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Cholestyramine

Updated: September 28, 2017.

OVERVIEW

Introduction

Cholestyramine is a nonabsorbed bile acid sequestrant that is used a therapy of hyperlipidemia and for the pruritus of chronic liver disease and biliary obstruction. Cholestyramine has been associated with mild and transient serum enzyme elevations during therapy, but has not been linked to cases of clinically apparent liver injury with jaundice.

Background

Cholestyramine (koe" le stye' ra meen) is a large, highly positively charged anion exchange resin that binds to negatively charged anions such as bile acids (as well as other organic compounds and some medications). The binding of bile acids to cholestyramine creates an insoluble compound that cannot be reabsorbed and is thus excreted in the feces. Bile acids ordinarily undergo extensive (>95%) enterohepatic recirculation, being secreted in bile, acting as fat solubilizing compounds in the upper intestine, and then being reabsorbed in the distal small bowel. Chronic loss of bile acids from cholestyramine use results in a contraction of the total bile acid pool. The liver compensates for this decrease by increasing bile acid synthesis, which directly competes with cholesterol synthesis resulting in a decrease in serum levels. In addition, cholestyramine may also decrease in serum cholesterol by direct inhibition of fat absorption caused by its binding to bile acids in the intestine. Cholestyramine was approved for use in the United States in 1973 and is one of the oldest and safest cholesterol lowering agents, but it is currently used largely as an adjunctive therapy when statins or other lipid lowering agents result in an inadequate decrease in cholesterol levels. Cholestyramine is also effective in reducing the pruritus of chronic liver disease, probably as a function of binding the “pruritogen” in the intestine (which is either a bile acid or an organic anion like a bile acid that undergoes enterohepatic circulation). Because cholestyramine binds to negatively charged molecules, it can also be used to reduce absorption of medications taken in toxic overdoses and has multiple drug-drug interactions. Cholestyramine is available in multiple generic forms and under the brand name of Questran as a powder or in single dose packet form, generally in 4 gram amounts. The usual dose of cholestyramine is 4 grams, given one to six times per day usually before meals and at bedtime. Other drugs should be given 1 hour before or 4 to 6 hours after cholestyramine. Cholestyramine is unpalatable and can be difficult to swallow. Side effects include abdominal discomfort, indigestion, nausea, flatulence and constipation.

Hepatotoxicity

There is little evidence that cholestyramine causes significant liver injury. However, mild elevations in serum aminotransferase levels occur in a proportion of patients on cholestyramine. The elevations have been mild,

transient and without accompanying symptoms or jaundice. In one prospective study, cholestyramine therapy was associated with serum ALT elevations above 3 times the upper limit of normal in 11% of subjects. In all cases, the abnormalities were asymptomatic and resolved rapidly upon stopping cholestyramine. Serum alkaline phosphatase levels are usually normal. A single case report of marked serum aminotransferase elevations on bile acid sequestrant therapy with rapid resolution on stopping has been published. However, there have been no reports of clinically apparent liver injury with jaundice attributed to cholestyramine or the other bile acid sequestrants. Cholestyramine is used in patients with liver disease to treat pruritus, and has little or no effect on serum enzyme or bilirubin levels.

Likelihood score: E (unlikely cause of clinically apparent liver injury with jaundice).

Mechanism of Injury

The mechanism by which cholestyramine causes serum aminotransferase elevations is not known. Because cholestyramine is not absorbed, it is surprising that it might cause liver injury, even mild and asymptomatic serum enzyme elevations. There is also little evidence that the contraction of the bile acid pool caused by its use harms the liver. Because cholestyramine can interfere with the absorption of other medications or vitamins, it may affect the levels of medications used for liver disease. These effects are particularly important for vitamins A, D, E, K, hormones such as estrogens, corticosteroids, and thyroid hormone, and medications such as thiazide diuretics, acetaminophen and digoxin.

References on the safety and hepatotoxicity of cholestyramine are given with those for colesevelam and colestipol in the Overview section on Bile Acid Resins/Sequestrants.

Drug Class: Antilipemic Agents, Bile Acid Resins/Sequestrants

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Cholestyramine – Generic, Questran®

DRUG CLASS

Antilipemic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Cholestyramine	11041-12-6	Unspecified