Metabolic Syndrome, Obesity, Insulin Resistance, Type 2 Diabetes and Bile Acids

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Microbiome, Antibiotics, Bile Acids and Insulin Resistance

The intestinal microbiome is referred to as a novel endocrine organ because it is able to influence the host via bile acids (Ridlon & Bajaj, 2015).

Since the landmark study by Karlsson et al. (2013) in which differences in the gut metagenome were explored in a cohort of European women with normal, impaired and diabetic glucose control, the intestinal microbiota is regarded as another (possibly modifiable) risk factor for obesity and type 2 diabetes (Tilg & Moschen, 2014), (Allin, Nielsen, & Pedersen, 2015). Although Karlsson et al.'s data (2013) are based on association and do not rule out reverse causality, a growing body of evidence is showing that, among lipopolysaccharides and short-chain fatty acids, bile acids may play a significant and possibly causal role.

Beneficial effects, although transient, were achieved by transferring “lean donor microbiota” to naive males with metabolic syndrome (Vrieze et al., 2012), (Khan, Nieuwdorp, & Bäckhed, 2014), or by changing the gut microbiota of obese male obese subjects through the administration of vancomycin, which reduced peripheral insulin sensitivity (Vrieze et al., 2014). A dramatic change was observed in the fecal bile metabolome because the secondary bile acids LCA and DCA decreased in very small quantities, but primary bile acids increased. Primary bile acids in plasma (measured as AUC after a meal) were somewhat reduced, but a 3.5-fold reduction was noted in the AUC of secondary bile acids as well as intestinal-derived FGF19 (AUC from 674 to 555 pg/ml), which is one of the downstream effectors of FXR. The authors did not measure the bile pool. Rather, their data were obtained from animal experiments (Sayin et al., 2013). The AUC data show that the pool size was very likely to have been considerably reduced. In observational studies, short- and long-term antibiotic treatment soon after birth was associated with obesity in later life. This suggests an almost everlasting epigenetic modulation or persistent population of altered gut microbiota.

Recording changes in the plasma bile acid metabolome before and after antibiotic treatment would be quite unusual in clinical routine, but may disclose novel predictive features in intensive care patients.

References


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