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CASE REPORT

Low-Dose Trimethoprim-Sulfamethoxazole Prophylaxis for *Pneumocystis jirovecii* Pneumonia in a Critically Ill Patient with HIV/TB Coinfection: Pharmacokinetics and Clinical Outcomes

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Background: *Pneumocystis jirovecii* pneumonia (PJP) is a life-threatening opportunistic infection disease in immunocompromised patients, particularly those with advanced HIV and tuberculosis (TB) co-infection. Trimethoprim-sulfamethoxazole (TMP-SMZ) is recommended for PJP prophylaxis, but its pharmacokinetics (PK) and clinical efficacy in critically ill patients receiving multi-drug therapies (anti-TB, antiretroviral, and antifungals) remain poorly characterized.

Case Presentation: This study reported the PK profile, multi-drug management strategies and clinical outcomes of low-dose TMP-SMZ (a combined dose of 480 mg once daily, 50% of the standard prophylactic dose) for PJP prophylaxis in a critically ill patient with disseminated TB, advanced HIV ($CD4^+$ count: 21 cells/μL), and concurrent infections. The patient received TMP-SMZ alongside anti-TB therapy (isoniazid, rifabutin, levofloxacin, linezolid), voriconazole, and antiretroviral therapy. Therapeutic drug monitoring (TDM) showed peak concentrations of sulfamethoxazole (SMZ) and trimethoprim (TMP) were 18.58 μg/mL and 0.48 μg/mL, with trough concentrations of 1.75 μg/mL and 0.03 μg/mL, respectively. No drug–drug interactions were observed with concurrent voriconazole. The patient achieved stable recovery and without PJP or TMP-SMZ-related adverse events occurred during treatment and 6-month follow-up.

Conclusion: This case reported the feasibility of low-dose TMP-SMZ for PJP prevention in high-risk, critically ill patients with HIV/TB coinfection, and described its PK characteristics. It provides a reference for optimizing prophylaxis in resource-limited settings or patients intolerant to standard regimens.

Keywords: TMP-SMZ, low-dose, pharmacokinetics, case report

Background

Pneumocystis jirovecii pneumonia (PJP) is a respiratory infection disease and predominantly affects immunocompromised individuals. PJP is one of the leading causes of morbidity and mortality among patients infected with human immunodeficient virus (HIV).[1,2] Trimethoprim-Sulfamethoxazole (TMP-SMZ) is the first-line treatment for PJP and can also be used for prevention of PJP in individuals with a history of at least one episode of PJP or HIV-infected adults with a $CD4^+$ T-cell count $\leq 200/mm^3$ or < 20% total lymphocytes.[3,4]

The TMP-SMZ used in clinical practice is a compound preparation, with each tablet containing 400mg of sulfamethoxazole (SMZ) and 80mg of trimethoprim (TMP). The recommended standard treatment regimen for PJP is TMP 3.75–5 mg/kg and SMZ 18.75–25 mg/kg, administered every 6 h. Alternatively, for prophylaxis of PJP in adults, the initial dose is TMP 160 mg and SMZ 800 mg (two tablets of compound preparation) twice daily, followed by the same dose either once daily or three times per week.[5] TMP-SMZ is rapidly and completely absorbed (>90%) after oral administration, reaching peak plasma concentrations (Cmax) within 1–4 h. After absorption, both components can be

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widely distributed in the whole body tissues and fluids. Both SMZ and TMP are primarily eliminated through glomerular filtration and renal tubular secretion, with mean elimination half-lives of approximately 10 h and 8–10 h, respectively. In patients with impaired renal function, the half-life is prolonged, necessitating dose adjustments.[6–8]

Currently, there is relatively limited data on the pharmacokinetics (PK) studies of TMP-SMZ as well as its appropriate dosing and efficacy for different types of infections. Although the efficacy and safety of TMP-SMZ in treating PJP in patients with HIV infection have been reported,[9,10] few studies have investigated its PK, particularly in critically ill patients with tuberculosis (TB) complicated by HIV infection. The PK characteristics of low-dose TMP-SMZ prophylactic use in this specific patient population remain unclear. Therefore, this case report described the clinical management of a critically ill patient with TB and HIV coinfection, focusing on the PK characteristics of low-dose TMP-SMZ and its correlation with clinical outcomes while highlighting potential host factors that may influence drug exposure in this complex population.

Case Presentation

The patient was a 33-year-old male, weighing 46 kg and measuring 178 cm, and was admitted to hospital with a one-week history of fatigue and malaise. The patient was transferred to our hospital due to a chest computed tomography (CT) scan result from local hospital revealed diffuse bilateral pulmonary lesions, tuberculosis of the T10 and T11 vertebrae with surrounding abscess formation, slightly hypodense lesion in the left liver lobe and with a serum sodium level of 115 mmol/L (normal range: 137–147mmol/L). The patient had been diagnosed with acquired immunodeficiency syndrome (AIDS) for over a decade and had received antiretroviral therapy (ART), but his recent medication adherence was unclear. He also had a history of treatment for syphilis.

The patient was admitted to hospital with provisional diagnoses of hematogenous disseminated pulmonary tuberculosis, tuberculous meningitis, HIV/AIDS with multiple opportunistic infections, suspected fungal infection, latent syphilis, hyponatremia, and vertebral tuberculosis. Upon admission, the patient underwent comprehensive diagnostic testing and was placed on oxygen therapy and continuous cardiac monitoring. Given his HIV history, multiple infections were suspected. Therefore, he was initially started on an anti-tuberculosis regimen consisting of intravenous isoniazid (0.3g/daily), levofloxacin (0.5g/day, intravenous infusion), and linezolid (0.6g/day, intravenous infusion). Additionally, intravenous voriconazole (0.2g, once every 12 hours, with doubled loading dose on the first day) was administered for antifungal coverage, meropenem (1.0g, once every 8 hours, intravenous infusion) was initiated for broad-spectrum antibacterial treatment, and TMP-SMZ (480 mg, three times a day, orally) was prescribed for PJP prophylaxis.

On day two of hospitalization, the patient's body temperature was normal. However, he continued to experience profound fatigue and altered mental status. Laboratory investigations revealed a blood pH of 7.484 (normal range: 7.35–7.45), partial pressures of 35.5 mmHg (normal range: 35–45 mmHg) for carbon dioxide and 83.0 mmHg for oxygen (normal range: 80–110 mmHg), lactate level of 1.60 mmol/L (normal range: 0.5–1.7 mmol/L), and D-dimer level of 1862.0 μg/L (normal range: 0–550 μg/L). Additionally, the level of hepatitis B surface antigen was 0.00 IU/mL (negative: <0.08 IU/mL), while the HIV antibody level (ELISA, types 1+2) was indeterminate. The syphilis-specific antibody test (chemiluminescence immunoassay) yielded a result of 13.69 (positive: >1.0). The hepatitis C virus antibody test (IgM +IgG) result was negative. The toluidine red unheated serum test for syphilis was positive (normal: negative). Chest CT findings suggested tuberculosis in the right lung with potential bilateral dissemination. Next-generation sequencing of sputum confirmed the presence of *Mycobacterium tuberculosis* complex with resistance to isoniazid. Based on the results, the anti-tuberculosis regimen was adjusted to levofloxacin (0.5g/day, intravenous infusion), linezolid (0.6g/day, intravenous infusion), and oral rifabutin tablet 0.3g/day. Meropenem and voriconazole were continued for coverage of bacterial and antifungal infection. Additionally, intravenous ganciclovir (250 mg once every 12 hours) was initiated for antiviral therapy, and TMP-SMZ (480mg, three times a day, orally) was continued for PJP prophylaxis.

On day four of hospitalization, the serum galactomannan (GM) assay (Platelia Aspergillus Antigen Test, Bio-Rad Laboratories) targeting *Aspergillus species* yielded a result of 0.04 ng/mL (cut-off value for positivity: ≥0.5 ng/mL). At the same time, considering that the patient did not have any clinical signs of fungal infection (such as persistent fever, new pulmonary infiltrates), the administration of voriconazole was discontinued. Blood samples were collected before withdrawal to monitor the serum drug level, revealing a voriconazole trough concentration of 4.84 μg/mL (normal range:

0.5–5.0 μg/mL). On day seven of hospitalization, the patient was given 0.3g/day of tenofovir dipifurate fumarate tablet and 0.35g/day of lamivudine dotilavir tablet for HIV treatment from an outside hospital.

On day eight of hospitalization, due to the patient's serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels increasing to 201 U/L (normal range: 9–50 U/L) and 131 U/L (normal range: 15–40 U/L), respectively, rifabutin was discontinued, and the dose of TMP-SMZ was adjusted to 480mg/day. Additionally, glycyrrhizin 100mL/day was administered intravenously for hepatoprotection, and regular monitoring of liver and renal function was advised.

On day nine of hospitalization, a chest CT scan revealed diffuse miliary nodules and widespread interlobular septal thickening in both lungs. Blood samples were collected 3 hours after administration of TMP-SMZ for peak concentration testing, and the results showed that the concentration of SMZ and TMP concentration was 18.58 and 0.48 μg/mL, respectively. On day 12 of hospitalization, the patient was diagnosed with tuberculous meningitis, and the treatment regimen was continued. Moreover, the trough concentrations of TMP and SMZ were measured, with respective concentrations of 0.03 and 1.73 μg/mL.

On day 16 of hospitalization, the patient exhibited reduced coughing and sputum production, with no hemoptysis or blood-streaked sputum. Due to hypoalbuminemia, intravenous human albumin (50 mL) was administered. Blood samples were collected again (3 h following administration of TMP-SMZ) to determine the peak concentration, the results suggested concentrations of TMP and SMZ were 0.46 and 16.51 μg/mL, respectively.

On day 19 of hospitalization, the patient had minimal cough and sputum production and did not experience abdominal pain, bloating, diarrhea, nausea, or vomiting. Laboratory tests revealed a WBC count of 3.3×10^9/L (normal range: $3.5–9.5 \times 10^9$/L), a neutrophil percentage of 78.5% (normal range: 46.5–76.5%), a hemoglobin (Hgb) level of 102 g/L (normal range: 120–170 g/L), and a platelet count of 142×10^9/L (normal range: $100–300 \times 10^9$/L). Biochemical testing revealed a serum glucose level of 5.66 mmol/L (normal range: 3.9–6.1 mmol/L), blood urea nitrogen (BUN) of 3.93 mmol/L (normal range: 3.1–8.8 mmol/L), creatinine of 21.2 μmol/L (normal range: 41–111 μmol/L), uric acid of 57 μmol/L (normal range: 155–428 μmol/L), albumin of 38.8 g/L (normal range: 40–55 g/L), ALT of 43 U/L (normal range: 9–50 U/L), AST of 29 U/L (normal range: 15–40 U/L), high-sensitivity C-reactive protein (hs-CRP) of 4.92 mg/L (normal range: 0–3.3 mg/L), sodium level of 130.0 mmol/L (normal range: 137–147 mmol/L), potassium level of 4.29 mmol/L (normal range: 3.5–5.3 mmol/L), and chloride level of 88.8 mmol/L (normal range: 96–108 mmol/L). Based on the results, severe tuberculosis complicated by HIV infection was considered. And since the patient's liver function stabilized, rifabutin (0.3g/day, orally) and (ethambutol 0.75g/day, orally) were added to the anti-tuberculosis regimen. On day 29 of hospitalization, the patient is in stable condition, and with normal liver function, the existing anti-tuberculosis and antiretroviral treatment regimen was continued.

On day 38 of hospitalization, the patient had a mild cough and less sputum production. There were no symptoms of nausea, vomiting, abdominal pain, bloating, diarrhea, or dyspnea. Laboratory results revealed WBC count 6.8 × 10^9/L, Hgb level 106 g/L, platelet count 265 × 10^9/L, BUN 2.87 mmol/L, creatinine 37.7 μmol/L, total bilirubin 7.25 μmol/L, total protein 56.6 g/L, albumin 34.0 g/L, ALT 20 U/L, AST 14 U/L, hs-CRP 15.31 mg/L, sodium level 139.8 mmol/L, potassium level 3.83 mmol/L, and chloride level 103.3 mmol/L. Therefore, considering that the patient was in stable condition after anti-tuberculosis, anti-infectious, anti-retroviral and nutritional support treatment, he was discharged on day 39 of hospitalization. Moreover, no incidence of PJP and TMP-SMZ-related adverse reactions was observed throughout the treatment course. He was advised to continue oral anti-tuberculosis and antiviral therapy, and undergo weekly monitoring of blood parameters, liver and renal functions, and vision after being discharged. The patient was followed up for 6 months and his condition remained stable A detailed treatment timeline is provided in Table 1. The changes of neutrophils (%), PLT levels, serum potassium and sodium levels throughout the treatment course are depicted in Figure 1. Changes in the lung CT images of the patient before treatment and 3 months after treatment are shown in Figure 2.

During the treatment course, TDM for TMP-SMZ and voriconazole were performed by a validated liquid chromatography with tandem mass spectrometry method. The linear detection ranges for TMP, SMZ, and voriconazole were 0.6–48, 3–240, and 0.25–20 μg/mL, respectively. The serum concentrations of TMP, SMZ, and voriconazole during treatment are summarized in Table 2.

Table 1 The Timeline of the Overall Treatment Process

Time	Laboratory Profile	Imaging Examination	Treatment
Before admission	Na+: 115mmol/L	Lung CT: diffuse lesions in both lungs, tuberculosis of the 10th and 11th thoracic vertebrae and peripheral abscesses	NR
Admission Day 1	T: 38.8 °C P: 125 R: 20 BP: 119/73	NR	H: 0.3g, qd, ivgtt. Lfx: 0.5g, qd, ivgtt. LZD: 0.6g, qd, ivgtt. VRZ: 0.2g, q12h, ivgtt. Meropenem: 1.0g, q8h, ivgtt. TMP-SMZ: 480mg, tid, po.
Day 2	pH: 7.484 PCO2: 35.5 PO2: 83.0 D-dimer: 1862.0 Syphilis testing: positive BUN: 3.78 Scr: 46.3 UA: 75 Alb: 29.3 ALT: 30 AST: 61 Na+: 115.3 K+: 3.69 WBC: 4.4 Hgb: 122 PLT: 95 CRP: 147.49	Lung CT: right pulmonary tuberculosis, with biculmonary spread considered; NGS of sputum: positive tuberculosis and INH resistance	Lfx: 0.5g, qd, ivgtt. LZD: 0.6g, qd, ivgtt. Rfb: 0.3g, qd, po. VRZ: 0.2g, q12h, ivgtt. Meropenem: 1.0g, q8h, ivgtt. TMP-SMZ: 480mg, tid, po. Ganciclovir:0.25g,q12h,ivgtt
Day 4	SPO_2: 96% C_{trough} of VRZ: 4.84 mg/L	Serum GM test: 0.04	Discontinue: VRZ
Day 7	WBC: 3.1 RBC: 3.84 Hgb: 116 PLT: 109 BUN: 3.07 Scr: 26.3 UA: 25 Alb: 26.9 ALT: 132 AST: 120 Na^+: 125 K^+: 3.77 CRP: 15.57	NR	Adding: Tenofovir dipifurate fumarate: 0.3g, qd, po. lamivudine dotilavir: 0.35g, qd, po. Discontinue: Ganciclovir
Day 8	Abnormal liver function (ALT: 201 AST: 131)	NR	Discontinue: Rfb: 0.3g, qd, po. TMP-SMZ: 480mg, tid, po. LZD: 0.6g, qd, ivgtt. Adding: TMP-SMZ: 480mg, qd, po. LZD: 0.6g, qd, po.
Day 9	C3h of SMZ: 18.58 μg/mL, C3h of TMP: 0.48μg/mL	Lung CT: right upper lung with multiple high-density shadows, extensive interlobular septal thickening	Discontinue: Ganciclovir: 0.25g, q12h, ivgtt.
Day 12	CSF testing: WBC: 26 RBC: 50 Pandy protein: positive Ctrough of SMZ: 1.73 μg/mL Ctrough of TMP: 0.03μg/mL	Head MRI (plain scan + DWI): a few subacute hemorrhages in the left occipital cortex and acute lesions near the left ventricular posterior horn.	/
Day 16	C3h of SMZ: 16.51 μg/mL C3h of TMP: 0.46μg/mL	NR	Discontinue: Meropenem: 1.0g, q8h, ivgtt

(*Continued*)

Table 1 (Continued).

Time	Laboratory Profile	Imaging Examination	Treatment
Day 19	WBC: 3.3 Hgb: 102 PLT: 142 BUN: 3.93 Scr: 21.2 UA: 57 TB: 14.20 DB: 5.7 Alb: 38.8 ALT: 43 AST: 29 CRP: 4.92 Na+: 130.0 K+: 4.29	NR	Adding: Rfb: 0.3g, qd, po. E: 0.75g, qd, po.
Day 29	WBC: 5.6 Hgb: 100 PLT: 284 BUN: 4.37 Scr: 25.8 UA: 83 Alb: 36.0 ALT: 45 Na^+: 137.3 K^+: 3.82	NR	/
Day 38	WBC: 6.8 Hgb: 106 PLT: 265 BUN: 2.87 Scr: 37.7 TP: 56.6 Alb: 34.0 ALT: 20 AST: 14 CRP: 15.31 Na+: 139.8 K+: 3.83	**Lung CT**: significant absorption of pleural effusion, and reduction in pulmonary infiltrates and nodules	/
Day 39 Discharge	NR	NR	Discharge medication: Lfx: 0.5g, qd, po. LZD: 0.6g, qd,po. Rfb: 0.3g, qd, po. E: 0.75g, qd, po. TMP-SMZ: 480mg, qd, po.

Abbreviations: Alb, Albumin (g/L); ALT, Alanine aminotransferase (U/L); AST, Aspartate aminotransferase (U/L); BP, Blood Pressure (mmHg); BUN, Blood urea nitrogen (mmol/L); CT, Computer tomography; CRP, Hypersensitive C-reactive protein (mg/L); C_{trough}, trough blood concentration; C_{3h}, Concentration of 3h after medication; CSF, Cerebrospinal fluid; D-dimer, D-dimer testing (μg/L); DB, Direct bilirubin (μmol/L); E, Ethambutol; GM, galactomannan test; Hgb, Hemoglobin (g/L); H, Isoniazid; Lfx, Levofloxacin; LZD, Linezolid; MRI, Magnetic resonance imaging; NGS, Next generation sequencing; P, Pulse (times/minute; PCO_2, Partial pressure of carbon dioxide (mmHg); PO_2, Oxygen partial pressure (mmHg); PLT, Platelets (×10^9/L); R, Respiration (times/minute); RBC, Red blood cells (×10^12/L); Rfb, Rifabutin; SPO2, Blood oxygen saturation (%); Scr, Serum creatinine (μmol/L); SMZ, sulfamethoxazole; T, Temperature (°C); TB, Total bilirubin (μmol/L); TP, Total protein (g/l); TMP, Trimethoprim; UA, Uric acid (μmol/L); VRZ, Voriconazole; WBC, White blood-cell counts (×10^9/L); Na+, Serum sodium level (mmol/L); K+, Serum potassium ion (mmol/L).

Discussion

Over the past few decades, the incidence of infections caused by opportunistic pathogens, including *P. jirovecii* and *Stenotrophomonas maltophilia*, has increased due to the rising number of immunocompromised patients.[11–13] TMP-SMZ remains the first-line drug for the treatment of mild, moderate, and severe PJP. Nevertheless, PK/PD data, susceptibility breakpoint, and comprehensive dosage and efficacy data of TMP-SMZ for various types of infections remain relatively scarce. This study demonstrated the clinical efficacy and pharmacokinetic characteristics of halved-dose TMP-SMZ in preventing PJP in patients with severe tuberculosis and HIV infection, which may provide references for TMP-SMZ clinical application.

TMP-SMZ remains first-line for PJP treatment but carries dose-dependent renal and hematologic risks.[14] While standard doses (15–20 mg/kg/d TMP; 75–100 mg/kg/d SMZ) are guideline-recommended,[15] they may not optimally balance efficacy and safety. A systematic review on low-dose TMP-SMZ therapy for PJP demonstrated that compared to the standard dosage, a TMP dose closer to 10 mg/kg/d was associated with satisfactory treatment outcomes while significantly reducing the incidence of severe adverse reactions.[16] Our case aligns with this finding but extends it to a more complex scenario: a critically ill HIV/TB coinfected patient on multi-drug therapy (anti-TB, ART, antifungals). Unlike the general PJP population in the review,[16] our patient had unique pharmacokinetic traits (substandard TMP/SMZ concentrations) likely due to high creatinine clearance (>200 mL/min) and drug interactions, yet still achieved effective PJP prophylaxis without adverse events. This suggests individualized low-dose regimens may be viable in high-risk, critically ill populations with altered drug clearance—an underaddressed aspect in prior reviews.[16]

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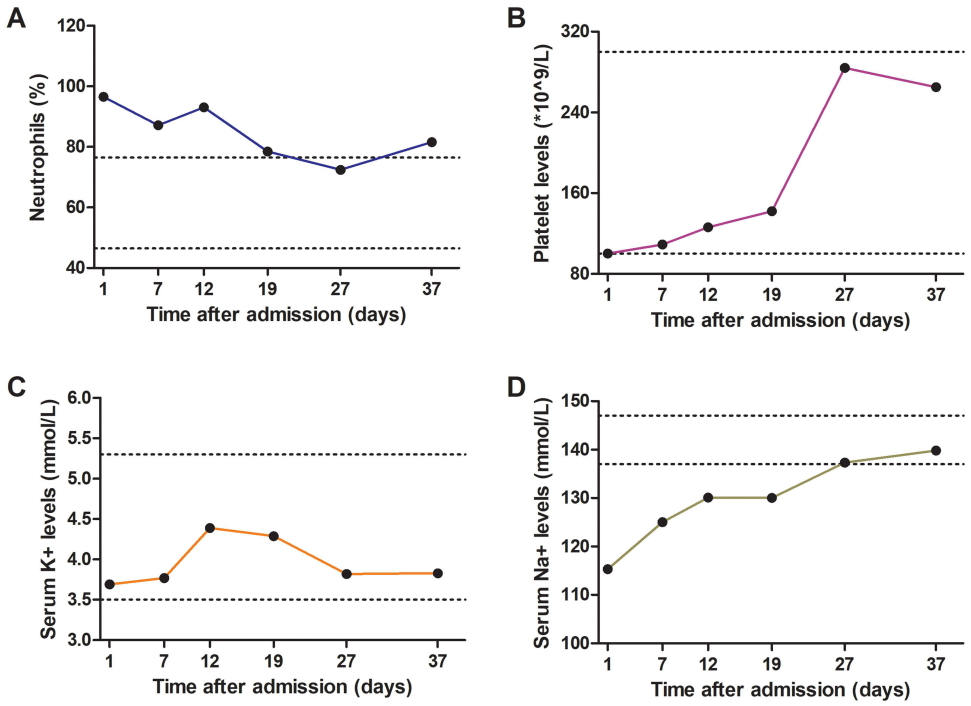

Figure 1 Changes of neutrophils, PLT levels, serum potassium and sodium levels throughout the treatment course. (**A**) neutrophils (%) levels; (**B**) PLT levels; (**C**) serum potassium levels; (**D**) serum sodium levels. The dashed lines represent the normal ranges for neutrophils, platelets, potassium ions and sodium ions, respectively.

For some patients (eg, critical illness or breakthrough PJP), early higher doses may still be needed. Here, TMP-SMZ was initially 480 mg thrice daily, then reduced to 480 mg daily (1.74 mg/kg/d TMP; 8.69 mg/kg/d SMZ) after one week due to liver function decline. This is half the label-recommended maintenance dose (960 mg daily or thrice weekly), yet the patient remained PJP-free with no drug-related adverse effects (eg, hypersensitivity, cytopenias, electrolyte disturbances). These findings support low-dose TMP-SMZ as a viable PJP prevention option in critically ill HIV/TB coinfected patients.

TMP-SMZ serum concentration exhibits substantial interindividual variabilities, and prolonged exposure to high serum drug levels may lead to toxic reactions. Routine TDM of TMP-SMZ is infrequently utilized in clinical practice.[17] Therefore, the authors' team has developed a mass spectrometry-based method for TMP-SMZ concentration measurements, which is currently applied in the TDM of immunocompromised or critically ill patients. According to the expert consensus on the clinical application of TMP-SMZ TDM,[17] TMP-SMZ TDM is mainly applicable to the following populations: (1) patients with infections caused by susceptible pathogens who exhibit suboptimal treatment responses, or patients with autoimmune diseases complicated by infections, in whom empiric dose adjustments based solely on clinical experience may increase the risks of toxicity, treatment failure, and the development of drug resistance; (2) critically ill patients or those receiving extracorporeal life support, whose PK may be altered by physiological and pathological changes; (3) patients with abnormal drug clearance, such as those with impaired renal function or receiving renal replacement therapy;[18] (4) patients treated for more than three months, those receiving high doses, those undergoing intravenous therapy, and individuals with a low body mass index or hypoalbuminemia who are suspected of developing toxic reactions; and (5) patients with poor medication adherence. The expert consensus also specifies that the TDM indicator for TMP-SMZ treatment of systemic infections should be the Cmax. The recommended respective target concentrations of TMP and SMZ are 1.5–2.5 and 30–60 μg/mL for common pathogens and 5–10 and 100–200 μg/mL for *Pneumocystis jirovecii*. Regardless, the optimal concentration range for TMP-SMZ prophylactic administration remains unclear. In this study, following administration of TMP-SMZ at 480 mg daily, the Cmax of TMP and SMZ was 0.48 and 18.58 μg/mL, respectively. These values are markedly below the therapeutic ranges recommended in the aforementioned guidelines. Besides the fact that the preventive dose used by this patient was significantly lower than the recommended

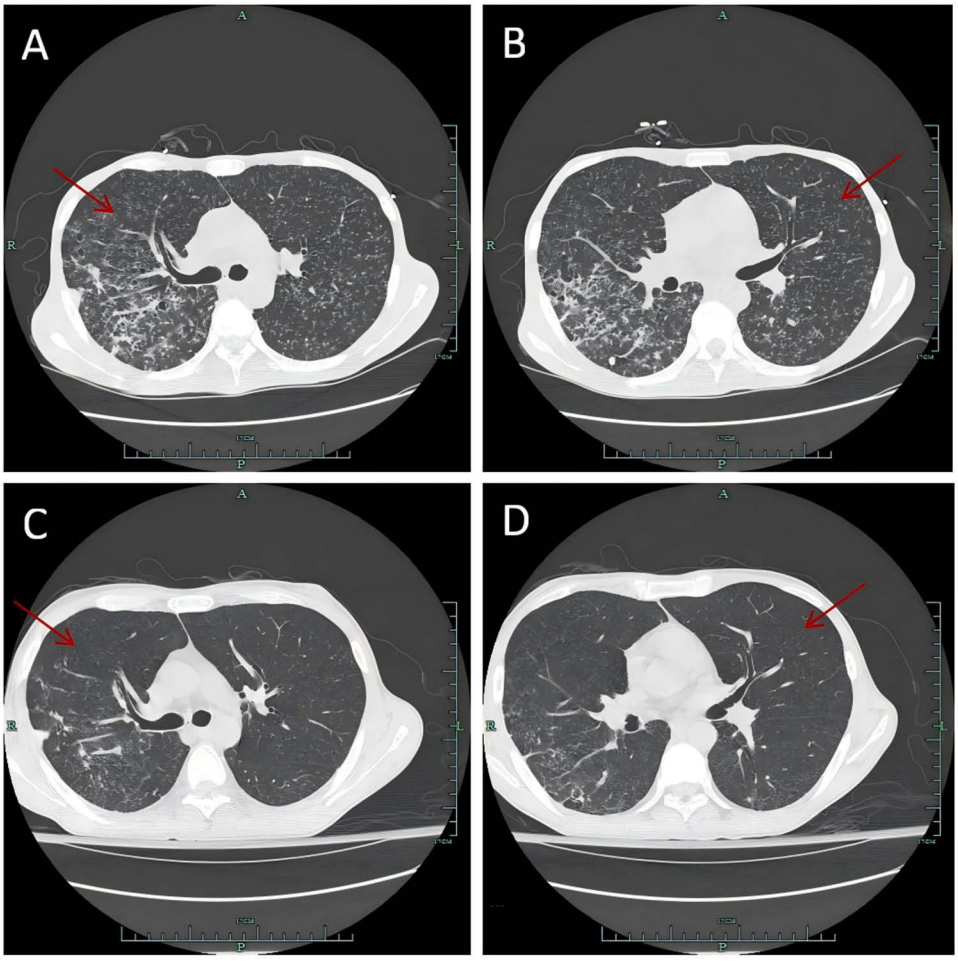

Figure 2 Changes in the lung CT images of the patient before treatment (**A and B**) and 3 months after treatment (**C** and **D**). (**A** and **B**) Diffuse miliary shadows in both lungs, with some confluent patchy opacities, more prominent in the right lung. (**C** and **D**) The diffuse miliary shadows in both lungs showed significant resolution compared to the previous imaging.

dose regimen, the state of renal ultrafiltration leading to accelerated drug elimination (during the treatment, the patient showed a creatinine clearance rate of more than 200 mL/min) might also be another reason.

The case in this study was a critically ill patient with tuberculosis and HIV co-infection. Consequently, during TMP-SMZ prophylactic administration, ART was administered simultaneously using a combination of tenofovir dipifurate fumarate tablet and lamivudine dotilavir tablet. Studies have found that TMP-SMZ concomitant use with dapsone, and zidovudine may increase the incidence of nephrotoxicity or bone marrow suppression. Therefore, when an ART regimen containing zidovudine is used concurrently with TMP-SMZ and dapsone, close monitoring of renal function and

Table 2 Concentrations of TMP, SMZ, and Voriconazole During Treatment

Time	SMZ	TMP	Voriconazole
Day 4	/	/	C_{trough}: 4.84 mg/L
Day 9	C_{3h}: 18.58 μg/mL,	C_{3h}: 0.48μg/mL	/
Day 12	C_{trough}: 1.73 μg/mL,	C_{trough}: 0.03μg/mL	/
Day 16	C_{3h}: 16.51 μg/mL,	C_{3h}: 0.46μg/mL	/

Abbreviations: C_{trough}, trough blood concentration; C_{3h}, Concentration of 3h after medication.

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hematologic parameters is warranted. Furthermore, TMP-SMZ (160 and 800 mg, respectively) increases lamivudine exposure by 40%, while lamivudine does not affect the PK of TMP or SMZ.[19,20] Thus, when TMP-SMZ are used in conjunction with ART medications, caution should be exercised as certain drug combinations may enhance the risk of adverse reactions.

This study has several limitations. First, PK analysis based on individual patient data has inherent limitations and challenges in generalizing findings to the broader population. Second, only peak and trough concentrations of TMP-SMZ were measured. Additional sampling points are needed to better characterize the PK profiles of both components. Third, further prospective studies are warranted to validate these findings and to provide more reliable information for clinical management.

Conclusion

This case reports the clinical outcomes and associated pharmacokinetic characteristics of low-dose TMP-SMZ for PJP prevention in a high-risk, critically ill patient with HIV/TB coinfection. The findings suggest that halved-dose TMP-SMZ may be an effective prophylaxis option in this population, with implications for optimizing individualized strategies—particularly in resource-limited settings or for patients unable to tolerate standard regimens.

Abbreviations

PJP, *Pneumocystis jirovecii* pneumonia; HIV, human immunodeficient virus; TMP-SMZ, Trimethoprim-Sulfamethoxazole; Cmax, peak plasma concentrations; PK, pharmacokinetics; TB, tuberculosis; CT, computed tomography scan; AIDS, acquired immunodeficiency syndrome; ART, antiretroviral therapy; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TDM, therapeutic drug monitoring; WBC, white blood cell; RBC, red blood cell; Hgb, hemoglobin; BUN, blood urea nitrogen; hs-CRP, high-sensitivity C-reactive protein.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was supported by the Ethics Committee of Zhejiang Hospital of Integrated Traditional Chinese and Western Medicine (Approval No.: 2022JS018) and was carried out in accordance with the ethical standards of the Declaration of Helsinki. Written informed consent was obtained from the patient.

Consent for Publication

Written informed consent was obtained from the individual, for the publication of any potentially identifiable images or data included in this article. Institutional approval for publication was obtained from the Ethics Committee of Hangzhou Red Cross Hospital.

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Disclosure

The authors report no conflicts of interest in this work.

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