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Dyselectrolytemias after single dose of Pamidronate Administration

Panday K,[1] Kanth R[2]

[1]Hospitalist at Rapid City Regional Hospital, Rapid City, S.D, USA, [2]Hospitalist at Marshfield Clinic, Marshfield, Wisconsin, USA.

ABSTRACT

Bisphosphonate such as pamidronate initially described for the treatment of neoplastichypercalcemia, currently is being used off label to treat sever hypercalcemia of any etiology. Multipledyselectrolytemias are a potential adverse effect of this drug, and are considered infrequent. We describe a case of transient electrolyte abnormalities after single dose of 60 mg intravenous pamidronate.

Keywords: dyselectrolytemias, hypercalcemia, hypocalcemia, hypophosphatemia, hypomagnesemia, pamidronate.

INTRODUCTION

Intravenous bisphosphonate like pamidronate is effective in the treatment of hypercalcemia especially caused by malignant tumors such as bone metastasis from solid organ tumors, multiple myeloma, Paget's disease and sever refractory hypercalcemia of any etiology after aggressive hydration and Calcitonin treatment. Though infrequent, transient to prolonged electrolytes abnormalities including sever life threatening hypocalcaemia have been reported after pamidronate administration. We present a case of severehypercalcemiawho developed hypocalcaemia, hypophosphatemia, hypokalemia and hypomagnesemia after single dose of 60 mg pamidronate infusion.

CASE REPORT

A42 year old Hispanic female with Acquired immune deficiency syndrome, CD 4 count of 95, anemia of chronic disease and seizure disorder was transferred from Nursing Home(sub acute care facility) secondary to poor oral intake, generalize malaise, lethargy and failure to thrive. On physical examination patient was hypotensive (BP 80/51), HR: 90, afebrile with dry mucous membrane. Laboratory tests revealed Calcium: 15.9 mg/dl, hematocrite of 27.5%, BUN/Creatinine: 47mg/dl /1.7 mg/dl, phosphorous: 3.7 mg/dl, Magnesium: 1.7 mg/dl, Albumin: 2.9 g/dl, and total protein: 6.4 g/dl. Patient was hydrated aggressively with normal saline and was treated with calcitonin 100 units subcutaneously every 12 hourly for 3 days followed by pamidronate 60mg infusion over 4 hours. Serial electrolytes were followed for 12 days. Serum vitamin D (25 OH vitamin D and 1-25, $(OH)_2$vitamin D) level as well as vitamin A level were within normal limits. Intact parathormone was 17.4pg/dl at admission which increased as patient became hypocalcemic. Work up for latent malignancy, as a cause for hypercalcemia, including Urine protein electrophoresis, serum protein electrophoresis, parathormone related peptide (PTHrP) and CT Scan of Abdomen /pelvis /chest were negative (Table 1).

Potassium and magnesiumlevels decreased with nadir on 2nd and 7th day. Hypokalemia was treated with intravenous and oral potassium and magnesium was replaced orally.

Multiple electrolyte abnormalities were noticed after single dose of pamidronate administration. Asymptomatic hypocalcemic with the trough on 5th day after pamidronate treatment gradually responded to oral calcium supplementation.Hypophosphatemia with the lowest value was observed on 5th day as shown in table 1 above.

Correspondence: Dr. KeshavPanday, Hospitalist at Rapid City Regional Hospital, Rapid City, S.D, USA. Email: kesu7np@yahoo.com

Table 1.Serial electrolytes measurement.

Agents	Reference value	Before treatment	2nd day after Pamidronate.	5th day after Pamidronate	7th day after Pamidronate	10th day after Pamidronate
Calcium	8.4 - 10.6 mg/dl	15.9	12.1	7.4	8.4	8.7
Phosphorous	2.5 - 4.5 mg/dl	3.7	2.4	1.7	2.1	3.4
Magnesium	1.3 - 2.2 mg/dl	1.7	1.2	1.1	1.0	1.3
Potassium	3.5 - 5.0 mEq/L	3.9	2.7	3.2	3.9	4.0
Creatinine	-	1.5	1.2	1.0	1.0	1.0

DISCUSSION

Sodium pamidronate belongs to the Bisphosphonate family of drugs, which decrease bone resorption by inhibiting osteoclast activity. They are synthetic structural analogues of pyrophosphate, a natural inhibitor of crystalline nucleus formation and of bone mineralization. Pyrophosphate, which is hydrolyzed by tissue alkaline phosphates, has a biological half-life of several minutes. Syntheticbisphosphonates are resistant to hydrolysis. They act in opposition to most of the mechanisms involved in stimulating bone resorption, involving PTH, 1-25 dihydroxyvitamin D, prostaglandins, retinoids, and some cytokines.[1]

Although, hypocalcemia is one of the known side effects of bisphosphonates it is described as an infrequent and usually as asymptomatic. Published recommendations from the American Society of Clinical Oncology do not mention an increased risk of hypocalcemia, [2] and Conte et al.[3]described a 17% incidence of hypocalcemic, all of which were asymptomatic.[4]

In our caseAsymptomatic hypocalcemic was noted on 5th day after treatment and was treated with oral calcium supplement. Three different mechanisms for bisphosphonate induced hypocalcemic seem to be involved. One is not of Parathormone related as the parathormone concentration is high during the hypocalcemic episode.[5,6]Second mechanisms is suggestive of decompensationof latenthypoparathyroidism due to previous surgery on the thyroid[7] or on the parathyroids, [6, 8] palliative radiotherapy in the cervical region, [9]or other origin.[4, 10, 11]

Third, Magnesium deficiency may act on bone directly to reduce calcium release independent of parathormone.[12]

Severe hypomagnesemia was observe on seventh day and was treated with oral supplementation. Hypomagnesemia is one of the known adverse effectsof pamidronate administration but no serious cardiac and neurological effect has been reported. The likely explanation for the low magnesium level could be secondary to low serum phosphorous level, which causes enhanced renal magnesium excretion.[12]As observed in our case low magnesium paralleled with low phosphorus level.

Our case report shows that multiple electrolytes abnormalities arerare but known side effects of pamidronate administration. As severe life threatening hypocalcemicafter intravenous pamidronateinfusion especially in vitamin D deficiency patient has been reported by Clifford J. Rosen.[13] We suggest that all patients receiving bisphosphonate be thoroughly screened for high risk factors leading to hypocalcemic like latent hypoparathyroidism after surgery, cervical radiotherapy, hypomagnesemia, and low 25 hydroxy vitamin D. All patients should have serial electrolytes checked after bisphosphonate administration, especially those at "high risk." It might be prudent to lower the dose of pamidronate administration to high risk patients to prevent overshoot towards hypocalcemia.

Further prospective study is warranted in this regards todetermine the exact incidence and risks factors ofmultiple electrolyte imbalance after bisphophonate administration along with dose determination in high risks group.

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