



A Case Report On Acute Very Severe Iatrogenic Hypercalcemia

Angel George¹, Dr. Sreenath R², Dr. Dona Maria Jetto³

¹Pharm D intern, ²M.B.B.S, M.D,D.M, ³Pharm D, Associate Professor,

^{1,3}Department of Pharmacy Practice , ²Department of Endocrinology

^{1,3}Nirmala College of Pharmacy, Muvattupuzha, Ernakulam, Kerala 686661

²Caritas Hosptial Thellakom, Kottayam 686630

***Corresponding Author:**

Angel George

Pharm D Intern, Department of Pharmacy Practice , Nirmala College of Pharmacy,
Muvattupuzha, Ernakulam, Kerala 686661

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Abstract

Hypoparathyroidism is a common complication in patients who undergo total thyroidectomy leading to low levels of calcium. Here, a 65-year-old female patient was admitted to the hospital for severe hypocalcemia after a total thyroidectomy. She was given standard-of-care treatment and also injection teriparatide as her calcium levels were not increasing. Later she was discharged with a stable calcium level. When she came for the second review she was disoriented, and confused and also gave a history of constipation. Blood biochemistry was done on an emergency basis and it revealed very severe hypercalcemia of 25.8mg/dl. After the treatment with IV Fluids, Loop diuretics, glucocorticoids, and injection of calcitonin, the calcium level dropped to 8.3mg/dl. This case report focuses on the management of hypocalcemia and the risk of occurrence of iatrogenic hypercalcemia during the treatment period.

Keywords: Total Thyroidectomy, Parathyroid Hormone(PTH), Hypocalcemia, Iatrogenic Hypoparathyroidism, Iatrogenic Hypercalcemia

Introduction

A typical side effect of bilateral thyroid surgery is postoperative hypoparathyroidism, which results in insufficient levels of the hormone PTH in the blood, which lowers calcium levels and raises phosphate levels. Calcium gluconate injections can be used to treat acute hypocalcemia. As soon as feasible, oral calcium supplementation should be started, and if necessary, therapy with vitamin D or its analogs should also be started. PTH action may become resistant due to hypomagnesemia. Hence, if hypomagnesemia is found, it should also be treated.

Vitamin D, vitamin D metabolite, or oral calcium (1 to 3 gram 3 to 4 separate doses) are all effective treatments for asymptomatic chronic hypocalcemia. Patients with hypoparathyroidism frequently require

activated vitamin D supplementation in the form of calcitriol 0.25 mcg and may require up to 0.5 mcg 4 times per day or alfacalcidol (1(OH)D3) or a combination of both because hypoparathyroidism affects the synthesis of active vitamin D. Thiazide diuretics can be administered to promote calcium reabsorption from renal tubules.

Conventional therapy with calcium supplements and vitamin D doesn't restore the action of PTH. In 2015, the US Food and Drug Administration approved the once-daily subcutaneous (SC) administration of recombinant human (rh) PTH(1-84) as an adjunctive treatment for adult patients with chronic hypoparathyroidism. Teriparatide (recombinant human PTH(1-34)) has the same actions as endogenous

PTH on calcium and phosphate homeostasis, it stimulates distal tubular reabsorption of calcium in the kidney and inhibits proximal tubular phosphate reabsorption, and activates the 1-alpha-hydroxylase enzyme in proximal tubules which converts the filtered 25(OH)D to 1,25(OH)₂D the most active vitamin D metabolite.

Patients who are receiving oral calcium supplements along with other hypercalcemia-inducing drugs like vitamin D, thiazides, and human recombinant PTH require frequent monitoring of serum calcium levels.

Case Report

A 65-year-old female patient with a history of follicular thyroid carcinoma underwent total thyroidectomy and radioiodine ablation in 2022 December. She presented with complaints of paresthesia and numbness in both hands. It was not associated with any pain. The patient was also suffering from type 2 DM, diabetic kidney disease, and systemic hypertension. On examination the patient was conscious, oriented, afebrile, bilateral pitting pedal edema, CNS-HMF normal, and No deficits.

The blood test showed severe hypocalcemia(5.1 mg/dL), and hypomagnesemia (1.1 mg/dL). She was diagnosed with iatrogenic hypoparathyroidism. Injection of magnesium sulfate 4 ampoules in 1-pint normal saline over 6 hours was given because of hypomagnesemia. The treatment for hypocalcemia was started with an infusion of calcium gluconate 10% w/v in 10-minute IV Q8H and the calcium level on the next day was 4.4mg/dl. From Day 2 onwards patient was treated with an infusion of calcium gluconate 6 ampoules 1pint normal saline Q6H and the calcium level on day 4 was 4.8mg/dL. Along with the infusion tablet containing calcium 500 calcitriol, 0.25 mcg, and vitamin K2-7 45 mcg was given with a frequency of 2 tablets 4 times daily, and calcitriol

0.25mcg two tablets 3 times was started and continued to day 7 and the serum calcium was 5.7mg/dl. Due to persistent hypocalcemia tablet hydrochlorothiazide 12.5 mg once daily was started .On day 13, the infusion was stopped and the calcium level again dropped to 7.3mg/dL [Table 1], [Figure1],[Figure 2]. Hence started injection of teriparatide 20mcg subcutaneously once daily. The patient was discharged with the medication of teriparatide 20mcg Subcutaneously, capsule calcitriol 0.25 mcg two tablets 4 times daily, cholecalciferol 60000IU Solution once monthly, tablet calcium 500 mg two tablets 4 times daily, and tablet hydrochlorothiazide 12.5 mg OD. On her first review after 5 days the calcium level was 8.2mg/dl and on her second review after 20 days was 9.4mg/dL.

Three days after the second review patient presented with decreased response and constipation. On systemic examination, the patient was conscious, and confused, No focal deficits. Her calcium levels and 25 OH vitamin D were 25.8 mg/dl and 113.4 respectively. She was diagnosed with iatrogenic hypercalcemia. She was admitted to the intensive care unit and all the medications given for hypocalcemia were temporarily stopped. Treatment was started with IV fluids, IV furosemide 20mg Q8H, IV dexamethasone 2mg Q12H and Subcutaneous calcitonin. Calcium levels came down progressively with the treatment. When the calcium level became 8.4mg/dl, she was started with oral calcium and calcitriol. iPTH was found to be less than 4ng/ml. On day 9, the patient was discharged with a calcium level of 8.2mg/dl and the condition was stable [Table 2]. She was given the medication of vitamin D 6000IU once a month, a Tablet containing Calcium 500 , calcitriol 0.25 mg and vitaminK2-7 45 mcg with a frequency of 1-2-1, and calcitriol 0.25 mcg three times daily.

Table 1: Serum Calcium and Magnesium level during first admission.

	SERUM CALCIUM	MAGNESIUM
day 1	5.1 mg/dl	
day 2	4.4 mg/dl	
day 3	4.6 mg/dl	1.1 mg/dl

day 4	4.8 mg/dl	2.4 mg/dl
day 5	5.9 mg/dl	1.8 mg/dl
day 6	6.6 mg/dl	2.3 mg/dl
day 7	5.7 mg/dl	3.9 mg/dl
day 8	6.2 mg/dl	2.2 mg/dl
day 9	7.2 mg/dl	1.6 mg/dl
day 10	6.3 mg/dl	1.4 mg/dl
day 11	9.4 mg/dl	2.8 mg/dl
day 12	8.8 mg/dl	2.1 mg/dl
day 13	8.6 mg/dl	
day 14	7.3 mg/dl	
day 15	9.2 mg/dl	
day 16	9.8 mg/dl	
day 17	9 mg/dl	

Table 2: Serum Calcium Level during the second admission

DAYS	SERUM CALCIUM
DAY 1	25.8 mg/dl
DAY 2	20.0 mg/dl
DAY 3	15 mg/dl
DAY 4	11.4 mg/dl
DAY 5	9.6 mg/dl
DAY 6	8.3 mg/dl
DAY 7	7.8 mg/dl
DAY 8	7.5 mg/dl
DAY 9	8.2 mg/dl

Figure 1: Graphical representation of serum calcium levels on different days during the first admission

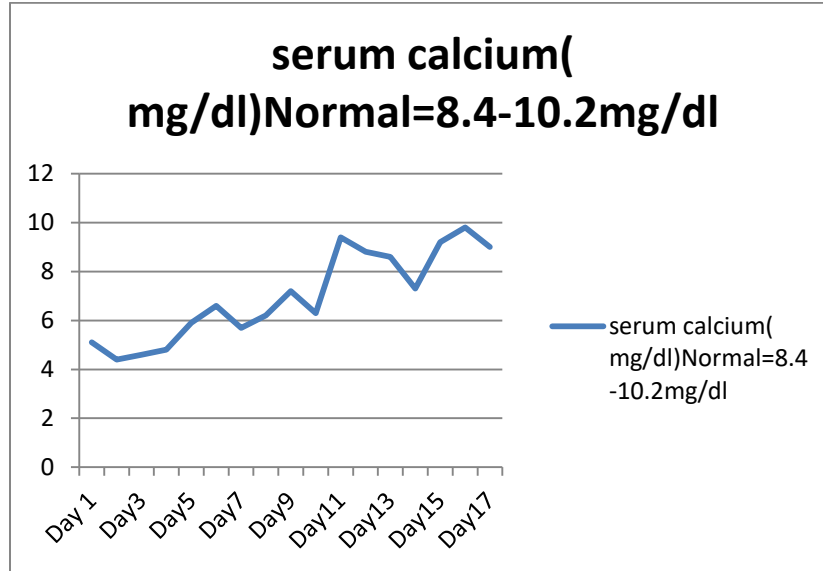
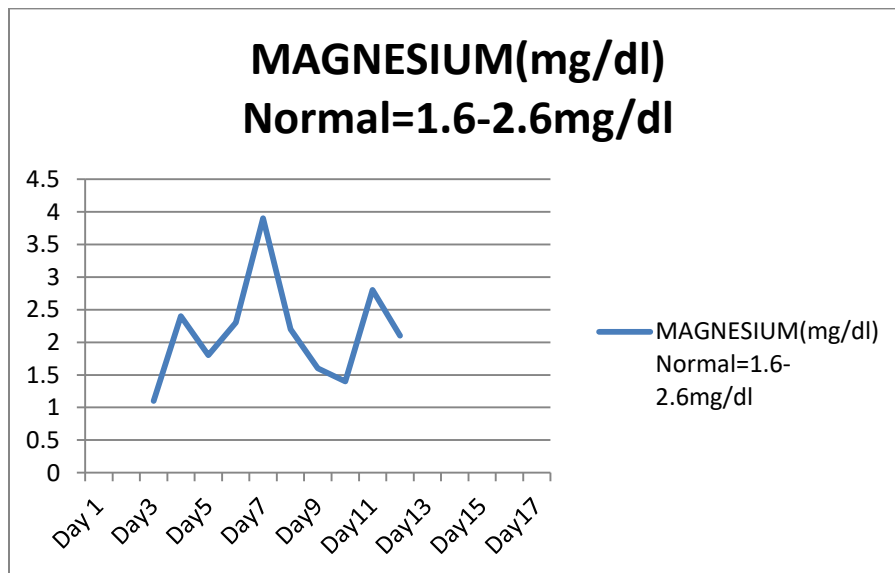


Figure 2: Graphical representation of Magnesium levels on different days during the first admission



Discussion

We describe a case of severe hypocalcemia in a patient with hypoparathyroidism and iatrogenic hypercalcemia in this report. Postoperative hypoparathyroidism, typically causes hyperphosphatemia and hypocalcemia[10]. After receiving treatment with calcium supplements, vitamin D, and thiazide diuretics, this patient was unable to maintain the desired calcium level. Replacement therapy with PTH(1-34) and (1-84) in hypoparathyroidism lessens the requirement for high doses of extra calcium and active vitamin D, maintains calcium levels, and improves the quality of

life. For the treatment of osteoporosis in men and postmenopausal women at high risk for fracture, PTH (1-34) is authorized in the USA and throughout the world[12]. 1-alpha hydroxylated vitamin D analogs can raise the calcium level in people taking vitamin D supplements by increasing intestinal and renal calcium absorption. Patients getting calcium and vitamin D supplements are more likely to develop hypercalcemia, especially if they have impaired renal function. Simultaneous injection of intravenous isotonic saline, subcutaneous calcitonin, and bisphosphonate can treat drug-induced hypercalcemia (iv zoledronic acid, pamidronate). Age and

concomitant diseases like renal failure affect the rate of infusion. By boosting renal excretion, calcitonin can lower serum calcium levels, however, its effectiveness is only lasting for the first 48 hours. Osteoclast activity may be inhibited by bisphosphonates. Glucocorticoids, zoledronic acid, or pamidronate can be used to treat hypercalcemia brought on by vitamin D and calcidiol. For a patient with renal and cardiac failure who cannot be safely hydrated, hemodialysis and peritoneal dialysis are the last options.

In conclusion, we report a case of severe hypocalcemia with hypoparathyroidism. Even after treatment with large doses of calcium and active vitamin D, serum calcium levels were not rising, hence opted to give PTH therapy. PTH replacement therapy with PTH (1-34) and PTH (1-84) is a promising therapeutic option for patients with hypoparathyroidism. Iatrogenic hypercalcemia occurred in this patient after the second review and the patient was managed with IV fluids, IV furosemide 20mg Q8H, IV dexamethasone 2mg Q12H, and subcutaneous calcitonin. Iatrogenic hypercalcemia is a complication in a patient who is under treatment for hypocalcemia especially those who have impaired renal function and require frequent monitoring of calcium levels.

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Authors

The first author (Angel George) collected the cases and drafted the manuscript, the Second author Dr. Sreenath R and the Third author (Dona Maria Jetto) reviewed the manuscript.

Abbreviations

PTH –Parathyroid Hormone, 25(OH)D – 25 hydroxyvitamin D, 1,25(OH)₂D - 1,25-dihydroxy vitamin D, iPTH –Early intact PTH, CNS-HMF – central nervous system-Higher Mental Function, DM –Diabetes mellitus

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