TESTS FOR MALABSORPTION

INTRODUCTION

In the assessment of patients with possible malabsorption, a wide variety of tests is available[1,2]. As a baseline, the estimation of full blood count, ESR, haematinics in the form of folate, B12 and iron status and serum albumin with serum calcium, phosphate and magnesium is routine. Liver and renal function tests and faecal microbiological assessment are indicated in some patients. Oesophagogastroduodenoscopy with small bowel biopsy for histology is very useful and enteroscopy with or without biopsy may have an increasing role. Small bowel and pancreatic radiology can also help to define much pathology.

The role of specific biochemical tests to assess function is discussed below. With all the tests, it is important to separate out tests which are performed for clinical reasons and those for research. In general, the tests which only have a research role are not discussed further.

TESTS FOR FAT MALABSORPTION

Every clinical gastroenterologist should have access to a test for fat malabsorption, particularly to assess patients with malabsorption who are proving difficult to diagnose. Either the ^{14}C-triolein breath test or faecal fat measurement should be available. The ^{14}C-triolein breath test can be useful to make a diagnosis of steatorrhoea in patients with difficult diarrhoea[3]. It has also been used to monitor pancreatic fat malabsorption. Its problems are that it gives a qualitative rather than a quantative result even if the area under the curve is assessed. Most laboratories sample the CO_2 for only six hours and, as the peak is between 5-7 hours, this is probably not long enough. There is also a problem with using an assumed CO_2 output in the calculation since measured values can vary widely from this value.

Although they tend to be offensive for the patients, ward and biochemical laboratory staff concerned, the assessment of faecal fats still has its advocates[4]. Ideally, a 70g fat diet should be taken for six days with isotopic or radio-opaque markers. Collection must be careful and methods for measurement uniform. Misleading results — especially false negative results — occur because of incomplete stool collection, uncontrolled fat intake and poor analytical performance.

The faecal microscopy and the butterfat tests are thought to be of very dubious value. Faecal microscopy has been poorly validated and tends to miss mild degrees of steatorrhoea. The butterfat test does not discriminate minor changes, has variable peak times because of variable absorption and, whatever metabolite is measured, it is associated with small peaks.

TESTS FOR PANCREATIC MALABSORPTION

Non-invasive pancreatic function tests include the pancreolauryl and para-amino benzoic acid (PABA) tests[5]. The pancreolauryl tests require the avoidance of Vitamin B and some drugs, and two consecutive day 10 hour urine collections. There is a kit and it is analytically very easy to perform. As it has been well standardised, it has advantages. The PABA test should be reported as a urinary PABA excretion index by coadministration of p-aminosalicyclic acid or ^{14}C-PABA. The PABA test has variable reference ranges at different hospitals with the lower limit of normal being accepted varying between 55-75%. Both these tests were thought acceptable as screening tests for pancreatic exocrine insufficiency. The faecal chymotrypsin level can be done with kits on random sample stools but its value is less well established.

The invasive tests (i.e. the secretin-cholecystokinin test and the Lundh test)[6]

are being used little and seem most appropriate to research.

SUGAR TESTS

Sugar tests are not widely done as a screen for malabsorption in the UK. It is thought that the various forms of the xylose test are no longer appropriate. The cellobiose/mannitol, lactulose/mannitol, lactulose/rhamnose and radio-labelled EDTA/rhamnose tests are sensitive for small bowel disease and useful screening tests for small intestinal function but would seem to fall more into the realms of research rather than routine clinical biochemistry[7].

DISACCHARIDASE MALABSORPTION

The lactose breath hydrogen test with a long fast and careful oral hygiene is an inexpensive and sensitive test[8]. Lactose tolerance tests give very variable results and cannot be recommended. There are advantages to looking simply at the clinical response to reduced lactose in the diet.

The measurement of disaccharidases, usually lactase, maltase and sucrase, is of limited use because of high coefficients of variation[9]. Standard assays should be performed with internal normal ranges. They have a role in diagnosing lactase deficiency and limited use for monitoring disaccharidase deficiencies in coeliac disease.

TESTS FOR LAXATIVE ABUSE

It is important for these tests to be available but there is concern that, when samples are passed between laboratories, numerous positive results are missed. Phenolphthalein can be assessed by faecal or urinary alkalinisation. Magnesium abuse can be excluded by magnesium concentrations of less than 30mmol/L in faecal water and/or faecal osmotic gaps of less than 100. A TLC screen of urine or faeces should be available for phenolphthalein, bisacodyl, sennosides and danthrone[10].

PROTEIN-LOSING ENTEROPATHY

It is reasonable to monitor this with a serum albumin. Measurement of alpha 1-antitrypsin had problems with reference ranges and methods and discriminates rather poorly between active and inactive inflammatory bowel disease. Chromium radiolabelled albumin or alpha-1 antitrypsin excretion are the definitive tests in difficult cases[11].

BILE ACID MALABSORPTION

It is important to make a diagnosis of bile acid malabsorption and the rare idiopathic cases must be searched for. The SeHCAT test with a seven day retention is useful[12] but, if unavailable, a simple assessment of the clinical response of diarrhoea to cholestyramine 4-8gms t.d.s. can be used.

SMALL BOWEL BACTERIAL OVERGROWTH

The aspiration of jejunal contents with anaerobic culture in laboratories specifically set up for these procedures is ideal[13]. The use of lactulose and glucose hydrogen breath tests and the glycocholate breath test are also helpful[14].

TESTS FOR VITAMIN B12 DEFICIENCY

The Schilling, Dicopac or similar tests should continue to be used for measuring the site of Vitamin B12 malabsorption in the stomach, ileum or pancreas[15].

GLIADIN ANTIBODIES FOR COELIAC DISEASE

The endomysial and IgA gliadin antibody tests have 90-95% sensitivity for diagnosing coeliac disease[16]. The predictive value of a positive result is about 50% in high disease frequency groups, emphasising the need to confirm the diagnosis by biopsy. They can be used to follow up coeliac disease to assess the effect of a gluten-free diet.

HORMONE MEASUREMENT

A plasma VIP is essential for diagnosing patients with VIP-secreting tumours in patients with secretory diarrhoea[17]. The measurement of pancreatic polypeptide (PP) is also helpful as it is often co-secreted in patients with pancreatic endocrine tumours[18]. The measurement should be performed in supraregional laboratories as it is difficult and is otherwise likely to lead to unacceptable levels of assay variation.

The measurement of urinary 5-HIAA, plasma gastrin and plasma calcitonin is also indicated in some patients.

ASPECTS OF QUALITY

In an audit for the British Society of Gastroenterology (unpublished), Dr. Duncan has identified some major problems in the performance of these tests. A major case can be made for centralising many of the tests in laboratories where there is particular expertise. The following major problems have been identified:

1. Laboratories in general are using published reference ranges rather than calculating their own from normal populations. It is important that laboratories which are offering the tests rectify this and provide their own normal ranges. Where it is impractical for laboratories to establish reference ranges, it is important that the method used is standardised to the published method by which the reference range was derived. Methods are often not transferable between laboratories. There is a need for clinical biochemists to develop uniform methods and tests.

2. There are wide variations in protocols for tests often between laboratories using the same reference range. It is important that individual laboratories and clinicians rectify this.

3. The quality of the analytical services is sometimes poor. Problems include high intra- and inter-laboratory coefficients of variation, dubious biochemical methods, absence of internal quality control, wrong calculation of results particularly when the tests are rarely used and clerical errors. Individual laboratories again need to audit this carefully.

RECOMMENDATIONS

There is a need for tests for malabsorption. Blood tests should be available for gastroenterologists throughout Britain but it is recommended that some of the tests should be centralised to laboratories with a particular interest. Laboratories should assess their protocols and methods of analysis and, when uniform procedures have been agreed, there should be standard UK reference ranges. It is essential to establish an external quality control scheme. New tests should be evaluated using co-operation between laboratories.

CONCLUSION

Some basic guidelines have been given in an area where it is impossible to be dogmatic. It is inevitable that different workers will have different opinions and problems with emphasis in some areas. These comments are meant as an introduction to a complex subject.

AUTHORSHIP

This guideline was prepared by members of the British Society of Gastroenterology, with valuable assistance from Dr G.M. Addison, Consultant Clinical Biochemist, Royal Manchester Children's Hospital, Dr P. Hill, Consultant Clinical Biochemist, Derbyshire Royal Infirmary and Dr G. Brydon, Clinical Scientist, Western General Hospital, and approved by Council.

We plan that this guideline will be revised from time to time. Comments or suggestions

for use in subsequent editions should be sent to: The Clinical Services and Standards Committee, British Society of Gastroenterology, 3 St Andrews Place, Regent's Park, London NW1 4LB.

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