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A positive SeHCAT test results in fewer subsequent investigations in patients with chronic diarrhoea

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Abbreviations: BA, bile acid; BAD, bile acid diarrhoea; PBAD, primary bile acid diarrhoea; SeHCAT, ^{75}Se-homocholic acid taurine.

ABSTRACT

Chronic diarrhoea is a common condition, resulting from a number of different disorders. Bile acid diarrhoea, occurring in about a third of these patients, is often undiagnosed. We hypothesised that a positive diagnosis of BAD would reduce the need for subsequent investigations for alternative diagnoses.

Methods: Patients previously recruited to a study of chronic diarrhoea who had SeHCAT testing and subsequent follow-up at our institution were identified. In a retrospective analysis, the numbers of defined investigations undertaken from the first three months after SeHCAT in the following 5 years were compared.

Results: 90 patients were identified with primary bile acid diarrhoea (SeHCAT retention <15%, n=36) or idiopathic diarrhoea (SeHCAT retention >15%, n=54). Follow-up had been performed on 29 and 39 subjects respectively, with no differences in previous investigations or the last contact date. In the follow-up period, the proportions of these patients who had undergone endoscopic procedures (gastroscopy, colonoscopy, sigmoidoscopy) were the same. However, there was a higher proportion of patients in the SeHCAT-negative group who had undergone other investigations, including imaging, physiological tests and blood tests (p=0.037). Use of cross-sectional imaging was significantly higher in this group (p=0.015) with greater proportions of subjects having CT (0.44 vs. 0.10) and MRI (0.26 vs. 0.07). Ultrasound use and the number of blood tests were also higher in the SeHCAT-negative group whereas the SeHCAT-positive group attended more clinic appointments (p=0.013).

Conclusion: A positive diagnosis of bile acid diarrhoea, made by a SeHCAT test, resulted in reduced use of diagnostic investigations over the subsequent five years.

INTRODUCTION

Chronic diarrhoea is a common presenting problem in primary and secondary care in the UK and elsewhere. After conditions including inflammatory bowel disease (ulcerative colitis and Crohn's), microscopic colitis, coeliac disease and colonic neoplasia have been excluded, many patients are told they have functional causes for the diarrhoea.[1] Functional chronic diarrhoea and irritable bowel syndrome (IBS) with diarrhoea are overlapping condition and estimates suggest 3% of the population may suffer from these.

It has been shown in multiple studies that around 25-33% of these people with functional chronic diarrhoea have primary bile acid diarrhoea (PBAD), also known as idiopathic bile acid malabsorption (BAM).[2,3] Diagnostic methods have been reviewed recently.[4] The SeHCAT test uses tauroselcholic [5] acid (SeHCAT) to identify excessive faecal bile acid loss by measuring whole body retention of radio-labelled ^{75}Se by gamma camera at 7 days. Retention values between 10 and 15% indicate mild bile acid loss, those between 5 and 10% moderate, and less than 5% indicating severe loss. Patients with PBAD will usually show a response to bile acid sequestrants such as colestyramine or colesevelam.[6] Alternative diagnostic methods include measurement in blood of a bile acid precursor, 7α-OH-4-cholestenone (C4), faecal bile acid quantification or a therapeutic trial of treatment.

Clear recognition and quantification of the excessive bile acid loss in PBAD enables the therapeutic options to be refined and modified so that optimal individualised patient responses can be obtained.[7,8] Although such expert opinion recognises the value of SeHCAT testing in clinical practice, an economic review for NICE in 2012 found there was insufficient data for clear conclusions to be drawn.[9] Guidelines for the investigation of chronic diarrhoea are in need of updating [10] and recent patient-reported symptoms and outcomes suggests many patients suffer for over 5 years as clinician awareness of appropriate diagnostic methods is not widespread.[11]

A potential benefit of a timely diagnosis of PBAD is that this could result in fewer investigations being performed to look for possible alternative diagnoses. This has not been assessed previously. We hypothesised there would be a lower subsequent use of investigations in patients who had a positive SeHCAT result. The aim of this study was to provide initial data on the use of investigations following a SeHCAT test to help in the evaluation of any economic benefit of an abnormal SeHCAT test.

METHODS

Patient groups

We previously recruited patients with chronic diarrhoea to a prospective study of chronic diarrhoea between January 2009 and July 2010.[12] They had all had SeHCAT testing and subsequent follow-up at our institution as part of a study approved by the Research Ethics Committee of Hammersmith and Queen Charlottes & Chelsea hospitals. Their clinical features have been described before.[12] We have now retrospectively analysed the investigations they had at the time of diagnosis and subsequently.

Two cohorts of patients were studied. The group with bile acid diarrhoea had a SeHCAT 7-day retention value of <15% ("SeHCAT positive"). Only those with PBAD were included; patients with secondary causes including Crohn's disease, ileal resection or post-cholecystectomy diarrhoea were excluded. The second group of idiopathic chronic diarrhoea ("SeHCAT negative") had a SeHCAT 7-day retention >15%. The cohorts were then restricted to those who had continued to be seen in any department of our healthcare trust for 5 years from the date of their SeHCAT investigation.

Investigations

Electronic medical records were searched systematically to identify the number, type and indication for defined pertinent investigations in all patients in the cohort. This included clinical correspondence, outpatient appointment, endoscopy, radiology, physiology and pathology report databases. Any overlap was accounted for.

Investigations undertaken for 5 years from the date of the SeHCAT scan in all patients were identified. Tests carried out within 3 months of the SeHCAT test date were analysed separately, as they were likely to have been ordered before the SeHCAT result was known. Any investigations undertaken after the 5-year follow-up period were not included.

All investigations performed for a gastro-intestinal condition, or relevant symptoms, were counted. These included: gastroscopy, colonoscopy, flexible sigmoidoscopy, ERCP, capsule endoscopy, CT, MRI, PET, US, abdominal X-ray, glucose- and lactose-hydrogen breath testing. All blood tests were recorded. Out-patient visits were identified, but only gastroenterology appointments following the SeHCAT result appointment were counted in order to assess the impact on subsequent follow-up.

Analysis

The number of specific and pooled investigations per patient and per group was compared between the two groups. Median numbers of investigations were compared by non-parametric Mann-Whitney U-tests and the proportions per group by Fisher's exact test. A *p* value of 0.05 was taken as significant.

RESULTS

A total of 114 patients from the previous study were seen at our institution and of these, 90 patients were identified with possible primary bile acid diarrhoea (SeHCAT <15%, n=36) or idiopathic diarrhoea (SeHCAT >15%, n=54). Follow-up date was available on 29 "SeHCAT-positive" and 39 "SeHCAT-negative" patients respectively (Table 1). There was no difference between these groups in the date of the last contact in our institution or the length of follow-up. Two patient included in the SeHCAT-negative group had died from unrelated conditions. The clinical features of the two groups did not differ from those we described before.[12] Endoscopic and other investigations were performed in similar proportions before the SeHCAT test (Table 1). There was also no difference in the number of these investigations performed in the 3 months immediately following the SeHCAT test (Table 2), which could have been ordered as part of the initial evaluation of diarrhoea.

Investigations

In the 5-year follow-up period, there was no significant difference in the proportion of patients who had undergone endoscopic procedures including gastroscopy, colonoscopy, flexible sigmoidoscopy, capsule enteroscopy and ERCP (Table 3). However, there were statistically significant greater proportions of the SeHCAT-negative group who underwent investigations when all imaging (CT, MRI, US), physiological tests and blood tests were analysed (p=0.037). Use of cross-sectional imaging (abdominal CT and MRI) was particularly higher in the SeHCAT-negative group (p=0.018). US use did not differ significantly. Six patients (five SeHCAT-negative, one SeHCAT-positive) had both CT and MRI.

More blood tests had been undertaken in the SeHCAT-negative group compared to the SeHCAT-positive group. This did not reach significance (p=0.085). However, the SeHCAT-negative patients had fewer gastroenterology out-patient clinic appointments than the SeHCAT-positive patients during the 5 year period of follow-up (p=0.013). As expected, the SeHCAT-negative patients had greater variability in both number of blood tests and in follow-up appointments.

DISCUSSION

This study has been performed to give initial data regarding how a positive diagnosis of primary BAD, made by SeHCAT testing, influences subsequent use of investigations over a 5-year period in a cohort of patients presenting with chronic diarrhoea. The greatest difference found was in the use of cross-sectional abdominal imaging by CT and MRI.

There are many causes of chronic diarrhoea, with primary BAD being found in a large proportion – 36% in the prospective series which included the patients studied here.[12] The diagnosis can be made by SeHCAT scanning in a relatively simple, non-invasive procedure, which gives a greater proportion of positive results than other, less proven tests.[4] Patients value having the correct diagnosis made in a timely fashion; almost half of those in a recent survey had waited for more than 5 years and felt that their symptoms had been dismissed before they were diagnosed with PBAD.[11] Treatment with bile acid sequestrants is effective in a majority, as demonstrated in 75% of these patients in our previous publication.[12] There are clearly patient benefits in being diagnosed in a timely manner. We have shown that there are also likely to be economic and organisational benefits in the usage of other diagnostic resources.

The use of endoscopic procedures to rule out important causes of chronic diarrhoea such as colorectal cancer and inflammatory bowel disease was similar in both groups. The BSG guidelines from 2003 [10] are currently undergoing revision and are expected to place the exclusion of these diseases as a high priority. Our data indicates that exclusion of BAD by SeHCAT will result in less use of cross-sectional imaging by CT and/or MRI. These are usually performed to exclude possible chronic pancreatic disease or small bowel pathology, not found on endoscopy or ruled out by other tests. The yield of these tests in our series of patients was very low but they are still likely to be performed if no definite diagnosis has been made in a symptomatic patient. Further tests will also be performed in the minority (25%) of SeHCAT patients who do not experience a satisfactory, full response to bile acid sequestrants.[12]

These results provide some data to help in the assessment of the economic benefits of diagnosing PBAD. We can assume that the SeHCAT-positive patients, had they not been diagnosed, would have had the same utilisation of other tests as the SeHCAT-negative patients. Using the difference in proportions undergoing these tests and their NHS unbundled tariffs,[13] net savings per patient would

be: from CT (0.34x£135=£46), MRI (0.19x£240=£46) and US (0.17x£56=£10) = £102. There would be further saving from the costs of blood tests. A more detailed study is needed to assess fully the economic benefits of potential improvements in the quality of life, including any reduction in primary care visits, as opposed to treatment and follow-up costs, and the cost of SeHCAT, in making the diagnosis of PBAD.

There are several limitations to our study. The size of the cohorts is not large, which has limited the power to detect significant differences. The analysis of these investigations has been performed retrospectively and we did not follow any specific defined protocols for further investigation or treatment but left these to the clinical judgment of the referring clinician. Although we have 5-year follow-up data on subsequent investigations, we cannot be certain that the patients have not attended other hospitals for investigations. However, as there were more out-patient attendances in the SeHCAT-positive group, but more investigations in the SeHCAT-negative group, this difference is likely to be greater if further investigations had been performed elsewhere. Furthermore, the greater number of out-patient attendances in the SeHCAT-positive group likely results from continued follow-up of these patients for potential therapeutic research and so may not be generalizable.

In conclusion, this study has shown that in a cohort of patients with chronic diarrhoea, there is a lower usage of other investigations in those with a diagnosis of PBAD in the five years after a SeHCAT test. This provides additional data to support measures to increase the awareness of bile acid diarrhoea and the benefits of making a positive diagnosis.

Table 1: Patient details and investigations performed before SeHCAT testing

	SeHCAT positive (<15%)		SeHCAT-negative (>15%)	
	Number	Tests/patient	Number	Tests/patient
No. of patients				
Diagnosed	36		54	
With 5 year follow up	29		39	
SeHCAT (7-day % retention)				
Mean	9.0		33.9	
Minimum	3.0		15.6	
Maximum	14.4		90.0	
Investigations before SeHCAT				
Endoscopy				
Colonoscopy	16	0.55	20	0.51
Flexible sigmoidoscopy	6	0.21	7	0.18
Gastroscopy	8	0.28	12	0.31
Physiology				
Glucose hydrogen-breath test	2	0.07	4	0.10
Lactose hydrogen-breath test	7	0.24	3	0.08

Data are shown as proportions of the patients in each group with 5-year follow up.

Table 2: Investigations performed in the 3 months after SeHCAT testing

	SeHCAT positive (<15%)		SeHCAT-negative (>15%)	
	Number	Tests/patient	Number	Tests/patient
No. of patients	29		39	
Endoscopy				
Colonoscopy	5	0.17	8	0.21
Flexible sigmoidoscopy	0	0.00	0	0.00
Gastroscopy	4	0.14	2	0.05
Physiology				
Glucose hydrogen-breath test	0	0.00	3	0.08
Lactose hydrogen-breath test	8	0.28	8	0.21

Table 3: Investigations performed between 3 months and 5 years after SeHCAT testing

	SeHCAT positive (<15%)		SeHCAT-negative (>15%)		
	Number	Tests/patient	Number	Tests/patient	
No. of patients	29		39		
Endoscopy					
Colonoscopy	6	0.21	7	0.18	
Flexible sigmoidoscopy	0	0.00	4	0.10	
Gastroscopy	6	0.21	4	0.10	
Imaging					
CT	3	0.10	17	0.44	[a]
MRI	2	0.07	10	0.26	
CT or MRI	5	0.17	27	0.70	[b]
US	16	0.55	28	0.72	
Abdo X-ray	9	0.31	15	0.38	
Physiology					
Glucose hydrogen-breath test	1	0.03	2	0.05	
Lactose hydrogen-breath test	0	0.00	3	0.08	
Other investigations	3	0.10	5	0.13	
Blood tests /patient					
Median		21		33	[c]
IQR		4-37		12-77	
Out-patient clinic visits /patient					
Median		4		1	[d]
IQR		2-8		0-6	

[a] p= 0.045; [b] p=0.015 two tailed Fisher's exact test. [c] p=0.086; [d] p=0.013; Mann-Whitney U-test.

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