Effects of Sevelamer on the gut microbiome in chronic kidney disease

Every human being hosts an enormous quantity and variety of microorganisms, which in their entirety represent the human microbiome (1). The gut microbiome is part of this microbiome and consists of all microorganisms living in the intestinal tract, most of which are bacteria. Under physiologic conditions, the gut microbiome has a large impact on health and carries out several functions, such as protection against invasive intestinal pathogens, stimulation and modulation of the host immunity. Beyond the synthesis of vitamins B and K, the gut microbiome contributes to various metabolic functions and new active metabolites are regularly being identified (2). Conditions of gut dysbiosis, i.e. changes in qualitative and quantitative composition of the gut microbiome of any cause may contribute to the development of several disease states. To name just a few, established associations between the gut microbiome and obesity (3), diabetes mellitus (4) or cardiovascular diseases have been already made (5). In chronic kidney diseases (CKD), some uremic toxins such as p-cresol, indole and trimethylamine n-oxide (TMAO) are produced by the gut microbiome and are associated with CKD progression and cardiovascular outcome (6-8).

Hypercholesterinaemia and hyperphosphatemia are two important factors contributing to vascular atherogenesis and calcification in CKD. In order to prevent hyperphosphatemia, treatment with phosphate-binders is widely approved and used. Several non-randomized clinical trials show that among phosphate binders, patients taking sevelamer hydrochloride (HCL) have significantly lower all-cardiovascular and all-cause mortality than patients taking calcium-containing phosphate-binders (9, 10). Sevelamer hydrochloride is a binding crosslinked polymer. It contains multiple amines which become partially protonated in the intestine and interact with phosphate ions through ionic and hydrogen bonding. By binding phosphate, its absorption decreases thus lowering serum phosphate concentration. Sevelamer hydrochloride is not systemically absorbed. In addition, sevelamer seems to offer other pleiotropic beneficial effects, such as reducing inflammation, lowering serum-lipid- and serum uric acid levels (9, 11, 12). It is somehow remarkable that sevelamer HCL has been shown to exhibit systemic effects, without being absorbed. So far, the pleiotropic and favourable effects of sevelamer have been explained by its binding effects on bile acid and endotoxins (13, 14). It is very likely that sevelamer influences the gut microbiome as well, either by binding bacterial metabolites or the bacteria itself. So far, no one investigated the interaction of sevelamer with the gut microbiome before.