Interruption of Bile Acid Recirculation

Philippe Boucher and Hans Gerhard Vogel

Contents

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Cholestyramine Binding

Purpose and Rationale

Cholesterol is metabolized in the liver by oxidation to bile acids which undergo enterohepatic circulation. In the untreated state, approximately 95 % of the bile acids that are secreted are reabsorbed and returned to the liver, while the small loss is replaced by de novo biosynthesis from cholesterol. Increased excretion of bile acids with the feces increases the rate of oxidation of cholesterol in the liver leading to a partial depletion of the hepatic cholesterol pool. A compensatory increase in uptake via the LDL receptors results in lower serum LDL levels. This can be achieved by addition of a bile acid-binding resin, e.g., cholestyramine, to the food. The binding of unconjugated and conjugated bile-salt anions can be tested in vitro (Johns and Bates 1969).

Procedure

Rabbits weighing 2.5–3 kg are switched from standard food to a diet containing 10–20 % polymeric basic-anion exchanging resin, e.g., cholestyramine. Cholesterol levels in serum are measured at the beginning and at the end of a 4-week feeding period.

Evaluation

Cholesterol levels as means ± SD are calculated for controls and treated animals and compared by statistical analysis.

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Modification of the Method

Tennent et al. (1960) tested polymeric organic bases for action on blood cholesterol in 4-day experiments and in experiments of 7–8-week duration in cholesterol-fed White Leghorn cockerels. The birds were given a diet containing 2 % cholesterol and 5 % cotton-seed oil with or without addition of polymeric bases. The increase of cholesterol and the incidence of aortic atheromatosis were decreased by polymeric organic bases.

Day (1990) compared the hypocholesterolemic activities of the bile acid sequestrants cholestyramine and cholestipol hydrochloride in cholesterol-fed sea quail.

Quaternary ammonium conjugates of bile acid inhibited cholic acid binding and transport in everted ileal sacs of guinea pigs in vitro (Fears et al. 1990).

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