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Porphyrias—An update on the management and unmet clinical needs

Porphyria is a group of metabolic disorders, due to specific abnormality in one of the eight enzymes of the heme biosynthetic pathway. These can be classified based on predominant site of enzyme defect into hepatic and erythropoietic types, and based on clinical presentation into acute neurovisceral and cutaneous blistering porphyrias. Hepatic porphyria includes acute intermittent porphyria (AIP); variegate porphyria (VP), hereditary coproporphyria (HCP), aminolevulinic acid dehydratase deficiency porphyria (ADP), and porphyria cutanea tarda (PCT). Of these, AIP and ADP are classified as acute porphyria, PCT as cutaneous, while VP and HCP present with both acute and cutaneous clinical manifestations. Porphobilinogen levels in spot urine sample is the initial screening test for the diagnosis of acute hepatic porphyria, and plasma with spot urine porphyrin levels is the initial screening test to approach patients suspected of cutaneous porphyria. Specific biochemical porphyrin profile for each porphyria helps in determining the specific diagnosis. Pain relief and elimination of triggering agents are the initial steps in managing a patient presenting with an acute attack. Intravenous glucose administration terminates the mild episode of acute porphyria, with intravenous hemin needed for management of moderate to severe episodes. Liver transplantation is curative and may be needed for patients with a life threatening acute porphyria attack or for patients with recurrent acute attacks refractory to prophylactic treatment. PCT is frequently associated with a combination of multiple susceptibility factors. Phlebotomy regimen and low dose hydroxychloroquine are effective and safe treatment options for management of PCT. Erythropoietic porphyria include congenital erythropoietic porphyria (CEP), erythropoietic protoporphyria (EPP), and hepatoerythropoietic porphyria (HEP). The latter presents like, PCT is usually in small children due to autosomal recessive mutation of the uroporphyrinogen decarboxylase enzyme. EPP is due to loss of function mutation of ferrochelatase enzyme. However, 10% of protoporphyria patients are due to gain of function mutation of the rate limiting enzyme ALA synthase in the heme biosynthetic pathway. Patients with protoporphyria irrespective of the mutation develop non-blistering photosensitivity usually in small children and adolescents, which can severely impair the quality of life. The diagnostic test is elevated protoporphyrins in the red blood cells, with high levels of free protoporphyrins and not the zinc bound levels. About 5-10% of these patients may develop intrahepatic cholestasis with severe liver disease or hepatopathy, which can often progress rapidly to liver failure requiring liver transplantation. Bone marrow transplantation should be considered at an appropriate time in these patients to prevent recurrence of EPP and graft involvement as the liver transplantation is not curative for protoporphyria.

Biography

Ashwani K Singal is working as Associate Professor of Medicine in division of Hepatology and Director of Porphyria Center at the UAB, Birmingham AL. His clinical research interests include alcohol and non-alcohol fatty liver disease, porphyria, and renal dysfunction in liver cirrhosis. He has over 110 publications, on editorial board of reputed journals, and research award committees of the AGA and AASLD. His research is funded from the Transplant Institute of the UAB, ACG, NIAAA and NIDDK from the NIH, and pharmaceutical industry.

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