

Metabolic alkalosis: A less appreciated side effect of Imipenem-cilastatin use

Sir,

Imipenem is a carbapenem group of antimicrobial agent that is structurally related to β -lactam group of drugs. To prevent the hydrolysis of imipenem by dehydropeptidase-I enzyme in the proximal renal tubule, cilastatin is combined with imipenem for its clinical use.^[1] We report occurrence of metabolic alkalosis with the use of imipenem-cilastatin in two of our patients.

Acinetobacter baumannii is a common nosocomial pathogen in our intensive care unit (ICU) for which we use imipenem-cilastatin as the first line antimicrobial agent. Our first patient was a 29-year-old male having cervical spinal cord injury and the second patient was a 37-year-old male having blunt trauma chest. Both of the patients required prolonged mechanical ventilation and eventually had *A. baumannii*-associated pneumonia which was treated with imipenem-cilastatin. Both of our patients showed clinical improvement with the treatment, but during the treatment both had persistent metabolic alkalosis (after 3 and 4 days of therapy in patient 1 and 2, respectively). There were no signs and/or symptoms of cardiovascular, hepatic or renal abnormality in any of the patient and their serum cortisol, potassium, calcium, and magnesium levels were within normal limits. The urinary chloride levels were 33 mEq/L and

41 mEq/L in patient 1 and 2, respectively. Apart from antimicrobial agents both of the patients were receiving enteral nutrition and multivitamin supplements only and none received any alkaline solution or massive blood transfusions.

Beta-lactam antibiotics^[2] (sodium penicillin, carbenicillin) use can be associated with metabolic alkalosis as these drugs act as non-absorbable anions which increases K^+ and H^+ excretion resulting in metabolic alkalosis.^[2,3] Metabolic alkalosis has been reported to be associated with meropenem,^[4,5] another carbapenem group of drug. The structural similarity between meropenem and imipenem lead us to believe similar kind of mechanism for the metabolic alkalosis in our patients. We substituted imipenem-cilastatin with piperacillin and tazobactam, following which the metabolic alkalosis in both of our patients subsided over a period of 36-48 hours.

The most common reported side effects of imipenem use are nausea, vomiting, diarrhea, reactions at the infusion site, skin rashes, and seizures,^[1] but we could not find any report of association of imipenem-cilastatin and metabolic alkalosis in the available literature. Due to the structural similarity between penicillin and imipenem (i.e., β -lactam ring), similar mechanism might have lead to metabolic alkalosis with imipenem-cilastatin use in our patients, and this fact was further supported by subsidence of metabolic alkalosis after discontinuation of imipenem-cilastatin in our patients.

Apathy, confusion, cardiac arrhythmias, neuromuscular irritability, and compensatory hypoventilation leading to hypoxia are problems associated with severe metabolic alkalosis, and arterial blood pH >7.55 should be treated with appropriate interventions.^[2] As the metabolic alkalosis was not associated with any clinical symptomatology and the blood pH was <7.55, we did not correct the alkalosis (except substitution of another antibiotics) in our patients. With this case report, we want to emphasize that imipenem-cilastatin can be a cause of metabolic alkalosis in ICU patients.

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