

Refractory Hypokalemia: A Rare Presentation of Hypomagnesemia

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Abstract: We describe a case of refractory hypokalemia associated with hypomagnesemia and with other clinical features, characteristic ECG changes of ventricular bigeminy, prolonged PR interval, 'U' waves and associated laboratory features. Intravenous magnesium therapy reversed the Hypokalemia, ECG changes and led to improvement in clinical symptoms. A brief review of literature is also presented.

INTRODUCTION

Magnesium is fourth most common extracellular and second most common intracellular cation of the body. It is required for activation of various cellular enzymes and is responsible for neurotransmission, hormone receptor binding and postreceptor activation. It is also required for maintenance of calcium and potassium homeostasis. Severe magnesium deficiency thus results in varied manifestations ranging from ECG changes, neuromuscular abnormalities and defects in electrolyte and hormonal homeostasis. Hypomagnesemia though relatively common in clinical practice, esp. in ICU setting, is relatively infrequently diagnosed, mainly due to low index of suspicion. This article highlights the clinical findings of hypomagnesemia and stress the need for proactive treatment.

CASE REPORT

70 yr old female patient was referred to medical emergency with presenting complaints of protracted vomiting for last 15 days associated with generalized weakness and decreased appetite. Her vitals were stable and no complaint of chest pain or palpitation was present. No history suggesting any chronic illness could be elicited. On examination she was severely malnourished and CNS examination suggested decreased tone and decreased power (grade 2) of all 4 limbs with depressed reflexes. Other systemic examination did not reveal any significant finding. She was carrying an ECG showing ventricular bigeminy with aberrancy of conduction which was not present in subsequent serial ECGs done by us, which however showed transient prolonged PR interval, followed by persistent U waves. This prompted us to look for electrolyte imbalance as the underlying cause. Further investigations revealed low serum potassium of <2 mEq/L (3.5-5.5) and normal Serum sodium 133mEq/L.

Patient continued to have refractory hypokalemia even after adequate replacement with potassium chloride. A 24 hr urinary K^+ level of 89mmol/24hrs (25-125) was found with metabolic acidosis. Serum Magnesium was 0.67 mg/dl (1.7-2.3) with 24 hr urine magnesium 8.0 mg/24hrs (75-125). Serum Ionized Ca^{2+} was 0.98mmol/l (1.10-1.35) & S. Phosphorus 2.5 mg/dl(3.5-5). The patient's potassium levels and symptoms improved remarkably after i.v. magnesium replacement. Subsequently raised parathyroid hormone (PTH) values of 201.50 pg/ml (15-68.30) and low normal 25- hydroxyl vitamin D (25-OHD) 30 ng/ml (11-70) were found. Also patient had low S. proteins. Liver and kidney functions and uric acid levels were unremarkable. Hypothyroidism was also documented with TSH >

100 IU/ml(0.5-5), Total T3- 20ng/dl (70-200) and Total T4- <1 mg/dl(5.5-13.5).

DISCUSSION

Magnesium is the fourth most abundant extracellular cation and second most abundant intracellular cation after potassium¹. A normal adult contains about 25 mEq/kg magnesium with only 1% of this magnesium present in the extracellular compartment. The rest of magnesium being present in bone (67%), and cells (31%)². Normal magnesium concentration is 1.7-2.1 mg/dl (0.7-0.9 mmol/l or 1.4-1.7 mEq/l)¹. Unbound intracellular magnesium is an integral part of the energy metabolism and catalyses phosphatases that hydrolyze and transfer organic phosphate and reactions that involve adenosine triphosphate (ATP). Magnesium is required for conversion of ATP to cyclic AMP by the enzyme adenylate cyclase. The substrate for adenylate cyclase is Mg^{2+} -ATP and in addition, magnesium appears to have a catalytic effect on adenylate cyclase activity. As ATP has a pivotal role to play in metabolism, magnesium deficiency has a potential to impair many critical cellular functions².

Proximal small bowel is the major site of magnesium absorption. Vitamin D may increase magnesium absorption³. Renal excretion of magnesium occurs by glomerular filtration and tubular reabsorption, mainly in thick ascending limb (TAL) of the Loop of Henle(60-70%)¹. Causes of hypomagnesemia can be due to gastrointestinal or renal losses. In gastrointestinal causes prolonged nasogastric suction or vomiting, acute or chronic diarrhea, malabsorption syndromes and protein calorie malnutrition may be responsible. 24hr urine Mg^{2+} excretion is generally less in gastrointestinal diseases. Renal loss occurs due to renal tubular acidosis, pyelonephritis, Bartter's & Gitelman's syndrome, osmotic diuresis as present in diabetes, mannitol administration, and due to high urea levels. Also increased renal losses may be due to alcohol or metabolic acidosis. Normal urinary excretion of magnesium in the normal range in presence of hypomagnesemia suggests a renal leak. Endocrine disorders like hyperthyroidism, hypercalcemia, hyperaldosteronism, phosphate depletion may be responsible.

Hypomagnesemia may coexist with hypokalemia, hypocalcemia & hypophosphatemia. Potassium depletion in hypomagnesemia may be multifactorial e.g. due to kaliuresis, altered cell membrane permeability, decreased Na^+ - K^+ ATPase activity, decreased inward rectification of K^+ and decreased Na^+ - K^+ cotransport. Thus Mg^{2+} has a pivotal role in maintaining K^+ homeostasis⁵.

Although, hypomagnesemia is usually associated with hypoparathyroidism, few cases with normal or high PTH values have been found in literature⁴. Our case has high PTH levels. In spite of high PTH levels, calcemic response of parathyroid hormone is not adequate. This may be due to End organ resistance to PTH at the level of bone and kidney. Due to low 25 hydroxy vitamin D, there is defective mineralization of osteoid tissue which leads to defective calcemic response of PTH. Even low magnesium levels are responsible for this end organ resistance. This may be explained by defective generation of cyclic AMP in kidney, bone and parathyroid gland resulting from magnesium deficiency as cyclic AMP is a mediator in the peripheral actions of PTH resulting in decreased renal and skeletal responsiveness to parathyroid hormone. In our case, there were low S. phosphorus levels, which may be due to low dietary phosphorus intake before admission and intravenous dextrose infusion given to patient after admission⁴. Hypothyroidism may be an isolated finding in this case. Thus prolonged protracted vomiting, led to loss of magnesium and low serum phosphorus levels were also responsible for low magnesium levels. Severe symptomatic hypomagnesemia should be treated with

intravenous magnesium. It can take up to 3 to 7 days to replenish the intracellular stores. So after intravenous therapy, oral magnesium supplementation is required.

Our patient achieved normal magnesium levels followed by normal potassium & calcium levels subsequent to intravenous replacement⁶. After about 2 months, magnesium was discontinued, and subsequent magnesium levels done are within the normal levels. The presence of resistant hypokalemia & hypocalcemia should alert the physician to look for underlying hypomagnesemia as the cause.

REFERENCES

1. Hypomagnesemia (online). 2009 (cited 2009 Jan21); Available from URL:<http://emedicine.medscape.com/a/246366>.
2. Rude RK. Magnesium Disorders. In: Kokko JP, Tannen RL (eds). *Fluids and Electrolytes*. 3rd ed. Philadelphia : WB Saunders Co. 1996: 421-45.
3. Brannan PG, Vergna-Marini P, Pak CYC, Hull AR, Fordtran JS. Magnesium absorption in the human small intestine. *J Clin Invest* 1996;57:412-8.
4. Rude RK, Oldham SB, Singer FR. Functional hypoparathyroidism and parathyroid hormone end organ resistance in human magnesium deficiency. *Clin Endocrinol* 1976;5:209-24.
5. Whang R, Hampton EM, Whang DD. Magnesium homeostasis and clinical disorders of magnesium deficiency. *The Annals of Pharmacotherapy* 1994;28: 220-5.
6. Rajput R, Kumar K, Dhingra A. Hypomagnesemic Tetany. A Rare presentation of uncontrolled hyperthyroidism. *The Endocrinologist* 2009;19:222-3.

LITERATURE REVIEW

Long-term Outcomes of Renal Transplants from Spousal and Living-related and Other Living-unrelated Donors: A Single Center Experience

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Deceased donor organ shortage has made living donors (LD) major source for renal transplantation (RTx) in India. Spouses represent an important source of allograft. We carried out a retrospective study of spousal RTx vs other LDRTx to compare long-term results. This retrospective single-center study was undertaken to evaluate demographic, patient survival, graft survival, function vis-à-vis serum creatinine (SCR) and rejection episodes in 1523 living donor renal allograft recipients from 1998 to 2009. It included spouse donors (n=337) (group 1), living related donors (LRD) (n=969) (group 2), and living unrelated donors (LUD) (n= 217) (group 3). Mean recipient age (years ± SD) was 41.48 ± 8.87, 30.49 ± 10.61, and 37.13 ± 13.25, respectively for the three groups who were followed for 4.47 ± 3.03, 4.47 ± 3.0 and 5.15 ± 3.28 years respectively. Female donors were 92.6%, 66.4%, and 41%, mean HLA match was 1.15 ± 0.93, 3 ± 1.05 and 1.30 ± 1.08 respectively. One, 5 and 12 year graft survivals among group 1 were 91.39 %, 75.49 %, and 73.13 %; 90.98 %, 74.10 % and 64.57% in group 2 and 94.92 %, 82.86 % and 70.31% in group 3. Patient survival for 1, 5 and 12 years were 89.31%, 72.55% and 66.58% in group 1, 93.57%, 82.25% and 72.23% in group 2, and 92.62%, 79.76% and 66.79% in group 3. Acute rejections were noted in 16.6 %, 15.8 % and 17% respectively. In circumstances of organ shortage and unavailability of well developed ABO incompatible transplants, spousal donation is viable option.

LITERATURE REVIEW

Vitamin D deficiency as the primary cause of musculoskeletal complaints in patients referred to rheumatology clinic: A clinical study

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To study vitamin D deficiency as the primary cause of musculoskeletal complaints in rheumatology clinic. Adult patients presenting with 'non-inflammatory' musculoskeletal pain to our rheumatology clinic between May 2009 and April 2011 underwent estimation of serum 25-hydroxyvitamin D [25(OH)D] and those with level < 20 ng/ml were recruited. Hypothyroidism, painful neuropathies, chronic kidney disease, malignancies, chikungunya, HIV, HCV and HBV were excluded. All study patients underwent complete physical examination and baseline estimation of serum calcium, phosphorus, alkaline phosphatase and PTH besides routine tests. Study patients received treatment with oral cholecalciferol and calcium and were re-assessed clinically and biochemically after 8 weeks. Serum 25(OH)D levels were also estimated in 92 asymptomatic controls. Thirty patients were found eligible for the study after screening a total of 95 (Male/Female: 12/18; mean age: 42.3 ± 13.2 years). Polyarthralgia was the commonest presenting complaint (46.6%). Other symptoms included myalgia, bone pains and chronic widespread pain. Physical examination showed joint and muscle tenderness in 10 patients each and joint swelling in one. Paired biochemical results at baseline and 8 weeks were: 25(OH)D (ng/ml) = 5.84 ± 2.71 and 34.45 ± 12.98, calcium (mg/dL) = 9.06 ± 0.58 and 9.16 ± 0.63, phosphorus (mg/dL) = 3.65 ± 0.95 and 3.84 ± 0.70. Paired median [IQR] values for alkaline phosphatase and PTH were 89 [66-181] and 68 [55-138] units/L, and 69.2 [47.6-106] and 38.8 [25-60] pg/ml respectively. Treatment was successful in all except 4. Improvement was found to be sustained in all cases at 6 months follow up. Although 75% of controls also had biochemical evidence of vitamin D deficiency, their vitamin D levels were significantly higher. Vitamin D deficiency is frequently the sole cause of polyarthralgia, myalgia, bone pain and chronic widespread pain in patients referred to rheumatology clinic. Referring physicians ought to have a lower threshold for this eminently curable condition.

Future Special Issues/ Symposia

Special Issues

- Constipation: Emerging Horizons-II
- Advances in Pediatric Surgery
- HIV/AIDS: Emerging Trends
- Injury/Trauma: An Epidemic of Modern Times (Tentative)

Symposia

- Advances in Endocrine Surgery
- Pain Management: Current Trends
- Sleep Disorders: Current Perspective