CASE REPORT

Sevelamer Hydrochloride for Tumor Lysis Syndrome-related Hyperphosphatemia

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Background: Tumour lysis syndrome is associated with high levels of uric acid, phosphate and potassium along with low levels of calcium and abnormal renal function. Sevelamer, an oral phosphate-binder is used in the treatment of hyperphosphatemia in children and adults on hemodialysis. **Case characteristics:** Two children with T-cell acute lymphoblastic leukemia who presented with a high tumour load and developed tumour lysis syndrome. **Observation:** Both children received Rasburicase and Sevelamer hydrochloride. The serum phosphate reduced to normal levels within 24-48 hrs of initiation of sevelamer hydrochloride. **Message**: Sevelamer appears to be an effective treatment for hyperphosphatemia associated with tumour lysis syndrome.

Keywords: *Acute lymphoblastic leukemia, Hyperphosphatemia, Sevelamer hydrochloride, Tumour lysis syndrome.*

Acute lymphoblastic leukaemia (ALL) is the commonest type of cancer seen among children contributing to almost one fourth of all childhood cancers [1]. In developing countries, these children present late when the disease has progressed to an advanced stage with a high tumour load [2], and hence have a high risk of developing a tumor lysis syndrome. The standard treatment of hyper-leukocytosis associated with tumor lysis syndrome is hyperhydration and allopurinol along with Rasburicase (Urate oxidase) to control very high uric acid levels. If in spite of hyper-hydration the serum phosphate levels remain high, it is then treated with aluminium hydroxide [3]. Sevelamer is a non-calcium phosphate binder which is not absorbed from the gastrointestinal tract, and has proven efficacy in reducing the serum phosphate levels in chronic kidney disease and in patients on hemodialysis [4,5]. We report two children with tumor lysis syndrome where we used Sevelamer hydrochloride to treat hyperphosphatemia**.**

CASE REPORT

Case* 1**: A seven-year-old boy reported with a 10 day history of progressive fever, associated with facial swelling and bruises for 2 days. On examination he had bulky lymph nodes in the neck associated with hepatosplenomegaly. His chest *X*-ray was suggestive of superior mediastinal lymphadenopathy. His initial blood results showed the following: Hb 9.3 g/dL, total leukocyte count 51×10^9/L, and platelet count 7×10^9/L. The blood film was suggestive of acute leukemia and was later confirmed to be T-cell ALL. His other blood tests revealed: uric acid 18 mg/dL, phosphate 8 mg/dL, potassium 4.6 mmol/L, calcium 8.6 mg/dL and LDH 1932 units. He was started on hyper-hydration ($3L/m^2$) by maintaining a urine output above 3mL/kg/hr using regular doses of furosemide. Following a dose of rasburicase (0.2 mg/kg), the uric acid levels came down to within the normal range (Fig.* 1**). The serum creatinine was initially 1.1 mg/dL and reached a maximum of 1.9 mg/dL. The serum phosphate level started to rise on the day 2 of admission to a maximum of 12 mg/dL, along with signs of hypocalcaemic tetany (Serum calcium 5.7 mg/dL), which was treated with calcium gluconate injections on two occasions. In addition to increasing fluids to a maximum 5 L/m^2, sevelamer hydrochloride 400 mg was given orally every 8 hrs, following which the phosphate levels were controlled in 48 hrs (***Fig.*1**). The child was started on UKALL 2003 protocol and is currently 6 months from the date of diagnosis.

Case* 2**: A 10-year-old boy presented with fever for 2 weeks associated with skin rashes, and facial swelling for 5 days. He had generalized lymphadenopathy with large cervical, parotid gland swelling and hepatosplenomegaly. The chest *X*-ray showed mediastinal widening. His initial blood results showed the following: Hb 3g/dL, total leukocyte count 395×10^9/L cells/cc, and platelets count of 40×10^9/L. The initial uric acid was 26.5 mg/dL (Fig.* 1**), LDH 5674 units, potassium 6.4 mmol/l, calcium 9 mg/dL, phosphate 5.5 mg/dL and the serum creatinine was

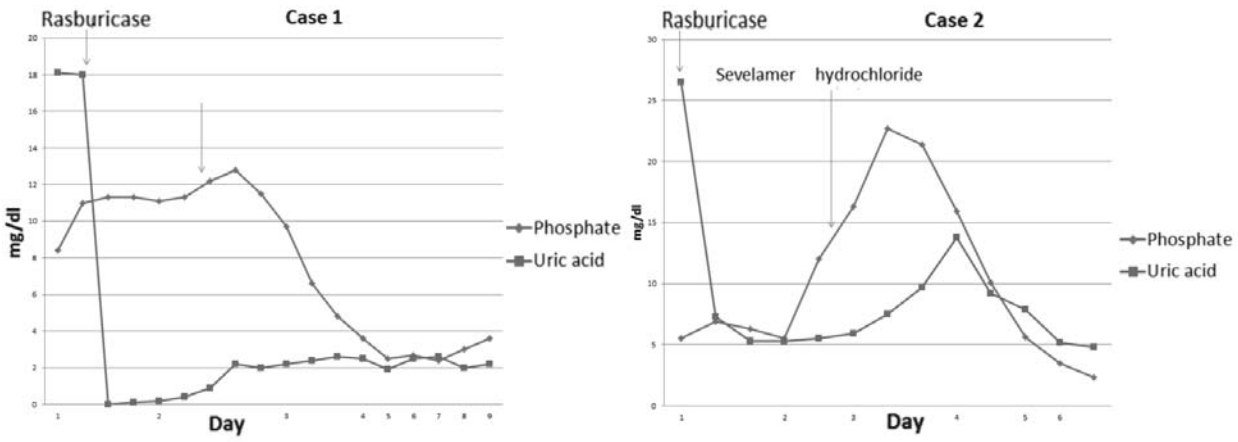

FIG.1 *Changes in phosphate and uric acid and sesporise to Sevelamer hydrochloride in the two children.*

2.0 mg/dL. He was started on intravenous fluids at 3 L/m^2/day. A single dose of rasburicase (3mg) controlled the hyperuricemia within 2 hours. However, serum phosphate and creatinine level started to rise by day-2, to 22 mg/dL and 2.4 mg/dL, respectively. Intravenous fluids were increased to 5 L/m^2/d and urine output was maintained throughout with regular furosemide doses. He also developed hypocalcemic tetany which was treated with calcium gluconate injection. Oral Sevelamer hydrochloride 400 mg, every 8 hrs, was given following which his serum phosphate levels came to within normal levels in 48 hours. The flow cytometry result confirmed T cell Acute Lymphoblastic Leukemia and the child was subsequently started on chemotherapy as per the UKALL 2003 protocol.

DISCUSSION

Hyperphosphatemia in children is usually defined when serum phosphate level is above 6.6 mg/dL (2.1 mmol/L). In malignancies, hyperphosphatemia occurs due to release of phosphate from the malignant cells during degradation. Hyperphosphatemia can cause nausea, vomiting, seizures, hypocalcemia, metastatic calcification, nephrocalcinosis and acute renal failure. In some cases of childhood cancers, phosphate level could go up in spite of aggressive hydration therapy, and may require hemodialysis. Aggressive hydration and aggressive diuresis will treat most cases of tumour lysis syndrome provided the kidney function is within normal limits [6].

Oral phosphate binders such as aluminium hydroxide can reduce serum phosphate level, but have adverse effects such as diarrhea. There are mainly three types of non-calcium-based phosphate binders available: Sevelamer, Lanthanum carbonate, and magnesium salts. Sevelamer is the only non-calcium-containing phosphate binder that does not have potential for systemic accumulation [6]. It is well tolerated except for an increased incidence of metabolic acidosis [7]. Other side effects include abdominal pain, diarrhea, nausea-vomiting, muscle cramps, hypocalcemia, headache and hypermagnesemia [8]. In children with end stage renal disease, it has been used in doses of 100 mg/kg/day to 130 mg/kg/day, every 8 hours [7,9].

In an earlier report [10], 13 children received sevelamer at a mean dose of 400 mg twice a day for treatment of tumor lysis syndrome related hyperphosphatemia. Significant reduction in serum phosphate was seen in 11 children. In both of our cases, serum phosphate levels were high enough to initiate hemodialysis; however, performing haemodialysis in newly diagnosed ALL is challenging in view of low platelet counts. Use of Sevelamer hydrochloride avoided hemodialysis and reduced the serum phosphate levels within 48 hours. We conclude that Sevelamer hydrochloride can be used for short duration to reduce the high phosphate levels associated with tumor lysis syndrome.

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