (0.67) vs. 6.38 (0.45) mg/kg/min) in the two groups proved a lack of significant insulin resistance in the presence of portal systemic shunting. We conclude that isolated portal systemic shunting leads to neither hyperinsulinemia nor insulin resistance.