

Overview on Causes and Updated Management of Favism

Abstract:

Favism is most common in those who have G6PD deficiency from the Mediterranean region. As hemolytic anaemia is the most common complication of G6PD deficiency, and it can be life-threatening in certain people. Infection, hyperglycemia, certain meals, and certain drugs can all cause hemolysis therefore, the most prevalent enzymopathy is glucose-6-phosphate dehydrogenase (G6PD) deficiency, which affects an estimated 400 million individuals, globally. Exposure to some medicines might cause hemolytic anaemia. The most important management technique is to avoid oxidative stresses by avoiding a hemolytic crisis. Also, avoidance of exposure to food and medicines that causes hemolytic anaemia episodes

This review looks at etiology, epidemiology, pathophysiology, evaluation and management of the disease.

Introduction:

Favism characterises a subgroup of patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency's susceptibility to, and clinical presentation of, acute haemolytic crises as a result of eating broad beans. The most prevalent enzymopathy is glucose-6-phosphate dehydrogenase (G6PD) deficiency, which affects an estimated 400 million individuals globally.[1]

Hemolytic anaemia is the most common complication of G6PD deficiency, and it can be life-threatening in certain people. Infection, hyperglycemia, certain meals, and certain drugs can all cause hemolysis. Though G6PD insufficiency is found in limited areas throughout Africa, the Middle East, and Southeast Asia, it affects around one in every ten African-American men in the United States. As global travel to the United States expands and immigrants gain access to the American health-care system, the disease may become more relevant in the future, resulting in a higher-than-expected prevalence.[1]

The enzyme glucose-6-phosphate dehydrogenase (G6PD) is found in the cytoplasm of all cells in the human body. It's a maintenance enzyme that protects cells from reactive oxygen species damage (ROS). This is accomplished by supplying substrates that prevent oxidative damage.[2]

Because of their involvement in oxygen transport and their incapacity to replace cellular proteins as mature cells, erythrocytes

are particularly sensitive to ROS. During times of heightened reactive oxygen species production, inherited deficits in glucose-6-phosphate dehydrogenase can cause severe hemolytic anaemia.[2]

Patients who depend on red blood cell (RBC) transfusions may be at a higher risk of receiving blood from G6PD-deficient donors. Sickle cell disease (SCD) patients for example, frequently require transfusions of blood group antigen-negative RBCs to avoid or respond to alloantibody formation; thus, based on blood group antigen frequencies, they are more likely to receive RBCs from African-American donors, who may be G6PD deficient.[5,4]

If these individuals have an infection or were given a drug that caused oxidative stress simultaneously, they would be at a greater risk (e.g. a pregnant SCD patient treated with nitrofurantoin for a urinary tract infection) .[5]

The most prevalent life-threatening manifestation of G6PD deficiency is hemolytic anaemia. Patients, typically report with symptoms such as jaundice, lethargy, back pain, tachypnea, and tachycardia. Reduced haemoglobin and red blood cell counts, reticulocytosis, elevated lactate dehydrogenase, and increased unconjugated bilirubin are all relevant diagnostic results.[1]

Etiology:

The G6PD enzyme is represented by the Gd gene. Because this gene is found on the long arm of the X chromosome, and is inherited in an X-linked manner. Mutations that affect the protein

structure and so limit its activity or the amount of enzyme generated, can cause G6PD deficiency. There are now 186 known human G6PD mutations, the majority of which are single-nucleotide variants. Complete inactivation of G6PD would be harmful to a growing embryo. None of the mutation patterns found in humans produce it. [2,3]

The G6PD gene is made up of 13 exons that cover about 18 kb. The gene's coding sequence is 1,545 base pairs (bp) long. It codes for 515 amino acids from the G6PD main sequence. G6PD insufficiency is the most prevalent human enzyme abnormality, affecting over 400 million people worldwide. A deficient hemizygote is a guy who inherits the damaged X chromosome from his mother and carries the deficient gene. Each parent's X chromosome is faulty in female homozygotes. Only one faulty X chromosome is passed down to female heterozygotes.[6]

Exposure to certain drugs that can cause episodes of hemolytic anemia: acetanilide, cotrimoxazole, dapsone, doxorubicin, furazolidone, methylene blue, moxifloxacin, nalidixic acid, naphthalene, niridazole, nitrofurantoin, norfloxacin, pamaquine to which a person is sensitive with pentaquin from person to person [7].

Epidemiology:

Due to X-linked inheritance, men are more typically impacted when compared to women. Individuals from the tropical areas are the

most affected Surprisingly, there is evidence that G6PD deficiency protects against uncomplicated malaria, however, not against severe malaria. G6PD deficiency and malaria have a protective mechanism that is still being researched. G6PD insufficiency is more common in people of African, Mediterranean, or Asian cultures, possibly because to its malaria-protective effect.[2]

G6PD is the rate-limiting first step of the pentose phosphate pathway, which converts nicotinamide adenine dinucleotide phosphate (NADP) to its reduced form, NADPH, using glucose-6-phosphate. NADPH is essential in red blood cells for preventing cellular components from damaged by oxygen-free radicles. It accomplishes this by acting as a substrate for the glutathione reductase enzyme. Reduced glutathione can be utilised to convert hydrogen peroxide to water and protect cellular components, especially the cell walls of mature red blood cells (RBCs), which have limited repair capacity. [2]

Pathophysiology:

The first step in the pentose phosphate pathway is catalysed by glucose-6-phosphate dehydrogenase (G6PD). Converting glucose to ribose-5-phosphate, a precursor of RNA, DNA, ATP, CoA, NAD, and FAD, is part of the pentose phosphate pathway (PPP). The route also involves the production of NADPH, which provides the cell with reducing energy by ensuring that reduced glutathione remains within

the cell. Reduced glutathione protects cells from oxidative damage by acting as an antioxidant.[2]

Most cells have a backup set of metabolic pathways that can generate the necessary intracellular NADPH. Red blood cells, on the other hand, lack the "other NADPH makers." As a result, G6PD deficiency is particularly dangerous in red blood cells, where any oxidative stress leads to hemolytic anaemia. Consumption of fava beans, certain medicines, infections, and certain metabolic disorders such as diabetic ketoacidosis can all cause oxidative stress.[7]

Pudding of haemoglobin occurs as a result of oxidative denaturation, and bite or hemiblisters cells form in the peripheral smear. Denatured haemoglobin precipitates, and can be seen as "Heinz bodies.". A normal peripheral blood smear, which shows red blood cells of uniform size and shape, can be distinguished [7].

Hemoglobin concentrations begin to recover after removal of the offending hemolytic agent, after 8 to 10 days; consequently, acute hemolysis seldom leads to severe anaemia which needs a blood transfusion (especially in infants) [7]

Post - operatively, the G6PD-deficient patient may exhibit clinical symptoms that necessitate further support or therapy. Hemolysis usually appears 1 to 3 days after contact with the triggering factors. Acute hemolysis is self-limiting, however, it can be severe enough to necessitate a blood transfusion in rare cases. Cyanosis, fatigue, tachycardia, dyspnea, lethargy, lumbar/substernal pain, abdominal

pain, splenomegaly, hemoglobinuria, and/or scleral icterus are all possible symptoms. Furthermore, haemoglobin breakdown products accumulate in the blood, causing jaundice. The breakdown products can be excreted in the urine, resulting in a dark brown discoloration. [7]

Avoidance of oxidative stresses is the major treatment for G6PD deficiency. Anemia can be severe to the extent of needing urgent blood transfusion. [9-11]

Hemolysis manifests itself clinically after 24 to 72 hours of medication administration, and anaemia develops until about day 7. This makes it difficult for doctors to detect a hemolytic crisis in patients undergoing outpatient or short-stay hospital operations (less than 24). Therefore, the most important management technique is to avoid oxidative stresses thereby avoiding a hemolytic crisis. Acute hemolysis in G6PD-deficient adults, on the other hand, is usually short-lived and does not require therapy. The offending agent should be eliminated in the event of a hemolytic crisis, and the patient should be continuously watched. A daily complete blood count should be performed at the very least to monitor the requirement for a blood transfusion.[7]

Evaluation :

- Neonatal evaluation:-

In newborn infants, check for jaundice by looking for a yellowish color on the skin in a well-lit room. In infants, total serum bilirubin

(TSB) or transcutaneous bilirubin (TcB) readings are more objective. A risk-stratified bilirubin nomogram can be used to help select the best treatment for newborns with elevated bilirubin levels.[2]

Although G6PD deficiency screening tests are available, they are not commonly used in the United States. However, screening should be explored in infants with severe jaundice that is resistant to phototherapy. Screening tests should also, be available to patients with a family history or ethnicity that suggests G6PD deficiency. To determine the production of NADPH from NADP, the most frequent screening approach is a fast fluorescent spot test. Quantitative spectrophotometric analysis can also be used for screening.[2]

- Children and adult evaluation:-

The evaluation of older individuals with G6PD deficient problems begins with a thorough medical history, including new drugs, and a search for a family history of related symptoms. In patients with G6PD deficiency, the stress of infection might induce a hemolytic event, so it's also important to check for infection.

CBC, bilirubin levels, reticulocyte count, serum aminotransferases, and lactate dehydrogenase levels are among the tests performed in the laboratory. Schistocytes may be seen on a peripheral blood smear, indicating hemolysis. [2]

Management :

- Neonates

The infant patient's treatment focuses on preventing kernicterus and minimizing jaundice. This includes phototherapy that follows stated standards. An exchange transfusion may be required in severe cases.[2,15]

- Adults and Children

The treatment of older individuals is mostly determined by the overall clinical picture. Supportive therapy, as well as the withdrawal and avoidance of the offending medications, can be used to manage less severe symptoms. Infections should be treated as suggested by the history and examination. Transfusions may be required in more severe situations. [2]

Avoidance of oxidative stresses is the major treatment for G6PD deficiency. Anemia can be severe enough to necessitate a blood transfusion in rare cases. Splenectomy is generally not advised. Although G6PD deficiency is frequently asymptomatic and the resulting hemolysis is usually short-lived, folic acid and iron may be beneficial in hemolysis. Antioxidants like vitamin E and selenium haven't been shown to help with G6PD deficiency.[9-11]

Favism is most common in those who have G6PD deficiency from the Mediterranean region[8].

To manage hemolysis in individuals with G6PD impairment, it is important to identify and eliminate the precipitating factor. Anemia should be treated appropriately, with the understanding that hemolysis is self-limiting and usually resolves in 8 to 14 days.

Transfusions are only used in exceptional circumstances. In most cases, splenectomy is ineffective.[12-14]

The majority of people who have glucose-6-phosphate dehydrogenase (G6PD) deficiency don't require treatment. They should, however, be educated to stay away from medications and chemicals that can induce oxidative stress. Broad beans should also be avoided by patients (ie, fava beans).[12-14]

Foods, medicines, and chemicals that can cause hemolysis should be avoided by people with G6PD deficiency. The degree of enzyme insufficiency and consequently the risk posed by such chemicals is determined, in part, by the person's G6PD variation.[12-14]

Fava beans are the most well-known food for causing hemolysis. Favism, or symptomatic attacks of hemolytic anaemia caused by eating fava beans, has been known since antiquity. Other foods to avoid for people with G6PD deficiency include the following:

- a glass of red wine
- Legumes in general
- Blueberries
- Products made from soya
- Water with a tonic effect [13,14]

Complications:

- Acute severe haemolytic anaemia causes death (relatively rare).

- Intraocular intravascular haemolysis causes ophthalmological damage. [16]

Patients with an acute onset of favism had severe ophthalmological problems, however, not all of patients suffered from generalised haemorrhagic symptoms at the same time.[17]

- Kidney injury that was severe.
- Infection susceptibility.[16]

Conclusion:

Fava beans are the most well-known food for causing hemolysis. Favism, or symptomatic attacks of hemolytic anaemia are caused by eating fava beans. The most important management technique is to avoid oxidative stresses and to avoid a hemolytic crisis. Acute hemolysis in G6PD-deficient adults, on the other hand, is usually short-lived and does not require therapy.

When managing with a G6PD-deficient patient, every health care professional must exercise caution.

Hemolysis can be caused by fava beans, certain medicines, infections, and metabolic disorders. Inadequate care for G6PD-deficient people who develop acute hemolytic anaemia can result in severe brain impairment or death.

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