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Clinical Consequences of Hyperphosphataemia

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Hyperphosphataemia is a major trigger for the onset of hyperparathyroidism in chronic renal failure, and may result in bone pain, pathological fractures, proximal myopathy and growth retardation in children. In addition, it contributes to the anaemia of renal failure, and it has been suggested that hyperphosphataemia accelerates the progression of chronic renal failure, by precipitation of calcium phosphate in renal tubules or interstitium, or by inducing glomerular hypertension.

Poor phosphorus control correlates significantly with morbidity and mortality among end-stage renal disease and dialysis patients. Arterial calcification is associated with elevated calcium x phosphorus product, and dialysis patients have been shown to have 2.5-5.0 times higher coronary artery calcification scores compared to non-dialysis patients, using electron beam computed tomography. This technique has been shown to have a high sensitivity (84%) for predicting coronary disease in the general population, where the calcification score correlates with luminal stenoses. However, in dialysis patients the calcification is often within the arterial wall, and therefore may not be contributing to luminal stenosis, so that extrapolation of risk may not be valid in this group of patients. However, Block et al. surprised the nephrology community with the finding that hyperphosphataemia is associated with reduced survival, and most of the excess deaths were from cardiac causes. The magnitude of the risk is illustrated by the fact that hyperphosphataemic compared with normophosphataemic patients have a 52% higher risk of death from coronary artery disease, a 26% higher risk of sudden death, a 34% higher risk from other cardiac causes and a 39% higher risk of death from cerebrovascular accidents. It is tempting to suggest that the excess cardiac deaths are directly related to higher calcification scores derived from CT studies but this remains unproven. Further prospective studies are required to confirm this.

The calcium x phosphorus product is now regarded by many nephrologists as the major determinant of the progression and regression of metastatic calcium deposits. These calcifications are widespread in chronic renal failure and affect peri-articular sites, large and small arteries, cornea and conjunctiva, lung, myocardium and heart valves, kidney, gastric mucosa and subcutaneous tissues. Calcification of the myocardium can cause a reduction in left ventricular function and may cause arrhythmias. Calcific aortic stenosis causes the usual features of that disease and has proved fatal. Large vessel calcification is often particularly prominent in patients with diabetes mellitus, and progressive calcification of small and medium vessels can cause digital gangrene, particularly in the limb bearing a shunt or fistula.

Data from a variety of national and international registries demonstrates clearly that current management of calcium and phosphorus control is inadequate, and up to 70% of patients exceed the recommended limit for serum phosphorus. Control

by dialysis and diet alone is inadequate, and oral phosphorus binders are required. Unfortunately existing phosphorus binders are insufficiently effective, or limited by side-effects, and do not enable good control to be achieved. Lanthanum carbonate (Fosrenol™, Shire Pharmaceuticals) is a potent, novel, non-calcaemic, oral phosphate binder, with a proven ability to control serum phosphorus and calcium x phosphorus product.