Dear Editor,

We want to draw attention to the important role of the parathyroid glands in maintaining normocalcaemia. A 50-year-old woman with known hypoparathyroidism secondary to Riedel’s thyroiditis initially presented with severe hypercalcaemia and acute renal failure luated by a gastroenteritis (table 1). Her medications dihydrotachysterol (DHT; 0.4 mg/day), calcium carbonate (3000 mg/day) and hydrochlorothiazide were stopped and she was treated with normal saline and a single dose of 60 mg pamidronate. After recovery of the hypercalcaemia she was discharged on her previous medication (figure 1). Five days later she presented again, now with severe hypocalcaemia necessitating treatment with intravenous calcium glubionate (2160 mg/day) and oral calcium carbonate (4500 mg/day) for several weeks, and a doubled vitamin D dose (table 1, figure 1). Only after 21 days the intravenous calcium supplementation was completely tapered. Twenty-three days after admission, she was discharged on oral calcium carbonate (6000 mg/day) and alfacalcidol (0.50 µg/day) (figure 1).

A clustering of features contributed to the bidirectional extreme calcium plasma concentrations in this patient. In normal conditions plasma calcium is tightly regulated by a dynamic hormonal system that controls its transport in the gut, kidney, and bone. Key players are the parathyroid hormone (PTH) and active vitamin D (1,25(OH)2D). Whereas normally any tendency towards hypocalcaemia or hypercalcaemia will result in a rapid increase or decrease in PTH secretion from the parathyroid glands, this response was obviously lacking in our patient. In addition, she was treated with calcium carbonate and DHT. The latter is a half synthetic vitamin D analogue that does not require renal hydroxylation. DHT is deposited in fat, liver, skin, muscle and bone. After withdrawal it may take up to nine weeks for the physiological effects to completely resolve. Thus, while gastroenteritis was the initial trigger for volume depletion, hypercalcaemia and renal insufficiency, the cascade was fuelled by continued use of calcium carbonate, DHT and hydrochlorothiazide. In this situation, intoxication with DHT is likely to occur with concomitant inappropriate ongoing intestinal calcium absorption.

Administration of pamidronate was the main trigger in the development of the severe hypocalcaemia. This synthetic analogue of pyrophosphate – a natural regulator of bone metabolism found abundantly in bone matrix – has several physiological effects resulting in a net decreased osteoclast activity. As a result the drug is very effective in correcting hypercalcaemia, especially in case of vitamin D intoxication, which is characterised by increased bone resorption. The appropriate pamidronate dose depends on patient characteristics, including the risk of hypocalcaemia, which is increased in the presence of hypoparathyroidism. A few case reports indicate low-dose pamidronate (15-20 mg) to be safe in hypoparathyroidism with DHT intoxication. Our patient received a higher dose (60 mg) instead. Although the plasma half-life of pamidronate is short, the inhibiting effect on osteoclasts persists for many weeks. Administration of APD in the presence of renal failure can result in prolonged and stronger inhibitory effects on osteoclastic activity, with a concomitant increased risk of prolonged hypocalcaemia. The long half-life of DHT, the vitamin D analogue used in our patient, is an unfavourable characteristic in the clinical situation in which immediate vitamin D effects are warranted. When the patient presented with hypocalcaemia, we therefore decided to replace the DHT by the short-acting active vitamin D analogue alfacalcidol.
In conclusion, this case illustrates the importance of functioning parathyroid glands for calcium homeostasis. In hypoparathyroid patients, bisphosphonates should be used cautiously as they can result in severe life-threatening and prolonged hypocalcaemia.

REFERENCES


