Case Report:

A Case Series of Piperacillin-Tazobactam Induced Hypokalemia in a Tertiary Care Hospital in South India

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Abstract: Potassium is an important intracellular cation responsible for action potential generation and normal functioning of muscles. Hypokalemia and hyperkalemia are both dangerous as they cause life threatening cardiac arrhythmias. Piperacillin tazobactam is a commonly used beta-lactam and beta-lactamase inhibitor combination for complicated abdominal and urinary tract infections. Under pharmacovigilance programme of India, few cases of hypokalemia which were attributed to piperacillin tazobactam therapy were reported. This is a case series of 10 patients who developed hypokalemia secondary to piperacillin tazobactam therapy.

Key Words: Potassium, Ureidopenicillin, Pharmacovigilance, Beta-Lactam, Beta-Lactamase inhibitor

Introduction:
Potassium is a major intracellular ion. It is necessary for the normal cardiac, smooth and skeletal muscle functioning. Normal potassium level ranges from 3.5 – 5.5 mmol/L.[1] Hypokalemia is condition in which potassium level is less than 3.5 mmol/L. It is either due to increased potassium loss or due to abnormal intra and extracellular distribution of potassium. At levels less than 1.5mmol/L, it can be life threatening due to cardiac arrhythmias.[1] Hypokalemia can be caused by severe dehydration due to diarrhoea and vomiting, aldosteronism, long-term diuretic therapy, aminoglycoside therapy, etc.[2]

Piperacillin Tazobactam is a beta lactam – beta lactamase inhibitor combination. Piperacillin, a ureidopenicillin, is used for treating serious gram negative infections. It is active against Pseudomonas, Klebsiella, Enterobacteriaceae, and few bacteroides[3] and has the broadest spectrum among the penicillins.[4]

There are earlier case reports of hypokalemia secondary to Piperacillin.[5-8] This is a case series of 10 cases that developed hypokalemia after receiving Piperacillin Tazobactam injection.

Adverse drug reactions were collected as part of adverse drug reaction monitoring program by department of Pharmacology in Kasturba Medical College from December 2014 – March 2015, a period of four months in department of general medicine.

Case Series
Case 1: A 75 year old male patient was stared on IV Piperacillin Tazobactam 4.5g every 8th hourly for lower respiratory tract infection. He developed mild hypokalemia on the 4th day of therapy. No correction was given and drug was continued.

Case 2: A 38 year old male patient was started on IV Piperacillin Tazobactam 2.25g 8th hourly for gram negative sepsis. He developed moderate hypokalemia on 2nd day of therapy. Syrup potassium chloride correction was given and drug was continued.
Case 3: A 73 year old male patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for pyelonephritis. He developed mild hypokalemia on 2nd day of therapy. No correction was given and drug was continued.

Case 4: A 45 year old female patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for gram negative sepsis. She developed mild hypokalemia on the 5th day of therapy. In this patient, drug was stopped but no potassium correction was given.

Case 5: A 52 year old female patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for lower respiratory tract infection. He developed mild hypokalemia on 8th day of therapy. Intravenous potassium correction was given and drug was continued.

Case 6: A 77 year old male patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for acute gastroenteritis. He developed moderate hypokalemia on 4th day of therapy. Intravenous potassium correction was given and drug was continued.

Case 7: A 51 year old male patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for UTI - E Coli. He developed mild hypokalemia on 2nd day of therapy. No correction was given and drug was continued.

Case 8: A 38 year old male patient was started on IV Piperacillin Tazobactam 2.25g 8th hourly for gram negative sepsis, acute kidney injury. He developed moderate hypokalemia in 6 days of therapy. In this patient, drug was stopped and no correction was given.

Case 9: A 45 year old male patient was started on IV Piperacillin Tazobactam 4.5g 8th hourly for gram negative sepsis. He developed moderate hypokalemia on 9th day of therapy. In this patient, drug was stopped and no correction was given.

Case 10: A 59 year old female patient was started on IV Piperacillin Tazobactam 4.5g Q8H for pneumonia. She developed mild hypokalemia on 2nd day of therapy. In this patient, drug was stopped and no correction was given.

**Discussion:**

There were ten cases of Piperacillin-Tazobactam induced hypokalemia. In all 10 cases, temporal association was seen (hypokalemia developed after piperacillin-tazobactam was started). Hypokalemia was mild in 6, and moderate in 4. In 4 of these cases, the offending drug was discontinued and the three patients recovered after oral potassium supplementation, and 1 required parenteral potassium correction. In the rest 6 cases, the drug was not discontinued because the patients had only a mild grade of hypokalemia. No potassium supplementation was given to them. Except for one case who was on torsemide, other nine cases were not taking any drug that would have deranged potassium levels. Even in that scenario, patient was on torsemide for more than two years and thus torsemide being the cause for hypokalemia in this patient is highly unlikely.

Two of the cases had renal failure. Renal failure is usually associated with hyperkalemia but these patients developed hypokalemia, hence making the hypokalemia more likely due to piperacillin-tazobactam therapy.

In the above 10 cases, it was noted that older patients developed hypokalemia in an average of 3.3 days, and younger patients in 4.5 days. Zaki et al have put forth 2 hypotheses for piperacillin tazobactam induced hypokalemia: (i) The drug acts as non absorbable anion increasing transepithelial electronegativity in the kidney (distal nephron). As a result, there is an increase in sodium delivery and excretion of potassium ions.[6] (ii) Piperacillin is administered along with large quantity of sodium which can lead to solute diuresis. This results in potassium excretion through BK channels.[6]

Another study by Kutluturk F et al attributed hypokalemia to tubular dysfunction.[8] Piperacillin-tazobactam causes mild to moderate hypokalemia. Piperacillin tazobactam induced hypokalemia is usually not severe enough to need correction. It becomes imperative to monitor potassium levels while starting this drug, especially when other drugs which lower serum potassium levels are being administered concomitantly, or when administered in elderly patients.

**References**


