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Dose Adjustment of Cefoperazone–Sulbactam in a Patient with Chronic Kidney Disease and Sepsis: A Case Report

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ABSTRACT: Chronic kidney disease (CKD) can lead to anemia and impaired excretion of metabolic waste products, characterized by elevated urea and creatinine levels (azotemia). Patients with CKD are also more susceptible to severe infections, including sepsis, which requires appropriate antibiotic therapy with careful dose adjustment. To report the use of cefoperazone–sulbactam in a patient with CKD and sepsis, emphasizing dose adjustment according to renal function. Case Presentation: The patient presented with anemia (Hb 10.2 g/dL; hematocrit 30.6%; erythrocytes 3.42 $\times 10^6$ /µL) and azotemia (urea 104–145 mg/dL; creatinine 6.28–7.15 mg/dL). Leukocytosis (14 $\times 10^3$/µL) with neutrophil predominance indicated bacterial infection. Creatinine clearance (CrCl) was calculated at 10–25 mL/min, indicating severe renal impairment. The patient was treated with cefoperazone–sulbactam 1 g every 12 hours. Cefoperazone–sulbactam therapy was considered appropriate, as the combination is more effective against resistant Gram-negative bacteria than cefoperazone monotherapy. Dose adjustment was required because sulbactam is renally excreted and may accumulate, leading to neurotoxicity.Cefoperazone–sulbactam is a rational antibiotic choice in CKD patients with sepsis, provided that the dose is adjusted based on renal function to maintain therapeutic efficacy while minimizing adverse effects.

KEYWORDS: Chronic Kidney Failure; Anemia; Azotemia; Sepsis; Cefoperazone; Sulbactam

I. INTRODUCTION

Acute Respiratory Infections (ARI) are among the most common infectious diseases encountered in both primary care and hospital settings, with treatment typically involving antibiotics and symptomatic medications [1]. In patients with normal renal function, such treatments are generally safe and effective. However, in patients with chronic kidney disease (CKD), the use of antibiotics for ARI requires special attention due to pharmacokinetic and pharmacodynamic changes resulting from impaired renal function [2].

CKD is characterized by a progressive decline in glomerular filtration rate (GFR), leading to impaired drug elimination through the kidneys [2], [3]. This condition increases the risk of drug accumulation, particularly for renally excreted agents such as aminoglycosides, cephalosporins, penicillins, and fluoroquinolones, which may cause nephrotoxicity, ototoxicity, and other systemic complications [4], [5]. In addition, symptomatic drugs such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are also nephrotoxic and may accelerate CKD progression [6].

Previous studies have reported that high-dose or long-term NSAID use in CKD patients is associated with an increased risk of acute kidney injury (AKI), electrolyte imbalance, hypertension, and accelerated decline of renal function [7], [8]. Literature reviews have also shown that inappropriate antibiotic prescribing in CKD patients—whether in terms of dose or interval—remains common, contributing to increased adverse events and worsened prognosis [9], [10], [11]. Therefore, drug selection, dose adjustment, and therapeutic monitoring are essential in the management of ARI in CKD patients to minimize complications and optimize treatment effectiveness.

II. METHODS

Case Presentation

A 60-year-old male patient was admitted to the hospital with complaints of severe shortness of breath, a persistent cough lasting more than one week, rhinorrhea, chest pain, difficulty expectorating sputum, and sore throat. The patient was diagnosed with impending respiratory failure, stage V chronic kidney disease (CKD), and hypertension.

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Table 1. Laboratory findings of the patient

Parameter	Reference Range	Result (Day 1)	Result (Day 5)	Result (Day 6)
Hemoglobin (g/dL)	13.2 – 17.3	10.2	–	–
Leukocytes (×10³/µL)	4.5 – 11.5	14	11.65	–
Eosinophils (%)	2 – 4	0.6	–	–
Neutrophils (%)	50 – 70	81.6	–	–
Lymphocytes (%)	18 – 42	9.3	–	–
Monocytes (%)	2 – 8	8.1	–	–
Total Lymphocytes (×10³/µL)	1.5 – 3.7	1.3	–	–
Neutrophil–Lymphocyte Ratio	< 3.13	8.77	–	–
Hematocrit (%)	40 – 54	30.6	–	–
Erythrocytes (×10^6 /µL)	4.50 – 14.5	3.42	–	–
Random Blood Glucose (mg/dL)	70 – 140	175.2	–	–
Urea (mg/dL)	17 – 54	104	145.1	55.2
Creatinine (mg/dL)	0.73 – 1.18	6.28	7.15	3.09

Table 2. Parenteral Medications Administered to the Patient

Drug Name	Dosage & Preparation	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Lasix	1 × 2 ampoules	✓	–	–	–	–	–	–	–
Furosemide 20 mg/2 mL	5 ampoules in 50 mL NS – infused at 2 mL/hour	✓	–	–	–	–	–	–	–
Furosemide 20 mg/2 mL	3 ampoules in 50 mL NS – infused at 4 mL/hour	–	✓	✓	✓	✓	✓	–	–
Cefoperazone–Sulbactam	1 g IV twice daily	–	✓	–	–	–	–	–	–
Cefoperazone	1 g IV twice daily	–	✓	✓	✓	✓	✓	✓	✓

Table 3. Non-Parenteral Medications Administered to the Patient

Drug Name	Dosage	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Oseltamivir	75 mg orally, twice daily	✓	✓	✓	✓	✓	✓	✓	–
Amlodipine	5 mg orally, once daily	✓	✓	✓	✓	✓	✓	✓	✓
Irbesartan	300 mg orally, once daily	✓	✓	✓	✓	✓	✓	✓	–
Decolgen (paracetamol + phenylpropanolamine + chlorpheniramine)	1 tablet orally, three times	✓	✓	✓	✓	✓	✓	✓	–

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	daily								
N-acetylcysteine (NAC)	200 mg orally, three times daily	✓	✓	✓	✓	✓	✓	✓	–
Longatin (ambroxol)	50 mg orally, three times daily	✓	✓	✓	✓	✓	✓	✓	–
Folic Acid	1 mg orally, three times daily	✓	✓	✓	✓	✓	✓	✓	–
Velutine Plus + Pulmicort (nebulization)	1 dose, three times daily	✓	✓	✓	✓	✓	✓	✓	–

III. RESULTS AND DISCUSSION

The patient's laboratory findings revealed several abnormalities, indicating anemia as shown by decreased hemoglobin (Hb) on Day 1 (10.2 g/dL), hematocrit (30.6%), and erythrocyte count (3.42×10^6 /µL). This condition may have been caused by the underlying chronic kidney disease (CKD). Renal dysfunction was further demonstrated by elevated creatinine levels on Day 1 (6.28 mg/dL), Day 5 (7.15 mg/dL), and Day 6 (3.09 mg/dL), as well as elevated urea levels on Day 1 (104 mg/dL), Day 5 (145.1 mg/dL), and Day 6 (55.2 mg/dL), indicating azotemia. Azotemia is defined as an increase in blood urea nitrogen (BUN) and creatinine levels due to impaired renal function [12]. This occurs because nitrogenous metabolic waste products accumulate in the blood as the kidneys are unable to excrete them effectively. In contrast, uremia is a more severe condition, representing advanced azotemia, and is characterized by symptoms such as nausea, vomiting, encephalopathy, and pericarditis [13], [14].

Hematological findings also showed leukocytosis on Day 1 (14×10^3/µL) and Day 5 (11.65×10^3/µL), which is a marker of infection. This was further supported by decreased eosinophils (0.6%), increased neutrophils (81.6%), decreased lymphocytes (9.3%), and elevated monocytes (8.1%) on Day 1. These findings strongly suggested bacterial sepsis. Based on this, the patient was treated with cefoperazone–sulbactam on Day 2, followed by cefoperazone monotherapy from Day 2 to Day 8.

Cefoperazone–sulbactam is a third-generation cephalosporin combined with a β-lactamase inhibitor, primarily indicated for severe infections, including sepsis and infections caused by resistant Gram-negative bacteria [15], [16]. The combination is superior to cefoperazone monotherapy because sulbactam protects against β-lactamase-mediated resistance. However, dosage adjustments are required in patients with hepatic and renal impairment [17].

Cefoperazone is mainly excreted through bile, unlike most cephalosporins that are eliminated via the kidneys. In contrast, sulbactam is renally excreted; therefore, in patients with reduced glomerular filtration rate (GFR), sulbactam may accumulate and increase the risk of adverse effects, including neurotoxicity such as seizures and encephalopathy.

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Table 4. Dose Adjustment of Cefoperazone–Sulbactam in Renal Impairment [17]

Renal Function (CrCl/GFR)	Cefoperazone Dose	Sulbactam Dose	Notes
Normal (≥30 mL/min)	2–4 g/day, divided every 12 h (max 8 g/day)	1–2 g every 12 h	No specific adjustment required
CrCl 15–30 mL/min	Same (2–4 g/day)	Max 1 g every 12 h	Sulbactam dose should be reduced due to renal excretion
CrCl <15 mL/min	Same (2–4 g/day)	Max 0.5 g every 12 h	Risk of sulbactam accumulation
Hemodialysis	Same (2–4 g/day)	Additional dose after dialysis	Sulbactam is partially removed during dialysis
Combined hepatic & renal failure	Reduced (e.g., 1–2 g/day)	Adjust according to CrCl	Close monitoring of drug levels and coagulation needed

Table 5. Patient's Creatinine Clearance (CrCl) Calculation

Day	Creatinine (mg/dL)	Estimated CrCl (mL/min)	Interpretation
H1	6.28	~12.4	Severe renal failure
H5	7.15	~10.9	Severe renal failure
H6	3.09	~25.2	Moderate–severe renal failure

Based on the patient's CrCl values on Day 1 and Day 5, renal function was classified as severe renal failure. Therefore, administration of cefoperazone–sulbactam at a dose of 1 g every 12 hours was considered appropriate. This adjustment was made because sulbactam, when administered at doses exceeding 500 mg, may accumulate in the kidneys, thus the lowest effective dose was chosen to

IV. CONCLUSION

In this case, the patient with chronic kidney disease presented with anemia and azotemia, indicated by elevated urea and creatinine levels, accompanied by leukocytosis suggestive of bacterial sepsis. Cefoperazone–sulbactam was selected as the antibiotic of choice, as this third-generation cephalosporin combined with a β-lactamase inhibitor is more effective against resistant Gram-negative bacteria compared with cefoperazone alone. Given that the patient had severe renal impairment (CrCl approximately 10–25 mL/min), dose adjustment was made by administering cefoperazone–sulbactam 1 g every 12 hours, ensuring therapeutic effectiveness while reducing the risk of sulbactam accumulation and potential neurotoxic adverse effects.

DECLARATIONS

Conflict of interest.

The authors declare that they have no conflicts of interest.

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REFERENCES

[1]. C. D. Mambo, A. S. R. Masengi, and D. A. Thomas, "Rasionalitas Penggunaan Antibiotik untuk Pengobatan Infeksi Saluran Pernapasan Akut pada Anak," Med. Scope J., vol. 6, no. 1, pp. 72–79, 2023, doi: 10.35790/msj.v6i1.45431.

[2]. S. Liabeuf et al., "Drug Exposure in Chronic Kidney Disease: It Is Not Just About the Glomerular Filtration Rate," Fundam. Clin. Pharmacol., vol. 39, no. 4, pp. 1–10, 2025, doi: 10.1111/fcp.70037.

[3]. A. Chapron, D. D. Shen, B. R. Kestenbaum, C. Robinson-Cohen, J. Himmelfarb, and C. K. Yeung, "Does Secretory Clearance Follow Glomerular Filtration Rate in Chronic Kidney

Diseases? Reconsidering the Intact Nephron Hypothesis," Clin. Transl. Sci., vol. 10, no. 5, pp. 395–403, 2017, doi: 10.1111/cts.12481.

[4]. R. E. Campbell, C. H. Chen, and C. L. Edelstein, "Overview of Antibiotic-Induced Nephrotoxicity," Kidney Int. Reports, vol. 8, no. 11, pp. 2211–2225, 2023, doi: 10.1016/j.ekir.2023.08.031.

[5]. [5] S. Nayak-Rao, "Aminoglycoside use in renal failure," Indian J. Nephrol., vol. 20, no. 3, pp. 121–124, 2010, doi: 10.4103/0971-4065.70839.

[6]. A. Whelton, "Nephrotoxicity of nonsteroidal anti-inflammatory drugs: Physiologic foundations and clinical implications," Am. J. Med., vol. 106, no. 5 B, pp. 13S-24S, 1999, doi: 10.1016/S0002-9343(99)00113-8.

[7]. T. Dreischulte, D. R. Morales, S. Bell, and B. Guthrie, "Combined use of nonsteroidal anti-inflammatory drugs with diuretics and/or renin-angiotensin system inhibitors in the community increases the risk of acute kidney injury," Kidney Int., vol. 88, no. 2, pp. 396–403, 2015, doi: 10.1038/ki.2015.101.

[8]. K. Gooch et al., "NSAID Use and Progression of Chronic Kidney Disease," Am. J. Med., vol. 120, no. 3, pp. 1–7, 2007, doi: 10.1016/j.amjmed.2006.02.015.

[9]. N. Al Himali, Y. M. Al Suleimani, I. Al-Zakwani, and A. M. Abdelrahman, "Antibiotics utilization patterns and dosage appropriateness among patients receiving hemodialysis," Saudi Pharm. J., vol. 30, no. 7, pp. 971–978, 2022, doi: 10.1016/j.jsps.2022.05.005.

[10]. B. Chahine, "Antibiotic dosing adjustments in hospitalized patients with chronic kidney disease: a retrospective chart review," Int. Urol. Nephrol., vol. 54, no. 1, pp. 157–163, 2022, doi: 10.1007/s11255-021-02834-6.

[11]. J. X. G. Zhu, D. M. Nash, E. McArthur, A. Farag, A. X. Garg, and A. K. Jain, "Nephrology comanagement and the quality of antibiotic prescribing in primary care for patients with chronic kidney disease: A retrospective cross-sectional study," Nephrol. Dial. Transplant., vol. 34, no. 4, pp. 642–649, 2019, doi: 10.1093/ndt/gfy072.

[12]. A. Tika, E. Irawati, Wayunah, B. Sakti, and F. Suprapti, KEPERAWATAN DEWASA SISTEM ENDOKRIN, IMUNOLOGI, PENCERNAAN, PERKEMIHAN DAN REPRODUKSI PRIA, 1st ed. Bandung: EUREKA MEDIA AKSARA, JUNI 2024 ANGGOTA IKAPI JAWA TENGAH NO. 225/JTE/2021, 2024.

[13]. E. Mikhail, A. Seri, K. Ralston, A. Valvani, and Z. Kalynych, "Urinothorax and pseudo-azotemia following total abdominal hysterectomy: a case report," AME Case Reports, vol. 8, pp. 25–25, 2024, doi: 10.21037/acr-23-146.

[14]. A. Tyagi and N. R. Aeddula, "Azotemia - StatPearls - NCBI Bookshelf," 2020. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK538145/

[15]. H. S. Sader, C. G. Carvalhaes, J. M. Streit, M. Castanheira, and R. K. Flamm, "Antimicrobial activity of cefoperazone-sulbactam tested against Gram-Negative organisms from Europe, Asia-Pacific, and Latin America," Int. J. Infect. Dis., vol. 91, pp. 32–37, 2020, doi: 10.1016/j.ijid.2019.11.006.

[16]. WHO, "Proposal to the 2025 WHO EML Expert Committee on AMR / AWaRe Classification regarding Cefoperazone / Sulbactam," 2025.

[17]. C. M. Chao, C. C. Lai, C. H. Lee, and H. J. Tang, "Optimal Dose of Cefoperazone-Sulbactam for Acute Bacterial Infection in Patients with Chronic Kidney Disease," Antibiotics, vol. 11, no. 5, pp. 2–9, 2022, doi: 10.3390/antibiotics11050610.