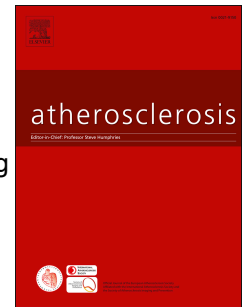


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Antiatherogenic potential of ezetimibe in sitosterolemia: Beyond plant sterols lowering

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Keywords: Atherosclerosis; Ezetimibe, Lipoproteins; Plant sterols; Sitosterolemia.

Sitosterolemia (OMIM 210250) is a rare autosomal recessively-inherited disorder caused by homozygous or compound heterozygous mutations affecting either adenosine triphosphate-binding cassette (ABC) transporters G5 or G8, which are located on human chromosome 2p21 in a head-to-head organization ¹. These two proteins form heterodimers, which act as efflux pumps to preferentially export free sterols from hepatocytes or enterocytes into the intestinal lumen ². For this reason, and in contrast to healthy individuals, the sitosterolemic subjects have a significant increase in circulating levels of plasma plant sterols including beta-sitosterol, campesterol and stigmasterol ¹. The presence of tendon and tuberous xanthomas, premature atherosclerosis and hematological abnormalities, such as hemolytic anemia and thrombocytopenia, are common clinical features of sitosterolemia ^{1, 2}. However, the clinical phenotype of these patients is characterized by a marked heterogeneity ³ and the evidence of premature atherosclerosis has not always been reported, despite having high levels of plasma plant sterols ^{4, 5}. This could indicate that premature atherosclerosis found in most of the sitosterolemic patients may not be caused exclusively by the higher circulating plant sterols.

Ezetimibe, a drug specifically targeting intestinal Niemann-Pick C1-Like 1 (NPC1L1)-mediated inhibition of sterols absorption, has emerged as a successful agent for sitosterolemia treatment since it significantly reduces plasma plant sterol levels, reverses xanthomas and normalizes most of the hematological abnormalities in

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