Bisphosphonates Prevent the Hungry Bone Syndrome

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Sir,

Bisphosphonates are a well-established treatment for hypercalcaemia of malignancy [1] and Paget’s disease of bone [2]. In recent years, bisphosphonates have also been used in the medical management of primary hyperparathyroidism for temporary control of hypercalcaemia or in patients who are unwilling or unfit for parathyroid surgery [3]. An important complication of parathyroidectomy for severe primary hyperparathyroidism is development of the ‘hungry bone syndrome’, which may cause severe, and sometimes life-threatening hypocalcaemia, post-operatively [4]. Active metabolites of vitamin D have been given pre-operatively in an attempt to prevent this syndrome, with variable effects. Here we describe a patient with severe primary hyperparathyroidism who had bisphosphonate treatment for hypercalcaemia pre-operatively and who did not develop post-operative hypocalcaemia despite extensive parathyroid bone disease.

A 62-year-old woman presented with a 6-month history of progressive lassitude, bone pain, intermittent nausea with accompanying abdominal pain, polyuria and mild confusion. She was found to be hypercalcaemic (serum adjusted calcium of 3.3 mmol/l; normal 2.1-2.6) and had a grossly elevated intact immunoreactive parathormone level (iPTH) of 1,271 ng/l (normal 10-65). Her urea was 22 mmol/l (2.5-6.5), creatinine 215 µmol/l (60-110) and serum alkaline phosphatase 360 units/l (45-105). Radiographs showed evidence of extensive hyperparathyroid-related bone disease in the hands, skull, spine and pelvis. Intravenous pamidronate 30 mg was given over 4 h, on 2 consecutive days. Prior to the second infusion her serum calcium had already fallen to 2.85 mmol/l and a nadir of 2.57 mmol/l was reached at 7 days. Satisfactory calcium levels were maintained without further intervention until she underwent parathyroidectomy 10 days later. The combined weight of the two parathyroid adenomata that were resected was 4.6 g. Post-operatively, serum calcium values were restored to normal; there was no acute hypocalcaemia, nor did she require calcium or vitamin D supplements. Serum calcidiol (25-hydroxy vitamin D₃) and calcitriol (1,25-dihydroxy vitamin D₃) levels were measured prior to pamidronate treatment, and then at regular intervals before and after surgery over the next 3 weeks. The levels reflected chronic renal insufficiency. Calcidiol levels were normal between 15 and 25 nmol/l (reference range 15-100) and were not affected by treatment. The calcitriol level was 23 pmol/l (20-120) before treatment and was less than 15 pmol/l on all subsequent estimations.

Between 13 and 30% of patients who undergo parathyroidectomy develop postoperative hypocalcaemia [4]. Clinical and biochemical features that appear to predict the occurrence of
the ‘hungry bone syndrome’ are high serum calcium, raised alkaline phosphatase and PTH levels, raised plasma urea, age, and size of the resected parathyroid adenomatous ( > 4.4 g) [4]. Despite having all of these features, this patient did not develop post-operative hypocalcaemia. In view of this, it is probable that the pre-operative bisphosphonate treatment may have prevented development of the hungry bone syndrome. What might be the mechanism of action? In addition to its potent inhibitory effect on osteoclast activity, pamidronate can also transiently inhibit bone mineralisation [5]. Since prolonged hypocalcaemia after parathyroidectomy is thought to arise as the result of adsorption of calcium onto bone matrix, we speculate that pamidronate-induced inhibition of mineralisation may have reduced calcium uptake by the skeleton so reducing the likelihood of acute hypocalcaemia post-operatively. A compensatory rise in circulating calcitriol, which has been observed in patients with Paget’s disease receiving intravenous pamidronate, was not noted in our patient [6]. Whatever the underlying mechanism, the above observations, while uncontrolled, raise the possibility that pre-operative treatment with bisphosphonates such as pamidronate, may help prevent the hungry bone syndrome. Bisphosphonates thus provide an alternative to hydroxylated derivatives of vitamin D, which can have the unwanted effect of worsening hypercalcaemia pre-operatively.

References


