

RESEARCH

What is the cost of delayed diagnosis of bile acid malabsorption and bile acid diarrhoea?

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ABSTRACT

Introduction ⁷⁵Selenium taurocholic acid (SeHCAT) scanning diagnoses bile acid malabsorption/bile acid diarrhoea (BAM/BAD) and defines optimal treatment. Approximately 2% of the population have BAM/BAD.

Aim To evaluate the cost of delayed diagnosis of BAM/BAD.

Methods Patients' notes who underwent SeHCAT scanning in three hospitals over a 1-year period were reviewed retrospectively. Scan results and treatment response were recorded. Package-of-care costs were calculated using costing tools from the National Institute for Health and Care Excellence and from United Lincolnshire Hospitals Trust business unit.

Results Between June 2016 and May 2017, 19 men and 37 women (median age 58 (range 19–83)) of 3860 new patients seen in gastroenterology clinics were referred for SeHCAT scanning. Sixty-four per cent of scans were abnormal: 13 demonstrated severe (<5% 7-day SeHCAT retention), 13 moderate (5%–10%), 5 mild (10%–15%) and 5 borderline (15%–20%) BAD/BAM. Likely causes included primary BAD (n=16), cholecystectomy (n=13), inflammatory bowel disease (n=4) and other (n=3). If SeHCAT scanning was ordered at first consultation (n=11), patients reported 24 months (median) of symptoms (range 6–360) and the median diagnostic package-of-care cost was £811.40 (95% CI £625.59 to £1508.20). If SeHCAT scanning was booked later (n=25), patients reported symptoms for 30 months (median, range 0.5–360) and the cost was £1568.31 (95% CI £1200.55 to £1713.18). Following diagnosis, treatment led to symptom improvement (n=24), no change/deterioration (n=3) and not reported (n=9).

Conclusions SeHCAT is underused. Late diagnosis leads to unnecessary demands for other services and treatment delay. Early

Significance of this study

What is already known on this topic

- ▶ Bile acid malabsorption/bile acid diarrhoea is often misdiagnosed as irritable bowel syndrome with 44% of patients having to tolerate their symptoms for 5 years before the correct diagnosis being made.

What this study adds

- ▶ The diagnostic ⁷⁵selenium taurocholic acid (SeHCAT) test remains enormously underused. Late diagnosis leads to unnecessary demands for other services which cost more than £750 per patient. Early diagnosis achieves health benefits while reducing costs.

How might it impact on clinical practice in the foreseeable future

- ▶ Use of the SeHCAT scan early in the diagnostic process for patients with appropriate symptoms will save many unnecessary endoscopic procedures, reducing waiting lists and significantly cut the number of patients who need to be seen in gastrointestinal clinics in secondary care.

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INTRODUCTION

Bile acid malabsorption (BAM) and bile acid diarrhoea (BAD) are two conditions characterised by symptoms which invariably include episodes of loose stool, but also can cause bowel frequency, urgency of defecation, faecal incontinence, nocturnal defecation, abdominal bloating, pain and steatorrhoea.¹

Bile acids are released from the gall bladder into the duodenum following the



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dietary intake of long-chain fatty acids, aromatic-aliphatic amino acids and intact proteins.² BAM occurs because of defective absorption in the terminal ileum due to ileal disease, mucosal dysfunction or surgical resection. BAD describes a syndrome characterised by the same symptoms (ie, not just diarrhoea) and is due to impaired FGF19 feedback inhibition by a non-diseased, intact ileum, resulting in excessive bile acid synthesis by the liver, overwhelming ileal absorptive capacity and resulting in excessive bile salts reaching the colon.³

Both conditions can be accurately diagnosed using a ⁷⁵selenium taurocholic acid (SeHCAT) scan by any nuclear medicine department with a gamma camera. This test has a sensitivity of 89%–97% and a specificity of close to 100% for the diagnosis of BAM/BAD.^{4,5} The severity of the BAM/BAD as assessed by the SeHCAT scan has also been shown to be useful at determining optimal treatment¹ with either low-fat diet or bile acid sequestrants or both which have been shown to lead to excellent symptom control.^{1,6,7} When SeHCAT is not available an alternative diagnostic test is 7 α -hydroxy-4-cholesten-3-one.⁸ Recent guidelines suggest that an empirical trial of a bile acid sequestrant should be avoided.⁸

Primary BAD affects approximately 1% of the British population, and is often misdiagnosed as functional diarrhoea or diarrhoea-predominant irritable bowel syndrome (IBS-D).⁹ Indeed, studies suggest 25%–33% of patients confidently diagnosed with IBS-D in fact have underlying primary BAD.^{10,11} There is a further large but as yet unquantified number of individuals who develop secondary BAM/BAD as a result of active Crohn's disease,¹² diabetes mellitus,¹³ cancer chemotherapy or radiotherapy,^{14–17} or following gastrointestinal surgery such as gastrectomy,^{12,18} cholecystectomy,¹² pancreatic resection¹⁸ and ileal resection or right hemicolectomy.^{19,20} Failure to make the correct diagnosis has huge implications for patient outcomes and leads to additional and unnecessary tests, ineffective prescribed treatments and dysfunctional clinical consultations.

The aim of our study was to identify whether delayed diagnosis of BAM/BAD had any cost implications and the effect on patients.

METHODS

The notes of all patients undergoing SeHCAT scanning in our trust over a 1-year period were reviewed retrospectively. The number of abnormal scans and patient response to treatment was recorded. Costs of additional clinics/tests/procedures performed before the diagnosis of BAM were calculated using the National Institute for Health and Care Excellence costing tools published from 2013 onwards (table 1) and from the business unit at United Lincolnshire Hospitals Trust. The cost of any prescribed treatments, however, was not included.

Table 1 Costs used from figures provided by United Lincolnshire Hospitals Trust and NICE costing tools

Appointment costs	
Gastroenterology new patient appointment	181.00
Gastroenterology follow-up patient appointment	72.00
Procedure costs	
SeHCAT scan	381.00
MRI scan with contrast	284.00
Ultrasound abdomen	77.61
CT scan abdomen and pelvis	172.00
Diagnostic upper GI endoscopy with biopsy	323.42
Flexible sigmoidoscopy with biopsy	365.59
Colonoscopy with biopsy	544.45
Hydrogen breath test	48.23
Blood tests/stool samples	
Full blood count	3.04
ESR	3.04
U&Es	3.88
LFTs	4.85
CRP	1.60
TFTs	1.60
Vitamin B ₁₂ , folate and ferritin	8.61
Vitamin D	17.00
Coeliac screen	1.60
Folate	8.61
Gut hormones	70.00
Faecal calprotectin	22.79
Faecal elastase	22.79
Stool for microbiology culture	7.49

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; LFT, liver function test; NICE, National Institute for Health and Care Excellence; SeHCAT, ⁷⁵selenium taurocholic acid; TFT, thyroid function test; U&E, urea & electrolytes.

The SeHCAT studies were undertaken using an uncollimated gamma camera. The SeHCAT capsule was administered to the patient and then 4 hours later, an anterior and posterior 5 min count (background corrected) was acquired. A second count was performed 7 days later and the percentage retention for the patient was calculated. Patients' response to treatment was assessed from information recorded in the clinic letters and hospital notes after the SeHCAT scan had been performed.

RESULTS

A total of 3860 new patients were seen in the gastroenterology clinics in our trust which comprises three different hospitals between June 2016 and May 2017. Of these, 1.5% (19 men and 37 women, median age 58 (range 19–83)) were referred for SeHCAT scanning. Of these scans, 64% were abnormal: 13 demonstrated severe (<5% 7-day SeHCAT retention), 13 moderate (5%–10%), 5 mild (10%–15%) and 5 borderline (15%–20%) BAM/BAD. Underlying causes for BAM/BAD included primary BAD (n=16), cholecystectomy

(n=13), inflammatory bowel disease (n=4), right hemicolectomy for bowel cancer (n=1), diabetes mellitus (n=1) and multiple possible causes (n=1).

If SeHCAT scanning was ordered at first consultation (n=11), patients reported 24 months (median) of symptoms (95% CI 6 to 360) and the median diagnostic package-of-care cost was £811.40 (95% CI £625.59 to £1508.20). Additional findings were found in four of these patients: diverticulosis (n=2), oesophagitis (n=1), adenomatous polyps (n=1) and duodenal diverticulum (n=1). If the SeHCAT scan was booked second line or later (n=25), patients reported symptoms for 30 months (median, 95% CI 3 to 240) and median diagnostic package-of-care cost was £1568.31 (95% CI £1200.55 to £1713.18). However, in these 25 patients nine additional abnormalities were found: vitamin D deficiency (n=3), diverticulosis (n=2), folate deficiency (n=1), oesophageal dysmotility (n=1), renal cell carcinoma requiring nephrectomy (n=1) and *Helicobacter pylori* gastritis (n=1). Following diagnosis, treatment led to reported symptom improvement (n=24), no change/deterioration (n=3) and not reported (n=9).

Patients with a normal SeHCAT scan were subsequently diagnosed with functional diarrhoea or IBS-D (n=13). Twelve of them were subsequently discharged from outpatient clinics with a satisfactory control of their symptoms using dietary manipulation, loperamide or amitriptyline. One patient with refractory symptoms was referred to the regional tertiary centre. Other diagnoses made included collagenous colitis (n=2), pancreatic insufficiency (n=1) and coeliac disease (n=1). Three patients were lost to follow-up following their negative SeHCAT scan, and no definite diagnosis was made before they were discharged.

DISCUSSION

BAM is a frequently overlooked condition in patients with ongoing episodes of loose stool.⁸ Our study has shown the cost saving benefits of performing tests for BAM/BAD first line with a median saving of more than £750 compared with performing it later on. Our data also suggest that patients who had a positive diagnosis made of BAM/BAD benefitted in terms of symptom improvement.

Gastroenterology departments in UK hospitals are struggling with ever increasing workload. Endoscopy waiting lists are often long. Our study suggests that significant cost savings and reduction in referral for diagnostic tests could be achieved while at the same time gaining improvement in health outcomes. This finding is supported by data from another recent study²¹; however, the size of the financial benefit from early diagnosis has not been estimated before.

Our finding that a positive diagnosis of BAM/BAD leads to improved symptoms in most patients is similar to that reported in at least one other study,²² although others have suggested the efficacy of treatment drops

off over time possibly because some sequestrants are unpalatable.²³ However, this study also suggested that sequestrants are often not given in optimal doses and dietary interventions to treat BAM/BAD which have been shown to be helpful are often not recommended.²⁴

The prompt diagnosis and management of BAM/BAD has a number of positive outcomes for patients. First, a better understanding of BAM/BAD by medical professionals can lead to more useful consultations and greater satisfaction for patients. Second, dietary changes, especially the avoidance of high-fat foods which trigger symptoms, can have long-term health benefits beyond the improvement of gastrointestinal symptoms.²⁵ Third, accurate diagnosis has a positive impact on the mental health of patients suffering from BAM/BAD with significant improvement seen in areas of embarrassment, low self-esteem and feeling nervous leaving home.²⁶

The financial implications of failure to make the diagnosis is enormous. Almost half of patients diagnosed with BAM/BAD have to wait for more than 5 years to be diagnosed and many patients feel that their symptoms are repeatedly dismissed until the diagnosis is made.²⁶ Yet, it has been estimated that a full-time general practitioner sees on average eight patients with IBS-like symptoms a week (one of whom is presenting for the first time)²⁷ and this costs the National Health Service £22 million for these consultations²⁸ and more than £70 million for prescribed treatments for IBS annually.²⁹ In secondary care, outpatient attendances to gastroenterology and colorectal surgery specialties in the UK for patients with IBS account for approximately 7.5% of total outpatient attendances across all specialties, costed at £12 million for 2012–2013, although this is likely to be an underestimate.²⁹ Despite this expenditure, at least 50% of patients will continue to have unresolved symptoms long term.^{30 31} The cost of undiagnosed organic pathology is not restricted to increased healthcare costs alone as the mean number of days lost to work because of IBS-like symptoms lies between 8.5 and 21.6 days per year.³²

One can try to calculate the saving early diagnoses would make for our trust. Approximately 50% of patients seen in gastroenterology clinics have IBS-like symptoms. Of these, one in three have diarrhoea-predominant symptoms (IBS-D) and one in three patients of these have BAD/BAM. So, just in this population who might have primary BAD, in our trust 428 (3860×1/3×1/3) SeHCAT scans should have been requested (according to the current guidelines), and more than 140 would have been positive. Early diagnosis would therefore likely have saved more than £100 000. If you add to this number, patients with IBS who have alternating diarrhoea and constipation some of whom will have BAD/BAM and other patients with secondary BAM/BAD, the savings would be considerably more.

While our study was performed in just one trust, the numbers of scans used in our trust are not particularly different from what is happening in many other trusts and the patient population in whom the scans are requested is also similar: fewer than half the scans were in patients with IBS-D.^{9 33} National figures suggest that >25 000 patients with IBS-D are seen as new patients in secondary care annually,¹⁰ yet SeHCAT usage in England, approximately 11 500 SeHCAT capsules sold in 2016 (data provided by the manufacturer, personal communication), suggests that this test remains significantly underused across the country. So it seems reasonable to suggest that early use of SeHCAT could equate to savings across all 135 non-specialist acute trusts, of the order of more than £13.5 million annually in England.

One limitation of this study is that we did not calculate the costs of treatments patients were prescribed before a positive diagnosis of BAM/BAD was made. However, given the average length of time patients waited before diagnosis, it is likely that the treatments they trialled would have significantly increased the costs in those diagnosed in tests performed second line or later.

A second limitation is that we do not know how many patients were treated in our trust with empirical bile acid sequestrants rather than undergoing a formal diagnostic test. Formal testing is now the diagnostic approach recommended.⁸ This seems entirely reasonable as it has become clearer that empirical therapy does not always give clear-cut results,³⁴ and this may contribute to the large group of patients with BAM/BAD who have had their diagnosis missed repeatedly, the so-called 'revolving door' effect where people with IBS-like symptoms have repeated referrals and investigations but do not respond to treatments offered.²⁶

CONCLUSION

In our trust, SeHCAT scanning is underused. Late diagnosis of BAM/BAD is associated with markedly increased costs, unnecessary demands for other services and treatment delay for patients. It is likely that that our findings are applicable across the UK. More emphasis to ensure early diagnosis of BAM/BAD, a frequent, unpleasant and treatable condition would bring the unusual but highly desirable result of significant health benefits while substantially reducing healthcare costs.

Contributors DCRF and DP helped develop the study concept, collected and analysed the data, wrote the first draft of the manuscript and approved the final version. LLW conceived and develop the study, identified the patients, contributed to the first draft of the manuscript and approved the final version. HJNA conceived and developed the study, contributed to all versions of the manuscript, edited the manuscript and is the study guarantor.

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Competing interests HJNA has received honoraria as a speaker and consultant for GE (manufacturer of SeHCAT) and Sanofi Aventis/Genzyme (manufacturers of colesevelam)

Patient consent Not required.

Ethics approval This study was approved by the audit committee for our trust.

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