Sulfamethoxazole-Trimethoprim Prophylaxis in Pediatric Oncology Patients with Glucose-6-phosphate Dehydrogenase Deficiency

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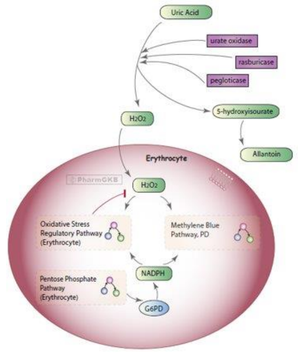
Background

- Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that generates NADPH to protect red blood cells against oxidative stress.
- G6PD deficiency predisposes individuals to developing acute hemolytic anemia in the presence of oxidative stress.
- Potential triggers of hemolysis are infection, certain foods, and certain medications.
- Historically, various regulatory agencies recommended against the use of sulfamethoxazole-trimethoprim (SMX-TMP) in patients with G6PD deficiency.
- As part of the 2022 CPIC guideline update, the author group evaluated the literature surrounding the use of SMX-TMP in patients with G6PD deficiency and found little to no evidence supporting an association with increased risk of hemolytic anemia.



- The recommendation was that SMX-TMP presents low-to-no risk of acute hemolytic anemia and therefore can be used regardless of G6PD status.
- There is currently a paucity of literature assessing the outcomes of SMX-TMP use in individuals with G6PD deficiency.

HIGH RISK MEDICATIONS
Avoid in patients with G6PD deficiency

- Dapsone
- Methylene blue
- Pegloticase
- Primaquine – standard dose
- Rasburicase
- Tafenoquine
- Toluidine blue

MEDIUM RISK MEDICATIONS
Use with caution in patients with G6PD deficiency

- Nitrofurantoin
- Primaquine – medium dose (0.75 mg/kg or 45 mg once weekly x 8 weeks) for *Plasmodium vivax* malaria

LOW-T0-NO RISK MEDICATIONS
Use without regard to G6PD status

- 4-aminosalicylic acid
- Aspirin (≤ 1g/day)
- Chloramphenicol
- Chloroquine
- Ciprofloxacin
- Dimercaprol
- Doxorubicin
- Furazolidone
- Glyburide
- Hydroxychloroquine
- Mafenide
- Nalidixic acid
- Norfloxacin
- Ofloxacin
- Phenazopyridine
- Primaquine – single low dose (0.25 mg/kg) for *P. falciparum* malaria
- Quinine
- Sulfadiazine
- Sulfadimidine
- **Sulfamethoxazole/ trimethoprim**
- Sulfanilamide
- Sulfasalazine
- Sulfisoxazole
- Tolbutamide
- Vitamin C & vitamin K

Table 1. Risk categories in 2022 update to the CPIC G6PD Guideline.

Objective

To investigate whether the use of SMX-TMP prophylaxis against *Pneumocystis jirovecii* pneumonia (PJP) in patients with G6PD deficiency is associated with an increased incidence of hemolysis as compared to non-deficient controls in a pediatric oncology population.

Methods

- Retrospective, single-institution cohort analysis (2005-2022)
- Control patients were matched for diagnosis and chemotherapy regimen, as well as age and sex when possible

SMX-TMP Dosing Table for PJP Prophylaxis at St. Jude	
Body Surface Area (m^2)	**Dose SMX-TMP (mg)**
<0.3	100-20 Q12H 3x/wk
0.3-0.79	200-40 Q12H 3x/wk
0.8-1.39	400-80 Q12H 3x/wk
1.4-1.89	600-120 Q12H 3x/wk
>1.9	800-160 Q12H 3x/wk

Table 2. Standardized dosing protocol for SMX-TMP prophylaxis.

Cohort 1: Cases
Patients with G6PD deficiency who received SMX-TMP prophylaxis for at least two weeks

Cohort 2: Matched Controls
Patients without G6PD deficiency who received SMX-TMP prophylaxis for at least two weeks

Results

All patients with G6PD deficiency as determined by activity or genotype who received SMX-TMP prophylaxis for at least two weeks (n=46)

→ All data available in EHR (n=40)

Excluded for missing data in EHR (n=6)

→ Appropriate matched control available (n=35)

Excluded for no available matched control (n=5)

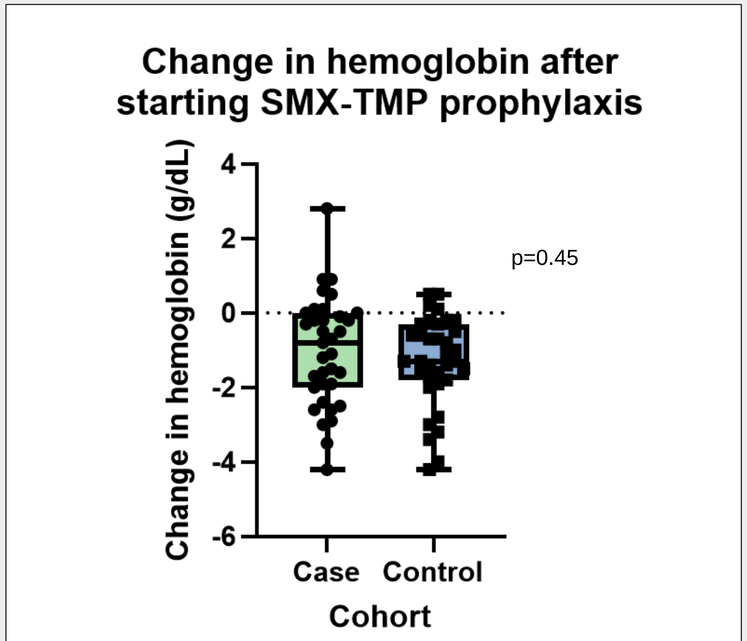
Demographics	Cases (n=35)	Controls (n=35)
Median age (range)	9 years (1-20 years)	8 years (1-19 years)
Sex	**N (%)**	**N (%)**
Male	25 (71%)	24 (69%)
Diagnosis	**N (%)**	**N (%)**
Acute Lymphoblastic Leukemia	14 (40%)	14 (40%)
Acute Myeloid Leukemia	6 (17%)	6 (17%)
Osteosarcoma	4 (11%)	4 (11%)
Medulloblastoma	3 (8%)	3 (8%)
Hodgkin's Lymphoma	2 (6%)	2 (6%)
Rhabdomyosarcoma	2 (6%)	2 (6%)
Aplastic Anemia	1 (3%)	1 (3%)
B-cell Lymphoma	1 (3%)	1 (3%)
CNS Germinoma	1 (3%)	1 (3%)
Nasopharyngeal Carcinoma	1 (3%)	1 (3%)
Baseline Transfusion Requirement	**N (%)**	**N (%)**
Patients requiring transfusions in 30 days prior to SMX-TMP	18 (51%)	17 (48%)

Table 3. Demographics of participants.

		Transfusion required 30 days after starting SMX-TMP		
		Yes	**No**	**p value**
Cohort	**Case**	21 (60%)	14 (40%)	0.62
	Control	23 (66%)	12 (34%)	

Table 4. Transfusion requirements after SMX-TMP initiation.

Results cont.



Conclusions

- There was no statistically significant difference in change in hemoglobin concentrations after starting SMX-TMP prophylaxis between patients with and without G6PD deficiency.
- This finding suggests no increased risk of hemolysis with the administration of SMX-TMP at prophylactic doses in a pediatric oncology population with G6PD deficiency.

References

1. Gammal RS, Pirmohamed M, Somogyi AA, et al. Expanded Clinical Pharmacogenetics Implementation Consortium Guideline for Medication Use in the Context of G6PD Genotype. *Clin Pharmacol Ther*. 2022;10.1002/cpt.2735.

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