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Case Report

Internal Medicine Section

Meropenem Induced Hypokalemia

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ABSTRACT

Meropenam, a beta-lactam antibiotic has been used for severe infections of skin, tissue, intra- abdominal and urogenital infections in hospitalized patients. The common adverse effects reported are diarrhoea, vomiting, rashes and hypersensitivity reactions. Here we report two cases of meropenam induced hypokalemia, wherein, meropenam was prescribed for cellulitis and urinary tract infection in the first and second case respectively. Hypokalemia can manifest as muscular weakness, fatigue, muscle cramps, constipation, ileus, flaccid paralysis, hyporeflexia, hypercapnia, tetany, rhabdomyolysis or respiratory failure. Hence, it is necessary to make physicians aware of such an adverse effect which can develop with meropenam.

Keywords: Antibacterial agents, Beta-lactam antibiotics, Hypokalemia, Infections

CASE 1

A 53-year-old female patient came with complaints of cough with greenish sputum which was thick and scanty. She also had an ulcer on the left lower limb which on examination was 10 cm × 3.5 cm × 1.5 cm in dimentions, with exposed bone, warmth and tenderness of surrounding area and peripheral pulses felt. She also had productive cough with fever. She was diagnosed as a case of bilateral pneumonia with left lower limb cellulitis. She was put on Inj. meropenem 1 gm TID for pneumonia and was advised ulcer debridement with regular dressing. Sputum culture showed the growth of *Acinetobacter baumannii* which was sensitive to carbapenems. Her concomitant medications included Inj. pantoprazole 40 mg OD, vitamin C, calcium and vitamin B-complex. Following six days of treatment she complained of weakness. Blood culture, complete haemogram and serum electrolytes were done. Blood culture did not show the growth of any organism. However, her hemoglobin (8 g/dl) and serum potassium (2.3 mmol/l) were low. The patient had no history of excessive loss of potassium due to diarrhoea or vomiting which is the most common cause of hypokalemia, there were no other causes that could have been attributed to hypokalemia. The differential diagnosis put forward by the clinicians were sepsis induced hypokalemia and drug induced hypokalemia. Hence, a detailed literature search was done. Two cases of meropenem induced hypokalemia had been reported which made the clinicians to think of hypokalemia as a probable cause. Hence, meropenem was thought to be the causative factor and was stopped after eight days and she was put on oral potassium supplementation 15 ml TID during the course of her hospital stay. Patient improved after the stoppage of the drug and her potassium levels also returned to normal.

Past history revealed that she had been diagnosed to have dengue fever one month back at a private hospital, where she was treated with Inj. meropenem 1gm TID for three days and she was intubated for four days following breathlessness. The laboratory reports at the private hospital also were suggestive of hypokalemia.

CASE 2

A 53-year-old female patient came with complaints of easy fatigability and malaise since two months and burning micturition since one month. The routine investigations including electrolytes were within normal limits. Her abdominal ultrasound scan showed right renal staghorn calculi with gross hydroureteronephrosis. Her urinary culture also showed *E. coli* and was sensitive to carbapenems, ciprofloxacin and gentamicin. She was a known case of diabetes mellitus type-2 and ischemic heart disease with inferior posterior wall hypokinesia. She was started on Inj. meropenem 1gm TID following which her laboratory parameters showed decreased serum potassium levels (3.1 mmol/L, 3.0 mmol/L) after two days. She was given oral potassium supplementation, 15 ml QID for a period of three days. Her concomitant medications included Tab. metformin 0.5 mg OD, Tab. aspirin 150 mg OD, Tab. clopidogrel 75 mg OD and Tab. atorvastatin 40 mg OD. She underwent percutaneous nephrolithotomy and was discharged. Follow up details were not available.

DISCUSSION

Meropenem is a dimethylcarbamoylpyrolidinyl derivative of thienamycin [1]. Meropenem, a broad spectrum, beta-lactam antibiotic acts by binding to the Penicillin Binding Proteins (PBP) and destroys bacterial cell wall integrity and synthesis. It has a broad spectrum of activity against many aerobic and anaerobic Gram-positive and Gram-negative organisms [2]. It is indicated for the treatment of severe or complicated skin, tissue, intra-abdominal and urogenital infections as well as sepsis due to susceptible organisms. Its use is generally reserved for severe infections in hospitalized patients. Here, we have presented two cases of hypokalemia due to meropenem.

In Case 1, patient had symptomatic hypokalemia, which resolved on stopping meropenem and there was no other concomitant medication that could have caused the same. Past history was suggestive of hypokalemia while being treated for dengue at a private hospital a month back. The patient had developed hypokalemia after three days of meropenem and was intubated for breathlessness. The authors are of the opinion that since hypoklaemia can also be caused during a dengue infection, it must have got worsened by treatment with meropenem and hence, necessitating an intubation. However, follow up details of the patients laboratory reports were not available as the patient was treated at a private set up. One month later, when the patient was put on meropenem for pneumonia she developed hypokalemia again, which suggests it to be due to meropenem itself as there were no other comorbid conditions or medications which could have caused hypokalemia in this patient. Hence, the causality assessment score based on Naranjo's algorithm was 9 [3]. Therefore, it is a "definite" adverse drug reaction.

In Case-2, patient developed hypokalemia following administration of meropenem which was asymptomatic and when potassium

supplementation were given the levels improved. In this case hypokalemia was detected during routine blood investigations. Since the clinicians already had a previous experience of treating meropenem induced hypokalemia, the drug was withdrawn for this patient and he did improve. Causality assessment score based on Naranjo's algorithm was 6. Therefore, it is a "probable" adverse drug reaction.

Zaki S and Shanbag P have reported a case of hypokalemia and metabolic alkalosis due to meropenem, wherein the condition resolved on stopping meropenem [4].

Bharti R et al., have also reported a case of weaning trials failure despite improvement in lung parameters probably because of persistent hypokalemia [5]. The β-lactam group of drugs (penicillin, carbenicillin, piperacillin) cause hypokalemia by distal delivery of non-resorbable anion which increases K+ and H+ excretion. Meropenem causes hypokalemia by the same mechanism due to structural similarities [4]. Hypokalemia can manifest as muscular weakness, fatigue, and muscle cramps, constipation, ileus, flaccid paralysis, hyporeflexia, hypercapnia, tetany, or rhabdomyolysis. Hence, meropenem needs to be stopped as hypokalemia can progress to respiratory failure. Hypokalemia can be treated with oral potassium supplementation in mild to moderate hypokalemia as it is the safest and easiest method. A dose of 20 mEq/day is generally sufficient. Intravenous potassium is indicated for patients with severe hypokalemia and for those who cannot take oral supplementation. However Electrocardiogram (ECG) monitoring may be required [6]. Another suitable antibiotic can be used for treating the infection.

CONCLUSION

Hypokalemia may be asymptomatic or can even lead to respiratory failure which can be life threatening. Hence, it is therefore essential for the physicians to be aware of these uncommon adverse effects of meropenem and also to treat it adequately as it can be life threatening.

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