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Stones in the common bile duct: experience with medical dissolution therapy

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Summary: Thirty-one patients with radiolucent common bile duct stones received medical treatment. Nineteen had Rowachol, a terpene preparation, eight (42%) achieving complete stone disappeance within 3 to 48 months. Fifteen (including 3 of the above) took Rowachol with bile acid (chenodeoxycholic in 11, ursodeoxycholic in 4) for 3 to 60 months: 11 (73%) achieved complete dissolution within 18 months. Persistent symptoms and complications settled on conservative management: 8 (25%) patients required admission (2 biliary colic, 1 obstructive jaundice, 4 cholangitis, 1 pancreatitis). One patient died of a myocardial infarction during recovery from pancreatitis; the others continued treatment, 2 achieving complete dissolution/disappearance. Oral dissolution therapy with Rowachol and bile acids should be considered when endoscopic sphincterotomy or surgery is not feasible, but careful attention to potential complications is required while stones persist.

Introduction

Although there is extensive published experience of oral dissolution therapy for gall bladder stones (Iser & Sali, 1981; Bachrach & Hofmann, 1982) relatively few patients with stones in the bile ducts have been so treated. The results were poor in early studies and the prevalence of complications high, so that the current view is that oral treatment has little or no place in the management of duct stones (Iser & Sali, 1981; Bouchier, 1983) for which alternative methods including endoscopic sphincterotomy, solvent perfusion and T-tube track extraction techniques are now available (Thistle, 1981; Dowling 1983).

We have a long standing interest in gall stone dissolution therapy for which we have used the proprietary terpene preparation Rowachol (Rowa Ltd., Bantry, Ireland) extensively, particularly in combination with chenodeoxycholic acid (CDCA) (Ellis *et al.*, 1981, 1984). Before the introduction of endoscopic sphincterotomy to Nottingham we also had some success using Rowachol for duct stones (Ellis & Bell, 1981). We were impressed with the good control of symptoms and lack of complications in this group, so we have continued, during the development phase of sphincterotomy in the city, to offer medical treatment to a selection of patients in whom a surgical approach was felt to be unwise or was refused, or sphincterotomy had failed.

This paper describes our further experience of treating duct stones with Rowachol, latterly in combination with either CDCA or ursodeoxycholic acid (UDCA), and our present view of the role of dissolution therapy in the management of ductal stones.

Patients, materials and methods

Thirty-one patients (20 female, 11 male, mean age 69 years, range 31–83, 24 over 60) were treated. All had radiolucent duct stones, diagnosed by T-tube cholangiogram in four and by infusion cholangiography in the remainder using iotroxamide (Schering Chemicals) according to our previously described method for obtaining optimal biliary opacification (Doran & Bell, 1980) and including tomography of the ducts and delayed gall bladder films as appropriate. The gall bladder was present in 16 cases, but non-functioning radiologically in 7. In 18 patients there was one duct stone, in 8 two and in the rest three or more: the mean stone diameter was 10 mm (range 4–22) and in 23 subjects stones were more than 7 mm across.

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Patients presented with a variety of symptoms; there was a history of biliary colic in 26, of jaundice in 15, of cholangitis in 11 and of pancreatitis in 3. Indications for medical treatment were unacceptable operative risk (11), failed endoscopic sphincterotomy (6) and refusal of surgical or endoscopic intervention (14).

All patients were given Rowachol capsules, initially in doses up to 7 capsules daily. Later, after we obtained experimental evidence that higher doses of Rowachol may paradoxically increase the cholesterol saturation of bile (Ellis & Bell, 1979; Ellis, 1983) doses of 3 capsules daily or less were used in all cases. One patient, however, had already achieved complete stone disappearance on 7 capsules daily when this policy was instituted.

In three patients who did not respond to Rowachol, bile acid therapy was given in addition after 18, 24 and 42 months respectively. A further 12 patients were given combinations of Rowachol and bile acid throughout. CDCA was used in 11 cases altogether, initially in low dosage (375 mg daily): after we had become confident, as a result of experience in treating gall bladder stones (Ellis *et al.*, 1981; 1984), that the combination was safe, higher doses were prescribed and the dose actually taken was determined by the individual subjects' tolerance to the dose-related diarrhoea produced by CDCA. A wide range of doses, from 3.8–16.7 mg/kg/d, was therefore employed in this group. UDCA was used in 4 patients; again because the safety of this drug in combination with Rowachol was not certain, we used moderate doses, 600 mg/d in 3 and 300 mg/d in the remaining subject, who was small. The resulting dose range was 4.5–7.1 mg/kg/d. Full details of the dosages used are given in Figure 1.

Patients were seen regularly for assessment and liver function test estimation. Infusion cholangiograms were performed after 3 to 6 months therapy and thereafter every 6 to 12 months.

Results

The overall results are given in Figure 1. Ductal stones disappeared completely within 48 months in 8/19

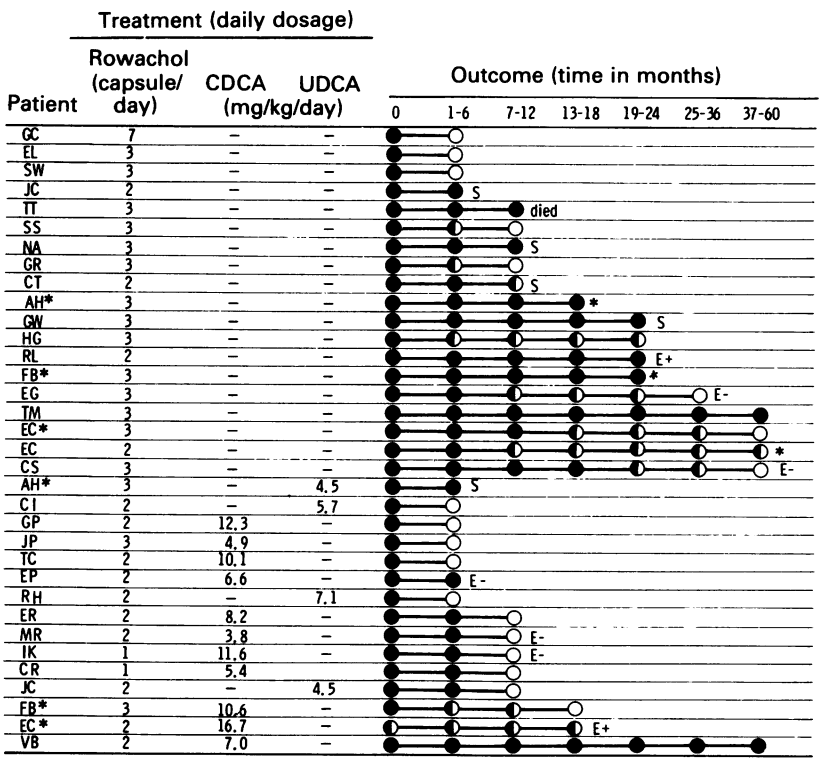

Figure 1 Treatment of bile duct stones in 31 cases. (●) No dissolution; (◐) partial dissolution; (○) complete dissolution; S = surgery performed; E+ = endoscopic sphincterotomy performed; E− = endoscopic sphincterotomy (failed).

(42%) of patients treated with Rowachol alone and in 11/15 (73%) of those receiving Rowachol and bile acid. During medical treatment endoscopic sphincterotomy was attempted in 8 patients but failed in 6; in four of these the stones eventually disappeared on treatment.

Of the twelve in whom stones persisted 4 required surgery, two had a successful endoscopic sphincterotomy and a further 5 are symptom-free and have continued therapy, in two cases for over five years.

Eight patients were admitted as emergencies while on therapy with biliary colic (2), painful obstructive jaundice (1), pancreatitis (1) or cholangitis (4). All were successfully managed conservatively and all but one (an elderly man who died of cardiac infarction following recovery from pancreatitis) continued with treatment afterwards.

The alkaline phosphatase (ALP) was raised in 10 patients at the start of treatment but became normal in five after either 6 months' medical treatment or stone disappearance. Of the others, two had surgery and three (one with Paget's disease) remain asymptomatic with modest ALP elevation. Cholangitis or biliary colic was usually accompanied by a rise in ALP (six of seven cases).

All patients whose stones disappeared have been followed up for at least one year without symptoms or rise in ALP levels.

Discussion

Although uncontrolled, our experience represents by far the largest series of medically treated patients with choledocholithiasis reported to date. The results with Rowachol alone (8/19 or 42% complete success) and in combination with a bile acid (11/15 or 73%) compare favourably with published experience of CDCA treatment used alone (Table I) and is similar to the 50% disappearance rate obtained in the only trial of UDCA (Salvioli *et al.*, 1983). Our dissolution figures, however, like those of Salvioli *et al.*, depend upon assessment by infusion cholangiography, a relatively insensitive imaging method. This requires comment.

There is no reliable non-invasive procedure for the detection of stones in the bile ducts. Ultrasonography, although very accurate in experienced hands for detecting gall bladder stones, has a low sensitivity for duct stones (as opposed to duct dilatation, which is not always present) and is thus not an adequate method (Einstein *et al.*, 1984; Espinoza *et al.*, 1984). Direct cholangiography by the percutaneous route is not acceptable for repeated monitoring of patients on treatment, nor is endoscopic cholangiography. If the latter is readily available, sphincterotomy will usually be indicated for patients with duct stones. If it is not, or fails, then another method must be used. We have a particular interest in the infusion cholangiogram and have refined the procedure, using iotroxamide, to a higher standard of duct visualization than that achieved previously (Doran *et al.*, 1981). Nevertheless we accept its limitations and have therefore followed our patients with apparent complete disappearance of stones with some care, seeking clinical, biochemical or, in some cases, further radiographic evidence to suggest that stones in fact persist. To date we have no reason to suppose that they do.

Common bile duct stones over 7 mm in diameter rarely pass spontaneously, particularly if multiple (Schein, 1978). Since the majority of our patients' stones were larger than 7 mm and over one third had multiple calculi it is unlikely that spontaneous passage of the stones occurred in a significant proportion. It is possible that the stones were sufficiently reduced in size by the combined cholelitholytic properties of the Rowachol and bile acid to pass through the ampulla of Vater. Rowachol, with menthol a major ingredient, has both choleretic (Morsdorf, 1965) and spasmolytic (Lamy, 1967) properties which could perhaps facilitate the passage of common duct stones once they have been sufficiently reduced in size.

Only one third of our patients had abnormal liver function tests and even those whose stones failed to dissolve or dissolved very slowly mostly remained symptom-free with normal liver function. It is uncertain whether this reflects treatment-induced relaxation of the sphincter of Oddi or whether choledocholithiasis, especially in the elderly, is more benign than is generally recognized. Complications, however, did

Table I Some published figures for successful dissolution of common bile duct stones using chenodeoxycholic acid (CDCA)

Authors	*No. of patients*	*Dose of CDCA*	*Complete disappearance*
Bateson *et al.* (1978)	10	750 mg/d (9)	
		500 mg/d (1)	1
Barbara *et al.* (1976)	8	2–15 mg/kg/d	3
Sue *et al.* (1981)	13	750 mg/d	3
Iser *et al.* (1975)	4	750–1500 mg/d	1
Thistle *et al.* (1978)	11	250–750 mg/d	5

arise in a number of cases; although these were managed successfully and did not preclude a later satisfactory outcome, patients do remain at some risk while their stones persist. This must be weighed against the risks of alternative approaches.

Surgery, when applied to the elderly patients such as ours, seems to be more hazardous, carrying an overall mortality of at least 5% in patients over 60 years of age (Glenn, 1975). This is not so in younger subjects however, in whom, if the gall bladder is *in situ*, an operation is normally indicated. Endoscopic sphincterotomy is not notably more dangerous in the elderly but there is an overall mortality of approximately 1% and, even in expert hands, in over 10% of cases duct clearance is not achieved (Cotton, 1984). There is therefore a group of patients, mainly elderly, in whom surgery is contra-indicated (or refused) and endoscopic treatment is unavailable or fails. Our experience suggests that these cases may be considered for medical dissolution therapy.

A decision to treat patients in this way, however, carries with it a responsibility to monitor progress very closely in order to detect and treat potential complications at the earliest possible stage. This includes making the patients, relatives and general practitioners aware of the need for prompt consultation with a view to immediate hospital admission if any but trivial symptoms occur.

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