Use of recombinant parathyroid hormone with significant improvement of debilitating hypocalcaemia and hypomagnesaemia.

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Introduction

Primary hypoparathyroidism has an incidence of 4 in 100,000 people, with postoperative and autoimmune aetiology being the commonest. Idiopathic hypoparathyroidism is unusual affecting 7.2 per million people. Although acute hypomagnesaemia increases parathyroid hormone (PTH) secretion, profound magnesium depletion paradoxically depresses PTH and increases resistance inducing severe hypocalcaemia. Teriparatide a type of recombinant PTH containing the biologically active N terminal of the hormone (1-34) when given intermittently leads to increased number and activity of osteoblasts.

Case

A 45 year old woman presented with gradually worsening paraesthesia and limb weakness. Clinical examination only revealed a positive Chvostek’s sign. Initial investigations showed low serum calcium of 1.58 (2.2 - 2.6 mmol/L), magnesium of 0.4 (0.7 - 1.05 mmol/L), potassium of 3 (3.5 - 5 mmol/L) and normal phosphate 1.21 (0.8 - 1.5 mmol/L), bicarbonate 27 (22 - 28 mmol/L), liver and renal function. ECG showed prolonged QTc segment. She was initially treated with intravenous calcium and magnesium and subsequently switched to oral supplements. She had recurrent admissions over a 10 month period with persistently low calcium and magnesium. Hypertension was diagnosed eight months after her initial presentation.

Investigations

She was found to be hypocalcaemic and severely hypomagnesaemic (Figure 1) in all occasions.

Further investigations showed low PTH at 0.6 (1.3 - 6.8 pmol/L) with elevated 24 hour urine calcium excretion of 13.1 (2.5 - 7.5 mmol/24hr), urine magnesium excretion of 3.9 (2.4 - 6.5 mmol/24hr), normal thyroid function, haematocrits and a basal cortisol of 375 nmol/L. She had osteopenia on dual energy X ray absorptiometry and normal whole body computed tomography, gastroscopy and coeliac screen.

Outcome and Follow Up

Recombinant PTH (1-34) (teriparatide) led to normalisation of calcium and no further hospital admissions. A 24 hour collection of urine electrolytes, while on teriparatide and oral supplements, showed a magnesium excretion of 8.1 (2.4 - 6.5 mmol/24hr), calcium of 11.2 (2.5 - 7.5 mmol/24hr), potassium of 72 (25 - 125 mmol/24hr) and phosphate of 20 (14 - 50 mmol/24hr). In hypomagnesaemia of extrarenal origin, 24 hour urine magnesium excretion remains below 1 mEq/day whereas in tubular defects is greater than 4 mEq/day. As a result her hypoparathyroidism is thought to be functional secondary to severe hypomagnesaemia suppressing the endogenous PTH production and increasing PTH resistance.

Conclusion

In our case, in view of her normal gastrointestinal investigations and excessive urine electrolyte losses, the hypoparathyroidism was attributed to a renal tubular defect related to an acquired mutation or a hereditary disorder clinically emerging in adulthood leading to excessive magnesium renal wasting. In the United Kingdom, the N terminal active fragment (1-34) of recombinant human PTH (teriparatide) is currently only licensed for the treatment of osteoporosis. In the United States, the full length PTH (1-84) was approved for the treatment of hypoparathyroidism in 2015. The “Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism” (REPLACE) study [1] showed good tolerance and therapeutic effect of PTH (1-84) in hypoparathyroidism. Further studies are required to evaluate the role and efficacy of PTH in the management of patients with resistant and/or persistent hypocalcaemia and hypomagnesaemia.