

A Brief Review on Renal Osteodystrophy

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ABSTRACT

Renal osteodystrophy is a type of bone disease. Renal bone disease occurs in patients with chronic kidney disease. In these cases there will be changes in the concentrations of calcium, phosphate, vitamin D and parathyroid hormone. Systemic complications include renal osteodystrophy and soft tissue calcification, which can direct to morbidity and mortality. As the changes of renal bone disease are potentially modifiable, early recommendation to a nephrologist for monitoring and treatment is suggested. Advice about diet and regular monitoring of calcium, phosphate and parathyroid hormone are necessary. Careful prescribing of drugs and dialysis to achieve specific biochemical targets can minimize the complications. Phosphate binders and vitamin D analogues are required by most patients with advanced renal failure.

Keywords: Osteodystrophy, Phosphate binders, Parathyroid hormone (PTH), Vitamin D.

INTRODUCTION

Renal osteodystrophy is a type of bone disease that occurs when the kidneys are unsuccessful to maintain proper levels of calcium and phosphorus in the blood. It is common in people with kidney disease and affects most dialysis patients. This condition is most serious in children because this slows bone growth and causes deformities. The bone changes from renal osteodystrophy can begin many years before symptoms appear in adults with kidney disease so it also called as silent cripler.¹

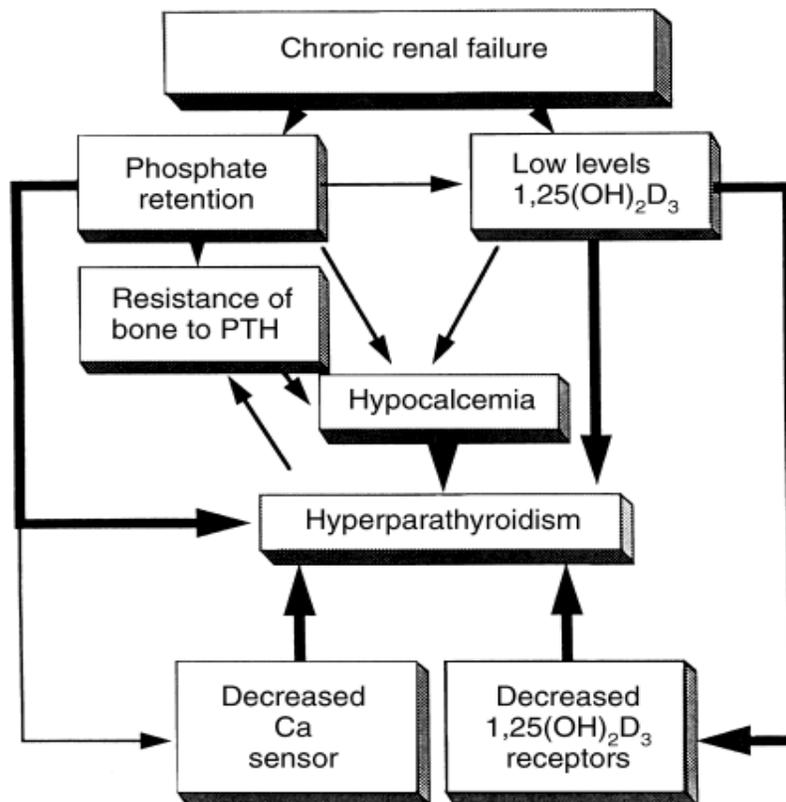
MECHANISAM & PATHOPHYSIOLOGY

The kidneys play an important role in maintaining healthy bone mass and structure by maintaining the levels of calcium and phosphorus in the blood. Healthy kidneys turn vitamin D into an active hormone (calcitriol), which helps increase calcium absorption from the intestines into the blood.^{2, 3} If calcium levels in the blood become too low, parathyroid glands release a hormone called parathyroid hormone (PTH). This hormone draws calcium from the bones to raise blood calcium levels. Too much PTH in the blood will remove too much calcium from the bones;

over time, the constant removal of calcium weakens the bones. Phosphorus also helps regulate calcium levels in the bones. Healthy kidneys remove excess phosphorus from the blood. When the kidneys stop working normally, phosphorus levels in the blood can become too high, leading to lower levels of calcium in the blood and resulting in the loss of calcium from the bones. If calcitriol levels drop too low, PTH levels increase, and calcium is removed from the bones. Calcitriol and PTH work together to keep calcium balance normal and bones healthy. In a patient with kidney failure, the kidneys stop making calcitriol. The body then can't absorb calcium from food and starts removing it from the bones.⁴⁻⁶

PATHOPHYSIOLOGY⁷

Renal osteodystrophy is the term applied to all pathologic features of bone in patients with renal failure. Impaired renal function leads to hyperphosphataemia & hypocalcaemia. If calcium levels in the blood become too low, parathyroid glands release PTH in the blood which will remove too much calcium from the bones, the constant removal of calcium weakens the bones. This can lead to renal bone diseases like renal osteodystrophy.

**SYMPTOMS⁸**

- Renal bone diseases are asymptomatic.
- With marked hyperparathyroidism there may be arthralgias, bone pains and deformity, neuropathy and marrow fibrosis with anaemia despite sufficient erythropoietin.
- These patients have an increased risk of fracture.
- In advanced disease, calcification of cutaneous blood vessels may rarely progress to thrombosis (calcific uraemic arteriopathy or calciphylaxis), resulting in painful ulcerating nodules that are associated with a high mortality.
- Renal osteodystrophy combines features of secondary hyperparathyroidism, rickets, osteomalacia, and osteoporosis. Findings of rickets and osteomalacia are present in children, and findings of osteomalacia and secondary hyperparathyroidism are present in adults.⁹

DIAGNOSIS¹⁰**Blood Tests**

- Calcium
- Phosphorus
- PTH
- Calcitriol

Bone biopsy

- Bone density

Radiography

- MRI helps evaluate the soft tissues for ligament rupture, and CT can help evaluate pathologic fracture. Amyloidosis may cause erosion in and around a joint, resulting in subtle radiographic signs, while amyloid deposits can be visualized directly on MRI.

DIFFERENTIAL DIAGNOSIS¹¹

To confirm diagnosis, renal osteodystrophy must be distinguished from

- Osteoporosis(Alk Phos and PO4 usually normal)
- Osteopenia
- Osteomalacia
- Hyperparathyroidism
- Multiple myeloma
- Soft tissue calcification¹²

- Chondrocalcinosis
- Hypervitaminosis

TREATMENT¹³

Preventing renal bone disease is a priority because advanced disease responds poorly to treatment.

- Phosphate binders reduce hyperphosphataemia and hyperparathyroidism.
- Calcium-containing phosphate binders also improve hypocalcaemia.
- Calcitriol improves hypocalcaemia and hyperparathyroidism.

1. Phosphate reduction^{14,15}

Controlling phosphate concentrations helps to control the secretion of parathyroid hormone.

Dietary restriction

Avoidance of foods high in phosphate, such as dairy products, cola soft drinks and nuts. The dietary restriction needs to be balanced against the risk of malnourishment.

Phosphate binders

These are taken with meals to adsorb dietary phosphate in the gut. Calcium salts are most commonly administered because they are cheap and help to maintain serum calcium.

Sevelamer and lanthanum¹⁶

These are newer drugs for patients intolerant of calcium salts. Sevelamer is a non-metal polymer-based binder that is not absorbed from the gut, while lanthanum is a rare earth metal which is minimally absorbed. These drugs are generally prescribed for hyperphosphataemia not controlled by calcium or when the calcium-phosphate product is greater than $4 \text{ mmol}^2/\text{L}^2$. Both drugs decrease phosphate absorption.

Aluminium salts

These are effective phosphate binders, but are not recommended because aluminium accumulates in renal impairment. This can cause anaemia and neurological complications. It is necessary to make sure that phosphate binder is aluminum-free because aluminum can be toxic and cause anemia.

Renal replacement therapy

Dialysis removes phosphate and this is enhanced if the duration and frequency of dialysis are increased.

2. Vitamin D analogues¹⁷⁻¹⁹

Multiple vitamin D analogues are available, but their relative advantages are not completely clear. Colecalciferol (vitamin D3), and less commonly ergocalciferol (vitamin D2) are oral formulations used by patients who do not require dialysis. In patients having dialysis, preliminary studies suggest colecalciferol partially corrects chronic kidney disease, mineral and bone disorder. Calcitriol is listed on the Pharmaceutical Benefits Scheme for hypocalcaemia due to renal failure, but in clinical practice it is mainly prescribed to suppress elevated parathyroid hormone concentrations. Calcitriol is a potent vitamin D analogue so careful monitoring for hypercalcaemia is necessary. Alfacalcidol (1- α -calciferol) and other dihydroxy vitamin D analogues such as paricalcitol (intravenous) and doxercalciferol are used less commonly. All vitamin D analogues can cause hypercalcaemia and hyperphosphataemia. Appropriate monitoring and dose adjustment of phosphate binders is therefore required.^{20,21}

3. Other treatments

Cinacalcet²²⁻²⁴

The drug cinacalcet hydrochloride (Sensipar), approved by the Food and Drug Administration in 2004, lowers PTH levels by imitating calcium. Cinacalcet is a calcium receptor sensitiser (calcimimetic) that inhibits parathyroid hormone release. It is usually used for patients receiving dialysis when parathyroid hormone exceeds 50 pmol/L , or is $15\text{--}50 \text{ pmol/L}$ with hypercalcaemia, despite conventional treatment. Doses are titrated from 30 mg to 180 mg daily.

Calcium salts

In addition to phosphate binding properties, calcium salts are often administered with vitamin D to suppress parathyroid hormone and to normalise body stores and ionised calcium for normal cell function. High doses should be avoided because they are associated with vascular calcification.

Sodium bicarbonate

Correction of metabolic acidosis may be useful because studies of alkali therapy in patients who are not in renal failure suggest an improvement in bone parameters. Sodium bicarbonate is poorly tolerated in higher doses due to flatulence, and imposes a sodium load which can exacerbate problems with fluid retention.

Bisphosphonates²⁵

Routine use of bisphosphonates is not currently recommended due to limited data on their efficacy and safety in patients having dialysis. Concerns include exacerbation of chronic kidney disease mineral and bone disorder and toxicity due to impaired clearance. However, they may reduce vascular calcification and limit hypercalcaemia when there is high bone turnover.

Surgical parathyroidectomy

This is indicated for severe secondary or tertiary hyperparathyroidism that fails to respond to optimum medical treatment, particularly if the patient is symptomatic or if there is coexistent hyperphosphataemia, hypercalcaemia or evidence of high turnover bone disease. Surgical parathyroidectomy is potentially avoidable with careful treatment of the mineral and hormonal disturbances in chronic kidney disease.

Exercise has been found to increase bone strength in some patients. It's important, to consult a health care professional before beginning any exercise program. A good treatment program, including proper attention to dialysis, diet, and medications, can improve your body's ability to repair bones damaged by renal osteodystrophy.

CONCLUSION

Renal bone disease is an important consequence of chronic kidney disease. Frequent monitoring of the plasma concentration of calcium, phosphate and parathyroid hormone is essential to minimise complications. Despite improvement in diagnostic imaging (bone density measurements), determination of biomarkers, mainly parathyroid hormone, still plays a central role. Treatment includes dietary advice and titrated doses of oral phosphate binders such as calcium salts, vitamin D analogues, sodium bicarbonate and cinacalcet. Dialysis is beneficial for patients with end-stage renal failure. Early referral to a nephrologist to guide monitoring and treatment is recommended. New treatment options resulted in improved bone health and also a reduction in mortality was achieved in adults with calcium-free phosphate binders. Substitution of active and inactive vitamin D is important and also has a beneficial effect on proteinuria.

Knowledge about the biochemical and molecular mechanisms of renal osteodystrophy is increasing significantly and has an impact not only to bone health but also overall morbidity and mortality. This will

ultimately lead to further improved diagnostic approaches and novel treatment options.

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