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Letter to Editor

Severe Hypernatremia Associated with Intravenous Fosfomycin: A Preventable Adverse Effect in the Intensive Care Setting

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Dear Editor,

In patients followed in intensive care units (ICU), electrolyte disturbances are common and often result from complex polypharmacy, impaired renal handling, or the use of broad-spectrum antibiotics. With the increasing use of fosfomycin for multidrug-resistant (MDR) infections, hypernatremia has emerged as a recurrent and clinically significant problem (1). We present two illustrative ICU cases to highlight this underrecognized yet preventable complication.

Fosfomycin is a broad-spectrum bactericidal antibiotic commonly used against Enterobacteriaceae and Pseudomonas aeruginosa (2). Each gram of intravenous fosfomycin disodium contains about 0.33 g (14.3 mEq) of sodium, meaning that a 16 g/day regimen provides more than 230 mEq of sodium daily, equivalent to 1 L of 3% saline (2). This sodium load can precipitate iatrogenic hypernatremia, particularly in critically ill or oliguric patients (3).

Case 1: A 69-year-old male with diabetes, chronic kidney disease (baseline creatinine 3.5 mg/dL), and laryngeal carcinoma was admitted to the ICU with respiratory failure after CABG. Due to MDR isolates, he received fosfomycin (4 g every 12 hours, total 8 g/day). His serum sodium rose from 141 to 155 mmol/L despite stable renal function and fluid balance. After discontinuation of fosfomycin, sodium levels decreased to 144 mmol/L. The clear temporal association suggested fosfomycin-induced hypernatremia. During this period, the patient was clinically euvolemic, was not receiving diuretics, hypertonic saline, or sodium bicarbonate, and enteral nutrition and fluid prescriptions remained unchanged. Fosfomycin therapy was discontinued prematurely due to progressive hypernatremia rather than completion of the planned treatment course.

Case 2: A 49-year-old paraplegic male with diabetes, hypertension, coronary artery disease, and prior Pott abscess surgery was admitted to the ICU after debridement of an infected pressure ulcer. Following initiation of intravenous fosfomycin (4 g every 12 hours, total 8 g/day), sodium rose from 139 to 163 mmol/L, then gradually decreased to 136 mmol/L after the drug was withdrawn, without other medication changes. The patient was clinically euvolemic, did not receive diuretics or additional sodium-containing infusions, and no changes in nutritional support or fluid management were observed during fosfomycin therapy. Treatment was discontinued early because of marked hypernatremia, after which serum sodium levels gradually normalized.

In conclusion, fosfomycin-induced hypernatremia is an underrecognized but preventable adverse effect. High-risk patients include those with renal dysfunction, oliguric states, or additional sodium loads (4). Regular sodium monitoring, dose adjustment, and avoiding sodium-containing diluents are essential preventive strategies. Early recognition and interdisciplinary collaboration among intensivists, nephrologists, and infectious disease specialists can minimize morbidity and improve outcomes.

This report aims to emphasize a side effect that we frequently observe in practice yet should never overlook, as timely awareness can make a significant clinical difference.

DECLARATIONS

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