Malabsorption syndrome due to various causes is associated with antroduodenal hypomotility

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Background: Patients with celiac disease who present with symptoms of gastrointestinal hypomotility have abnormal antroduodenal manometry. There are no data on antroduodenal manometry in malabsorption syndrome (MAS) due to causes other than celiac disease.

Methods: Fasting, post-prandial and post-octreotide antroduodenal motility parameters were compared in 18 untreated patients with MAS presenting with chronic diarrhea (tropical sprue 10, small bowel bacterial overgrowth 3, celiac disease 2, common variable immunodeficiency 1, AIDS with isosporidiasis and bacterial overgrowth 1, giardiasis 1) and 8 healthy subjects.

Results: Number of patients with MAS and controls having spontaneous migratory motor complexes (MMC) during fasting was comparable (11/18 vs 7/8; p=ns). Fasting contraction amplitude was weaker in MAS than in controls in the gastric antrum (median 42 [range 17-90] vs 80 [31-120] mmHg; p=0.001), proximal duodenum (50 [18-125] vs 72 [48-107]; p=0.013) and distal duodenum (45 [20-81] vs 76 [51-98]; p=0.001). In the fed state too, contraction amplitudes were weaker in patients with MAS in the antrum (32 [15-110] vs 76 [61-103] mmHg, p=0.002), proximal duodenum (57 [20-177] vs 73 [56-113]; p=0.07) and distal duodenum (45 [24-87] vs 75 [66-97]; p<0.0001). Patients with MAS had lower fasting and post-prandial antral and duodenal motility indices than healthy subjects. Intravenous octreotide induced MMC in all patients and controls.

Conclusions: MAS due to various causes is associated with antroduodenal hypomotility typical of myopathic disorders.

Original Article

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Conclusions: MAS due to various causes is associated with antroduodenal hypomotility typical of myopathic disorders.

Though a few reports from Western countries have described multiple abnormalities in both fasting and fed-state antroduodenal manometry (ADM) in patients with MAS due to celiac disease, most of them had symptoms of gastrointestinal hypomotility instead of chronic small bowel diarrhea. Further, there is no study on ADM in patients with MAS from the tropics, where causes of MAS are heterogeneous. We studied ADM in patients with MAS due to various causes presenting with chronic small bowel diarrhea.

Methods

Eighteen consecutive patients with MAS due to various causes attending the Luminal Gastroenterology Clinic at our tertiary center and agreeing to participate in this study were included. Patients with uncontrolled diabetes mellitus, chronic renal failure or small intestinal stricture on barium small bowel series were excluded. MAS was diagnosed based on clinical presentation, absorption defect of two unrelated substances such as abnormal 5-g D-xylose test (normal ≤1 g/5 g/5 h) and increased fecal fat excretion (normal <7 g/d on 72-h estimation using van de Kamer’s method [n=16] or <10/high power field on Sudan III–stain on spot stool specimen [n=10]). The cause of MAS was investigated using a standard protocol described previously. Eight healthy subjects were studied as controls.

Patients and controls underwent ADM after informed consent. Drugs that may influence gastroduodenal motility and antibiotics were not used within the previous four weeks; none of the patients with MAS received specific treatment before ADM. Our institution’s ethics committee approved the study.

Antroduodenal manometry

ADM was done after an overnight fast using a water-perfusion system and a low-compliance polyvinyl catheter (Redtech, Calabasas, CA, USA). The catheter, with eight sideholes placed 3 cm apart from each other, was passed through the nose without any sedation or anesthesia, over a guidewire, and was positioned under fluoroscopy such that at least two proximal ports were in the antrum and the remaining ports were in the duodenum.

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Fasting motility was recorded for at least 120 min. A meal containing approximately 450 KCal (60% carbohydrate, 15%-20% each of fat and protein) was then given, followed by post-prandial motility recording for at least 90 min. At this stage, 50 μg octreotide (Octride; Sun Pharma, India) was given intravenously over 2-3 min and antroduodenal motility was recorded for at least 30 min.

The signal was visually scanned to remove artifacts (e.g., those due to cough), filtered (9 and 24/min for antral and duodenal frequency limits, respectively), and then analyzed (by UCG) using GiPC motility software (Redtech). In the fasting record, presence of spontaneous migratory motor complex (MMC) and its duration was looked for. Post-prandial record was evaluated for conversion from fasting to fed pattern. Amplitude of contractions in the antrum and proximal and distal duodenum was measured using average of all ports in antrum, proximal two and the remaining ports in duodenum, respectively. MMC in the duodenal ports after octreotide injection were analyzed similarly.

Manometric patterns were defined using established criteria. Motility index (MI) for every 15-minute period during fasting and post-prandial phase was calculated as described previously using the GiPC software. MI in the antrum and proximal and distal duodenum was calculated using average values of all ports in antrum, proximal two and the remaining ports in duodenum, respectively. Average values in the second 15-min period in fasting and post-meal periods were compared between patients and controls.

Statistical analysis

Categorical and continuous variables were analyzed using chi-squared test with Yates’ correction and Mann-Whitney U test, respectively. Alpha value of 0.05 was considered as significant.

Results

Patients with MAS and controls were comparable in age (42 [20-67] vs 33 [26-48] y) and gender distribution (13 vs 8 males). All patients presented with chronic diarrhea. Causes of MAS included tropical sprue (n=10), SIBO (3; systemic lupus erythematosus, peripheral vasculitis and jejunal diverticulae in one each), celiac disease (2), common variable immunodeficiency (1), acquired immunodeficiency syndrome with isosporidiasis and SIBO (1), and giardiasis (1). Median urinary D-xylene excretion, number of fat droplets on Sudan III-stained spot stool specimens and 24-h fecal fat excretion were 0.48 g/5 g/5 h (range: 0.16 to 0.79), 16 (6-35) droplets per high power field, and 8.0 g/24 h (4.8-14.4), respectively. Of the 16 patients in whom fecal fat excretion was estimated quantitatively, four had normal value (<7.0 g/d); however, they had abnormal number of fat droplets on Sudan III staining.

Antroduodenal manometry (Table 1, Fig.)

The median duration of fasting record in patients with MAS and controls was comparable (160 [range 120-186] vs 147 [120-180] min; p=0.94). Spontaneous MMC was observed as frequently in patients as in controls. The duration of spontaneous MMC in the fasting state in patients with MAS and controls was comparable. Fasting contraction amplitude was weaker in MAS than in controls, in the antrum and duodenum. In the fasting state, discrete clustered contraction (DCC) was observed in one patient with MAS (Fig. 1D) and none of the controls.

After meal ingestion, fed pattern was observed in all study subjects except in one patient; this patient showed DCC during the fed state (Fig. 1D). In two other patients, the fed pattern was prematurely interrupted after 25 min and 30 min by DCC and a spontaneous MMC, respectively. In the fed state, contraction amplitude in antrum and duodenum were weaker in MAS.

Table 1: Manometry parameters in patients with malabsorption syndrome (MAS) and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MAS (n=18)</th>
<th>Healthy subjects (n=8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of spontaneous MMC while fasting</td>
<td>11/18</td>
<td>7/8</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of spontaneous MMC (min)</td>
<td>6(2-9)</td>
<td>8(4-12)</td>
<td>0.07</td>
</tr>
<tr>
<td>Fasting antral amplitude (mmHg)</td>
<td>42(17-90)</td>
<td>80(31-120)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting duodenal amplitude (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal Distal</td>
<td>50(18-125)</td>
<td>72(48-107)</td>
<td>0.013</td>
</tr>
<tr>
<td>Conversion to fed pattern after meal</td>
<td>17/18</td>
<td>8/8</td>
<td>ns</td>
</tr>
<tr>
<td>Post-prandial antral amplitude (mmHg)</td>
<td>32(15-110)</td>
<td>76(61-103)</td>
<td>0.002</td>
</tr>
<tr>
<td>Post-prandial duodenal amplitude (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal Distal</td>
<td>58(21-177)</td>
<td>73(56-113)</td>
<td>0.07</td>
</tr>
<tr>
<td>Distal</td>
<td>45(25-87)</td>
<td>75(66-97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset of MMC with octreotide</td>
<td>18/18</td>
<td>8/8</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of post-octreotide MMC (min)</td>
<td>9(2-21)</td>
<td>15(6-17)</td>
<td>0.08</td>
</tr>
<tr>
<td>Amplitude of post-octreotide MMC (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal duodenum Distal duodenum</td>
<td>30(12-76)</td>
<td>63(43-78)</td>
<td>0.003</td>
</tr>
<tr>
<td>Distal duodenum</td>
<td>27(13-59)</td>
<td>64(45-75)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

MMC: Migratory motor complex
Octreotide led to induction of MMC in all patients and controls. The amplitude of octreotide-induced MMC was weaker in patients than in controls though the duration of MMC and frequency of contractions during MMC (median: 10 per min) were comparable. In two patients with MAS and none of the controls the duration of post-octreotide MMC was shorter than 5 min. One patient and no control had retrograde contractions with vomiting during the study.

Both fasting and fed-state motility indices were lower in patients than in controls (Table 2).

**Discussion**

This study shows that patients with MAS due to various causes often have abnormalities of ADM in the form of reduced amplitude of contractions in fasting and post-prandial states both in the antrum and duodenum, and reduced motility index.

Similar observations have been reported previously in two studies, one each in children and in adults. However, all these patients had celiac disease. Moreover, most of these patients presented with symptoms of gastrointestinal dysmotility rather than chronic diarrhea. Ours is perhaps the first study from the tropics on ADM in patients with MAS due to other causes, particularly tropical sprue; further, all our patients presented with chronic diarrhea and not symptoms of gastrointestinal dysmotility.

The motility abnormalities found in this study are quite expected. The small bowel in patients with MAS is usually atonic with dilatation and increase in luminal fluid. Reduced amplitude of contractions...
and reduced MI found in the present study are associated with myopathic conditions of the gut. Since myopathy is associated with reduced propulsive movement, these results may explain the dilatation of the gut in patients with MAS. We presume that abnormal ADM is associated with diffuse motility abnormality of the whole small bowel. This may also explain the prolonged oro-cecal transit time (OCTT) that is known to be associated with secondary bacterial overgrowth, in patients with MAS due to tropical sprue and celiac disease. Since previous reports documented that this prolonged OCTT may normalize after specific treatment directed towards these diseases, further work is needed to evaluate whether such normalization is associated with correction of ADM abnormalities.

The pathogenesis of this altered antroduodenal motility in patients with MAS is unclear. It may be related to chronic inflammation, immune-mediated changes, alteration in mast cells, or changes in enteric neuropeptides, all of which have been proposed to explain intestinal hypomotility observed in a few patients with celiac disease.

Induction of MMC in most patients with MAS by intravenous injection of octreotide is another interesting finding in this study. Absence of MMC may be associated with SIBO, which often complicates MAS due to various causes and poses special problems in diagnosis and management of these patients. In fact, octreotide has been used in the treatment of refractory diarrhea and SIBO. Our study documents that even in the presence of marked antroduodenal hypomotility, the gut responds to intravenous octreotide by generating MMC, though somewhat weaker and shorter than in healthy subjects.

In conclusion, we have shown that patients with MAS exhibit fasting and fed-state antroduodenal hypomotility; such manometric abnormalities in patients with tropical sprue have not been reported previously. Antroduodenal hypomotility may have pathophysiological significance as prolonged OCTT is common in these patients, which might result in SIBO.

References

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