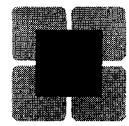

INTRODUCTION

Medical Grand Rounds is an integral part of the academic life at the Cleveland Clinic Foundation. As Chairman of the Medical Grand Rounds Committee and a frequent attendee, I continue to be impressed by the authoritative nature of the information presented and the clinical relevance of these sessions. To share some of the positive experiences of the Medical Grand Rounds with our readers, the *Cleveland Clinic Journal of Medicine* has inaugurated this new section, in which selected presentations will be summarized. We hope this section will prove a valuable source of current medical knowledge.

WILLIAM S. WILKE, MD, SECTION EDITOR
CHAIRMAN, MEDICAL GRAND ROUNDS COMMITTEE

ORAL DISSOLUTION OF GALLSTONES

Cholecystectomy is both accepted and effective treatment for symptomatic cholelithiasis. Recently available alternative therapies for cholelithiasis include oral dissolution therapy, biliary lithotripsy, and direct contact solvents. Two compounds effective in the treatment of selected patients with cholelithiasis are chenodeoxycholic acid and ursodeoxycholic acid.

PRE-THERAPY EVALUATION

The oral dissolution agents are effective in cholesterol cholelithiasis. It is estimated that 70% of gallstones in Western populations are pure cholesterol stones or "mixed" stones made up of greater than 60% cholesterol. It is likely that radiolucent stones with rounded borders are predominately cholesterol in composition; however, at least 15% of such stones will not dissolve at all with oral dissolution therapy, implying that these criteria are not infallible. Oral cholecystography is a useful test in the evaluation of patients being considered for oral dissolution therapy, as both gallbladder function and stone characteristics can be assessed. If the gallbladder cannot be visualized, the patient is generally not a candidate for oral dissolution therapy.

CLINICAL TRIALS

As part of the National Cooperative Gallstone Study, 916 patients with radiolucent stones were treated over a two-year period with chenodeoxycholic acid, 350 mg per day or 750 mg per day, or with placebo (Schoenfield et al). Of the patients receiving 750 mg per day of chenodeoxycholic acid, 13.5% had complete gallstone dissolution, and another 27.3% had partial (greater than 50%) dissolution. It has been suggested that the dose of chenodeoxycholic acid utilized in this study was below optimum for a large number of patients involved, accounting in part for the overall low dissolution rates (Fromm and Bazzoli). Side effects from chenodeoxycholic acid therapy included diarrhea occurring in up to 40% of patients, increases in serum cholesterol, seen in up to 80% of patients on therapy, and clinically significant hepatotoxicity, occurring in 3% of patients. The hepatotoxicity was biochemically reversible.

Ursodeoxycholic acid therapy was utilized over a 12-month period in 151 patients with radiolucent gallstones, in the Tokyo Cooperative Gallstone Study. Patients were treated with either 150 mg per day or 600 mg per day of ursodeoxycholic acid or placebo. Complete dissolution or decrease in stone volume occurred in 34.5% of patients receiving 600 mg per day, compared to 5% in the placebo group. In patients with floating gallstones (implying a large cholesterol content) less than 15 mm in size, efficacy was 83% in the 600 mg per day group. Side effects were in general much less than in the chenodeoxycholic acid study, with transient diarrhea in 6% and increased serum liver function tests in 3%.

In summary, chenodeoxycholic acid and ursodeoxycholic acid are effective cholelitholytic agents in selected patients with cholelithiasis. The two agents appear to be of equal efficacy, but side effects are far less frequent with ursodeoxycholic acid.

Pre-therapy selection of appropriate patients can significantly increase the likelihood of therapeutic success.

In addition to the limitations in efficacy detailed above, after dissolution is achieved, factors necessary for

gallstone formation are still present. It is estimated that the re-formation rate after dissolution is as high as 30% to 40% in the first five years after dissolution therapy. These stones can generally be dissolved with another course of therapy.

GREGORY ZUCCARO JR., MD
Department of Gastroenterology

BIBLIOGRAPHY

1. Fromm H, Bazzoli F. Medical dissolution of cholesterol gallstones. [In] Cohen S, Soloway RD, eds. Gallstones. New York, Churchill Livingstone, 1985.
2. Fromm H, Roat JW, Gonzalez V, Sarva RP, Farivar S. Comparative efficacy and side effects of ursodeoxycholic and chenodeoxycholic acids in dissolving gallstones: a double-blind controlled study. Gastroenterology 1973; **85:**1257–1264.
3. Pitt HA, McFadden DW, Gadacz TR. Agents for gallstone dissolution. Am J Surg 1975; **153:**233–246.
4. Roda E, Bazzoli F, Labate AM, et al. Ursodeoxycholic acid vs. chenodeoxycholic acid as cholesterol gallstone dissolving agents: a comparative randomized study. Hepatology 1982; **2:**804–810.
5. Schoenfield LJ, Lachim JM, Baum RA, et al. Chenodiol (chenodeoxycholic acid) for dissolution of gallstones: the National Cooperative Gallstone Study. A controlled trial of efficacy and safety. Ann Intern Med 1981; **95:**257–282.
6. Tint GS, Salen G, Colalillo A, et al. Ursodeoxycholic acid: a safe and effective agent for dissolving cholesterol gallstones. Arch Intern Med 1982; **97:**351–356.
7. Tokyo Cooperative Gallstone Study Group. Efficacy and indications of ursodeoxycholic acid treatment for dissolving gallstones: a multicenter double-blind trial. Gastroenterology 1980; **78:**542–548.

HYPERCHOLESTEROLEMIA: ROLES OF THE PHYSICIAN AND REGISTERED DIETITIAN

An increasing number of patients consult their physicians because they have been told their blood cholesterol level is elevated. A difficult problem for the clinician in a busy office practice is the issue of what to tell patients about a cholesterol-lowering diet, within the time frame the office setting allows.

Data from the Multiple Risk Factor Intervention Trial (MRFIT) has shown that certain high-fat eating behaviors are easier for patients to change than others,[1] and these changes can be recommended by the physician in a few minutes. Changes made with relative ease include 1) increasing consumption of fish and poultry and reducing intake of fatty red meat, 2) use of skim or low-fat milk products, 3) substituting polyunsaturated margarines for butter, 4) use of polyunsaturated oils for cooking, and 5) reducing the consumption of egg yolks. When these changes are made, diet specifications generally approach the National Cholesterol Education Program (NCEP) Step 1 diet (less than 30% calories as fat and less than 300 mg cholesterol/day).[2]

However, most people find it more difficult to reduce meat consumption to less than six to seven ounces per day, avoid high-fat cheeses and high-fat snacks such as crackers and potato chips (which contain a high content of saturated fat) and/or eliminate consumption of high-fat processed meat such as sausage and lunch meats. It may be necessary to make these changes if blood cholesterol levels fail to fall after a three- to six-month trial on the Step 1 diet. When this is the case, referral to a registered dietitian can be quite helpful because considerable time must be spent to implement the level of fat restriction specified in the NCEP Step 2 Diet. This diet contains less than 7% calories as saturated fat and less than 200 mg of cholesterol/day.

The dietitian is instrumental in helping patients achieve specified dietary goals, because patient education and behavior modification are required. Most clinicians in an office practice are not able to devote the 40 to 60 minutes typically required for a comprehensive nutritional evaluation.

Furthermore, many patients have already made substantial dietary changes before seeing their physician. We reviewed results of three-day food records of 384 patients referred to our lipid clinic. It was interesting to note that approximately 60% of these patients were already on a low-fat Step 1 diet (less than 30% of total calories as fat) at the time of the initial visit. Fat intake was less than 25% of calories in 145 (38%) of the 384 patients, 25-30% in 88 (23%) patients, and more than 30% in 151 (39%) patients.

This referred population is obviously not representative of the general public, but our data raise the important point that many persons who are aware of a blood cholesterol problem have already made many diet changes before they consult a physician. For these patients, a brief discussion with a physician about the principals of dietary therapy for hypercholesterolemia is likely to be of limited benefit. When this situation arises, it is desirable to have access to a registered dietitian who can provide the level of support required to further lower blood cholesterol levels by dietary means.

In our lipid clinic, food diaries have been useful as educational and self-monitoring tools. Diaries are analyzed using a computerized nutrient data base. This provides information about the average daily intake of cholesterol as well as the distribution of calories as fat, protein, and carbohydrate. Our lipid clinic nutritionists use these food records to point out areas where further dietary changes can be made. Using this approach, ap-