Role of sex steroids, intrahepatic fat and liver enzymes in the association between SHBG and metabolic features

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**BACKGROUND:** SHBG and liver enzymes levels are both associated with the risk of type 2 diabetes. However, the relationship between SHBG with liver enzymes and intrahepatic fat content remain poorly understood.

**OBJECTIVE:** To investigate whether SHBG is correlated with glucose and lipids levels and whether this association depends on fatty liver content, liver enzymes or sex hormone concentrations.

**DESIGN AND PATIENTS:** We studied 233 dysmetabolic men with measures of plasma SHBG, total testosterone, 17β-oestradiol, glucose, adiponectin, liver enzymes and hepatokines. Intrahepatic liver fat and visceral fat contents were measured by magnetic resonance imaging in 108 of these individuals.

**RESULTS:** After adjustment for age, SHBG concentration was inversely correlated with fasting glucose ($\beta_{\text{standardized}} = -0.21, P = 0.0007$), HbA1c ($\beta_{\text{standardized}} = -0.27, P < 0.0001$), triglycerides ($\beta_{\text{standardized}} = -0.19, P = 0.003$) and positively correlated with HDL-Cholesterol ($\beta_{\text{standardized}} = 0.14, P = 0.03$). These correlations persisted after adjustment for either total testosterone or 17β-oestradiol levels. SHBG was not related to either fetuin A or FGF 21 concentrations. The inverse association of SHBG with HbA1c and glycaemia was not altered after adjusting for liver markers but was no longer significant after adjustment for hepatic fat content.

**CONCLUSION:** The significant association between SHBG and fasting glycaemia, HbA1c and lipid levels in dysmetabolic men was not related to either sex hormones or markers of liver function, but was dependent on intrahepatic fat. This suggests that intrahepatic fat, but not alterations in liver function markers, may be involved in the association between SHBG and glucose and lipid metabolism.

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