IMAGING THE PANCREATICO BILLIARY SYSTEM WITH MAGNETIC RESONANCE CHOLANGIOCREATOGRAPHY

Sir,

We read with interest the recent article by Ballantyne *et al.* concerning the use of magnetic resonance cholangiopancreatography (MRCP) in imaging the pancreatico-biliary system.[1] We agree with their comment about the role of MRCP rather than diagnostic ERCP in evaluating patients with suspected choledocholithiasis, although much of the evidence for this is not based on controlled data. In our institution, MRCP has proved particularly useful in the evaluation of patients with suspected choledocholithiasis and has largely replaced ERCP as a diagnostic tool. A disadvantage of MRCP is that visualisation of the distal common bile duct (CBD) and ampulla of Vater may be poor.[2] This suboptimal visualisation is thought to be due to relatively slow flow of bile in the region secondary to sphincter constriction (as mentioned in the author's article). The distal CBD is enveloped by smooth muscle fibres and it has been shown that antispasmodic agents such as glucagon and hyoscine can cause relation of this smooth muscle with consequent sphincter dilatation, thereby potentially improving visualisation during MRCP.

We investigated ampullary visualisation using glucagon in 42 patients undergoing MRCP for suspected choledocholithiasis.[3] Initial MRCP was performed using a turbo-spin echo fat-saturated T2-weighted sequence (HASTE). Imaging was then repeated three minutes after intravenous administration of 1 mg of glucagon. Maximum intensity projections (MIPs) were obtained post-processing, optimised to visualise the common hepatic duct, CBD and the ampulla of Vater. The common bile and common hepatic ducts were assessed using a four-point grading system and the ampullary region was graded as to whether it was visualised or not. Maximal visualisation of the CBD was found in 17/42 patients pre-glucagon and 31/42 patients post glucagon administration. Visualisation of the ampulla was diagnostic in 15/42 patients pre- and 33/42 patients post-glucagon administration. Intraductal calculi were also identified in an additional three patients following glucagon administration. Significant differences in visualisation of the common hepatic duct region following glucagon administration were not identified – this may be because there is no smooth muscle at this level.

The efficacy of glucagon and hyoscine in smooth muscle relaxation is not dissimilar. Glucagon is considerably more expensive but has far fewer side effects than hyoscine, especially in older subjects. The use of an intravenous antispasmodic may reduce the incidence of non-diagnostic MRCP and should be considered in patients undergoing MRCP if the distal common bile duct or ampulla are not well visualised on initial sequences.

DC HOWLETT
Consultant Radiologist
Eastbourne District General Hospital

AD SMITH
Consultant Gastroenterologist
Eastbourne District General Hospital

AA DUNK
Consultant Gastroenterologist
Eastbourne District General Hospital

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SHORT-TERM REST AND 'NORMAL' BLOOD PRESSURE

Sir,

It is well known that blood pressure (BP) tends to be higher when taken by a doctor or other health professional than at complete rest ('white-coat hypertension') and that long-term monitoring or self-estimation will achieve lower values than occasional readings by another person.[1]

At medical examinations insurance companies will accept a single reading of 140/90 mm Hg, but if higher than that they ask for further readings, usually after five and ten-minute intervals and occasionally, if the desired level has not been achieved, further readings on another day. However it is now believed that even a blood pressure of over 120/80 mm Hg may be abnormal.[2]

The effect of short-term rest when an initial value of 140/90 mm Hg has been found is not requested, so this study was undertaken to quantify any change after ten minutes' rest. The subjects were all recumbent and a standard mercury sphygmomanometer was used with a sufficiently large cuff for the size of the subject's upper arm and readings taken to the nearest 5 mm Hg. The fifth phase was used for the diastolic pressure. A final check was made on the opposite arm to ensure there was no gross discrepancy between the two sides.

We examined 598 subjects altogether. All those with initial BPs of more than 140/90 mm Hg were rejected; also those on hypotensive therapy and a very few in whom the second BP had inadvertently not been

TABLE 1
Gender, number, ages and BMIs of cohort.

Gender	All cases	Males	Females
Number	390	310 (80%)	80 (20%)
Age (years)			
Mean	43·4	43·9	41·4
SD	10·1	10·1	10·0
Range	23–74	24–72	23–74
BMI			
Median	25·3	25·4	25·2
Range	17·3–46·0	17·3–46·0	19·1–43·0

recorded. This left 390 subjects with initial BPs of 140/90 mm Hg or less. An analysis of their ages and body mass indexes (BMIs) is shown in Table 1. Reductions in mean BP after ten minutes' rest are shown in Table 2.

One subject showed an increase in BP after ten minutes, easily explained because he allowed his mobile telephone to ring during the examination (and insisted on answering it!). His data have been included in the analysis.

It can be seen that in the 390 subjects, 73% showed a fall in systolic BPs and in the average of the systolic and diastolic BPs but only in 53% of the diastolic BPs. Similar falls are seen for both males and females; all are highly significant ($p < 0{\cdot}001$).

Further analysis has shown no significant relationship between gender between those showing a fall in BP and those that did not (systolic p=0·53, diastolic p=0·79: Chi squared test). There was also no significant association between the ages of those showing a fall in BP and those that did not (systolic p=0·64, diastolic 0·38; two sample t-test).

There was, however, a significant association between the fall in BP and the BMI. Those showing a fall in BP had a significantly lower BMI compared to those whose BP did not fall (systolic: median BMI 25·2 vs 26·6; p=0·008, diastolic: median BMI 25·2 vs 26·2; p=0·021; Mann–Whitney U-test).

Those subjects showing a fall in BP had an average drop of 8·9 mm Hg and 7·1 mm Hg in systolic and diastolic pressure respectively (the fall ranging from 5–20 mm Hg).

We conclude that in subjects with an initial BP of 140/90 mm Hg, nearly three-quarters show a highly significant drop in BP with ten minutes' rest.

It is not known whether this feature has any beneficial effect on eventual prognosis but it might be worth insurance companies asking for repeat BPs in every case and evaluating the long-term outlook over many years.

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CDR PENGELLY
Physician
Altrincham

J MORRIS
Senior Statistician
University Hospital of South Manchester

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TABLE 2
Effect of ten minutes' rest on BP.

Blood pressure type	Subjects & gender subgroups (no.)	Percent showing fall in BP with rest (no.)	Mean BP (SD) and p values			
			Initial reading	After 10 mins' rest	Difference	p value
Systolic	All (390)	73% (284)	130·1 (9·3)	120·5 (9·1)	6·4 (5·9; 7·0)	<0·001
	Males (310)	72% (223)	128·5 (8·7)	122·2 (8·6)	6·3 (5·7; 7.0)	<0·001
	Females (80)	76% (61)	121·0 (8·9)	114·1 (8·4)	6·9 (5·9; 8·1)	<0·001
Diastolic	All (390)	53% (207)	76·8 (7·4)	73·0 (7·5)	3·7 (3·3; 4·2)	<0·001
	Males (310)	52% (163)	77·7 (7·1)	74·0 (7·2)	3·7 (3·2; 4·2)	<0·001
	Females (80)	55% (44)	72·9 (7·4)	69·1 (7·2)	3·8 (2·9; 4·7)	<0·001
Average of systolic and diastolic	All (390)	73% (286)	101·9 (7·5)	96·8 (7·3)	5·1 (4·7; 5·5)	<0·001
	Males (310)	72% (223)	103·1 (7·0)	98·1 (6·9)	5·0 (4·6; 5·5)	<0·001
	Females (80)	79% (63)	97·0 (7·3)	91·6 (6·9)	5·3 (4·4; 6·2)	<0·001

RE: FLUCTUATION IN LEVELS OF BIOCHEMICAL PARAMETERS IN CHOLEDOCHOLITHIASIS

Sir,

When reviewing the biochemical results of a patient with the provisional diagnosis of choledocholithiasis, the question which sometimes arises is whether a fall in the serum alkaline phosphatase signifies spontaneous expulsion and clearance of a common bile duct (CBD) calculus, or whether the biochemical profile has improved in spite of continuing retention of calculi within the CBD.[1] In the event of the former, endoscopic retrograde cholangiopancreatography (ERCP) and its adjunctive therapeutic modalities will no longer be necessary, and the patient spared all attendant complications. In the event of the latter, both modalities will have to be activated to pre-empt potential complications of choledocholithiasis. An estimate of the probability of continuing retention of CBD calculi is afforded by a personal series which has increased since the original publication,[1] and now consists of 88 patients (mean age 82, range 57–99, including 61 females), in whom the diagnosis of choledocholithiasis was validated either by subsequent ERCP or by subsequent choledochlithotomy in 87 instances, or by subsequent magnet resonance cholangiopancreatography (MRCP) in one instance. Among these 88 patients were 16 (none with Mirizzi syndrome) in whom the serum alkaline phosphatase (serum alk phos) spontaneously reverted to the normal range despite continuing retention of CBD calculi. In the latter subgroup, mean age on presentation was 80, and 12 were females. For the purpose of this analysis, concurrent mean levels of each of the biochemical parameters in the rest of the 'hepatic screen' have been documented in association with the mean level of the peak serum alk phos. Reference ranges are documented in parentheses.

Peak serum alk phos: mean value for 16 patients = 244·3 iu/l (25–125), concurrent serum bilirubin: mean value for 16 patients = 39·4 mcmol/l (3–21), concurrent gammaglutamyl transferase (GGT): mean value for 16 patients = 470·9 iu/l (0–50), concurrent aspartate transaminase (AST): mean value for 16 patients = 165·6 iu/l (11–37).

Over a period averaging 36 days (range 3–133) antedating the use of ERCP (15 patients) or the use of MRCP (one patient) for validation of choledocholithiasis, serum alk phos fell to nadir levels, and the mean value of the nadir levels was documented as follows, together with mean values of concurrent biochemical parameters in the 'hepatic screen': alk phos = 86·3 iu/l (all alk phos levels having reverted to the normal range), bilirubin = 10·4 mcmol/l, GGT = 103·6 iu/l, AST = 25·4 iu/l. Prior ultrasonography had detected CBD calculi in only three of these patients, and gall bladder calculi in 11; one other patient had undergone cholecystectomy 11 years previously. A CBD diameter of 6 mm or more was documented by ultrasonography in eight patients, including a CBD diameter of 12·5 mm in the patient with previous cholecystectomy. The diagnostic quality of ultrasonography was suboptimal in two cases, including one in whom poor quality was attributable to pneumobilia.

Notwithstanding conventional wisdom which holds that elevation in the serum alk phos is a cardinal feature of biliary obstruction,[2, 3] this parameter can revert to the normal range in as many as 18% of patients with retained CBD calculi, the most plausible underlying mechanism being disimpaction of a retained CBD calculus.

Decisive validation of the diagnosis of choledocholithiasis was obtained by ERCP in 15 instances; in another case, in whom the diagnosis was established by MRCP, validation by ERCP was vitiated by inability to cannulate the CBD – the patient was subsequently referred to a surgical team, but I was unaware of the outcome at the time of my retirement.

In some of these patients circumstantial evidence of choledocholithiasis is suboptimal, consisting only of ultrasonographic documentation of risk factors such as ascholelithiasis, or indirect evidence of CBD obstruction such as ultrasonographic documentation of biliary dilatation. It is then left to the clinician to 'factor in' the index of clinical suspicion, based on age, and presenting symptoms and signs. In consequence, choledocholithiasis continues to be one of the most intellectually challenging diagnoses in the entire repertoire of clinical medicine.

OMP JOLOBE
NHS Consultant
Tameside General Hospital
Ashton under Lyne

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INVISIBLE OEDEMA

Sir,

It was a busy 'diabolic' clinic and patients with diabetes, obesity or other metabolic disorders streamed in endlessly. By the time it was Mrs F's turn I was keeping up a steady flow of sympathetic noises in response to the litany of complaints and excuses, whilst scanning the notes for weight, body mass index, blood pressure, lipids . . .

'My GP doesn't believe a word of it!' she was saying as her daughter nodded in sad agreement. 'And why not?' I asked, courteously but unenthusiastically. Mrs F was obese and depressed, and was attending for weight management. 'Well, see for yourself,' she said, unapologetically handing over an opened envelope addressed to 'Doctor in Charge, Diabetic Clinic.' It was from her general practitioner. In a curt disbelieving tone, he described how Mrs F had reported to him on a few occasions, complaining of swelling of the hands and face from time to time, which was never present when he saw her. He had referred her to a nephrologist, who had suggested testing for proteinuria and, as this was negative, she had not been offered an appointment.

Somewhat sheepishly, I asked her to recount her symptoms again and as I listened, things fell into place. There were tears in her eyes ('You believe me, doctor!') as I explained that the poorly-understood disturbances in the microcirculation associated with idiopathic oedema were often cyclical, which was perhaps why the swelling had cleared in the time it took to get an appointment at the surgery.

Idiopathic oedema is seen almost exclusively in women. Affected individuals suffer from recurring attacks of oedema of the hands, face, breasts and thighs, abdominal distension and large diurnal fluctuations in body weight of several pounds due to orthostatic retention of sodium and water.[1, 2] Psychological or emotional disturbance is often present along with an obsessive desire to lose weight. The diagnosis is made by exclusion of organic diseases such as the nephrotic syndrome, cardiac failure, cirrhosis, hypoalbuminaemia and hypothyroidism.[2] Reductions in plasma volume with secondary activation of the renin-angiotensin-aldosterone system and impaired suppression of vasopressin release have been implicated.[3, 4] Some cases appear to be diuretic-induced, salt-retaining mechanisms overcompensating for chronic blood volume depletion.[5] Salt-restriction, rest in the supine position at regular intervals, and wearing of elastic stockings may reduce symptoms. Diuretics are best avoided.

To be sceptical of the weird and the wonderful is second nature to us doctors. However, it has been aptly said that 'what the mind does not know, the eye does not see'. For once I felt grateful to the college for those meaningless 'grey cases' in the membership examination!

AA SYED
Specialist Registrar
University of Newcastle, Department of Diabetes & Endocrinology, Queen Elizabeth Hospital, Gateshead

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ALLOPURINOL INDUCED DIABETES MELLITUS

Sir,

A long way down the list of side-effects of allopurinol is mentioned diabetes mellitus. It is so far down that when I developed diabetes after taking allopurinol 300 mgms a day for six months, not one of the five doctors in my GPs practice or two consultant rheumatologists had heard of it, and a consultant endocrinologist had his doubts as to its existence. A telephone call to two suppliers of the drug produced no references to confirm the existence of the condition.

In April my plasma glucose was 9·7 mmols/L, and my HbAc1 was 8·7%: irrefutable evidence of diabetes mellitus. I promptly discontinued the allopurinol. Six weeks later my plasma glucose was 6·2 mmols/L (now 5·2), and my HbAc1 6·6%. My blood cholesterol, which had been raised, returned to normal. The weight loss that I had been suffering and the polyuria both disappeared; this improvement without any attempt at treatment with either diet or drugs.

An oral fasting blood sugar test peaked at 10·2 mmols/litre (a little high, but not in the diabetic range), and an abdominal ultrasound investigation revealed no evidence of pancreatic pathology.

The picture could be confused by the fact that I have taken a thiazide diuretic for 20 years, but I did not discontinue this drug during the period of improvement in plasma glucose levels, and leaving it off and restarting since has made no difference to the blood sugar.

It looks, therefore, as if I developed an almost unknown complication of allopurinol, which was only recognised by my insistence that it existed. But allopurinol has been available for 40 years worldwide, and gout and diabetes being both common and co-existent must mean that thousands of people, receiving allopurinol, have developed diabetes. I wonder in how many cases their physicians considered that allopurinol might be the link?

The matter is of more than academic interest as allopurinol can be replaced by a uricosuric drug thus encouraging an alleviation or even remission of the diabetes. In this connection, I should say that I have no connection with any pharmaceutical company. There

seems to be no doubt that allopurinol affects glucose metabolism, though the literature appears very sparse.

AC GIBSON
Woking

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