USE OF BILE ACID SEQUESTRANT IN TREATMENT OF PRURITUS ASSOCIATED WITH BILIARY CIRRHOSIS*

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Pruritus is usually a major complaint of patients with biliary cirrhosis. This symptom can be so severe and unremitting that the patient may contemplate suicide (1). When there is interference with normal excretion of bile, as in biliary cirrhosis and other forms of bile stasis, itching may be an early and persistent symptom. There appears to be a lack of correlation between degree of bilirubinemia and pruritus. Attempts to correlate presence of pruritus with degree of retention of bile acids have yielded conflicting results (2).

It is well known that patients with cholestasis may obtain relief from itching following surgical biliary drainage. Until recently, medical management of the pruritus associated with biliary cirrhosis has been unsatisfactory. A new approach to the problem was suggested by availability of procedures believed to promote fecal excretion of bile acids. These include administration (a) of diets rich in polyunsaturated fatty acids (3, 4), and (b) of an anion exchange resin (MK-135) capable of binding bile acids in the gut and thereby preventing their reabsorption (5).

SUBJECTS

Four women with primary biliary cirrhosis and severe, sustained pruritus were studied (Table 1). Each of them had experienced the insidious onset of pruritus, jaundice, and, after several years, generalized xanthomatosis. Exploratory laparotomy was performed in three of the patients. In each case, this procedure failed to disclose extrahepatic biliary obstruction. Liver biopsy studies in all four patients were consistent with the clinical diagnosis of biliary cirrhosis. Two of the patients obtained relief of their itching during the temporary external biliary drainage that followed laparotomy. At the time of admission, each of the four patients complained of intractable pruritus and marked insomnia for two to three years. Two patients had entertained suicidal ideas, and another patient had become temporarily psychotic.

PROCEDURES

Two patients were treated with formula-type diets, prepared in a dairy-type homogenizer in which safflower or corn oil was the sole fat source. The fat constituted 40 per cent of the total daily calories, dextrose 43 per cent, and casein 17 per cent. The safflower-oil formula was given to one patient‡ for a period of six weeks. The corn-oil formula was given to a second patient for a period of four weeks. On another occasion, this same patient was also treated with a bile acid sequestrant (MK-135) 15 gm. per day in divided dosage for a period of two months while on a regular diet. Two additional patients were similarly treated with the bile acid sequestrant, while on a regular hospital diet (Table 1). MK-135§ is a basic anion exchange resin which has a marked affinity for bile acids in vitro. The resin forms an insoluble complex with bile acids which is neither digested nor absorbed. When fed to experimental animals (5) and human subjects (6), this agent lowers serum cholesterol levels, and in higher doses, induces steatorrhea (7).

RESULTS AND DISCUSSION

All four patients experienced dramatic relief of the itching within one to two weeks after onset of treatment with either formula or resin. Relief was complete in three patients and partial in one (Table 1), and was sustained as long as treatment was continued. In no instance was there a rise in serum bilirubin or any adverse effect of treatment on liver function as measured by standard tests. There was a striking improvement in the morale and well-being of the patients. Disappearance of pruritus did not correlate well with changes in serum lipids.

The mechanism of pruritus in biliary cirrhosis and other forms of cholestasis remains unknown. Attempts to correlate the pruritus with serum levels of bilirubin or serum lipids have not been successful. A rough correlation appears to exist between serum bile acid levels and presence or absence of pruritus, but it has not been possible to correlate pruritus with individual values of serum bile acids (2). Nevertheless, patients can

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This work was supported by grants from the Nutrition Foundation, Inc., New York, N. Y., and Merek-Sharp, & Dohme, Rahway, N. J.

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Received for publication May 23, 1960.

‡ This patient was treated in collaboration with Dr. Kendall Emerson, Peter Bent Brigham Hospital, Boston, and Dr. Leonardo Sinisterra, now at Universidad del Valle, Cali, Colombia.

§ Kindly supplied by Dr. E. W. J. DeMaar of Merek-Sharp & Dohme Research Laboratories.
obtain relief from pruritus following external drainage of bile. The modes of treatment used in the present series are analogous to external biliary drainage in that there is enhanced excretion of fecal bile acids during administration of polyunsaturated fats or the bile acid sequestrant. It is possible that the relief of pruritus in these cases was related to mobilization of bile acids deposited in the skin attendant, in turn, upon an increase in fecal excretion of bile acids.

**SUMMARY**

Four patients with intractable pruritus associated with primary biliary cirrhosis were treated by measures calculated to promote fecal excretion of bile acids.

Two patients were placed on formula-type diets containing plant seed oils rich in polyunsaturated fatty acids. On another occasion one of these patients and two additional patients remained on regular hospital diets but were given an anion exchange resin (MK-135, 15 gm. per day in divided dosage) with bile acid sequestering properties.

All four patients obtained dramatic relief from their pruritus and insomnia within two weeks of the start of treatment, with an associated improvement in morale and sense of well-being. Relief was complete in three of the subjects and partial in one.

It is believed that relief of pruritus in these cases was related to mobilization of bile acids deposited in the skin accompanying increased fecal excretion of bile acids.

**REFERENCES**


