Secondary hyperparathyroidism: present and future therapeutic implications

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Secondary Hyperparathyroidism: Present and Future Therapeutic Implications was the first programme in a series of clinically oriented Masterclasses in Nephrology which took place in Vienna, Austria in November 2001. Designed to heighten awareness and understanding within specific areas of nephrology, this masterclass examined issues surrounding the pathogenesis, epidemiology, health consequences and medical management of secondary hyperparathyroidism (HPT) in patients with chronic renal failure (CRF).

The pathogenesis of secondary HPT in CRF is associated with disturbances of calcium and phosphate metabolism. The three major factors involved in triggering an increase in parathyroid hormone (PTH) secretion appear to be low plasma calcitriol, hypocalcaemia and hyperparathyroidism (HPT) in patients with chronic renal failure (CRF).

Epidemiological studies investigating the incidence of parathyroidectomy (PTx) among uraemic patients have provided conflicting results. The Lombardy epidemiological study [1] found that the prevalence and incidence of PTx in Lombardy was lower than that previously reported for Europe and Italy, probably because of improvements in the monitoring and management of dialysis patients. However, in more recent years as the Lombardy study has continued, no additional decrease in the incidence of PTx has been observed.

One major health consequence of secondary HPT is renal osteodystrophy (ROD). ROD includes bone remodelling disorders, where bone quality is altered, and bone loss disorders, where bone mass is reduced; both abnormalities being potentially associated. Adynamic bone disease is now the most common bone remodelling disorder found in patients with end-stage renal disease [2], while osteoporosis is a significant risk factor for both pre-dialysis and dialysis patients.

The dose requirements of recombinant human erythropoietin (rHuEpo) in patients with CRF vary considerably, and many patients do not achieve recommended target haemoglobin levels of >11 g/dl. Some evidence suggests that HPT may have an inhibitory effect on erythropoiesis. However, other factors, such as inflammation and iron deficiency, might play a more predominant role in rHuEpo hyporesponsiveness.

Control of hyperphosphataemia and maintenance of normocalcaemia form the basis of medical management of secondary HPT. Novel approaches include the use of non-calcium-based phosphate binders, different dialysis modalities, new vitamin D metabolites, second-generation calcimimetics and advances in surgical techniques.

- The use of calcium-based phosphate binders may be associated with an increase in cardiovascular disease among patients on dialysis. Ongoing studies are therefore investigating the efficacy of non-calcium-based phosphate binders.
- Conventional dialysis alone is unable to adequately control hyperphosphataemia. In contrast, nocturnal dialysis 6–7 times a week has been shown to remove 50% more phosphorus owing to the longer duration and increased frequency of this modality [3].
- Newer vitamin D sterols, such as paricalcitol and doxercalciferol, have been shown to reduce intact PTH levels, apparently with less risk of hypercalcemia and hyperphosphataemia than calcitriol and alfalcacidol.
- Second-generation calcimimetics have been shown to suppress PTH levels without increasing calcium × phosphate product.
Patients with severe HPT that cannot be controlled medically, may be treated by PTx. The two main surgical strategies are total PTx with autotransplantation or subtotal PTx [4]. Both techniques retain adequate parathyroid function, thus avoiding hypoparathyroidism and low bone turnover.

In conclusion, secondary HPT is a frequent complication in patients with CRF and is associated with significant morbidity. The use of novel approaches to control hyperphosphataemia and maintain normocalcaemia should help to provide better treatment for these patients.

References