Idiopathic Malabsorption Syndrome in India Diagnosis, Nutritional Evaluation and Management

V. I. MATHAN

Tropical sprue (idiopathic tropical malabsorption syndrome) is defined as a primary malabsorption syndrome affecting residents of, or visitors to, tropical regions. It must be emphasised that most of the diseases causing secondary malabsorption do occur in tropical countries and the diagnosis of tropical sprue in the individual patient is dependent on the demonstration of malabsorption and the exclusion of secondary malabsorption. The clinical picture of tropical sprue is dominated by diarrhoea and the prevalence of a wide variety of nutritional deficiency syndromes. The assessment of the nutritional status of the patient therefore is an important part of the total clinical evaluation. In the management in addition to measures to specifically cure malabsorption the nutritional deficiency issues have to be corrected.

Epidemiology

Tropical sprue has been reported from many tropical areas, India, most of the South East Asian countries, Central and some areas of South America, and the Caribbean islands. Interestingly in the Caribbean, it does not occur in Jamaica. It is known to occur in Hong Kong, but has not yet been reported from tropical Australia. There are only very few reports from sub-Saharan Africa.

In India, on epidemiological grounds, two types of patients with tropical sprue have been identified. The first endemic tropical sprue, are patients who present for investigation to the clinician who do not have any temporal or spatial association with other such patients. Such patients have been seen all over the Indian subcontinent. However, several epidemics of tropical sprue have been reported from the North Arcot district of Tamil Nadu (formerly Madras State). They have characteristic epidemiological features: the epidemic in any one village takes months or years to evolve; adults are affected earlier and with greater frequency in these epidemics; during the first few days of diarrhoea malabsorption of nutrients can be demonstrated in these patients. Careful analysis of the epidemiological data clearly shows that these epidemics are likely to be due to an infectious agent. However, bacteriological and virological studies up to now have not demonstrated such an agent. The only other epidemics of tropical sprue that have been documented occurred during the second world war in the Burma theatre of war, with British and Indian troops.

Diagnosis

The patients usually complain of diarrhoea which has lasted for months or years. The evolution of various nutritional deficiencies over this period is obvious when a careful and detailed history is taken. Investigations are aimed to establish the presence of malabsorption and to demonstrate a mucosal lesion in the small intestine which is the basis for malabsorption. In addition, investigations have to exclude the different diseases which can give rise to secondary malabsorption syndromes.

Investigations to establish malabsorption

It is theoretically possible to test the absorption of any nutrient to establish malabsorption. Conventionally the absorption of fat, D-xylose and vitamin B₁₂ are tested. Fat and D-xylose absorption reflect damage to the upper small intestinal mucosa while vitamin B₁₂ absorption, when it is abnormal after the addition of intrinsic factor, evaluates the function of the ileum.

Faecal fat excretion: The classical method of van de Kamer et al is still the best way of estimating the faecal fat by saponification. It has been shown by a variety of tests that an exact faecal balance technique is not necessary but if it

*Professor of Medicine & Gastroenterology
Wellcome Research Unit & Department of Gastroenterology, Christian Medical College & Hospital,
Vellore 632 004, India.
is ensured that the patient is maintained on a diet containing approximately 50 grams of fat per day, an excretion of more than 5 grams per day on a three-day-mean-study should be considered steatorrhoea. However, many of the South Asian and South-East Asian population groups have a very low fat intake in their diet, the bulk of the calories being supplied by carbohydrates and possibly faecal fat estimation in such population groups is not of great physiological significance.

D-xylene absorption. The absorption of D-xylene is the most widely used test of intestinal function world wide. Most reports from the western hemisphere use 25 gram doses of D-xylene. Studies in this Unit have confirmed that a 5 gram dose of D-xylene and fractionated urine collection gives very good and reproducible results. Subsequently the test has been further modified and the surface area - corrected 1 hour serum xylose concentration is now used as a good test of absorption of D-xylene. Since D-xylene is a carbohydrate and most of the populations of South and South-East Asia eat mainly carbohydrates, it may be thought that this is a good physiological test. Recent data suggest that the mechanism of absorption of D-xylene is different from that of the absorption of glucose and that the D-xylene absorption test is more likely to be a measure of intestinal surface area than an actual test of active glucose transport measuring carbohydrate absorption.

Vitamin B\textsubscript{12} absorption. The classical Schilling test where the 24 hour urinary excretion of radioactive vitamin B\textsubscript{12} after oral administration, with a simultaneous parenteral injection of a pharmacological dose is the most widely used test. This test was evaluated in the southern Indian population and was found to give rise to 16% of falsely abnormal results. These false malabsorbers occur because, in spite of careful instructions, the completeness of the urine collection cannot be fully guaranteed even in the metabolic ward. The whole body retention technique using a whole body counter can overcome this problem but such counters are not widely available. An alternative method to measure the percent of administered dose in the serum 8 hours after the oral dose has been standardised. Retention of more than 0.2% per litre of plasma, of the oral dose at 8 hours or more is within normal limits. This test was shown to discriminate between absorbers and malabsorbers very clearly.

Is there an alternative good test of intestinal function?

As mentioned above, there are problems with the use of either the faecal fat excretion of D-xylene absorption in assessing the absorption of physiologically important nutrients in the population of South and South-East Asia. Preliminary experiments in this laboratory to study the absorption of nutrient calories by bomb calorimetry of 24 hour faecal collections indicate that this is likely to be a good test discriminating between the normal population and those with malabsorption and is more useful than xylose absorption in detecting malabsorbers. The methodology is simple, the ballastic bomb calometer is not expensive and it is likely that this is the test which would be used in the future.

Other tests such as vitamin A tolerance, folate acid absorption, faecal nitrogen estimation and the absorption of various other nutrients can also be used, but in the clinical situation, the combination of faecal fat estimation, D-xylene absorption and vitamin B\textsubscript{12} absorption, with the possible addition of faecal calorimetry should be able to determine whether a patient has malabsorption or not.

Tests to determine the cause of malabsorption

It is essential when malabsorption has been demonstrated in a patient, to determine whether this is a primary or idiopathic malabsorption syndrome or secondary malabsorption. Some of the tests which can be done by the clinical biochemistry laboratory for such discrimination include the estimation of immunoglobulins, beta lipoproteins and the evaluation of the endocrine peptide hormones related to the gut. However, the careful determination of the primary aetiology of malabsorption is dependent on careful radiology and good histological examination of the jejunal mucosa. The techniques and problems involved in such studies have been reviewed elsewhere.

Nutritional evaluation

Tropical sprue was initially considered a haematological illness because of the widespread prevalence of megaloblastic anaemia associated with vitamin B\textsubscript{12} and folate acid deficiency in these patients. It is only with the wide availability of tests of intestinal absorption that it was recognised that tropical sprue is a primary gastrointestinal illness. At this time it was suggested that the
disease manifesting as a gastrointestinal abnormality with alterations in the small intestinal mucosa could be caused by nutritional deficiency. The epidemiological data on the prevalence of this disease affecting population groups with good nutritional status and poor nutritional status with equal frequency did not support this hypothesis. The prevalence of a variety of nutritional parameters such as glossitis, the presence of Bitot's spots, skin changes and oedema, and objective measurements of nutrients including haemoglobin concentration, serum folate, serum vitamin B₁₂, serum albumin and serum iron concentrations were done in a consecutive series of 400 patients studied in detail at Vellore. The duration of symptoms of these patients was also known. If nutritional deficiency was causal in the syndrome, the prevalence, but not necessarily the severity, of the deficiency states should be similar during the first few days of illness as well as in more chronic patients. The data clearly showed that the prevalence of nutritional deficiency states whether identified clinically or by laboratory parameters increased significantly in patients with increasing duration of illness. This in addition to the epidemiological data clearly suggests that malnutrition is not likely to be the primary cause of idiopathic malabsorption syndrome. The data from the second World War in occupants of concentration and prisoner of war camps also does not suggest that severe malnutrition can give rise to a small intestinal mucosal lesion. In experimental animal situations there are certain extreme conditions where severe protein deficiency appears to produce a mucosal lesion. However a clinical counterpart of this has not yet been clearly identified.

The assessment of the nutritional status of the individual patient is cardinal to planned and proper management of the nutrition of the patient. The assessment is by standard techniques of estimating haemoglobin, serum folate, serum vitamin B₁₂, serum iron, serum albumin and serum protein concentrations. The necessity for good quality control especially for assays such as the vitamin B₁₂ and folate concentration in the serum cannot be over emphasised.

Management of idiopathic malabsorption syndrome

The therapy of these patients is based on three approaches. Since the majority of these patients have diarrhoea, loss of appetite and occasional vomiting, appropriate therapy by simple means has to be given. Mixtures containing kaolin and bismuth have been found to be quite useful. In a few resistant subjects, tincture opium or other drugs such as Lomotil or Imodium may have to be used.

The second aspect of the management is nutritional rehabilitation. The majority of patients are anaemic and hypoproteinaemic. Physiological amounts of vitamin B₁₂, folic acid and iron is very useful for their treatment. For improving their protein nutritional status, a well-balanced nutritional diet appears to be best.

Specific therapy for tropical sprue is not clearly established since the aetiology of the disease is not yet known. In the Caribbean region and in expatriates who develop illness when they visit tropical countries treatment with tetraacycline, folic acid and vitamin B₁₂ in pharmacological doses has been found to be quite useful. However, the experience in India is that while a proportion of untreated patients appear to recover spontaneously, the recovery in patients given tetraacycline, folic acid and B₁₂ was no higher.

Conclusions

Idiopathic tropical malabsorption syndrome also known as tropical sprue is a clinical condition that has been described from many different parts of the tropical world. The epidemiology of this disease shows some interesting features and there is some evidence to suggest that there is a form of this disease known as epidemic tropical sprue which may be caused by an infectious agent. The evaluation of patients involves the determination of intestinal absorptive capacity, determination of the nutritional status and special tests to see whether malabsorption is primary or secondary. Treatment is difficult as there is no specific therapeutic measure and the response to treatment has to be monitored by biochemical tests of intestinal function and nutritional status.

REFERENCES

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