INTRODUCTION

Piperacillin/tazobactam is a combination of semi-synthetic ureidopenicillin and \( \beta \)-lactamase inhibitor, with broad spectrum antimicrobial activity that is useful in treating polymicrobial and gram-negative bacterial infection.\(^1\) It is mainly eliminated by glomerular filtration.

There are reported cases which described electrolytes imbalance,\(^2\) and other adverse effects with different antibiotics;\(^3-7\) however, this is an unusual case of a rare but severe hypokalemia induced by piperacillin/tazobactam in a postoperative patient who was treated for aspiration pneumonia.

CASE REPORT

A 76-year-old woman was admitted from Accidents and Emergency Department with a fractured neck of right femur and wound to her right ear after a fall. She had no significant past medical history apart from being suffering from anxiety for which she was taking chlorpromazine for the last 6 years. She did not have any drug allergy. She was independently mobile at home.

On physical examination the patient was apyrexial (36.9°C) with 93/minutes pulse, blood pressure of 173/86 mm/Hg, respiratory rate of 18/minutes and oxygen saturations of 97% on air. Her chest was clear on auscultation; abdomen was non distended, soft and non tender with positive bowel sounds. Right leg was shortened and internally rotated with right hip kept in flexed and abducted position. There was no neurovascular deficit. X-ray showed subtrochanteric fracture of the right femur. Her haemoglobin was 10.7 g/dL and white cell count was 13.8 \( \times 10^3 \) with normal liver function test, urea and electrolytes.

She was immediately resuscitated with 4 litres of intravenous (IV) normal saline within 48 hours and was taken to theatre for proximal femur nailing on the 3rd day of her admission. On the 2nd postoperative day she complained of nausea, vomiting and difficulty in breathing. On physical examination, pulse was 80/minutes, blood pressure of 96/70 mmHg, temperature of 37.7°C and respiratory rate of 22/minutes with oxygen saturation of 93% on air. Chest examination revealed bilateral lower zone crepitations. Chest X-ray showed left lower lobe shadowing (consolidation). She was started on IV Tazocin 4.5 g (piperacillin 4 g, tazobactam 500 mg), 3 times a day for lower respiratory tract infection. This was done according to the hospital protocol after discussing her case with the microbiologist. She had full blood count, liver function tests, urea and electrolytes checked every day. On the 1st postoperative day, before starting piperacillin/tazobactam, her serum potassium level was 4.2 mmol/l. On the 2nd postoperative day, she was started on piperacillin/tazobactam therapy for chest infection. Within 24 hours after commencing piperacillin/tazobactam therapy, her serum potassium level dropped to 3.6 mmol/l. Her progressive hypokalemia was treated with 80 mmol KCL in normal saline over 24 hours. Within 48 hours after commencing piperacillin/tazobactam therapy, her serum potassium level dropped to 2.9 mmol/l and sodium level increased to 150 mmol/l with normal renal function. There was no apparent cause for her deteriorating hypokalemia and hypernatremia. At 72 hours of initiation of piperacillin/tazobactam therapy, her general condition deteriorated further and on urgent lab analyser, serum potassium level was 2.4 mmol/l and sodium was 158 mmol/l. Electrolytes changes summarised

ABSTRACT

Electrolytes imbalance has been reported with the use of several antimicrobials. We report a case of severe hypokalemia secondary to piperacillin/tazobactam in a patient with normal renal function and normal serum potassium level who had presented with a fractured neck of femur. The electrolytes abnormality was corrected once piperacillin/tazobactam was stopped. To our knowledge, this is the first case to describe an early severe hypokalemia induced by piperacillin/tazobactam therapy in an otherwise healthy individual.

Key words: Hypokalemia. Hypernatremia. Piperacillin/tazobactam. Electrolytes imbalance.

Electrolytes Imbalance: A Rare Side Effect of Piperacillin/Tazobactam Therapy

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Received March 18, 2009; accepted February 23, 2010.
in Table I. The piperacillin/tazobactam therapy was stopped and intravenous co-amoxiclav (amoxicillin with clavulanic acid) 1.2 g was started 3 times a day, to treat her chest infection. Piperacillin/tazobactam was stopped as it was felt that this was the most likely reason for the patient’s deranged electrolytes. After 24 hours patient’s serum potassium level raised from 2.4 to 3.1 mmol/l and sodium dropped from 158 mmol/l to 149 mmol/l. On the subsequent day potassium and sodium levels normalized to 4.2 mmol/l and 139 mmol/l respectively. Oral potassium was only given for 3 days after potassium level reached 4.2 mmol/l and then it stayed within the normal limits thereafter.

**Table I: Laboratory test results.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Admission</th>
<th>72 hours post-antibiotic therapy</th>
<th>3 days after cessation</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/l)</td>
<td>140</td>
<td>158</td>
<td>139</td>
<td>135-145</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>4.8</td>
<td>2.4</td>
<td>4.2</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>Urea (mmol/l)</td>
<td>6.7</td>
<td>3.7</td>
<td>3.6</td>
<td>2.5-6.7</td>
</tr>
<tr>
<td>Creatinine</td>
<td>74</td>
<td>80</td>
<td>53</td>
<td>70-150</td>
</tr>
<tr>
<td>LFT’s</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>---</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.4</td>
<td>8.8</td>
<td>9.5</td>
<td>13.5-18</td>
</tr>
<tr>
<td>WBC count (x10³)</td>
<td>15.9</td>
<td>13.5</td>
<td>2.4</td>
<td>4.0 – 11</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>68</td>
<td>88</td>
<td>88</td>
<td>2-32</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>244</td>
<td>86</td>
<td>105</td>
<td>0-10</td>
</tr>
</tbody>
</table>

LFT’s = Liver function tests; WBC = White blood cell; ESR = Erythrocyte sedimentation rate; CRP = C-reactive protein.

**DISCUSSION**

Piperacillin/tazobactam is used widely in patients of all age groups to treat various infections. Potassium and magnesium losses are reported in patients with piperacillin therapy on intensive care units with multiple co-morbidities including renal impairment. The adverse effects reported with piperacillin/tazobactam therapy are; type-I hypersensitivity, acute delirium, neutropenia, rash, delayed type hypersensitivity reaction and paresthesia. The authors could not find any reported cases of hypokalemia occurring in patients treated with piperacillin/tazobactam in other wise healthy patient with no renal impairment. Use of the Naranjo probability scale and the Drug Interaction Probability Scale (DIPS) indicated a probable relationship between hypokalemia and the administration of piperacillin/tazobactam.

Most of the adverse effects of piperacillin/tazobactam are associated with long-term therapy such as, delayed type hypersensitivity, neutropenia or parasthesiae. Prolonged therapy with piperacillin/tazobactam rarely results in electrolyte imbalance in healthy individuals. However, patients with pre-existing renal impairment are more prone to develop hypokalemia with piperacillin/tazobactam therapy.

In this patient, apart from treating with piperacillin/tazobactam, there was no obvious cause for the electrolyte imbalance. Following cessation of piperacillin/tazobactam therapy the patient’s electrolytes returned to normal and therefore, one could presume that the piperacillin/tazobactam therapy was responsible for the electrolyte imbalance. A secondary effect of piperacillin/tazobactam therapy is hypernatremia as was noted in this patient.

To conclude, hypokalemia is a known but uncommon adverse effect of piperacillin/tazobactam therapy. This report describes the first case of severe hypokalemia induced by piperacillin/tazobactam therapy in a patient with normal renal function and normal potassium level. Serum sodium level should also be monitored in all patients receiving piperacillin/tazobactam therapy. It is suggested to closely monitor electrolytes in patients treated with piperacillin/tazobactam.

**REFERENCES**