

due to underlying duct ectasia or chronic breast disease provides a suitable nidus for the deposition of these anaerobes.

- ¹ Leach RD, Eykyn SJ, Phillips I, Corrin B. Anaerobic subareolar breast abscess. *Lancet* 1979;i:35-7.
- ² Wilson WR, Martin WJ, Wilkawske CJ, Washington JA. Anaerobic bacteremia. *Mayo Clin Proc* 1972;47:639-46.
- ³ Lefrock JL, Ellis CA, Turchik JB, Weinstein L. Transient bacteremia associated with sigmoidoscopy. *N Engl J Med* 1973;289:467-9.

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St Thomas's Hospital, London SE1 7EH

R D LEACH, MB, FRCS, honorary senior registrar, surgical unit (now lecturer in surgery, Westminster Medical School)

SUSANNAH J EYKYN, MB, MRCPATH, senior lecturer

IAN PHILLIPS, MD, MRCPATH, professor of microbiology

Treatment of biliary duct stones with a terpene preparation

Biliary duct stones are often found in patients who present with gall-bladder disease and are poor surgical risks. Retained stones may persist after cholecystectomy, despite recent developments in non-operative methods of extraction and in-situ litholytic agents. When facilities for endoscopic papillotomy are lacking, reoperation is contraindicated or further procedures refused, and spontaneous passage is unlikely on grounds of stone size, an alternative approach is needed. We used Rowachol (Rowa Ltd, Bantry, Ireland), a monoterpene mixture with cholelitholytic potential.¹

Patients, methods, and results

We treated nine female and two male patients with radiotranslucent ductal stones of a diameter greater than 7 mm and absent, infrequent, or mild symptoms (group 1) and four postoperative patients with retained stones, whose elective reoperations were either refused or considered to be undesirable (group 2). Endoscopic papillotomy was not available at the start of the study. In group 1 three patients had previously undergone cholecystectomy and three had, or developed, non-functioning gall bladders.

Maintenance dosage of Rowachol was with three capsules daily (some patients started at higher doses); symptoms and liver function were monitored six-weekly. Intravenous cholangiography was repeated after six and 12 months.

Treatment was well tolerated, a slightly sore mouth in one case being the only side effect. Results of liver function tests remained normal in six patients and improved in four asymptomatic patients with initially abnormal values. Five patients developed transient abnormalities after attacks of colic or jaundice.

The two male patients were withdrawn, one after five months when surgery was recommended for increasing colic and jaundice, the other after seven months on his death from cardiac infarction. Thirteen patients, all female, took Rowachol for one year or until the stone dissolved, if this was earlier. One of these had bile-duct dilatation and recurrent jaundice; after repeated advice she eventually accepted surgery, but at cholecystectomy no duct stones were found. The table shows details of gall-stone dissolution. One patient is not included because inadequate radiography precluded assessment. Of the four non-responders, two had large calculi after cholecystectomy 30 years previously.

Comment

The results of treating common bile duct stones with Rowachol are encouraging and compare well with published results obtained using bile-acid treatment. The best reported success rate achieved using chenodeoxycholic acid is five out of eight cases (62.5%),² but other series of patients have fared less well. Bateson *et al* had only one success in 10 cases and reported a high incidence of severe symptoms.³ Most of our patients presented with biliary symptoms, but only two required surgery during treatment with Rowachol, which suggests that the antispasmodic properties of the constituent terpenes⁴ may be of value. Rowachol also has the advantages of low cost and virtual absence of side effects. Thus, when other treatments for ductal stones are unacceptable or impracticable and long-term medical treatment is indicated, we suggest that Rowachol should be used, possibly in

combination with small doses of chenamic acid, which is our present practice. Such management in no way precludes subsequent definitive treatment by surgery or other methods should this become available or desirable; indeed, two of the patients described above subsequently underwent endoscopic papillotomy.

Response of biliary duct stones to treatment with Rowachol

Duration of treatment	No of patients treated	No with partial dissolution†	No with complete disappearance	Response rate
6 months	13	2	4	6/13 (46%)
12 months	12*	2	6	8/12 (67%)

*Includes patients treated for less than 12 months but until the stones disappeared.
†Reduction in size or number of stones.

The reasons why Rowachol should be more successful in ductal than gall-bladder⁵ disease are not clear. A flushing effect of the choleresis for which Rowachol is marketed may be contributory.

Full details of the patients and the results of liver function tests are available on request from Dr G D Bell, University Department of Therapeutics, City Hospital, Nottingham NG5 1PD.

- ¹ Doran J, Keighley MRB, Bell GD. Rowachol—a possible treatment for cholesterol gallstones. *Gut* 1979;20:312-7.
- ² Barbara L, Roda E, Roda A, *et al*. The medical treatment of cholesterol gallstones: experience with chenodeoxycholic acid. *Digestion* 1976;14:209-19.
- ³ Bateson MC, Ross PE, Murison J, Bouchier IAD. Comparison of fixed doses of chenodeoxycholic acid for gallstone dissolution. *Lancet* 1978;i:1111-4.
- ⁴ Boettge K. Ätherische Öle und Spasmolyse. *Med Monatsschr* 1954;8:444-6.
- ⁵ Ellis WR, Bell GD. Rowachol treatment for gallstones—small doses are best. *Gut* 1979;20:A931.

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University Department of Therapeutics, City Hospital, Nottingham NG5 1PD

W R ELLIS, MA, MRCP, research fellow and honorary senior registrar
G D BELL, MD, MRCP, senior lecturer

Adjunct to bile-acid treatment for gall-stone dissolution: low-dose chenodeoxycholic acid combined with a terpene preparation

Chenodeoxycholic acid is an established treatment for cholesterol gall stones. Bile is desaturated by reducing the output of cholesterol relative to bile acids; possible mechanisms of action include inhibition of hepatic S-3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR), the rate-limiting enzyme for cholesterol synthesis.^{1 2}

The recommended dose of chenodeoxycholic acid (15 mg/kg/day) causes diarrhoea in one-third of cases; reduction in dosage may alleviate this problem, but treatment is ineffective in doses of under 500 mg daily.¹ When full dosage is tolerated response rates are poor in obese patients and when stone diameter exceeds 15 mm.² A further serious disadvantage of chenodeoxycholic acid is its cost (over £600 per year for a 70 kg man at 15 mg/kg/day). Adjuvant treatments such as phenobarbitone, β -sitosterol, and restriction of dietary cholesterol have hitherto either failed to increase the efficacy of chenodeoxycholic acid (and thus reduce cost and side effects) or given only marginal benefit.¹

Rowachol (Rowa Ltd, Bantry, Ireland) is a well-tolerated, inexpensive preparation containing six cyclic monoterpenes: it inhibits hepatic HMGR,³ alters biliary cholesterol saturation,⁴ and can dissolve gall stones but is more effective in low than high dosage.^{4 5} This may reflect differences in the effects of individual constituent terpenes on HMGR.³ We report our experience of using Rowachol in combination with a small (and hence on its own probably ineffective)^{1 2} dose of chenodeoxycholic acid in an unselected series of patients with gall stones.

Patients, methods, and results

Thirty-two patients with radiotranslucent stones in functioning gall bladders were treated with Rowachol (two or three capsules daily) and chenodeoxycholic acid (375 mg at bedtime). Six further patients were treated with the same dose of chenodeoxycholic acid alone, and 13 with Rowachol alone (three capsules daily). Patients were assessed clinically and biochemically every six weeks, and oral cholecystography was repeated after six and 12 months.

The combination was well tolerated: only one patient noticed bowel disturbance sufficient to prevent continued treatment. Hypertransaminasemia occurred only in association with episodes of biliary colic, and only three patients had biliary symptoms severe enough to require surgery before completing six months' treatment. Two more patients elected to have surgery at six months rather than continue treatment. Medication was changed in three patients for other reasons, one before and two after six months. One patient developed a persistently non-functioning gall bladder within six months. Thus five patients were withdrawn before the first repeat cholecystogram was obtained and five afterwards. No patient voluntarily defaulted; total withdrawals were thus 10 out of 32 (31%). All the patients taking single preparations completed six months' treatment. The table shows the results of the trial in terms of gall-stone dissolution.

Comment

Gall-stone dissolution was more common with the combined treatment than when either drug was used alone. The success rate is greater when patients are selected for analysis as they would be for treatment according to currently recommended practice.² Thus, at no cost in terms of efficacy, we reduced the chenodeoxycholic acid dose requirement by almost two-thirds; this resulted in a great improvement in patient tolerance and reduced by half the total cost of treat-

ment. Formal double-blind assessment of optimal dosage of chenodeoxycholic acid, alone and in combination with Rowachol, is now indicated.

Full details of the patients and the results of liver function tests are available on request from Dr G D Bell, University Department of Therapeutics, City Hospital, Nottingham NG5 1PB.

- ¹ Bouchier IAD. The medical treatment of gallstones. *Ann Rev Med* 1980; 31:59-77.
- ² Dowling RH. The gallstone dissolution story. *Hospital Update* 1979;5: 1081-103.
- ³ Clegg RJ, Middleton B, Bell GD, White DA. Inhibition of hepatic cholesterol synthesis and S-3-hydroxy-3-methylglutaryl reductase by mono and bicyclic monoterpenes administered in vivo. *Biochem Pharmacol* 1980;29:2125-7.
- ⁴ Doran J, Keighley MRB, Bell GD. Rowachol—a possible treatment for cholesterol gallstones. *Gut* 1979;20:312-7.
- ⁵ Ellis WR, Bell GD. Rowachol treatment for gallstones—small doses are best. *Gut* 1979;20:A931.

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University Department of Therapeutics, City Hospital, Nottingham NG5 1PB

W R ELLIS, MA, MRCP, research fellow and honorary senior registrar
G D BELL, MD, MRCP, senior lecturer

Department of Biochemistry, Medical School, Queen's Medical Centre, Nottingham

B MIDDLETON, MA, PHD, lecturer
D A WHITE, BSC, PHD, lecturer

*Results of treating gall-bladder stones with low-dose chenodeoxycholic acid (CDCA) (375 mg daily) or Rowachol (2-3 capsules daily), or both**

Treatment	Duration	Details of patients treated			No with complete dissolution	No with partial dissolution	Response rate
		No	Mean (±SD) weight (kg)	Mean (±SD) dose of CDCA (mg/kg)			
Rowachol	6 months	13 (10)	67.8 ± 13.0		0 (0)	2 (1)	2/13 = 15% (1/10 = 10%)
CDCA	6 months	6 (4)	68.4 ± 17.5	5.78 ± 1.37	0 (0)	0 (0)	0/6 = 0% (0/4 = 0%)
CDCA and Rowachol	6 months	27 (15)	69.0 ± 13.4	5.64 ± 1.09	4 (3)	7 (6)	11/27 = 41% (9/15 = 60%)
	12 months or earlier dissolution	22 (13)	68.7 ± 14.4	5.69 ± 1.16	6 (5)	7† (5†)	13/22 = 59% (10/13 = 77%)

*Results in parentheses are those achieved when patients in excess of 110% ideal body weight or with no stones less than 1.5 cm in diameter are excluded from the analysis.
†Includes two patients with partial responses at 6 months that left only stones greater than 1.5 cm in diameter: one developed obstruction of the gall bladder at one year.
Comparison of response rates at 6 months shows no significant difference between the three treatment groups but a definite advantage of combined treatment over the single-drug regimens considered together (p = 0.026, Fisher's exact test (one tail)).

BORAGE AND BUGLOSS. These are so well known to the inhabitants in every garden that I hold it needless to describe them. To these I may add a third sort, which is not so common, nor yet so well known, and therefore I shall give you its name and description. It is called *Langue de Boeuf*; but why then should they call one herb by the name of Bugloss, and another by the name *Langue de Boeuf*? it is some question to me, seeing one signifies Ox-tongue in Greek, and the other signifies the same in French.

The leaves whereof are smaller than those of Bugloss but much rougher; the stalks rising up about a foot and a half high, and is most commonly of a red colour; the flowers stand in scaly round heads, being composed of many small yellow flowers not much unlike to those of Dandelion, and the seed flieeth away in down as that doth; you may easily know the flowers by their taste, for they are very bitter. It grows wild in many places of this land, and may be plentifully found near London, as between Rotherhithe and Deptford, by the ditch side. Its virtues are held to be the same with Borage and Bugloss, only this is somewhat hotter. They flower in June and July, and the seed is ripe shortly after.

They are all three herbs of Jupiter and under Leo, all great cordials, and great strengtheners of nature. The leaves and roots are to very good purpose used in putrid and pestilential fevers, to defend the heart, and help to resist and expel the poison, or the venom of other

creatures: the seed is of the like effect; and the seed and leaves are good to increase milk in women's breasts; the leaves, flowers, and seed, all or any of them, are good to expel pensiveness and melancholy; it helps to clarify the blood, and mitigate heat in fevers. The juice made into a syrup prevails much to all the purposes aforesaid, and is put, with other cooling, opening and cleansing herbs to open obstructions, and help the yellow jaundice, and mixed with Fumitory, to cool cleanse, and temper the blood thereby; it helps the itch, ringworms and tetter, or other spreading scabs or sores. The flowers candied or made into a conserve, are helpful in the former cases, but are chiefly used as a cordial, and are good for those that are weak in long sickness, and to comfort the heart and spirits of those that are in a consumption, or troubled with often swoonings, or passions of the heart. The distilled water is no less effectual to all the purposes aforesaid, and helps the redness and inflammations of the eyes, being washed therewith; the herb dried is never used, but the green; yet the ashes thereof boiled in mead, or honied water, is available against the inflammations and ulcers in the mouth or throat, to gargle it therewith; the roots of Bugloss are effectual, being made into a licking electuary for the cough, and to condensate thick phlegm, and the rheumatic distillations upon the lungs. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)