CASE REPORT

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Efficacy and Tolerability of Alendronic Acid for Primary Hyperparathyroidism

A Case Report and Review of the Literature

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The bisphosphonates are effective for the treatment of various diseases of bone and calcium metabolism that are characterised by increased bone resorption, including Paget's disease, hypercalcaemia of malignancy and metastatic bone disease. More recently, bisphosphonates have been proposed for the treatment and prevention of bone loss in several forms of osteoporosis;[1] alendronic acid (alendronate) is the first drug approved worldwide for this indication. While alendronic acid is generally well tolerated, oesophagitis is a not rare complication.[2] However, despite high bone turnover induced by overactivity of osteoclasts, primary hyperparathyroidism is not commonly recognised as an indication for bisphosphonates. A potential setback for administering bisphosphonates for a high-turnover bone disease may be the formation of an adynamic bone. This metabolic condition may result in a higher rate of fractures because of reduced bone resistance to trauma.

In this report we describe an elderly woman who was maintained successfully on alendronic acid with normalisation of serum calcium levels.

Case Report

A 75-year-old female was found to have asymptomatic hypercalcaemia on routine blood tests. The serum calcium level was 11 mg/dl (normal 8 to 10.5 mg/dl) and the serum phosphorus level was 3 mg/dl (normal 2.5 to 4.5 mg/dl). The intact parathyroid hormone (PTH) level was 60 ng/L (normal 12 to 72 ng/L). 24-hour urine collection showed a daily calcium excretion rate of 210mg and a daily phosphorus excretion rate of 720mg. The patient had been taking enalapril 10 mg/day for essential hypertension and aspirin 100 mg/day. She was otherwise healthy with no family history of endocrine disorders or tumours. She did not take oral calcium supplements, retinol (vitamin A), colecalciferol (vitamin D), lithium or thiazides.

Ultrasound revealed one enlarged parathyroid gland, which was probably an adenoma. She had no bone pain, nephrolithiasis, peptic ulcer disease or mental dysfunction. Bone x-rays were negative for cysts, but revealed mild osteopenia. Bone densitometry showed a mild reduction in mineral bone density, but this was normal for her age. The patient refused bone biopsy and partial parathyroidectomy and was started on alendronic acid 10 mg/day. Serum calcium levels decreased to 10.5 mg/dl within 3 weeks and the patient was maintained on this dosage. However, after 6 months the serum calcium levels increased to 11.2 mg/dl, while serum phosphorus levels were 2.9 mg/dl. Repeat intact PTH was now 221 pg/ml.

The patient still refused parathyroidectomy and the dose of alendronic acid was increased to 20 mg/day. Serum calcium levels decreased to 10.7 mg/dl and were maintained at this level for 2 years without further changes in the dosage of alendronic acid. She remained mentally and physically asymptomatic.

Discussion

Bisphosphonates are analogues of inorganic pyrophosphate, a naturally occurring chemical in bone. Phosphate-carbon-phosphate bonds with various carbon side-chains compose their basic chemical structure. The phosphate groups are responsible for the adsorption to bone mineral and rapid excretion in the urine. Based on the carbon side-chains, bisphosphonates can inhibit osteoclastic bone resorption with potencies that differ by as much as 10 000-fold among compounds. The most potent inhibitors are probably the aminobisphosphonates.[3]

Studies of the aminobisphosphonate alendronic acid show preferential uptake at sites of bone resorption. In these sites alendronic acid effectively blocks osteoclastic activity by inhibiting the ruffled border formation. Bisphosphonates other than alendronic acid are the treatment of choice for hypercalcaemia of malignancy, where a single infusion with a potent bisphosphonate will normalise serum calcium levels in 80% of patients.[4] However, Paget's disease also shows an excellent long-term response to alendronic acid, but usually necessitates a prolonged and high dosage. A dose between 10 and 20mg of oral alendronic acid may also successfully maintain normocalcaemia in patients with immobilisation hypercalcaemia and chronic hypercalcaemia of unknown cause.[5]

Mode of action studies have demonstrated that alendronic acid localises at sites of bone resorption and inhibits osteoclastic activity.[6] In secondary hyperparathyroidism caused by calcium-deficient diets in the rat, alendronic acid reduced bone loss.[6] In a comparative study between alendronic acid and etidronic acid (etidronate), alendronic acid appeared to be 1000-fold more potent in inhibiting bone resorption, and had at least a 1000-fold higher tolerability margin with respect to inhibition of mineralisation and osteomalacia.[6]

Bisphosphonates are effective therapeutic agents in several conditions characterised by increased bone turnover. Disorders where the underlying feature of the pathology is an increased bone resorption, including Paget's disease, hypercalcaemia of malignancy, and metastatic bone disease, are an accepted indication for use of bisphosphonates.[7] However, primary hyperparathyroidism is usually an indication for parathyroidectomy and not for pharmacological agents. In this case, however, the patient's refusal to undergo surgery and the mechanisms by which alendronic acid is effective, made it a logical choice which appeared successful in normalising serum calcium levels.

Recently, a 10-year prospective study of primary hyperparathyroidism has shown that uncomplicated primary hyperparathyroidism may be safely observed with or without parathyroid surgery.[8,9] In this single case, alendronic acid was used at least temporarily for the control of serum calcium levels in primary hyperparathyroidism. However, care must be taken not to neglect careful clinical, biochemical and radiological follow-up of the patient's bone mineral status. Parathyroid surgery undoubtedly remains the procedure of choice for symptomatic hyperparathyroidism.

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