Regulation of intestinal phosphate transport

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Increase in serum phosphate (Pi) level (hyperphosphataemia) is a common clinical problem in chronic kidney disease (CKD). Hyperphosphataemia is associated with progression of kidney disease, endothelial dysfunction, atherosclerosis, vascular calcification, and accelerated cardiovascular disease. Recent studies indicate that in addition to the kidney, intestinal Pi transport also plays an important role in regulation of serum Pi and positive Pi balance. This is of major concern in view of the increasing and easily absorbable inorganic Pi content of fast foods and food additives. Modulation of intestinal Pi transport is therefore an important target in prevention of hyperphosphatemia and the associated cardiovascular complications in CKD. Intestinal Pi transport is mainly mediated by the type IIb sodium phosphate (NaPi) co-transporter NaPi-2b (SLC34A2) which is expressed in the intestinal apical microvilli. Pit-1 (SLC20A1) is also expressed in the intestinal apical microvilli but its function in regulation of intestinal Pi absorption remains unknown. In response to a high Pi meal, we have found marked increases in serum Pi. The increase in serum Pi persists for several hours. This occurs in spite of gradual downregulation of renal Pi reabsorption mediated by the renal NaPi transporters, first NaPi-2a (SLC34A1) followed by delayed and eventual downregulation of NaPi-2c (SLC34A3) and Pit-2 (SLC20A2). However, we have found an unexpected paradoxical increase in intestinal Pi reabsorption which is mediated by increased expression of NaPi-2b protein. In recent studies in animals with CKD we have found that following a high Pi meal there is a further marked increase in serum Pi. The increase may be mediated by persistent expression of the intestinal NaPi transporter NaPi-2b as well as increase in intestinal permeability as determined by increased intestinal flux of FITC-dextran (4kDa).