Cholestyramine Effect on Plasma Triglycerides in Normolipidemic Patients* (33509)

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Cholestyramine is a quarternary ammonium exchange resin; when given internally it sequesters bile acids in the gut. It thus prevents reabsorption and increases excretion of bile acids (1). In association with the primary effect on bile acids, a very considerable lowering of plasma cholesterol occurs in most subjects (2). Bressler *et al.* reported that in patients with elevated cholesterol as well as elevated triglycerides, a fall in cholesterol and triglycerides occurred during cholestyramine therapy (3). These authors provide no information regarding the dietary program used in their hyperlipidemic subjects. No other reports on triglyceride changes during cholestyramine treatment have been published.

Materials and Methods. Five normolipidemic subjects were kept on quantitatively constant hypocaloric formula diets for periods up to 5 months. The diets provided 40% of calories from fat, 35% from carbohydrate, and 25% from protein. The fat used was oleic-safflower oil, which consists of oleic acid (80%), linoleic acid (15%), and palmitic acid (5%). The iodine number is 91. The patients underwent 4-week periods of cholestyramine therapy (16 g/day) in alternation with 4 weeks without treatment or treatment with cholestyramine placebo.

Four-week periods of cholestyramine[3] treatment ("on") and periods of the same duration without any treatment ("off") were as follows for the five patients on the study: Patient no. 1, off, on, off, on, off; Patient no. 2, on, off, on; Patients nos. 3 and 4, off, on, off; Patient no. 5, off, on. A comparison of the plasma total cholesterol (TC) and plasma triglyceride (TG) values during "treatment" and "off-treatment" periods was made. Plasma TC was estimated by the AutoAnalyzer technic (4); plasma TG was determined by the Michaels technic (5).

Results. The expected fall in plasma TC was seen in all patients on resin therapy, the decreases ranging from 8–37% of the previous levels; this was promptly reversible when cholestyramine was discontinued. Coincident with the fall in TC, there was an unexpected rise of plasma TG immediately after cholestyramine therapy was begun. This effect on plasma lipids, too, was entirely reversible when the drug was discontinued. The patterns in two representative patients are shown in Fig. 1. The actual triglyceride values (mean ± SD) in the five patients are as follows (mg/100 ml):

Patient no. 1: 137 ± 19 (off); 156 ± 21 (on); 144.5 ± 7 (off); 144.0 ± 14 (on); 124 ±13 (off); number of determinations were 5, 10, 8, 9, 11, respectively; the differences in TG values were statistically significant ($p < 0.025$) for all but the third transition.

Patient no. 2: 172 ± 12 (on); 143 ± 6 (off); 157 ± 3 (on); number of determinations were 4, 3, 3, respectively; $p < 0.025$ in both cases.

Patient no. 3: 130 ± 24 (off); 176 ± 22 (on); 142 ± 11 (off); number of determinations were 6, 9, 6, respectively; significance in both cases was $p < 0.005$.

Patient no. 4: 106 ± 5 (off); 137 ± 21 (on); 114 ± 6 (off); number of determinations were 7, 10, 10, respectively; p-values for the differences between the therapy period and the cholestyramine-free periods, respectively, were $p < 0.005$.

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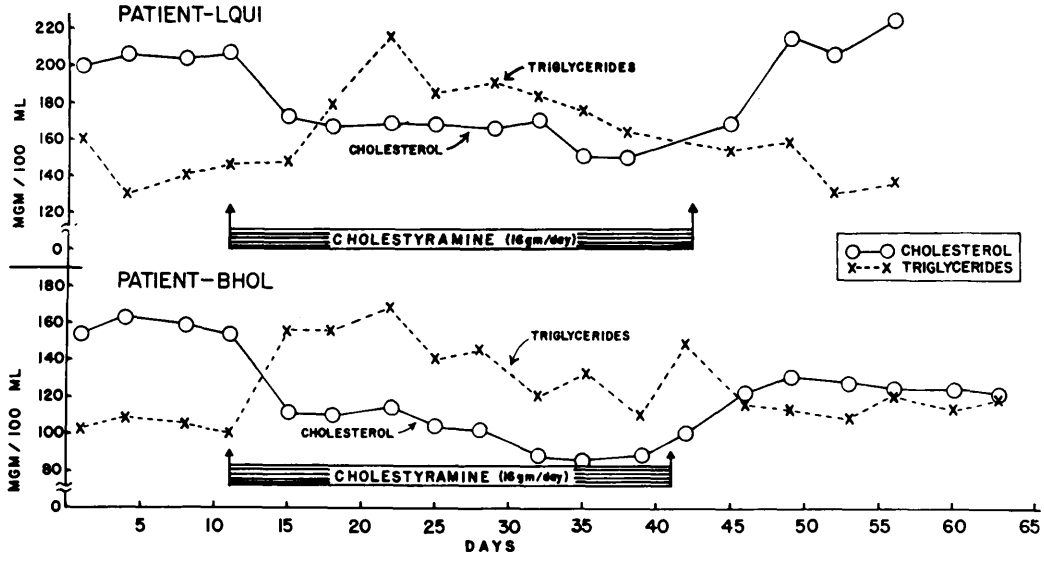

FIG. 1. Changes in plasma total cholesterol and triglyceride concentrations in response to cholestyramine treatment. Dietary intake was quantitatively constant throughout the study.

Patient no. 5: 142 ± 19 (off); 158 ± 12 (on); number of determinations were 10 and 9, respectively; $p < 0.005$.

The intermittent elevation of TG is especially surprising in view of the fact that all of the patients were on hypocaloric diets during the entire study. All of the patients had a continuous loss of weight, a metabolic state that is usually thought to reduce rather than elevate plasma TG.

During cholestyramine administration, lipoprotein electrophoresis revealed a distinct increase of the pre-beta (very low density) lipoprotein (VLD-LP) band, indicating that the rise in plasma TG is attributable to an increased concentration of endogenous VLD-LP. A possible mechanism is increased hepatic synthesis of VLD-LP in association with decreased low density lipoprotein formation, the latter resulting from decreased availability of cholesterol during cholestyramine administration.

Summary. Cholestyramine (16 g/day) was given to five normolipidemic subjects for periods of 4 weeks. A significant rise in plasma TG was seen in all patients in addition to the expected fall in plasma TC. Cessation of therapy was followed by a return of both TG and TC to normal values. Lipoprotein electrophoretic studies suggest that the rise in TG is due to a rise in VLD-LP.

1. Tennent, D. M., Siegel, H., Zanetti, M. E., Kuron, G. W., Ott, W. H., and Wolf, F. J., J. Lipid Res. 1, 469 (1960).

2. Hashim, S. A. and Van Itallie, T. B., J. Am. Med. Assoc. **192**, 289 (1965).

3. Bressler, R., Nowlin, J., and Bogdonoff, M. D., Southern Med. J. **59**, 1097 (1966).

4. AutoAnalyzer Manual, Technicon Instruments Corp., Chauncey, New York (1964).

5. Michaels, G. D., Metabolism **11**, 833 (1962).

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