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A Rare Case Series on Cefoperazone Sulbactam Induced Uremia: A Matter of Concern and Awareness

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Uraemia is a clinical syndrome marked by elevated concentrations of urea in the blood and is associated with fluid, electrolyte, hormone imbalances and metabolic abnormalities. Cefoperazone + sulbactam is a combination of two medicines: cefoperazone and sulbactam. Cefoperazone is an antibiotic that works by preventing the formation of the bacterial protective covering, which is essential for the survival of bacteria [1]. Sulbactam is a beta-lactamase inhibitor that reduces resistance and enhances the activity of cefoperazone against bacteria [2].

Pharmaceutical agents play a central role in diagnostic and therapeutic activities for patient care. However, all agents carry the risk of adverse drug effects. While most of these are clinically insignificant, some drugs may cause unacceptable toxicity that negatively impacts patient morbidity

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and mortality [3]. Recognizing adverse effects is important for administering appropriate drug doses, implementing preventive strategies, and discontinuing the offending agent when toxicity occurs [2]. In most cases, nephrotoxicity leads to discontinuation of the causative drug, thereby limiting treatment options.

One of the biggest challenges lies in our ability to identify nephrotoxicity in its early stages. Monitoring serum creatinine and blood urea nitrogen (BUN) levels is an effective method for identifying renal diseases [4]. In this study, the authors report three cases of isolated cefoperazone-sulbactam-induced uraemia in patients without chronic kidney disease (CKD). A Naranjo assessment score of 5 was obtained for the three case scenarios, indicating a probable relationship between the patient's uraemia and use of the suspected drug.

Keywords: Uremia; kidney disease; kidney injury; kidney failure; renal dysfunction; renal perfusion; hemodialysis.

1. INTRODUCTION

Uraemia more commonly develops with chronic kidney disease (CKD), especially in the later stages of CKD, but it can also occur with acute kidney injury (AKI) if there is a rapid loss of kidney function. Urea itself has both direct and indirect toxic effects on a range of tissues [5]. Several substances with toxic effects, such as parathyroid hormone, beta-2 microglobulin, polyamines, advanced glycosylation end products, and other middle molecules, are thought to contribute to the clinical syndrome [6].

Cefoperazone, a third-generation cephalosporin antibiotic, is widely used in clinical practice for the treatment of various bacterial infections [4]. While effective in targeting and eliminating bacterial pathogens, like any medication, cefoperazone is not without its potential side effects [7]. One rare but severe complication associated with cefoperazone use is the development of uremia.

Cefoperazone-induced uremia poses a significant challenge for health care providers as it requires prompt recognition and management to prevent further complications.

2. CASE PRESENTATION

2.1 Case 1

A 62-year-old male patient with past medical history of diabetes mellitus and on medication arrived with complaints of a sudden onset of lower body ache and right sciatica in the last 10 days. On systemic examination, patient was found to be best forward and more comfortable when seated. The straight leg raise test showed 45-degree for right leg. MRI showed bone spurs and tissues associated with arthritis of the spine between L4 and L5. The final diagnosis revealed prolapsed, herniated or extruded intervertebral disc (PIVD) between L4-L5 with sub ligamental extrusion.

Laminectomy and dissection were done for the patient. Laboratory investigations revealed normal values for urea (37 mg/dl) and serum electrolytes(sodium-137mEq/l) on the day of admission. However, during the course of admission in the hospital the patient was prescribed with inj. Cefoperazone and sulbactam for 6 days. Following administration, there was found to be a spike in the urea level (48mg/dl) and decreased serum electrolytes (Na-131mEq/l). On day three following administration of cefoperazone-sulbactam, urea level was raised to 55mg/dl, and on day five, it was further raised to 62mg/dl. Causality assessment using Naranjo scale was done and obtained a score of 5.

2.2 Case 2

A 67-year-old male patient with past medical history of COPD, HTN and type 1 respiratory failure arrived with complaints of breathing difficulty in the last 1 day, fever for 10 days, and cough. His past medication history includes tab cilnidipine 5 mg od, and Levo-salbutamol and ipratropium bromide as nebulisations as well as tab Acebrophylline bd. On systemic examination, the patient was found to have wheezing and acute exacerbation of COPD. The final diagnosis divulged COPD exacerbation, type 1 respiratory failure and systemic hypertension.

Laboratory investigations suggests normal urea level (27 mg/dl) on the day of admission. Following administration of inj. cefoperazone sulbactam for 6 days, there is an elevation of urea to 58 mg/dl on day one. Further investigations on day three and day five showed

Table 1. Urea level on the day of admission and following administration of suspected drug

Cases	Day of admission	Day 1	Day 2	Day 3
CASE 1	37 mg/dl	48mg/dl	60mg/dl	62mg/dl
CASE 2	27mg/dl	58mg/dl	60mg/dl	63mg/dl
CASE 3	30mg/dl	55mg/dl	58mg/dl	63mg/dl

an elevation in urea level to 60mg/dl and 63mg/dl respectively. On stoppage of medication the urea level was checked, and was found to be normal. A score of 5 was obtained when causality assessment was done using Naranjo scale.

2.3 Case 3

An 87-year-old female patient with no comorbidities except intermittent constipation, arrived to the hospital with altered sensorium for the past two days and bleeding for one day. On systemic examination, the patient was confused, restless, dehydrated, and showed signs of pallor and icterus. Per rectal examination indicated impacted stools with altered blood. The patient was diagnosed with chronic liver failure with hepatic encephalopathy and coagulopathy.

During the course of admission, the patient was on inj. Cefoperazone sulbactam 2gm iv bd, tab Ursodeoxycholic acid, tab rifaximin 550 mg bd, inj. Pantoprazole 40 mg iv od and Syp. Duphalac 30 ml TID. There was a drastic change in the urea level of the patient from the day of admission which is 30mg/dl to 55mg/dl after the intravenous administration of antibiotic cefoperazone sulbactam. Subsequent investigations to assess the urea levels indicated a rise which is 58mg/dl and 63mg/dl on third and fifth day. The normalization of urea level after the discontinuation of cefoperazone sulbactam indicates that this drug is a suspected agent for uraemia. The Naranjo scale was used for causality assessment, and a score of 5 was obtained for this case, which indicates a probable relationship between the suspected drug and the elevated urea level.

3. DISCUSSION

Cefoperazone sulbactam is a combination antibiotic widely used in clinical practice to treat severe bacterial infections. While it is generally considered safe and well tolerated there have been rare reports of cefoperazone sulbactam induced uraemia, a condition characterised by elevated blood urea nitrogen (BUN) and creatinine levels.

The clinical presentation of cefoperazone sulbactam induced uraemia can vary widely. Patients may exhibit symptoms such as decreased urine output, fatigue, oedema, hypertension, electrolyte imbalances, and altered mental status. Laboratory investigations typically reveal elevated BUN and serum creatinine levels, along with other signs of renal dysfunction. Timely recognition of these clinical features is crucial to differentiate cefoperazone sulbactam induced uraemia from other causes of renal impairment.

The foremost priority is to discontinue the offending medication and ensure adequate renal perfusion. Supportive care measures, including correction of fluid and electrolyte imbalances maybe necessary. In severe cases, renal replacement therapy, such as haemodialysis or continuous renal replacement therapy, may be required to provide temporary renal support. Furthermore, close monitoring of renal function and follow-up investigations are essential to assess the recovery of renal function and prevent long term complications.

4. CONCLUSION

Cefoperazone-sulbactam induced uraemia is a serious condition that can arise as a result of treatment with this antibiotic combination. Uraemia occurs when the kidneys are unable to effectively remove waste products from the body, leading to an accumulation of toxins in the bloodstream. Cefoperazone-sulbactam is a potent antibiotic used to treat a variety of bacterial infections, but it can have adverse effects on kidney function in some individuals [8].

The development of urea due to cefoperazone-sulbactam necessitates immediate medical attention and intervention. The discontinuation of the antibiotic is typically the first step, followed by supportive care to manage the complications associated with uraemia [9]. It is crucial for the healthcare providers to be vigilant in monitoring patients receiving cefoperazone-sulbactam therapy, especially those with pre-existing kidney disease or risk factors for renal impairment.

Furthermore, efforts should be made to raise awareness among healthcare professionals about the potential risk associated with cefoperazone-sulbactam use and the importance of monitoring renal function during treatment [10]. Improved surveillance and reporting systems can help identify cases of cefoperazone-sulbactam induced uraemia and contribute to the understanding of its incidence and risk factors [11-15].

CONSENT

It is not applicable.

ETHICAL ASPECTS

Written informed consent was not obtained from the patient since patient details are not disclosed.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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