

Promoting pharmacovigilance through glucose-6-phosphate dehydrogenase deficiency screening

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Adverse drug reactions are a leading cause of morbidity and mortality worldwide; thus, efforts focused on preventing unnecessary harm should be integral to public health policy. Drug induced hemolysis is one such example that can occur with some drugs and is more likely when glucose phosphate dehydrogenase (G6PD) enzyme is deficient.

G6PD supplies nicotinamide adenine dinucleotide phosphate, which maintains reduced glutathione concentration in red blood cells; providing protection of the cells from oxidative stress. The World Health Organization estimates more than 400 million people carry this X-linked chromosome disorder and recommends routine screening of new born infants for G6PD deficiency in countries where prevalence in males is more than 3% [1]. For many of the countries, even those fitting the prevalence established by WHO, testing for G6PD deficiency only occurs when new born infants present with signs of jaundice. This is the most common clinical manifestation of this disorder in new born infants; however, not all infants with G6PD deficiency will experience this complication. Furthermore, the importance of being aware of G6PD status extends beyond association with the development of neonatal jaundice to include positively impacting pharmacovigilance efforts.

The desire to prevent adverse drug reactions is one of the parameters of pharmacovigilance and therefore focus should be placed on monitoring exposure to drugs which may increase the risk of hemolysis in this patient group. The antimalarial drug primaquine for example, is established as requiring G6PD status determination before starting therapy to protect patient from drug induced hemolysis [2]. It is one of the many drugs included on listings of drugs characterised as having high potential for inducing hemolysis in G6PD deficient patients at therapeutic doses, as well as other drugs with evidence of hemolysis only with overdose [3]. Additionally, quick reference to the drugs to avoid is provided at the website of Italian G6PD Deficiency Association, or Associazione Italian Favismo - Deficit di G6PD (www.g6pd.org).

Although listings of potential drug triggers of hemolysis exist, awareness of their significance in patient care is being missed. Sheh recently reported a case of a 46 year old female presenting with trimethoprim/ sulphamethoxazole induced hemolysis; one of the known triggers to avoid. G6PD deficiency was suspected and was confirmed at this time of presentation, although the patient's history documented hemolysis also occurring with other known drug triggers, nitrofurantoin, phenazopyridine, ciprofloxacin, levofloxacin, and ibuprofen [4]. With the current worldwide estimates of the size of this population, efforts to make healthcare providers more aware of known drug triggers may be important to prevent this complication.

Whether current list of drugs is complete is questionable, especially since G6PD deficiency does not form part of standard patient

assessment. Metformin, a first line drug used in the management of diabetes mellitus is not currently included, although case reports have suggested metformin-induced hemolysis in patients confirmed to have G6PD deficiency [5-7]. Contradicting patient cases are also documented [8-10]; however, on review of these contradicting reports, it was noted that G6PD concentrations were determined during the time of insult and this can result in incorrect enzyme determinations [4].

Additionally, G6PD deficiency association with the increased risk of developing type two diabetes mellitus has been reported. In a recent meta-analysis of studies identified on Medline, EMBASE, AMED and CENTRAL databases between January 1966 and September 2016, Lai et al reported higher risk of diabetes mellitus among subjects with G6PD deficiency [11].

Advances in pharmacovigilance have fostered greater emphasis being placed on mining adverse drug reaction data. One such database is the Vigibase system of the World Health Organization global monitoring program, which boasts over sixteen million patient case reports (<https://www.who-umc.org/vigibase/vigibase/>). The availability of adverse drug reaction databases and knowledge of G6PD status may facilitate a greater understanding of the association between other drug triggers. With the ultimate focus of pharmacovigilance being to ensure benefits of drugs outweigh risks, routine screening for G6PD status offers an opportunity to ensure safe use of drugs in this large patient group.

References

1. Glucose-6-phosphate dehydrogenase deficiency (1989) WHO Working Group. *Bull World Health Organ* 67: 601-611. [[Crossref](#)]
2. Howes RE, Battle KE, Satyagraha AW, Baird JK, Hay SI (2013) G6PD deficiency: global distribution, enetic variants and primaquine therapy. *Adv Parasitol* 81: 133-201. [[Crossref](#)]
3. Youngster I, Arcavi L, Schechmaster R, Akayzen Y, Popliski H, et al. (2010) Medications and glucose-6-phosphate dehydrogenase deficiency: an evidence-based review. *Drug Saf* 33: 713-726. [[Crossref](#)]
4. Sheh T, Tsai IS (2016) G6PD Deficiency and a Family's Myth of Medication Allergies. *Proceedings of UCLA Healthcare* 20.
5. Ruggiero NA, Kish TD, Lee ML (2016) Metformin-induced hemolytic anemia in a patient with glucose-6-phosphate dehydrogenase deficiency. *Am J Ther* 23: e575-578. [[Crossref](#)]

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6. Meir A, Kleinman Y, Rund D, Da'as N (2003) Metformin-induced hemolytic anemia in a patient with glucose-6-phosphate dehydrogenase deficiency. *Diabetes Care* 26: 956-957. [[Crossref](#)]
7. Blum A, Ghaben W, Slonimsky G, Simsolo C (2011) Metformin-induced hemolytic anemia. *Isr Med Assoc J* 13: 444-445. [[Crossref](#)]
8. Lin KD, Lin JD, Juang JH (1998) Metformin-induced hemolysis with jaundice. *N Engl J Med* 339: 1860-1861. [[Crossref](#)]
9. Kashyap AS1, Kashyap S (2000) Haemolytic anaemia due to metformin. *Postgrad Med J* 76: 125-126. [[Crossref](#)]
10. Kirkiz S1, Yarali N, Arman Bilir O, Tunc B (2014) Metformin-induced hemolytic anemia. *Med Princ Pract* 23: 183-185. [[Crossref](#)]
11. Lai YK, Lai NM, Lee SWH (2017) Glucose-6-phosphate dehydrogenase deficiency and risk of diabetes: a systematic review and meta-analysis. *Ann Hematol* 96: 839-845. [[Crossref](#)]