Severe Symptomatic Hypocalcaemia Associated with Zoledronic Acid in a Patient of Ca Prostate: Case Report and Literature Review

Abstract: Zoledronic acid is a parenteral long acting bisphosphonate that has been used widely in the management of osteoporosis, bone metastasis and malignancy induced hypocalcaemia. Zoledronic acid is well tolerated but rarely severe hypocalcaemia and nephrotoxicity may occur. Here we report a case of 62 year male patient of metastatic Ca prostate who had severe hypocalcaemia after receiving intravenous zoledronic acid and docetaxel. Patient was hospitalized and managed with intravenous calcium supplementation and remained admitted for several days. Post recovery he was again started on zoledronic acid therapy and chemotherapy.

Keywords: ECOG – Eastern Cooperative Oncology Group, PTH – parathyroid hormone.

CASE REPORT
A 62 year old patient presented with complaints neck pain, lower backache and increased frequency of micturition in our department. He was known hypertensive. Examination revealed tenderness on scapular region. Digital rectal examination revealed enlarged prostate which was hard & non mobile. Patient underwent bilateral orchidectomy in the department of surgery and was started on tab bicalutamide. Lab results showed anemia (7.2gm/dl), total bilirubin 0.2mg/dl, AST 18, ALT 14, alkaline phosphatase levels were raised (1470U/L). X-ray lumbar spine & pelvic bones showed lytic and sclerotic lesions suggestive bone metastasis(Fig-1).

Patient was started on chemotherapy docetaxel (75mg/m²) intravenously and zoledronic acid therapy. Tablet bicalutamide (50mg) OD was continued. Cycle to be repeated after 21 days.
Patient reported after 3 days of therapy with complaints of tingling in hands and painful spasm of upper and lower limbs. On examination ECOG score was 1, trousseau’s sign was positive. His pulse rate was 96/min and BP 130/94 was mm of Hg. Lab results showed corrected serum calcium 4.7mg%, serum magnesium 1.7meq/L, serum urea/creatinine 52/1.2mg/dl, serum electrolytes levels were sodium 143meq/L, potassium 3meq/L, chloride 99meq/L. Urgent ECG showed prolonged QT interval (Fig-2).

Patient was hospitalized and managed with immediate 6gm of calcium gluconate diluted in 50ml of normal saline@ 1.5ml/hr. Serum magnesium was also corrected with intravenous infusion of 2gm of magnesium. After 5 days of admission he had fever which was managed with intravenous antibiotics. Patient also developed ulcer at cannulation site (Fig-3). He was managed with repeated calcium gluconate injections and after a period of 20 days he was discharged.

![Fig-2: Lesion on the Site of Cannulation](image)

![Fig-3: ECG Done on Admission Showing Prolongation of QT Interval](image)

Patient reported in our OPD one month later and after fresh blood investigation he was again started on docetaxel chemotherapy but zoledronic acid therapy was stopped. Till now he has completed 6 cycles of chemotherapy with maintained calcium levels.

**DISCUSSION**

Zoledronic acid is a highly potent intravenous amino bisphosphonate that is effective in benign and malignant metabolic bone disease. It is commonly used due to its high potency and ease of administration. Mild and asymptomatic hypocalcaemia is common in cancer patients with bone metastasis after intravenous zoledronic acid therapy.

The plasma concentration of zoledronic acid is maximal at the end of IV infusion, then declines rapidly to 10% in 4hrs and less than 1% in 24hrs. About 61% of the dose administered is taken up by bone tissues and 39% is taken excreted unchanged by kidneys with long elimination half life of 146hrs. Therefore zoledronic acid clearance is dependent on renal function, should not be administered in patients with creatinine clearance ≤35ml/min.
Zoledronic acid is potent inhibitor of osteoclasts and it reduces the mobilization of calcium from the bones to the circulation. Therefore it may lead to mild secondary hyperparathyroidism. Increased PTH cause increased renal reabsorption of calcium, and 1,25(OH)2D production leading to increased intestinal absorption of calcium. So the patients with vitamin D or renal impairment may not be able to correct hypocalcaemia and may become symptomatic. It is therefore necessary to correct vitamin D deficiency and have adequate daily intake of calcium. Since magnesium is required for PTH release, magnesium deficiency may further increase the risk of hypocalcaemia by inhibiting compensatory increase in PTH secretion. Thus impaired renal function, vitamin D deficiency, hypoparathyroidism and hypomagnesemia are significant risk factors of bisphosphonate induced hypocalcaemia.

Our patient developed severe symptomatic hypocalcaemia after 3 days of zoledronic acid transfusion therapy for Ca prostate with bone metastasis. He had no prior assessment of calcium and vitamin D levels. He also had coexisting but unrecognized vitamin D deficiency. Thus it is prudent to measure 1,25(OH)2D, calcium, phosphorous and PTH before starting the treatment with zoledronic acid. Also patient should not have creatinine clearance <35ml/min. Furthermore high risk patients should be monitored closely after start of zoledronic acid treatment to detect hypocalcaemia and impaired renal function.

**REFERENCES**


