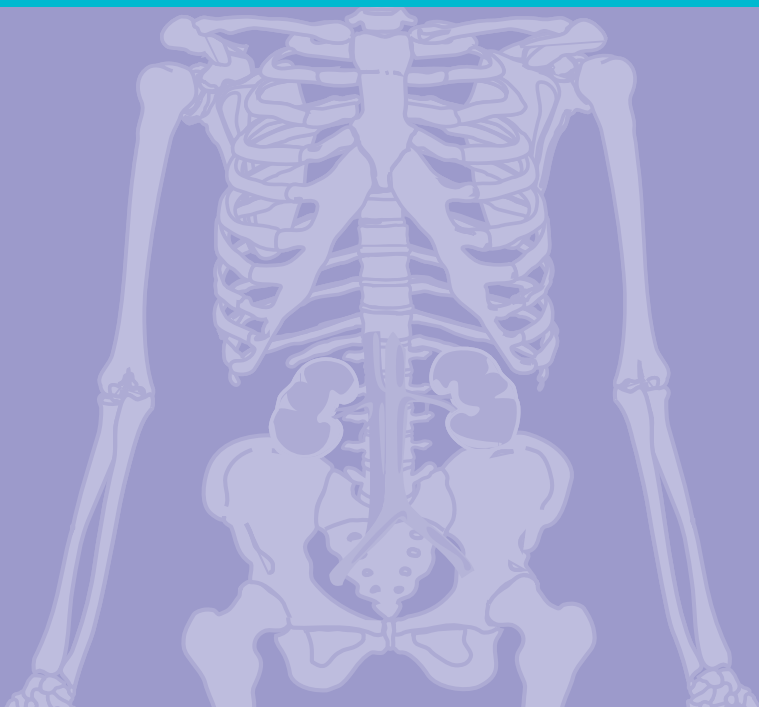


UNDERSTANDING AND PREVENTING

RENAL BONE DISEASE



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Understanding and Preventing Renal Bone Disease

Understanding Bones

Bone is a dynamic tissue, which constantly undergoes growth and remodelling. Healthy individuals have a complex system of metabolic checks and balances. The main factors controlling these processes are parathyroid hormone (PTH), calcitriol (active vitamin D) and also serum calcium and phosphorus levels. Together, these factors control the rate and nature of bone growth. Anything that disrupts these cycles can lead to abnormal, weak bone prone to pain or even fracture.

What is Renal Bone Disease?

Renal bone disease (also known as renal osteodystrophy) is due to changes in mineral metabolism and bone structure and occurs to some degree in everyone with progressive renal disease. Renal bone disease can be slowed or perhaps even prevented with early intervention using dietary measures and medications such as phosphate binders and calcitriol. Recently, new phosphate binders and a new class of drugs, the calcimimetics, have been introduced. Sometimes surgery (parathyroidectomy) is needed.

The Main Types of Bone Disease that Affect People with Chronic Kidney Disease (CKD):

- **“Osteitis Fibrosa”, caused by secondary hyperparathyroidism**
- **Osteomalacia (inadequate mineralisation)**
- **Low Turnover Bone Disease**
- **Osteoporosis**

“Osteitis Fibrosa” caused by Secondary Hyperparathyroidism

This can occur early in kidney disease. Bone turnover (the formation and removal of bone) is increased due to a process called secondary hyperparathyroidism (SHPT). This type of bone disease is due to changes in the balance of **calcium, phosphate and vitamin D that act to increase parathyroid hormone**. The kidneys play a key role in this balance. Parathyroid hormone (PTH) is produced by the parathyroid glands, 4 small glands in the neck.

As renal failure progresses, the kidneys are less able to remove phosphate, leading to higher than normal phosphate levels. These high phosphate levels, plus the underlying kidney disease, reduce the kidney's ability to make active vitamin D (calcitriol). Calcitriol is involved in regulating the blood level of calcium, by influencing the absorption of calcium from food. Levels of calcium in the blood therefore tend to fall when there is not enough calcitriol. Taken together, the lower calcium and active vitamin D levels and higher phosphate levels increase PTH release, a condition known as secondary hyperparathyroidism (SHPT). The excess parathyroid hormone then acts on bone to increase the release of calcium and phosphate. The blood levels of calcium and phosphate then increase, while the bones become weaker, with increased marrow fibrosis (hence “osteitis fibrosa”).

SHPT develops early in renal failure, even before the need for dialysis and is a "silent disease", just like blood pressure, because it is often unrecognised until symptoms occur. However, side effects of this imbalance (with elevated PTH and phosphate levels, and normal or high calcium levels) can cause itching, loss of mineral from the bones, pain, fractures and calcium deposits in blood vessels. Fortunately, most of these effects are entirely preventable through early and continuing treatment.

Osteomalacia (Inadequate Mineralisation)

In osteomalacia, bone requires crystals made from calcium and phosphate for its strength and rigidity. In osteomalacia, not enough of these crystals are formed. Osteomalacia is an important component of bone disease in some people with CKD. It can be due to vitamin D deficiency and acidosis, because bones take up acid that is normally removed by the kidneys and exchange it for calcium. In the past, many cases were caused by aluminium deposition in the bone. This is now unusual due to effective water treatment for haemodialysis and a decreased use of aluminium tablets taken to control phosphate.

Low Turnover Bone Disease

In low turnover bone disease, bone cell activity is reduced or absent (when this happens it is called ‘adynamic bone disease’). In contrast to osteomalacia, there is no increase in bone lacking mineral.

Low turnover bone disease was first noted in the early 1980s. It is often associated with the presence of diabetes and of older age. Amongst some patient populations, it has been described as the most common form of renal bone disease. Two additional factors which may be important in its development are the use of calcium and calcitriol, which suppress the release of PTH. Aluminium is how a factor in only a minority of cases. People with adynamic bone disease have a tendency to develop more fractures and blood vessel calcification.

Osteoporosis

It is also worth noting that renal bone disease occurs alongside the more common process of **osteoporosis**. Osteoporosis is associated with reduced levels of sex hormone (oestrogen and testosterone), ageing, reduced vitamin D levels and the use of medications such as glucocorticoids (steroids / prednisone).

Mixtures of the Above

In many cases a mixture of these processes is present, particularly a mixture of hyperparathyroid bone disease and osteomalacia.

Prevention and Treatment of Renal Bone Disease

Although symptoms such as bone pain and fractures might not occur until after dialysis has commenced, symptom free disease begins early. This is why early treatment is important in maintaining healthy bones. There are a number of strategies which, if employed and maintained, can help prevent the development of bone disease and calcification of blood vessels. Blood tests can be taken to measure calcium, phosphate and PTH levels, and treatment can be commenced to correct the changes.

Dietary and Medical Management

In early CKD, reduction of dietary phosphate can help to maintain normal PTH levels. However, phosphate restriction must be balanced against the risk of malnutrition. Phosphate is high in such foods as meat, beans, peas, chocolate, nuts, cola, most dairy products such as cheese (except full-fat soft cheese such as Philadelphia) and yoghurt, and shellfish and prawns. Renal dietitians can assist in identifying sources of dietary phosphate and can identify ways of reducing its intake, without risking malnutrition. In cases of mild to moderate renal impairment, low dose calcitriol has been shown to be effective in reducing parathyroid hormone by increasing the absorption of calcium from the intestines and directly inhibiting PTH production. Phosphate binders such as calcium carbonate are also used to reduce parathyroid hormone in the pre-dialysis stage and in cases of hyperparathyroidism. Calcium carbonate should be taken just at the start of meals, so that it can bind phosphate in the food and be excreted from the bowel.

Phosphate binders containing aluminium are also very effective in reducing phosphate. These should be used cautiously, if at all, because of the risk of aluminium intoxication. The absorption of aluminium is increased when medications are taken on an empty stomach or when taken with citric acid (found in orange and lemon juices). Children also have a tendency to absorb more aluminium. New oral phosphate binders (sevelamer and lanthanum) that don't contain calcium or aluminium, are especially useful for people with high phosphate levels when the calcium level in the blood is also high. These are not currently available before dialysis has been started.

Cinacalcet hydrochloride is a "calcimimetic" drug, which can trick the parathyroid cells into perceiving the level of calcium in the blood to be higher than it really is. The parathyroid glands then reduce PTH production. Calcimimetics are useful in reducing PTH and as a consequence, calcium and phosphate levels, in patients who have started dialysis.

Medications that can be used to improve low bone density are oral bisphosphonates, hormone replacement therapy (HRT), raloxifene, sometimes intravenous bisphosphonates and strontium. In patients with CKD, these treatments should only be used after specialist advice.

Surgical Management

Sometimes, the parathyroid glands will not decrease the production of PTH, regardless of medical management. In these cases, it is advisable that the parathyroid glands be removed (parathyroidectomy). Calcification of blood vessels in the skin with ulceration (calciophylaxis) may also be an indication for removal of these glands if levels of PTH are high.

Other Types of Bone Disease

Bone Disease Following Transplantation

Following transplantation, prednisone, cyclosporin and tacrolimus may reduce bone density. Both calcitriol and bisphosphonates have been shown to reduce loss of bone density following transplantation.

All patients need adequate calcium, vitamin D, nutrition and exercise. Hormone replacement therapy may occasionally be used in men or women.

High calcium levels due to hyperparathyroidism usually improve after transplantation. If they do not, parathyroidectomy is occasionally necessary. Pre-existing bone disease usually improves if good renal function is achieved after transplantation.

Bone Disease Associated with Long Term Dialysis Treatment

A condition known as amyloid bone disease develops in some people who have been on dialysis for many years. This is caused by the deposition of a small protein (Beta 2 microglobulin) in the soft tissues and joints. This protein is normally excreted by the kidneys. In the case of dialysis patients, it accumulates, as it is not completely removed during dialysis.

The commonest symptom of amyloid is a "carpal tunnel" syndrome. The median nerve to the hand can be compressed at the wrist, as it runs through the carpal tunnel. A small operation can release it. Other symptoms of amyloid can include pain, stiffness and swelling around the hands, shoulders and hips

These days, high flux dialysis membranes are more efficient in removing the amyloid protein. Also, ultrapure dialysate preparations may reduce the production of Beta 2 microglobulin. Hopefully, these improvements will result in a reduced incidence of this condition.

Transplantation is the treatment of choice for dialysis related amyloidosis. It lowers the blood concentration of Beta 2 microglobulin to normal, thus halting the progression of the disease. In fact, symptoms such as joint pain, swelling and stiffness can disappear within the first week after transplantation.

Taking Control

Renal bone disease is a complex disease process that starts early in kidney failure. Learning about this disease is the first step in taking control and preventing its effects. Follow the advice of your renal physician, dietitian, nurses and pharmacist by following any dietary recommendations and always taking your medication. **Taking an active role in your health management will maximise the possibility of a good outcome in all aspects of your treatment.** Ultimately, good management will help to maintain healthy bones and preserve an active lifestyle.

	Management of High Phosphate	Management of Hyperparathyroidism	Management of Low Turnover Bone Disease
TREATMENT	<ol style="list-style-type: none"> 1. Dietary phosphate reduction. 2. Phosphate Binders <ul style="list-style-type: none"> - Calcium - Sevelamer - Lanthanum - Magnesium - Aluminium 	<ol style="list-style-type: none"> 1. Calcium, Calcitriol 2. Reduce blood levels of phosphate. 3. Calcimimetics. 4. Surgery 	<ol style="list-style-type: none"> 1. Reduce Calcium or Calcitriol intake. 2. Sometimes reduce Calcium in the dialysis fluid. 3. Stop any Aluminium ingestion
COMPLICATIONS	<ul style="list-style-type: none"> • Blood Vessel and Skin Calcification • SHPT 	<ul style="list-style-type: none"> • Blood Vessel and Skin Calcification • Bone Pain • Itch • Fractures 	<ul style="list-style-type: none"> • Blood Vessel and Skin Calcification • Fractures