CASE REPORT

The association of hypokalemia with meropenem administration: A case report and literature review

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We report the case of a 72-year-old woman who was admitted following a fall and sustained a right neck of femur fracture. Prior to this admission, she was undergoing chemotherapy for lung cancer. Upon this admission, it was noted that she had developed neutropenic sepsis. She was initially treated with teicoplanin and ciprofloxacin. However, her neutrophil count dropped further, and she continued to have a high temperature, hence her treatment was switched to meropenem. Administration of meropenem was associated with persistent and difficult-to-correct hypokalemia. The hypokalemia resolved, and potassium levels returned to normal a few days after completing the course of meropenem therapy. To our knowledge, there is a very rare association between hypokalemia and the administration of meropenem. Therefore, clinicians need to be aware of this, especially in cases of refractory hypokalemia.

Key words: Fracture neck of femur, hypokalemia, lung cancer, meropenem

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INTRODUCTION

Potassium homeostasis is crucial for the normal function of various physiological processes, such as acid–base balance, nerve conduction, and both cardiac and skeletal muscle contraction.[1] Hypokalemia remains one of the most commonly seen electrolyte abnormalities in clinical practice. It is generally defined as a serum potassium level of <3.5 mEq/L (3.5 mmol/L).[2] Numerous diseases or conditions, injuries, and certain medications can trigger hypokalemia. The underlying mechanisms typically involve excessive intracellular shifting of potassium, inadequate potassium intake, and increased renal and gastrointestinal potassium loss.[3] Patients with hypokalemia typically present with fatigue, leg cramps, malaise, constipation, and arrhythmias, with the most significant consequence being cardiac arrest. Antibiotics are widely used in the treatment of various infections. Some of these antibiotics have been shown to be associated with hypokalemia. For instance, the administration of piperacillin/tazobactam (Tazocin), flucloxacillin, cephalexin, and vancomycin has been associated with hypokalemia.[3-6]

Meropenem is a carbapenem antibiotic with a broad spectrum of activity. It acts by binding to the penicillin-binding proteins and disrupting bacterial cell wall integrity and synthesis. A very small number of case reports have shown that the administration

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of meropenem can be associated with hypokalemia.[7-9] It is thought that antibiotic-induced hypokalemia occurs through increased urinary potassium loss. To our knowledge, our case represents the fourth case in the literature to demonstrate the association of hypokalemia with meropenem administration.

CASE REPORT

A 72-year-old woman was admitted following a fall, sustaining a right neck of femur fracture. She has a past medical history of nonsmall cell lung cancer, diagnosed 6 months before this admission, and treated with a right lung lobectomy. She began chemotherapy 2 weeks prior to this hospital admission. Her past medical history also includes atrial fibrillation treated with bisoprolol and apixaban therapy. On admission, her blood tests showed neutropenic sepsis and acute kidney injury (AKI) stage 2. She was thus started on a renal dose of teicoplanin and ciprofloxacin and maintained normal potassium levels. She underwent a right hip hemiarthroplasty, and postoperatively, her neutrophils dropped further, prompting a switch to meropenem [Table 1]. Subsequent blood tests showed a deterioration of her potassium levels, likely connected to meropenem. She received intravenous potassium replacement, but ongoing monitoring showed little improvement, despite maintaining magnesium levels at a mean level of 6 mmol/L (normal range: 0.7–1 mmol/L) and receiving magnesium replacement. The corrected calcium levels were within the normal range before, during, and after treatment with meropenem. However, albumin levels ranged between 22 and 25 g/L during the treatment (normal range: 35–50 g/L) [Table 2]. During treatment with meropenem, there were no reports of any episodes of vomiting or diarrhea, and the rest of her medications were not associated with hypokalemia. Eventually, when the meropenem course was completed, her potassium levels returned to baseline [Figure 1] and also renal function and neutrophils and white cell counts were all back to normal range [Table 2]. The patient consented to the publication of this case report.

DISCUSSION

Meropenem is used in the treatment of different types of severe infections, such as soft-tissue and skin infections, severe intra-abdominal infections, and urogenital infections, and it is best used under the guidance of a microbiologist.[10] In a randomized, double-blind, parallel-group, phase 3, noninferiority trial conducted in 76 centers across 17 countries in Asia, Europe, and the USA, the impact of cefiderocol versus high-dose, extended-infusion meropenem was compared in adults with nosocomial pneumonia. In this trial, hypokalemia was found in 15% of the meropenem group.[11] Administration of meropenem was also associated with hypokalemia in 5% of the infant population.[12] In addition, meropenem has been found to be among the antibiotics that can induce life-threatening potassium disturbances.[13] Importantly, the calculation of the Naranjo algorithm for adverse drug reaction causality assessment produced a score of 6, suggesting that the adverse drug reaction was probably related to meropenem.[14] Zaki and Shanbag showed that in a 6-year-old girl, the administration of meropenem was associated with hypokalemia and metabolic alkalosis, which resolved 3 days after stopping meropenem.[7] Anuhya *et al*. reported the presence of hypokalemia in two patients treated with meropenem.[8]

The exact mechanism by which meropenem can lead to hypokalemia is not fully known. It is thought that due to structural similarities between meropenem and the β-lactam group of drugs (penicillin, carbenicillin, and piperacillin), it is likely that meropenem induces hypokalemia in a similar way as the β-lactam group, through the formation of a nonresorbable anion that leads to an increase in urinary K+ and H+ excretion.[3-5,7-9] Further research is needed to establish (i) if meropenem can also impact the secretion of aldosterone or the aldosterone receptors, (ii) whether prior treatment with β-lactam group drugs may make individuals more prone to hypokalemia with meropenem administration, and (iii) why hypokalemia

Table 1: The dose, route, frequency, and manufacturer brand of meropenem

Dose	500 mg
Route of administration	Intravenous
Frequency	Three times per day
Manufacturer brand, product number	Synchrony pl 34958/0003 for 500 mg Bowmed meropenem and for 1 g pl 05539/0004

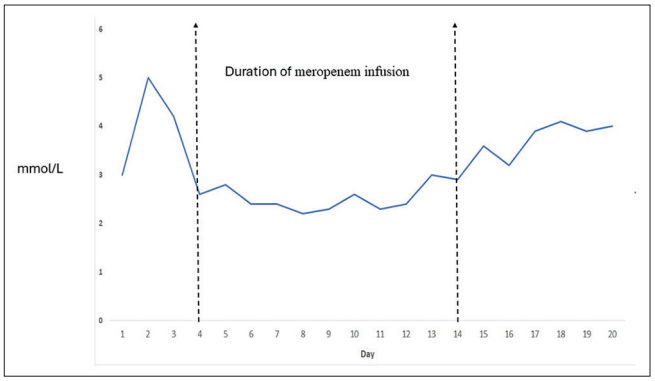

Figure 1: Hypokalemia with meropenem infusion and normal plasma potassium level after completion of meropenem therapy (normal reference range for potassium is 3.5–5.3 mmol/L). The blue line is the plasma potassium level, and the dotted line shows the duration of infusion of meropenem. Day 1 and day 3 represent the duration before meropenem infusion. Day 15 up to day 20 represent the duration of when meropenem infusion stopped. Potassium was measured by indirect method for electrolytes using Beckman analyzer (AU 5000/800)

Table 2: Different biochemical and hematological changes

Day	Biochemical and hematological changes during meropenem infusion									
	1	2	3	4	5	6	7	8	9	10
Hb	88	98	95	91	84	87	90	94	86	83
WCC	0.2	0.3	1	4.4	9.9	17.7	17.5	16.3	13.1	10.2
PLT	72	78	76	77	72	82	112	187	271	443
Neutrophil	0	0.1	0.8	3.3	8.8	15.7	13.8	14.3	11.1	8.7
Sodium	145	142	146	147	148	148	149	144	141	141
GFR	43	39	40	61	63	70	76	>90	>90	>90
Albumin	22	25	25	25	22	21	23	23	22	20

The neutrophils, WCC, PLTs, and renal function function improved at day 10 of infusion and normalized. No changes were noticed in plasma albumin or hemoglobin level. Albumin reference range (35–50 g/L), Sodium normal reference range 133–145 mmol/L. Hb=Hemoglobin (normal reference range 110–150 g/L); PLT=Platelets (normal reference range 150–450); WCC=White cell count (normal reference range 3.7–11.1); GFR=Glomerular filtration rate (normal reference range >90 mL/min)

induced by meropenem is refractory and not correctable with intravenous potassium replacement in the context of normal plasma magnesium levels.

Our case is unique, as it occurred in a patient with lung cancer on chemotherapy who sustained a neck of femur fracture and developed neutropenic sepsis. The presence of lung cancer, AKI, sepsis, and chemotherapy may act as confounding factors. However, hypokalemia was only observed during the administration of meropenem, and normal potassium levels were observed once meropenem was discontinued. This case will increase awareness among clinicians to look for the association of hypokalemia with meropenem administration.

One challenging question on the horizon is the best strategy to treat severe hypokalemia if meropenem is the only antibiotic able to eradicate the infection. In such a situation, possible options include oral and intravenous potassium replacement and encouraging the patient to eat potassium-rich foods such as bananas and tomatoes.

Presentation of abstract

The case was presented as a poster in the Society for Endocrinology Meeting-UK (SFEBES2023) in November 2023 and abstract only published in Endocrine Abstracts (2023) 94 P197 | DOI: 10.1530/endoabs. 94.P197.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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