**Hepatic Lipid Profile Improvement after Murine Sleeve Gastrectomy: The Role of Bile Acid Signaling.**

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Vertical Sleeve Gastrectomy (VSG) leads to metabolic improvements prior to, and beyond those that result from weight loss. We have shown previously that VSG increases serum bile acid concentration which feeds back negatively through the FXR-SHP pathway to down regulate lipogenesis and bile acid synthesis genes.

**Aims/hypotheses**

We considered whether short heterodimer partner (SHP) is necessary for the improvement of hepatic steatosis seen in mice following VSG surgery. In order to investigate the role of SHP we looked at the effects of VSG on hepatic steatosis, bile acid synthesis and transport genes, and bile acid metabolism in whole-body SHP-knock out mice. We also ruled out biliary obstruction or liver damage caused by VSG.

**Methods**

SHP-KO mice and their WT littermate controls were placed on high-fat diet (60% fat) until reaching an average of more than 30 grams the cut-off for obesity in mice. They then underwent either VSG or sham surgery. Post-surgery, weight was measured and blood samples were collected every 2 weeks. At sacrifice, 60 days post-surgery, liver and serum samples were collected for qPCR, liver/serum triglyceride and cholesterol, bile acid, and bilirubin and ALT assays. All assays were run with commercially available kits.

**Results**

SHP-KO VSG mice were lighter, had less body fat, and ate less than SHP-KO sham mice. However, there was no difference in liver triglyceride and cholesterol between SHP-KO VSG and SHP-KO sham mice. SHP-KO and WT mice post-VSG lost weight, had increased serum bile acids, and decreased bile acid synthesis gene expression. Despite this though, liver triglyceride and ALT reduction was not observed in SHP-KO VSG mice as seen in their WT littermates.

**Summary/Conclusions**

An intact SHP transcription factor is necessary for the improvement of non-alcoholic fatty liver disease seen after VSG in obese mice. It also appears that suppression of bile acid synthesis in SHP-KO VSG mice may be SHP independent. Further work investigating the ileal FXR-FGF15-FGFR4 pathway may explain this finding.

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