Favism, that is G6PD deficiency, and drugs for Covid-19

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A document, vital for people having Glucose-6-phosphate dehydrogenase deficiency (favism) is available. The link is https://www.epicentro.iss.it/coronavirus/pdf/en-report-covid-19-14-2020.pdf . In this document it is told that "Chloroquine and hydroxychloroquine currently applied to COVID-19 patients should be avoided in those with severe G6PD deficiency as they could trigger a hemolytic crisis in the patient". Other very important references are also given. Besides Chloroquine and hydroxychloroquine, Primaquine and 8-Aminoquinolines are considered.

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Favism is the popular name of the Glucose-6-phosphate dehydrogenase deficiency (G6PDD).

"It is an inborn error of metabolism that predisposes to red blood cell breakdown. Most of the time, those who are affected have no symptoms. Following a specific trigger, symptoms such as yellowish skin, dark urine, shortness of breath, and feeling tired may develop. Complications can include anemia and newborn jaundice. Some people never have symptoms". Wikipedia - https://en.wikipedia.org/wiki/Glucose-6-phosphate_dehydrogenase_deficiency

In Wikipedia it is also told that "About 400 million people have the condition globally.[1] It is particularly common in certain parts of Africa, Asia, the Mediterranean, and the Middle East.[1] Males are affected more often than females.[1] ... Carriers of the G6PDD allele may be partially protected against malaria. [1]". To [1] corresponds link https://ghr.nlm.nih.gov/condition/glucose-6-phosphate-dehydrogenase-deficiency . There we find: "An estimated 400 million people worldwide have glucose-6-phosphate dehydrogenase deficiency. This condition occurs most frequently in certain parts of Africa, Asia, the Mediterranean, and the Middle East. It affects about 1 in 10 African American males in the United States".

It is clear that a large number of people suffering of favism can be also affected by Sars-Cov-2, and therefore have Covid-19. A vital document for these persons is available at the following link https://www.epicentro.iss.it/coronavirus/pdf/en-report-covid-19-14-2020.pdf

The document is concerning the drugs used against Covid-19. It is entitled "Interim guidance for the appropriate support of people with enzymopenia G6PD (favism) in the current SARS-CoV-2 emergency scenario". Version April 14, 2020. The document has been prepared by the ISS COVID-19 Rare Diseases Working Group.

In the section entitled "G6PD enzymopenia and drugs for SARS-CoV-2". It is told that "The AIFA has authorized the off-label use of some drugs, paid by the NHS, in derogation of Law 648/1996 such as the lopinavir / ritonavir association (and in the alternative darunavir in combination with cobicistat or ritonavir) and chloroquine or hydroxychloroquine, to deal with the pandemic coronavirus SARSCoV-2 in the absence of proven treatment ... Both chloroquine and hydroxychloroquine can have serious side effects, even in subjects without G6PD deficiency, especially at high doses or in combination with other drugs. They must not be used without prescription and without medical supervision, and the prescription in case of COVID-19 must refer only to the case of clinical trials or protocols agreed at national level (EMA/170590/2020)".

The authors of the document are telling that we are facing a potential widespread of the use of these drugs to all symptomatic patients. "It is therefore of extreme importance to recall to all the healthcare professionals to extend to all patients the warning relating to the use of chloroquine and

hydroxychloroquine, in case of presence of impaired activity of the glucose-6-phosphate dehydrogenase (G6PD). People with G6PD deficiency have greater difficulties in metabolizing oxygen free radicals (ROS), developing in some cases severe forms of hemolytic anemia".

The document explains that the "Hemolysis is determined - with very rare exceptions - by a triggering factor such as the ingestion of fava beans and the intake of some drugs with intracellular oxidizing action. Chloroquine and hydroxychloroquine are among these drugs, having an oxidizing action. However, under normal conditions and in monotherapy, they do not give hemolysis, while other factors, such as the patient's immune status, bacterial or viral infections, the dose of the oxidizing drug and / or drugs interaction may contribute to determine this effect. Therefore, for subjects with G6PD deficiency, SARS-CoV-2 infection represents an additional risk factor. Chloroquine and hydroxychloroquine currently applied to COVID-19 patients should be avoided in those with severe G6PD deficiency as they could trigger a hemolytic crisis in the patient".

What is stressed in the document is the following. "Consequently, considering that the G6PD deficiency is an endemic condition in our country [Italy], and in order to guarantee the correct care of SARS-Cov2 positive patients it is necessary to assure the condition of the G6PD status before starting the pharmacological treatment with chloroquine or hydroxychloroquine, through a medical history and, if this is not possible and depending on the situation, through the screening or quantitative test of the G6PD activity. It is necessary to keep in mind that the absence of previous hemolytic crises in a person with G6PD deficiency does not lead to a reduction in risk, even in old age". The document is also considering the case "if the treatment with chloroquine or hydroxychloroquine has already been started without the possibility to obtain timely a dosage of the enzyme and in presence of both a drastic drop in hemoglobin 7 values, ... [see details in the document] it is necessary to consider the presence of a deficiency of G6PD and to discontinue the treatment".

Of course, the document is important for all people in the world.

Let us also consider primaquine.

"G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria Endemic Countries: A Geostatistical Model-Based Map" by Rosalind E. Howes, Frédéric B. Piel, Anand P. Patil, Oscar A. Nyangiri, Peter W. Gething, Mewahyu Dewi, Mariana M. Hogg, Katherine E. Battle, Carmencita D. Padilla, J. Kevin Baird, and Simon I. Hay. "Primaquine is a key drug for malaria elimination. In addition to being the only drug active against the dormant relapsing forms of Plasmodium vivax, primaquine is the sole effective treatment of infectious P. falciparum gametocytes, and may interrupt transmission and help contain the spread of artemisinin resistance. However, primaquine can trigger haemolysis in patients with a deficiency in glucose-6-phosphate dehydrogenase (G6PDd). Poor information is available about the distribution of individuals at risk of primaquine-induced haemolysis. We present a continuous evidence-based prevalence map of G6PDd and estimates of affected populations, together with a national index of relative haemolytic risk".

Primaquine is mentioned in Eye Reports as used against Covid-19.

https://www.eyereports.org/index.php/eyereports/article/view/99/PDF-EyeReports2020v6pS7 - "A recommendation for the use of chloroquine, hydroxychloroquine, primaquine, or tafenoquine for prophylaxis against the 2019 novel coronavirus (COVID-19) with note to the ophthalmic considerations", by Fouad Alshaban.

"With the ongoing pandemic of infectious disease termed coronavirus disease 2019 (COVID-19) caused by the novel coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), prevention of infection and spread is critical in preventing morbidity and mortality. Prophylaxis, specifically chemoprophylaxis, is particularly critical to breaking the spread and rapid rate of increase of SARS-CoV-2. Pre-exposure and post-exposure prophylaxis are both required components of this public health measure. As the use of anti-malarial agents, specifically the 4-

aminoquinolones, chloroquine and hydroxychloroquine, for the treatment of SARS-CoV-2 is now being reported, attention must be turned to their role in the chemoprophylaxis of SARS-CoV-2. In a search of the peer-reviewed medical literature (using MEDLINE and cross-referenced literature), this report is first peer-reviewed publication to present the use of these anti-malarial agents as prophylaxis against SARS-CoV-2" In the text, it is told "Notably, the 8-aminoquinolines are contraindicated in individual who have glucose-6phosphate dehydrogenase (G6PD) deficiency as hemolytic anemia may occur and may be fatal".

In "The friendly use of chloroquine in the COVID-19 disease: a warning for the G6PD-deficient males and for the unaware carriers of pathogenic alterations of the G6PD gene", by Ettore D. Capoluongo, Felice Amato, and Giuseppe Castaldo, it is told "The benefits of chloroquine therapy strongly depend on: (i) the age of the patient; (ii) the clinical presentation and (iii) the stage of the COVID-19 disease. Noteworthy, the use of this drug is contraindicated in some conditions, particularly the glucose-6-phosphate dehydrogenase (G6PD) deficiency. The latter is a condition that has not been deeply taken into account particularly when, on the web, there has been a “viral” spread of news emphasizing the safe use and the free availability of chloroquine".

In the "G6PD deficiency in COVID-19 pandemic: “a ghost in the ghost” ", Sameer Al-Abdi and Maryam Al-Aamrid tell that "There are about 350 million people with glucose-6-phosphate dehydrogenase (G6PD) deficiency worldwide. The highest prevalence of G6PD deficiency is in the Arabian Peninsula and tropical Africa. ... Hydroxychloroquine has been proposed as a treatment for COVID-19 and clinical trials have been started evaluating this proposal. Hydroxychloroquine has oxidative properties that could decrease glutathione levels and may cause severe hemolysis in G6PD-deficient patients. If hydroxychloroquine is found to be the silver bullet for COVID-19, then this may be a big challenge in treating COVID-19 in G6PD-deficient patients. Accordingly, it is prudent to use additional precautionary measures to prevent COVID-19 from reaching G6PD-deficient individuals".

In "COVID-19 infection and treatment with hydroxychloroquine cause severe haemolysis crisis in a patient with glucose-6-phosphate dehydrogenase deficiency", Yan Beauverd, Yannick Adam, Benjamin Assouline, Kaveh Samii tell that "Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited genetic disorder caused by red cell enzymatic defects and is associated with haemolytic crisis when patients are exposed to oxidative agents (fava beans, drugs, infections). Hydroxychloroquine is suspected to trigger haemolytic crisis in G6PD-deficient patients, and off-label administration of this drug to patients infected with the novel coronavirus (SARS-CoV-2) could cause concern". In the article the authors report "the first case of severe haemolytic crisis in a patient with G6PD deficiency, initiated by severe COVID-19 infection and hydroxychloroquine use. With worldwide spread of COVID-19, especially in regions with a high prevalence of G6PD deficiency, our case should alert physicians to this possible correlation".

Besides the drugs used, in "Glucose-6-phosphate dehydrogenase deficiency and risk of cardiovascular disease: A propensity score-matched study", by Giovanni Mario Pes, Guido Parodi, Maria Pina Dore, it is told that "G6PD deficiency is significantly associated with increased risk of CVD (cardiovascular disease), although the underlying mechanisms are still poorly understood. The loss of important protective pathways against oxidative stress, especially in the early stages of atherogenesis, might play a crucial role".

References

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