

Association of Gastrointestinal Physiologists (AGIP) Proposed Standardised Testing Protocol for Hydrogen/Methane Breath Testing (HMBT) to Assess Small Intestinal Bacterial Overgrowth (SIBO) and Carbohydrate Malabsorption

Introduction

Hydrogen and methane gases are not produced by the human body directly but both are produced as a bi-product of microbial fermentation of undigested food within the gut. A proportion of the produced gas passes through the gut wall into the blood and is then excreted via the lungs. Detection of these gases in samples of excreted breath is possible using various techniques and this forms the basis of hydrogen and methane breath testing (HMBT). HMBT is used as a diagnostic tool to detect small intestinal bacterial overgrowth (SIBO) and carbohydrate malabsorption (CM).

Despite HMBT being a well-established diagnostic test (1) it is performed by a broad range of healthcare professionals using various methodologies and the interpretation of the results is inconsistent between centres. This has led to some controversy about the use and interpretation of breath testing in the UK (2, 3). A similar situation was apparent in the North America and to address this a panel of expert Gastroenterologists from the region reviewed the scientific literature and developed a consensus document based on best evidence to try and standardise HMBT methods and, to an extent, interpretation (4).

Following publication of this North American consensus statement, The Association of Gastrointestinal Physiology (AGIP) committee of the British Society of Gastroenterology has reviewed the scientific evidence and proposed the following 'Standardised Testing Protocol' which should act as a starting point to standardise how HMBT is performed in the UK. Once technical standardisation is adopted, this will allow acquired data to be directly comparable across UK HMBT testing centres. This will represent a considerable advancement in the area of HMBT testing, bringing it in line with other modalities of commonly used GI physiological tests. Once data are obtained in a standardised manner, objective outcomes data can be used to further assess the clinical utility of these techniques.

Objective of AGIP guidance

The purpose of this guidance is to provide a standardised methodology for the assessment of HMBT, so that clinical studies can be correctly compared with available literature and interpreted within internationally accepted standards. AGIP encourage the use of these standards within clinical research in order to provide objective evidence of the clinical utility of HMBT.

HMBT Do's and Don'ts

- Breath gas measurement equipment should be regularly calibrated and maintained as per manufacturer's instructions and a log kept of this
- Methane should be measured as well as hydrogen throughout the test. Additional measurement of methane significantly increases the likelihood of a positive result and

reduces the risk of a false negative result. Approximately 20% of patients will be methane producers, and this proportion is further raised in patients with chronic constipation (5)

- A means of assessing quality of breath sample by measurement of oxygen or carbon dioxide levels should be used to confirm the adequacy of the breath sampling

Preparation

Patients should prepare for a HMBT in the following way:

- Antibiotics should be avoided for 4 weeks
- Patients should not have had colonoscopy or any full bowel cleansing preparation, including colonic lavage, for at least 1 week
- Patients should ideally have refrained from motility enhancing drugs or laxatives for a week
- Administration of a suppository prior to testing to ensure recent bowel motion at the time of the test is acceptable
- Patients should refrain from fermentable foods e.g. complex carbohydrates for at least 24 hours. A suggested menu and list of foodstuffs to avoid should be provided for the patient to follow. Only the following foods are permitted during the 12-hour preparatory diet period:
 - Baked or grilled seafood, chicken, turkey, lean beef, or pork
 - Eggs
 - Plain white rice
 - Plain coffee or tea or water
 - Minimal oils for cooking, salt and pepper

All other foods not listed above are not allowed during the 12-hour preparatory diet. Foods such as, but not limited to: alcohol, dairy, beans, wheat, grains, fruits and vegetables, and high-fibre containing foods are not allowed. If patients have special dietary requirements they should contact the Physiology Unit to discuss.

- Patients should fast for 12 hours. Drinking of some water is acceptable in the 12 hours preceding the HMBT
- Patients should not smoke tobacco products or e-cigarettes on the day of the test
- There is no clear guidance on stopping PPI's prior to HMBT, so at present studies can be performed on PPI therapy
- There is no clear guidance on stopping probiotics before breath testing. However, as taking probiotics introduces bacteria into the upper gut we suggest stopping probiotics at least 1-week prior to testing
- Patients should be warned of the potential for increased symptoms resulting from the substances being administered
- Written consent is recommended

Performance of the Investigation

- Assessment for SIBO is recommended before assessment of carbohydrate malabsorption as the presence of SIBO will lead to false positive results for malabsorption testing
- Whilst there are arguments for the use of glucose or lactulose as a first line assessment in SIBO the fact that lactulose will give a full bowel assessment and identify non-hydrogen producers means that we recommend Lactulose in preference to glucose for SIBO

assessment as a first assessment. Glucose is absorbed in the proximal small bowel and therefore is unlikely to provoke a positive breath result in the presence of bacterial colonisation of the distal small bowel. Glucose is highly sensitive if positive and should be used if a lactulose study is equivocal e.g. unable to distinguish between small bowel overgrowth or rapid transit and colonic fermentation (a large rise in gas production in the second half of the study) in the large bowel. Glucose may also be used in patients with short small bowel (for example following bariatric surgery)

- **The recommended dose for lactulose (SIBO assessment) is 10g with or in 300ml water**
- **The recommended dose for glucose (SIBO assessment) is 75g with or in 300ml water**
Rapilsoe OGTT solution is a 300ml solution containing 75g glucose in a ready-to-drink pouch and could be used as the test solution for SIBO assessment
- **The recommended dose for lactose is 25g with or in approximately 300ml water**
- **The recommended dose for fructose is 25g with or in approximately 300ml water**
- Patients may clean their teeth and/ or rinse with a mouth wash prior to baseline breath measurement and following ingestion of the provocation dose, but the toothpaste or mouthwash should not be swallowed and the mouth should be rinsed with water as both products can contain artificial sweetener
- Baseline hydrogen and methane levels prior to ingestion of the provocation dose should be <10ppm. The investigation may still be considered with higher baseline measures if these are stable on multiple measurements
- Breath sampling should be performed at least every 15 minutes for the first 90 minutes of an investigation
- In SIBO studies the investigation should last for at least 2 hours following ingestion. The investigation should then continue until either unequivocal evidence of fermentation of lactulose in the large bowel has been observed or 3 hours has elapsed following ingestion
- Carbohydrate malabsorption studies should continue for at least 3 hours following ingestion
- Patients should refrain from physical activity during the investigation or sleeping
- Baseline symptoms should be recorded before substrate ingestion using a visual analogue scale (0-10) so that the development of symptoms during the test can be accurately recorded

Interpretation of the Investigation

The recent North American Consensus document on breath testing (2) suggests that a rise above the baseline hydrogen level of ≥ 20 ppm of hydrogen within the first 90 minutes following ingestion of the provocation dose (lactulose or glucose) is normally considered positive for assessment of SIBO.

As mentioned earlier, AGIP recommends lactulose as a first line assessment as it will give a full bowel assessment. However, there are concerns that a 90-minute cut off may increase the incidence of false positive results (i.e. the lactulose arriving in the proximal colon within 90-minutes) which could then lead to an increase in inappropriate antibiotic use. Some centres define a shorter time period and use the Ledochowski cut off values of a rise of ≥ 10 ppm within 60-minutes as positive for SIBO (6) which is a more conservative value but conversely increases the risk of a false negative result. Therefore clinical judgement by an experienced Clinician and / or discussion within a multi-disciplinary team should be used with borderline positive results (i.e. a rise seen between 60-90

minutes) and a glucose HMBT could be undertaken to provide more confidence in a SIBO positive diagnosis. Further advice will be given as data emerge in this area in terms of the positive predictive value of cut offs in terms of treatment outcomes.

- A methane level ≥ 10 ppm at baseline or at any point during the test should be considered positive for methanogenesis. As methane may affect transit times it is difficult to say with certainty whether the methanogenic organisms are in the small bowel or colon so no comment on SIBO should be made in the absence of a concomitant rise in hydrogen
- Methane levels are often >10 ppm at baseline despite adherence to the pre-study diet so high baseline methane is not an indication to stop the test and a full study should still be performed with the substrate administered. This is more common in patients with bloating and constipation
- The time from ingestion to the rise in breath levels associated with large bowel fermentation should not be used as a diagnostic tool for estimating small bowel transit. However, it may be used to give some indication of the minimum required time for measurement of subsequent carbohydrate malabsorption studies.
- A rise above the baseline hydrogen or methane level of ≥ 20 ppm of hydrogen or methane at any time during the assessment is considered positive for carbohydrate malabsorption in the absence of SIBO
- In the presence of confounding factors such as partial small bowel resection, gastroparesis or bariatric surgery, clinical judgement should be used to interpret the findings of the HMBT procedure and glucose used as a first line investigation
- A flat-line response may be associated with patients that predominantly produce hydrogen sulphide. Whilst current equipment cannot detect hydrogen sulphide, if a flat line response is seen in patients that predominantly present with diarrhoea and symptoms of mal-odorous flatulence this may be a contributing factor

Preparation and Procedure for Patients who are Diabetic.

Diabetic patients are at risk of poor glycaemic control before and during HMBT due to the challenging requirements of preparation for and undertaking HMBT. The patient preparations and the procedure should be modified following a specific local protocol written for this situation. Such a protocol would be expected to include the following:

- Regular blood sugar sampling should be performed to ensure blood sugar levels are acceptable
- The patient should not be left unaccompanied during this assessment

Further Steps

AGIP would encourage further research and audit to improve the evidence base for HMBT for SIBO and carbohydrate malabsorption, and expect recommendations to change in the light of further evidence. A next logical step would be to establish a UK HMBT user group to gather data and make further recommendations when appropriate AGIP hopes to create a UK HMBT user group imminently to hopefully address some of the concerns surrounding test validity and clinical relevance.

Acknowledgements

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