Case Report

Symptomatic hypocalcaemia in hypermagnesaemia-induced hypoparathyroidism, during magnesium tocolytic therapy—possible involvement of the calcium-sensing receptor

Haim Mayan¹, Ariel Hourvitz², Eyal Schiff² and Zvi Farfel¹

¹Department of Medicine E and ²Department of Obstetrics and Gynecology, Chaim Sheba Medical Center, Tel-Aviv University, Tel Hashomer, Israel

Introduction

High dose magnesium therapy, which causes profound hypermagnesaemia, is an established therapy for eclampsia and premature labour. Usually the hypermagnesaemia is tolerated well. More than two decades ago hypocalcaemia was described in two obstetric patients receiving magnesium [1,2]. Cholst et al. [3] studied a group of seven pregnant women and showed that hypermagnesaemia-induced hypocalcaemia was associated with transient hypoparathyroidism. Of note is the lack of symptoms in the women who had hypocalcaemia. We present two patients who had magnesium tocolytic therapy, and during hypermagnesaemia developed prolonged symptomatic hypocalcaemia and undetectable PTH concentrations. We propose the involvement of the calcium-sensing receptor in hypermagnesaemia-induced hypocalcaemia.

Case 1

A 27-year-old woman on the 19th week of her pregnancy was admitted due to suspected twin to twin transfusion. During her stay in the ward premature labour occurred. As she did not respond to β-adrenergic agonists and indomethacin, she was started on intravenous magnesium sulfate (a loading dose of 5 g and a maintenance dose of 2 g/h). On the second day a routine blood chemistry analysis showed a calcium level of 6.5 mg/dl (1.62 mmol/l). On the third day of labour, she had vaginal bleeding and premature delivery. She was started on oral magnesium treatment she complained of hoarseness, muscle spasms, and was found to have tetany. Physical examination showed a positive Chvostek sign with marked hyperreflexia. Initial laboratory tests on admission including renal function were within normal limits. When symptoms occurred laboratory results showed the following serum concentrations: magnesium, 6.5 mg/dl (2.67 mmol/l); total calcium, 5.3 mg/dl (1.32 mmol/l); ionized calcium, 0.71 mmol/l; albumin, 3.3 g/dl (33 g/l); and phosphorus, 4 mg/dl (1.29 mmol/l). Twenty four hour urinary calcium excretion was 300 mg. A day later plasma PTH (intact PTH immunoassay kit, Nichols Institute Diagnostics, San Juan Capistrano, CA, USA) level was <8.5 pg/ml (normal range 10–65 pg/ml). Intravenous calcium was given but due to continued labour and symptomatic hypocalcaemia, magnesium therapy was stopped (Figure 1). The symptoms of hypocalcaemia resolved with the rise of serum calcium and the decline of serum magnesium. Plasma PTH level increased to 26 pg/ml on day 3. She gave birth on the 25th week of her pregnancy.

Case 2

A 28-year-old woman after in vitro fertilization procedure was pregnant with twins. On the 24th week of pregnancy she had vaginal bleeding and premature labour. She was started on oral β-adrenergic agonists and 4 days later intravenous magnesium sulfate was administered. Twelve hours after a loading dose of 5 g of magnesium sulfate and a maintenance dose of 2 g/h, she complained of diplopia, general malaise, and paresthesia especially over the face and extremities. On examination a prominent Chvostek sign with marked hyperreflexia were noticed. There were no signs of toxaemia. EKG showed a prolonged Q-T interval. Initial laboratory tests done on admission were within normal limits. When symptoms appeared, laboratory results showed the following serum concentrations: magnesium, 6.5 mg/dl (2.67 mmol/l); total calcium, 5.3 mg/dl (1.32 mmol/l); ionized calcium, 0.71 mmol/l; albumin, 3.3 g/dl (33 g/l); and phosphorus, 4 mg/dl (1.29 mmol/l). Twenty four hour urinary calcium excretion was 300 mg. A day later plasma PTH (intact PTH immunoassay kit, Nichols Institute Diagnostics, San Juan Capistrano, CA, USA) level was <8.5 pg/ml (normal range 10–65 pg/ml). Intravenous calcium was given but due to continued labour and symptomatic hypocalcaemia, magnesium therapy was stopped (Figure 1). The symptoms of hypocalcaemia resolved with the rise of serum calcium and the decline of serum magnesium. Plasma PTH level increased to 26 pg/ml on day 3. She gave birth on the 25th week of her pregnancy.

Correspondence and offprint requests to: Haim Mayan MD, Department of Medicine E, Sheba Medical Center, Tel-Hashomer 52621, Israel.
Fig. 1. Magnesium and calcium serum concentrations during tocolytic therapy in patient 1. Ionized calcium concentrations are in parenthesis. Timing of the start and the end of magnesium sulfate infusion is shown by arrows. Symptoms occurrence is also indicated.

Symptomatic hypocalcaemia and hypermagnesaemia (Figure 2). PTH levels were below detectable limits (<8.5 pg/ml) on three different days during magnesium therapy, and after discharge, rose to 10 pg/ml. Nifedipine and indomethacin were started, with resolution of the premature contractions. She was discharged and resumed her pregnancy to full term.

Discussion

Hypermagnesaemia is a known cause for hypocalcaemia [1–6]. Usually the hypocalcaemia is asymptomatic [7]. We have found only two published case reports of symptomatic patients. The reported cases were pregnant women who also had other conditions which might have contributed to the hypocalcaemia.

The first observation of symptomatic hypocalcaemia induced by hypermagnesaemia was of a 20-year-old woman who developed toxaemia and was treated by magnesium sulfate [1]. Serum magnesium concentration was 10 mg/dl (4.11 mmol/l) while serum total calcium level was 6.7 mg/dl (1.67 mmol/l), with serum albumin of 2.3 g/dl (23 g/l). The patient had severe aspiration pneumonia which necessitated intubation and mechanical ventilation. Hypocalcaemia could be attributed also to her critical state including the severe hypoalbuminaemia. Magnesium concentration in this patient was higher than the usual concentration of 5–7 mg/dl (2.05–2.88 mmol/l), obtained with the current recommended dose of magnesium sulfate.

A second report of symptomatic hypocalcaemia [2] was that of a 29-year-old woman, who developed hypocalcaemia (4.9 mg/dl, 1.22 mmol/l) 2 days after magnesium therapy was stopped, while magnesium levels were within normal range. Plasma PTH level

Fig. 2. Magnesium and calcium serum concentrations during tocolytic therapy in patient 2. Blood ionized calcium concentrations are in parenthesis.
was low. It should be noted that the patient had thyroidectomy a few years earlier.

Our two patients were different from the above cases. They both developed hypocalcaemia while magnesium was administered. There was no other condition or cause exposing them to hypocalcaemia. In both, hypocalcaemia appeared within hours after starting magnesium administration. Symptoms of hypocalcaemia appeared within 1–2 days later. This was accompanied by a decrease in plasma intact PTH concentration, which in the first patient lasted for at least 24 h, and in the second patient persisted for 8 days despite ongoing hypocalcaemia.

Cholst et al. [3] studied prospectively seven pregnant women who were given magnesium tocolytic therapy, consisting of a loading dose followed by a maintenance dose over 3 h. Mean serum magnesium increased to 6.1 mg/dl (2.51 mmol/l), and mean serum total calcium decreased from 8.6 (2.14 mmol/l) to 7.6 mg/dl (1.89 mmol/l), without symptoms. Plasma PTH concentration, measured using an antibody directed against PTH C-terminus, decreased from 13.1 to 7.8 pg/ml after 60 min, but increased after 3 h to levels not different from baseline levels. The authors suggested that the decrease in PTH level was due to inhibition of the parathyroid gland by the hypermagnesaemia. They ascribed the persistent hypocalcaemia partially to the low initial PTH levels, and could not rule out a renal effect.

Why did our patients develop symptomatic hypocalcaemia? A possible explanation is that the absolute reduction in blood calcium concentration was greater, 3.8 mg/dl (0.95 mmol/l) and 2.7 mg/dl (0.68 mmol/l) respectively, compared to the mean reduction of 1 mg/dl (0.25 mmol/l) reported by Cholst et al. Another possibility is the difference in the behavior of the PTH concentration during hypocalcaemia. While Cholst et al. [3] observed a return of PTH to baseline after 3 h, in our 6.


References


