

Renal Osteodystrophy Treatment and Cause

Abstract

The term “renal osteodystrophy” is used to describe the wide variety of skeletal deformities that affect people with chronic kidney disease. The two primary disorders are adynamic bone disease, which has low bone turnover and low levels of circulating PTH, and osteitis fibrosa, which is characterised by fast bone turnover, enhanced osteoclastic and osteoblastic activity, and high levels of circulating parathyroid hormone (PTH).

Renal osteodystrophy is primarily caused by the retention of phosphorus, decreased blood levels of calcitriol, lower levels of serum ionised calcium, decreased numbers of vitamin D receptors and calcium sensors in the parathyroid gland, and skeletal resistance to PTH's calcemic activity. The current strategy for treating renal osteodystrophy will be discussed in this review [1].

Keywords: Calcitriol • Hypophosphatemia • Hypocalcaemia • Parathyroid hormone • Chronic kidney disease

Introduction

For more than 60 years, it has been recognised that bone abnormalities are related to chronic renal disease. The term “renal osteodystrophy” is used to describe the wide variety of skeletal deformities that affect people with chronic kidney disease. Osteitis fibrosa, which has a rapid bone turnover rate, is a symptom of the impact of high levels of parathyroid hormone (PTH) on bones. Extremely little bone turnover is a feature of osteomalacia of aluminium buildup and adynamic bone disease. The latter disease, however, has an overabundance of osteoid tissue. In general, low levels of circulating PTH are linked to adynamic bone disease [2].

Mixed renal osteodystrophy is a disorder that can result from these two kinds of bone problems happening simultaneously. As a result of the buildup of β_2 -microglobulin, other processes like amyloidosis can also affect the skeleton. Finally, additional disorders like osteoporosis, which can occur postmenopausally or as a result of corticosteroid medication, can also have an impact on the bones [3].

It was observed that a buildup of aluminium from dialysis water and aluminium salts used as phosphate binders produced osteomalacia and an adynamic bone disease in the 1970s and 1980s. As a result of the discovery of these conditions, the range of renal osteodystrophy was widened, and calcium carbonate was substituted for aluminium salts in dialysis fluids. As a result, aluminum-related bone disease is becoming less common.

But in order to achieve normal bone histology, osteitis fibrosa and aluminium intoxication avoidance may not be sufficient. Patients may suffer from mild or adynamic bone diseases (early osteitis fibrosa) [4].

Renal osteomyelitis therapy

The goals of treating osteodystrophy in patients with kidney failure are to:

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Received: 02-Aug-2022, Manuscript No. OAIN-22-72738; **Editor assigned:** 04-Aug-2022, PreQC No. OAIN-22-72738 (PQ); **Reviewed:** 18-Aug-2022, QC No. OAIN-22-72738; **Revised:** 23-Aug-2022, Manuscript No. OAIN-22-72738 (R); **Published:** 30-Aug-2022
DOI: 10.37532/oain.2022.5(4).40-43

- (1) Keep blood calcium and phosphorus levels as close to normal as possible.
- (2) Stop the secretion of PTH if parathyroid hyperplasia has already developed.
- (3) Prevent calcium from building up outside of the skeleton.
- (4) Stop or reverse the buildup of materials like aluminium and iron that can negatively impact the skeleton.

Treatment

Phosphate, calcium, vitamin D, and PTH must all be kept under close supervision as part of the therapy of renal osteodystrophy. The following are the elements of a management strategy for conditions with high bone turnover and increased PTH [5]:

Vitamin D: A 20,000 U/day dose of vitamin D₂ is advised if blood levels of vitamin D are less than 30 ng/ml. PTH will be suppressed as a result, which will then affect osteoblasts. Analogs of vitamin D shouldn't be utilised in cases of adynamic bone disease. Depending on their potencies, these analogues could cause hypercalcemia. Since calcitriol is the most powerful and carries the greatest risk of hyperphosphatemia, which is also present to some extent with all vitamin D analogues, it is advised to avoid using it if the blood phosphate level is higher than 5.5 mg/dL. Among the several vitamin D analogues in use are paricalcitol and falecalcitriol.

Cinacalcet: This drug increases the sensitivity of the calcium-sensing receptors in the parathyroid glands, lowering PTH levels. It has been demonstrated to assist patients receiving dialysis in achieving PTH level goals when administered in conjunction with the other elements of the therapy regimen for renal osteodystrophy.

Phosphate: It's critical to keep the serum phosphate level below 5.5 mg/dL in order to reduce the high PTH levels. A phosphorus-restricted diet is strongly advised, and vegetarian meals are favoured since vegetarian protein has a poor bioavailability of phosphorus. The step-up intervention to maintain the appropriate phosphate levels is phosphate binders taken with meals. Because they don't affect calcium levels, non-calcium binders like sevelamer and lanthanum are favoured. However, calcium-

containing binders like calcium acetate and calcium carbonate might be administered in hypocalcemia situations when a calcium supplement is required. In these cases, the daily recommended intake of elemental calcium should not exceed 2 g.

Calcium: By adjusting the concentration of calcium in the dialysate, the amount of calcium is kept close to the upper end of the normal range. This reduces the calcium and phosphorus (Ca X P) product while maintaining the PTH's suppression.

Types of Osteodystrophy

Mild osteodystrophy: Having normal mineralization and a small increase in bone turnover as its primary symptoms.

Osteitis fibrosa: Characterised by accelerated mineralization and rapid bone turnover, leading to the development of weak and misaligned bones.

Osteomalacia: Reduced bone turnover and aberrant mineralization, which lead to the development of "soft" bones that are brittle and prone to breaking.

Atypical osteodystrophy: Characterised by acellularity and a reduction in bone turnover ("true bone").

Mixed osteodystrophy: Accelerated bone turnover and aberrant mineralization are its defining features.

Adynamic renal osteodystrophy

One of the histopathologic bone lesions identified in individuals with chronic renal failure is adynamic renal osteodystrophy, which is very different from the skeletal lesions caused by secondary hyperparathyroidism. Bone biopsy and histomorphometric analysis are required for conclusive evidence that adynamic bone is present in a certain patient. Histopathologically, adynamic bone is identified by a general decline in bone cellular activity.

Osteoblast and osteoclast counts are declining together. When bone samples from individuals with adynamic renal osteodystrophy are analysed by quantitative histomorphometry, the quantity of osteoid, or unmineralized bone collagen, is either normal or decreased. This alteration explains why there are very few areas of active new bone formation.

Although the rate of bone collagen production by osteoblasts and its subsequent mineralization are both below normal, both processes go forward at about the same speed. Therefore, in adynamic renal osteodystrophy, mineralization keeps up with or slightly exceeds the rate of collagen deposition by osteoblasts, in contrast to osteomalacia, where mineralization lags behind collagen synthesis, resulting in the accumulation of extra osteoid and an increase in osteoid seam width. As a result, in the adynamic lesion, the breadth of the osteoid seams is normal or reduced [6].

By using the technique of double tetracycline labelling on iliac crest bone biopsy specimens acquired from individuals with adynamic bone, the rate of bone growth is either subnormal or cannot be evaluated. With the use of these measures, it is possible to categorically separate individuals with adynamic lesions from those who have normal or higher rates of bone production and turnover. Secondary hyperparathyroidism's histologic alterations are conspicuously missing. Both the number of sites for osteoclastic bone resorption and the number of osteoclasts are decreased, and there is no peritrabecular or marrow fibrosis.

Diagnosis

It may be more crucial to do a bone biopsy in order to obtain an appropriate diagnosis now that it is understood that renal osteodystrophy covers a wide range of illnesses. Adynamic bone disease patients often have normal or decreased bone density, hardly raised serum alkaline phosphatase levels, generally normal blood parathyroid hormone levels, no bone aluminium, and hypercalcemia. Measurements of parathyroid hormones can be used to distinguish between adynamic bone disease and osteitis fibrosa or mixed illness, but they are insufficient to determine the specific kind of osteodystrophy in a given patient, particularly if calcitriol has been given.

Due to the pain of the procedure and the ability to predict the presence of osteitis fibrosa based on elevated serum concentrations of parathyroid hormone and alkaline phosphatase, the standard clinical practise for treating patients with end-stage renal disease and renal osteodystrophy has moved away from performing a diagnostic bone biopsy before the start of therapy. Additionally, blood aluminium levels, particularly following

deferoxamine therapy, point to the existence of bone disease linked to aluminium. The best method for determining the kind of renal osteodystrophy is still a bone biopsy [7].

Additionally, modifications in biopsy methods have lessened postoperative discomfort. The optimal blood parathyroid hormone concentration in a patient with end-stage renal disease is unknown, but it is now feasible to modify dialysate calcium concentrations, provide calcium salts, and deliver vitamin D preparations to keep serum parathyroid hormone concentrations within a specified range. Due to the down-regulation of parathyroid hormone receptors, the condition is linked to a resistance to the effect of parathyroid hormone [8].

However, the characteristics of adynamic bone disease imply that other mechanisms support resistance to the effects of parathyroid hormone and the increased serum Potentially necessary parathyroid hormone concentrations to overcome the suppression of factors that promote bone remodeling or the lack of bone-forming elements in advanced cancer kidney illness Probably, serum parathyroid hormone values should be kept between three and four times the regular maximum value, yet in recent research, children with increased parathyroid hormone serum hormone levels in patients taking calcitriol Despite treatment, the bone condition persisted [9].

Conclusions

The discovery that a variety of diseases can cause renal osteodystrophy comes as our knowledge of the disease's aetiology is getting better. Our understanding of the pathogenesis of renal osteodystrophy will improve with new knowledge about the physiology of bone remodelling in relation to the effects of cytokines and growth factors. Improved methods for the prevention and treatment of renal osteodystrophy may result from the potential identification of other chemicals that play significant pathophysiologic roles in osteitis fibrosa and adynamic bone disease [10].

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