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Treatment of renal bone disease
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1. INTRODUCTION

Renal osteodystrophy is a disorder of bone and mineral metabolism that has long been recognized as a consequence of renal dysfunction. Disturbances in calcium and phosphorus homeostasis, reduced synthesis of 1,25-dihydroxyvitamin D₃, altered metabolism of parathyroid hormone (PTH), impaired renal clearance of PTH fragments and accumulation of substances, such as aluminum and β₂-macroglobulin, play a critical role in the pathogenesis of the renal bone diseases.

Renal osteodystrophy represents a spectrum of skeletal lesions that range from high-turnover disorders (osteitis fibrosa and mild lesions of secondary hyperparathyroidism) to low-turnover bone diseases (osteomalacia and adynamic lesion). Mixed lesions of renal osteodystrophy have histologic evidence of both osteomalacia and hyperparathyroidism. The rate of bone formation in mixed lesions depends on the predominant lesion. Although the performance of bone biopsies is the most accurate test for the diagnosis of the different subtypes of renal bone diseases, they are not routinely performed and PTH levels are utilized as surrogates of bone formation and to guide the response to therapy.

Accordingly, serum PTH has been widely used as a non-invasive marker for distinguishing patients with low-turnover lesions from those with secondary hyperparathyroidism. While the type of renal bone disease is primarily determined by serum PTH levels, additional factors that modify bone formation and turnover include calcium, phosphorus, vitamin D analogs, growth hormone (GH), and aluminum.

Thus, the control of secondary hyperparathyroidism and the prevention and management of the state of low bone turnover are critical elements in the care of pediatric patients treated with dialysis in order to prevent potential serious long-term consequences such as bone deformities, growth retardation and vascular calcifications.

2. TREATMENT OF RENAL OSTEODYSTROPHY

The treatment of children with renal osteodystrophy should include consideration of the following goals: (a) to maintain normal rates of bone formation and turnover; (b) to maintain normal serum calcium and phosphorus levels; (c) to maintain serum PTH levels that correspond to normal rates of skeletal remodeling; and (d) to prevent extraskeletal and vascular calcifications. Early diagnosis and appropriate treatment of renal bone disease is essential to prevent the debilitating consequences of this disorder for the growing skeleton. In this chapter, we will review the appropriate dietary management, the use of the different phosphate binding-agents, and the indications for therapy with vitamin D.

2.1. Role of dietary phosphate restriction

The development of hyperphosphatemia occurs in the vast majority of patients treated with maintenance dialysis. Therefore, a number of strategies are utilized to prevent the consequences of elevated serum phosphorus levels. Dietary phosphorus restriction is most often necessary to prevent the development and progression of secondary hyperparathyroidism in the early stages of renal failure and to prevent extraskeletal calcifications in patients with advanced renal failure. In addition, hyperphosphatemia and an elevated calcium \times \text{ phosphorus} product have been reported as independent risk factors for vascular calcifications and mortality in adult dialysis patients\textsuperscript{7}. Treatment goals include maintaining serum phosphorus levels within normal limits for age and avoiding a calcium \times \text{ phosphorus} product above 50–60.

The average phosphorus intake of a child in the US population is approximately 1500–2000 mg/day with 60–70% absorption of the dietary intake. Patients who develop hyperphosphatemia associated with renal insufficiency are usually instructed to reduce phosphate intake according to the age appropriate recommendations. Patients treated with dialysis also require dietary phosphorus restriction since the quantity removed by the current standard prescription of peritoneal dialysis (PD) (approximately 300–400 mg/day) or hemodialysis (HD) (800 mg/treatment) is insufficient to maintain normal serum phosphorus levels. On the other hand, the recent use of daily slow continuous HD has been associated with excellent control of serum phosphorus levels allowing phosphate binder agents to be discontinued\textsuperscript{8}. Furthermore, some of these patients developed hypophosphatemia and phosphate supplements were added to the dialysate solution to prevent the long-term consequences of hypophosphatemia\textsuperscript{8}. This technique has not yet been utilized in pediatric patients with end-stage renal disease (ESRD).

Strict adherence to dietary phosphate restriction is often difficult in children as an adequate protein and nutritional intake is necessary for growth and low phosphate diets are unpalatable, especially to older children. Thus, the additional use of phosphate-binding agents is required to maintain age-appropriate serum phosphorus levels in most patients treated with dialysis. It is essential to monitor serum phosphorus levels regularly to prevent hypophosphatemia, which may result from aggressive dietary restriction and the use of large doses of phosphate-binding agents. Infants are particularly at risk for hypophosphatemia due to a