Recent Advances in the Management of Hyperphosphataemia

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Three main methods of achieving control exist; reduction of dietary intake, removal by dialysis, and reduction of gastrointestinal absorption by oral binding agents.

Patients on maintenance dialysis, who are usually catabolic, require a diet containing 1.0-1.2 g/kg/day of protein, which contains approximately 800-1,200 mg (20-40 mmol) of phosphate.

Usually this obligatory intake cannot be balanced by the decreasing phosphate excretion of the failing kidneys, or by the dialytic phosphate removal in patients on maintenance dialysis.

Thus, around 90% of dialysis patients require further therapeutic manoeuvres to control hyperphosphataemia.

An ideal oral phosphate binder would have a high affinity for binding phosphorus rapidly, across a range of pH, with low solubility and no systemic absorption. In addition, it should be non-toxic, in a solid oral dose form, and palatable, thus encouraging compliance.

Although a wide range of oral phosphate binders exists, none fully satisfies these criteria.

Calcium based binders are associated with a high incidence of hypercalcaemia, often severe enough to require withdrawal of the binder. Prior to 1985, aluminium-containing P binders were standard treatment for ESRD, forming insoluble and nonabsorbable aluminium phosphate precipitates in the intestinal lumen. However, once the risk of toxicity from oral aluminium was appreciated their widespread use rapidly declined. Synthetic hydrolysed ferrous sulphate (sodium ferrous citrate) and ferrihydrite have a significant capacity for adsorbing phosphorus but there is little experience with their use although the benefit of some iron absorption may be appreciated.

Sevelamer hydrochloride is a water-absorbing, non-absorbed hydrogel-cross-linked polyallylamine hydrochloride that is free of aluminium and calcium. It is probably resistant to digestive degradation, and therefore not absorbed from the intestinal tract. As a binder, it is as effective as calcium acetate but also binds certain fat-soluble vitamins such as 1,25 dihydroxyvitamin D3 and vitamin K. The long-term consequences of this remain unknown.

Nevertheless, the introduction of sevelamer gives clinicians a valuable new tool with which to attack hyperphosphataemia, but its expense has limited worldwide usage.

Lanthanum is a rare earth element with an atomic weight of 139 Da. It is present in tap water but in minute quantities. It binds phosphate ionically at all pH values, to form lanthanum phosphate, which is highly insoluble. In vitro studies suggest comparable efficacy to aluminium salts (>97%). Lanthanum carbonate has been studied in over 1,800 HD and CAPD patients in both Europe and the USA. These studies show good control of phosphate levels and calcium X phosphate products significantly less than 5.0 $(mmol/L)^2$. The incidence of adverse events was comparable to the placebo group and no safety

issues were identified.

Bone biopsy results indicate no evidence of direct toxic effects on bone; indeed potentially beneficial changes were seen from adynamic and osteomalacic states to more normal histology after one year of treatment. The full results of phase IV bone biopsy studies are awaited but it appears to be a highly promising addition to the range of oral phosphorus binders, with high potency and efficacy but no evident toxicity.