Use of Trimethoprim-Sulfamethoxazole in Patient with G6PD Deficiency for Treating Pneumocystis Jirovecii Pneumonia

Ya-Wen Lu1* and Tsung-Chia Chen2

1Department of Pharmacy, Taichung Hospital, Taiwan
2Department of Internal Medicine, Taichung Hospital, Taiwan

Abstract

Case Report: A fixed dose of Trimethoprim-Sulfamethoxazole (TMP/SMZ) is the treatment of choice for Pneumocystis Jirovecii Pneumonia (PJP) recommended by Infectious Diseases Society of America (IDSA). However, TMP/SMZ has been reported to cause hemolysis when administered to patients with deficiency. PJP might be fatal without receiving treatment. Therefore, there is a dilemma on the use of TMP/SMZ in G6PD deficient patients. Herein, we report a G6PD deficient patient with PJP treated successfully with 21 days of TMP/SMZ without any signs and symptoms of hemolysis.

Conclusion: It might be safe for the Southeast Asia population with a history of G6PD deficiency to administer TMP/SMZ under expert surveillance.

Keywords: Glucose-6-phosphate dehydrogenase deficiency; HIV; Pneumocystis pneumonia; Trimethoprim-sulfamethoxazole

Introduction

Pneumocystis Pneumonia (PCP) is an opportunistic and fatal infection caused by the fungus Pneumocystis jirovecii. As per guideline, Trimethoprim-Sulfamethoxazole (TMP/SMZ) is the recommended regimen for managing Pneumocystis jirovecii Pneumonia (PJP) [1]. However, TMP/SMZ is associated with the serious side effect of drug induced hemolytic anemia associated with Glucose-6-Phosphatase Dehydrogenase (G6PD) deficiency. Although substitute regimen does exist, the success rate of using those alternative regimens is below 80% except for the combination use of TMP and dapsone, which is also a medication contraindicated in patients with G6PD deficiency. Jennifer et al. [2] therefore suggested avoiding using TMP/SMZ in patient with the deficiency of G6PD. On the other hand, a literature reviews done by Youngster et al. [3] Suggested that TMP/SMZ is probably safe when given in usual therapeutic dose. Together with the inconclusive recommendations, there was also no real-world experience on the use of TMP/SMZ in G6PD deficiency patients in Taiwan. In this article, we reported a G6PD deficient patient whom recovered from PJP by administration of TMP/SMZ.

Case Presentation

A 31-year-old Han Taiwanese man with a history of G6PD deficiency was admitted due to fever, cough, fatigue, muscle soreness and occasional dyspnoea for 20 days. After admission, Chest X-Ray (CXR) revealed bilateral infiltration. The White Blood Cell (WBC) count was 5200 cells/mL, N-Seg 72.3%, lymph 19.2%, Hemoglobin (Hb) 13.2 g/dL, platelet 231,000/mL, Blood Urea Nitrogen (BUN) 16 mg/dL, Creatinine (Cr) 0.8 mg/dL, Sodium (Na) 136 mmol/L, Potassium (K) 3.6 mmol/L, Aspartate Transaminase (AST) 30 U/L, Alanine Amino Transferase (ALT) 21 U/L.
and total bilirubin 0.7 mg/dL. Blood and sputum acid fast satins, 
TB culture, pneumococcal and legionella urinary antigen test, 
_Mycoplasma IgM, Chlamydia IgM, Toxoplasma IgG_ all showed 
negative. High-Resolution Computed Tomography (HRCT) was 
arranged and showed diffuse Ground-Glass Opacities (GGO) and 
thickening of interlobular septum. PJP was then considered. HIV 
EIA and HIV western blot showed positive result. CD4 counts 
were 50 cells/mm³. HIV RNA (Ribonucleic Acid) load was 45588 
copies/ml. Oxygen supplement was delivered and TMP/SMZ 240 
mg/1200 mg intravenously was given every eight hours. At Day-13 of 
TMP/SMZ treatment, a review of medication was preformed and the 
issue of G6PD deficiency history was raised. The blood test was done 
directly and Hb was 11.6 g/dL, total bilirubin was 0.7 mg/dL, 
direct bilirubin was 0.3 mg/dL. With no obvious sign and symptoms 
as well as episode of acute hemolytic, the TMP/SMZ treatment 
was continued. At Day-16, under stable condition, the patient was 
discharged with oral TMP/SMZ 240 mg/1200 mg three times a day for 
five more days and an Out-Patient Department (OPD) appointment 
was arranged. After 21 days of PJP treatment completed, a prophyllaxis 
dose of TMP/SMZ 160 mg/800 mg once daily was given until CD4 
reach 200 cells/mm³. The G6PD enzyme activities were measured 
by quantitative fluorescence assay and showed a level of 0.6 U/g Hb 
(reference range: 6.4 U/g Hb to 12.9 U/g Hb) which was classified as 
severe enzyme activity deficiency by the definition defined by World 
Health Organization (WHO) [4].

**Discussion**

G6PD deficiency is the most commonly inherited Red Blood 
Cell (RBC) enzymatic defect, affecting around 400 million people 
worldwide [5]. About 7.5% of the world population carries one or 
two genes for G6PD deficiency. It is an X-linked genetic disorder 
with 187 known allelic mutations [6]. In Taiwan, G6PD deficiency 
prevalence between male and female were approximately 2.81% and 
0.7% respectively [7].

TMP/SMZ is used in a variety of infectious diseases and is 
the recommended treatment option in current practice for 
managing PJP [8]; however, it is associated with hemolysis when 
administered to G6PD deficient patients. Chisholm-Burns et al. [9] 
demonstrated a case with _African ethnicity_ with G6PD deficiency 
that experienced hemolysis after administration of double strength 
of TMP/SMZ orally for eight days. Reinke et al. [10] also reported 
a black woman with HIV infection who received only one dose of 
TMP/SMZ intravenously for managing PJP which then resulted in 
acute hemolysis. On the contrary literature had reported challenging 
G6PD subjects with genetic variant alleles. A commonly observed 
in the African population, with TMP/SMZ at the dose of 320/1600 
mg every 12 h. The level of hemoglobin did not decrease significantly 
nor did any hemolysis occur throughout the trial [11]. The possible 
explanation was that the regeneration rate of hemoglobin was faster 
than destruction of hemoglobin in G6PD A-variant population. 
However, the severity of hemolytic anemia varies among individuals 
with G6PD deficiency. Specific G6PD alleles are associated with 
G6PD variants with different enzyme activity and, therefore, result 
in different levels of disease severity [12]. In Southeast Asia, the most 
common variant alleles appear to be G6PD Kaiping and Canton, 
which are different from the western or African ethnicity [13]. To 
date, there is still insufficient evidence for the population in Taiwan 
to suggest a robust relationship between our G6PD variant alleles and 
the degree of disease severity with regards to the safety in the use of 
TMP/SMZ in G6PD deficiency [14].

**Conclusion**

The experience and evidence regarding safety in the use of 
TMP/SMZ in G6PD deficient HIV infected patients is not yet clear. 
Herein, we documented a case of a G6PD deficient HIV infected man 
successfully treated the PJP with high dose of TMP/SMZ without any 
signs and symptoms of hemolysis.

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**References**

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