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Antilithiasic Effect Of ß-Cyclodextrin In LPN Hamster: Comparison With Cholestyramine

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Abstract

ß-Cyclodextrin (BCD), a cyclic oligosaccharide that binds cholesterol and bile acids in vitro, has been previously shown to be an effective plasma cholesterol lowering agent in hamsters and domestic pigs. This study examined the effects of BCD as compared with cholestyramine on cholesterol and bile acid metabolism in the LPN hamster model model for cholesterol gallstones. The incidence of cholesterol gallstones was 65% in LPN hamsters fed the lithogenic diet, but decreased linearly with increasing amounts of BCD in the diet to be nil at a dose of 10% BCD. In gallbladder bile, cholesterol, phospholipid and chenodeoxycholate concentrations, hydrophobic and lithogenic indices were all significantly decreased by 10% BCD. Increases in bile acid synthesis (+110%), sterol 27-hydroxylase activity (+106%), and biliary cholate secretion (+140%) were also observed, whereas the biliary secretion of chenodeoxycholate decreased (-43%). The fecal output of chenodeoxycholate and cholate (plus derivatives) was increased by +147 and +64%, respectively, suggesting that BCD reduced the chenodeoxycholate intestinal absorption preferentially. Dietary cholestyramine decreased biliary bile acid concentration and secretion, but dramatically increased the fecal excretion of chenodeoxycholate and cholate plus their derivatives (+328 and +1940%, respectively). In contrast to BCD, the resin increased the lithogenic index in bile, induced black gallstones in 34% of hamsters, and stimulated markedly the activities of HMG-CoA reductase (+670%), sterol 27-hydroxylase (+310%), and cholesterol 7α-hydroxylase (+390%). Thus, ß-cyclodextrin (BCD) prevented cholesterol gallstone formation by decreasing specifically the reabsorption of chenodeoxycholate, stimulating its biosynthesis and favoring its fecal elimination. BCD had a milder effect on lipid metabolism than cholestyramine and does not predispose animals to black gallstones as cholestyramine does in this animal model.

Keywords

Lipoproteins; HMG-CoA reductase; cholesterol 7alpha-hydroxylase; sterol 27-hydroxylase; LDL receptor; intestinal cholesterol absorption; hepatic bile secretion; gallbladder bile; fecal sterols; bile acids; beta-cyclodextrin; cholestyramine