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Erythropoietic Protoporphyria in Latin America

Porphyrias are a group of diseases due to an alteration in the metabolism of porphyrins, which generates an increase in the accumulation and excretion of their intermediate chemicals. They can be classified according to their main manifestations as cutaneous, acute, or mixed, or by the location where the enzymatic deficiency predominates, as hepatic or erythropoietic.

Erythropoietic protoporphyria (EPP) is a rare inherited inborn error of porphyrin metabolism caused by decreased enzyme activity of ferrochelatase. The decreased enzyme activity is a consequence of the different mutations on both alleles of the ferrochelatase gene. EPP is characterized by severe phototoxicity (intolerance of light) of the skin resulting in intolerable pain, swelling, and scarring, usually of exposed areas such as the face, hands, and feet. Children and adults living with EPP must avoid sunlight and any other source of light of the visible spectrum, often staying indoors or wearing protective clothing.

EPP affects approximately 10.000 people globally. In Latin America, the prevalence varies in each country. In Argentina, reported EPP prevalence is around 1:900.000, clustered around 44 diagnosed families. Among these, a molecular fingerprinting study of the gene coding for ferrochelatase was performed in 16 families and discovered up to 15 different mutational profiles. In Colombia, the prevalence is around 1:65.000, affecting men and women equally.

According to a Brazilian KOL "*the prevalence in Brazil is hard to get because there is no network to centralize the diagnostic reports, as it happens for other rare diseases*". However, based on patient records from the Brazilian Porphyria Patient Association (ABRAPO), they report an EPP frequency of 4% (18 patients) among 439 patients with porphyria (data from 2007 to 2015).

The diagnosis of EPP is established based on the characteristic clinical features of the disease and confirmed by lab tests showing increased levels of protoporphyrins in blood. However, in Brazil "*the public system does not provide either porphyrin or genetic testing for EPP diagnosis*", as mentioned by a local KOL. Furthermore, there are few laboratories capable of performing the protoporphyrin testing in Brazil.

In Argentina, there is a reference center for Latin America operating since 1978 and dedicated exclusively to the genetic and biochemical diagnosis, treatment, and patient follow-up of those suffering from porphyria - *Centro de Investigaciones sobre Porfirinas y Porfirias* (CIPYP) - located at the Hospital de Clínicas José de San Martín, CONICET and University of Buenos Aires. In Colombia, issues with lab testing availability and quality of the results have led to delays in diagnosis and erroneously diagnosed porphyria cases.

Regarding treatment, most available options (e.g., beta-carotene, N-acetyl-L-cysteine, and vitamin C) have shown no clear benefit in clinical trials. On the other hand, hepatic or bone marrow transplant are a good alternative but of limited application. Usually, when there is high accumulation of the porphyrins in the liver that impairs its function, the patient has a liver transplant and then followed by bone marrow transplant. Recently, a new drug has been developed for EPP, afamelanotide (Scenesse®, Clinuvel Pharmaceuticals). It is a potent analogue of α-melanotide stimulating hormone, which has shown to reduce the incidence and severity of phototoxic reactions and to improve quality of life in the long-term. Although this drug is not yet available in Latin America is has shown a good result in Europe, where it is approved.

References

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