Non-ulcer Dyspepsia: A Clinical Trial Evaluating Efficacy and Safety with a Natural Antacid - Himcocid

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ABSTRACT

Dyspepsia encompasses a variety of upper abdominal symptoms i.e., pain and discomfort, bloating, fullness, nausea, anorexia, heartburn and belching. Herbal drugs have been known to provide a new therapeutic approach to treat non-ulcer dyspepsia. Fifty patients with symptoms of non-ulcer dyspepsia were treated with an herbal preparation Himcocid for a period of 6 weeks. The dosage of Himcocid was 2 teaspoonsful, twice a day. After 6 weeks, there was 96.5% relief from epigastric discomfort (p<0.0001), total relief from heartburn (p<0.0001) 95.32% relief in nausea relieved and 98.48% (p<0.001) relief in vomiting. There was 100% relief from belching, flatulence and fullness in the stomach (p<0.001). Abdominal distension was relieved in 98.25% (p<0.0001). There was no untoward side effect such as rebound gastritis in any of the patients. The study shows promising treatment of non-ulcer dyspepsia with Himcocid.

INTRODUCTION

The term “dyspepsia,” derived from the Greek words dys (bad) and pepsis (digestion), refers to symptoms thought to originate in the upper gastrointestinal tract. Dyspepsia is often used to refer to upper abdominal pain or discomfort but may also encompass symptoms of early satiety, postprandial abdominal bloating or distension, nausea and vomiting. Although only 20-25% of persons with dyspepsia seek medical care, the problem is responsible for 2 to 5 percent of visits to the physicians. Non-ulcer dyspepsia results in substantial health care costs, both in direct costs of visits to doctors, expensive tests and medications, and absenteeism from work and diminished productivity at the workplace.

Functional or idiopathic dyspepsia commonly occurs as a chronic digestive disorder affecting 20-40% of the general population. This condition is characterized by a recurring variable cluster of upper abdominal symptoms associated with food intake for which no evidence of organic disease can be found. Like other functional disorders of the gastrointestinal system such as irritable bowel syndrome and gastro-oesophageal reflux, the understanding of the pathophysiological mechanisms underlying this condition remains elusive. Motor, neurohumoral and sensory abnormalities in both the stomach and small bowel have been demonstrated in some patients with functional dyspepsia, but attempts to classify patients into dyspepsia subgroups based on predominating symptoms linked to such disturbances (dysmotility-like, ulcer-like, reflux-like dyspepsia) do not seem helpful. Many patients have more than one symptom in non-ulcer dyspepsia. Moreover, about one third of patients with functional dyspepsia also have symptoms associated with irritable bowel syndrome. This may
explain why the response to drug treatment of dyspepsia based on a symptom-oriented classification may be too narrow an approach.

In the investigators’ meeting in Rome in 1991, it was decided that the criteria for diagnosing non-ulcer dyspepsia are chronic or recurrent upper abdominal pain or discomfort for a period of at least 1 month, with symptoms present more than 25 percent of the time. There should also be an absence of clinical, biochemical, endoscopic and ultrasonographic evidence of organic disease that would account for the symptoms\(^9\). Despite these criteria, there is still some overlap between the symptoms of dyspepsia and those of irritable bowel syndrome.

The Rome group also suggested that it might be useful to subcategorize non-ulcer dyspepsia into ulcer-like, reflux-like, dysmotility-like, and nonspecific dyspepsia. Reflux-like dyspepsia is characterized by heartburn, regurgitation, or both, with dyspeptic symptoms and no endoscopic evidence of oesophagitis. Epigastric pain is the predominant symptom of ulcer-like dyspepsia. Symptoms of nausea, vomiting, early satiety, and abdominal bloating or distension characterize dysmotility like dyspepsia. The usefulness of this sub-classification based on symptoms has been questioned, since studies have reported a marked overlap among the subtypes. Also, the symptom-based sub-classification provides little information about the underlying pathophysiologic abnormality, such as gastroduodenal ulcer or gastroparesis\(^10\). In recent times many herbs have been used to treat dyspeptic symptoms and also for the treatment of peptic ulcers. Many advance research laboratories have been established to find herbal remedies for various disorders, which are devoid of adverse side effects. Thus, we decided to study a herbal preparation known as Himcocid. Himcocid contains herb such as Varatika, which is helpful in the treatment of symptoms of non-ulcer dyspepsia. Yasthimadhu is well known for it’s anti-ulcer properties. Dugdhapashna and Moutika Sukti, the other ingredients of Himcocid, are helpful in reducing the symptoms of non-ulcer dyspepsia.

In a clinical study, after 45 days of Himcocid therapy, the result showed that all the symptoms of non-ulcer dyspepsia were reduced which was evident when the scaling of the symptoms was considered. Initially the symptom score of epigastric discomfort, heartburn, nausea, vomiting, belching, flatulence, fullness in stomach and abdominal distension ranged from \(0.38 \pm 0.73\) to \(2.24 \pm 0.84\). At the end of the study all the symptoms were relieved and the symptom score was \(0\)\(^11\). In another study, there was reduction in all the symptoms from 2 weeks onwards. It was observed that there was excellent to good response in 86 – 87% of the patients after treatment. At the end of the study, the investigators rated efficacy and tolerance of treatment as excellent to good in 90% of the patients. Endoscopy was repeated in a majority of cases, and the results showed a significant improvement in healing\(^12\).

**MATERIAL AND METHODS**

The study was planned in 50 patients with non-ulcer dyspepsia with symptoms of epigastric discomfort, heartburn, nausea, vomiting, belching, flatulence, fullness in stomach and abdominal distension. Pain attributed to angina or gallbladder stones was ruled out after history-taking of the patients. Patients who suffered from thyroid and parathyroid disorders, hypertension, gastric carcinoma and diagnosed peptic or duodenal ulcer were also excluded. Of 50 patients there were 31 males and 19 females, aged between 18-60 years. All the patients had epigastric discomfort, 39
patients had heartburn, 18 patients had nausea, 3 patients had vomiting, 12 patients had belching, 13 patients had flatulence, 26 patients suffered from fullness in stomach and 16 patients had abdominal distension. The patients were dispensed Himcocid suspension and advised to take the medicine at a dose of 2 teaspoonsful twice a day for 6 weeks. They were evaluated every 2 weeks for improvement in the dyspeptic symptoms and to observe for any adverse events.

RESULTS
All the 50 patients completed the 6 weeks study period. It was found that relief was observed from the 2nd week onwards and at the end of 6 weeks they were very few negligible symptoms of dyspepsia. The assessment was done by grading the symptoms as 4 – very severe (unbearable), 3 - severe, 2 - moderate, 1 - mild and 0- no symptom.

At the beginning of the study all 50 patients had epigastric discomfort, 39 patients had heartburn, nausea was present in 18 patients, vomiting in 3, belching in 12, flatulence in 13, fullness in stomach in 36 and abdominal distension was present in 16 patients. After 2 weeks of therapy, epigastric discomfort was relieved in 17 patients, after 4 weeks, 32 patients and at the end of the therapy, 48 patients were completely relieved of the symptoms. Heartburn was relieved in 13 patients after 2 weeks in 29 patients after 6 weeks and in 39 patients after 6 weeks. Six patients were relieved from nausea after 2 weeks, 12 patients after 4 weeks and 17 patients after 6 weeks. Vomiting was relieved in 1 patient after 2 weeks, in 2 patients after 4 weeks and in 3 patients after 6 weeks.

Belching, flatulence and fullness of stomach was relieved in 4, 5 and 11 patients, respectively, after 2 weeks, 9, 10 and 20 patients after 4 weeks and total relief after 6 weeks. Abdominal distension was relieved in 6 patients after 2 weeks, in 11 patients after 4 weeks and in 15 patients after 6 weeks of Himcocid therapy (Table 1). No adverse reaction was observed in any of the patients.

DISCUSSION
A number of hypotheses have been proposed to explain the pathogenesis of non-ulcer dyspepsia. The gastric acid hypothesis advocates that either hypersecretion of gastric acid or increased sensitivity to it is responsible for dyspeptic symptoms. The motor-disorder hypothesis suggests that motor disorders of the upper gastro-intestinal tract, such as gastroesophageal reflux disease, gastroparesis, small-bowel dysmotility, and biliary dyskinesia cause dyspeptic symptoms. The hypothesis of augmented visceral perception suggests that dyspeptic symptoms are exaggerated responses to physical stimuli such as pressure, distension and temperature. Finally, the food-intolerance hypothesis proposes that certain foods may cause dyspeptic symptoms by triggering secretory motor or allergic responses.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of patients</th>
<th>After 2 weeks</th>
<th>After 4 weeks</th>
<th>After 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epigastric discomfort</td>
<td>50</td>
<td>17 (34%)</td>
<td>32 (64%)</td>
<td>48 (96%)</td>
</tr>
<tr>
<td>Heartburn</td>
<td>39</td>
<td>13 (33.33%)</td>
<td>29 (74.35%)</td>
<td>39 (100%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>18</td>
<td>6 (33.33%)</td>
<td>12 (66.66%)</td>
<td>17 (94.44%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>1 (33.33%)</td>
<td>2 (66.66%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>Belching</td>
<td>12</td>
<td>4 (33.33%)</td>
<td>9 (75%)</td>
<td>12 (100%)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>13</td>
<td>5 (38.46%)</td>
<td>10 (76.92%)</td>
<td>13 (100%)</td>
</tr>
<tr>
<td>Fullness in stomach</td>
<td>26</td>
<td>11 (42.30%)</td>
<td>20 (76.92%)</td>
<td>26 (100%)</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>16</td>
<td>6 (37.5%)</td>
<td>11 (68.75%)</td>
<td>15 (93.75%)</td>
</tr>
</tbody>
</table>
Despite the use of the term “non ulcer dyspepsia,” which suggests an idiopathic functional disorder, a number of non-motility and motility disorders have been identified as potential causes. For years, physicians have treated patients with pain like that associated with ulcer (epigastric pain that occurs after meals and at night and that is relieved with antacids), but with no ulcer on examination\textsuperscript{13}. In some patients, subsequent endoscopy may reveal an ulcer, suggesting that the initial symptoms were those of an “ulcer diathesis”\textsuperscript{14}. In some patients with dyspeptic symptoms, the duodenal mucosa may appear mottled, hyperemic, or irregular on endoscopy, with duodenitis noted on biopsy\textsuperscript{15}. The clinical significance of histologic duodenitis is doubtful, since it is often found in healthy adults and since there is little improvement in the appearance of the mucosa with treatment, regardless of the symptomatic response\textsuperscript{16}.

Few cases of dyspepsia may represent various stages of \textit{Helicobacter pylori} infection and may subsequently progress to ulcer disease\textsuperscript{17}. \textit{H. pylori} infection has a prevalence of upto 1 percent per year of age. The age-related prevalence may be higher in patients with non-ulcer dyspepsia, but this finding has not been confirmed by all investigators\textsuperscript{18,19}. Dyspeptic symptoms have been reported after intentional self-infection with \textit{H. pylori}\textsuperscript{20}. Although some studies have demonstrated an improvement in dyspeptic symptoms after the eradication of \textit{H. pylori}, an equal number of studies did not\textsuperscript{21,22}.

Another potential cause of non-ulcer dyspepsia is reflux of bile into the stomach. However, objective studies have shown that patients with dyspepsia who have not undergone prior surgery do not have elevated bile acid concentrations in the stomach\textsuperscript{23}. Medicines to treat this type of gastritis are unavailable or ineffective.

When one cannot explain a patient’s intractable symptoms, there is often supposition that it could be a manifestation of an underlying psychiatric disorder. Regardless of whether the cause is functional or organic, patients with abdominal pain have higher scores for depression, anxiety, neuroticism, and hypochondriasis than patients without abdominal pain. Exacerbations of non-ulcer dyspepsia are often attributed to stressful events. One study suggests that patients with non-ulcer dyspepsia and patients with other disorders have similar numbers of stressful events in their lives but that patients with dyspepsia report greater stress.

In upto 60 percent of patients with dyspepsia, the diagnostic evaluation discloses no underlying organic cause\textsuperscript{24}. Such patients are labeled as having non-ulcer, or functional, dyspepsia. This disorder is considered to be part of a continuum of functional gastrointestinal disorders that include irritable bowel syndrome, functional heartburn, and non-cardic chest pain.

The pathophysiology of non-ulcer dyspepsia is poorly understood\textsuperscript{25,26}. In more than half of affected patients, inflation of an intragastric balloon will cause pain at volumes significantly lower than those that cause pain in healthy subjects, suggesting the presence of increased visceral sensitivity. Upto half of patients have delayed gastric emptying of solids or postprandial antral hypomotility. Unfortunately, the demonstration of these abnormalities does not correlate with symptomatic improvement after treatment with agents that promote motility, such as cisapride. As compared with healthy subjects, patients with non-ulcer dyspepsia have higher scores for anxiety, neuroticism, and
depression on personality assessment, but it is unclear whether these traits merely reflect the fact that these patients will seek health care. Extensive, and many a times inconsistent, data on the treatment of non-ulcer dyspepsia are present. Treatment approaches that have been extensively prescribed included the use of antacids, the use of H$_2$ receptor antagonists and antibiotics for the eradication of $H. pylori$. Several careful meta-analyses have been performed, allowing some general statements about treatment for non-ulcer dyspepsia. In clinical studies, higher doses of acid-suppressing agents had a positive effect on the symptoms, with improvement reported in 35 to 80 percent of patients receiving the acid-suppressing agents, as compared with 30 to 60 percent of those receiving placebo. In two preliminary studies of omeprazole, a proton-pump inhibitor for the treatment of non ulcer dyspepsia, only 50 percent of the patients treated with omeprazole responded, as compared with 25 percent of those who received a placebo.

It is not advisable to perform extensive diagnostic tests such as esophago-gastroduodenoscopy, biliary tract ultrasonography, or even abdominal computed tomography in all patients. Whether all patients who present with dyspeptic symptoms should at least undergo initial endoscopy is controversial. Empirical therapy is advisable in patients who do not have signs or symptoms of an underlying organic disorder, such as gastric ulcer or cancer. This was the reason why we did not subject the patients in the study to gastroendoscopy.

In this study, the epigastric discomfort that was present in all the patients disappeared after six weeks of Himcocid therapy and only 3.5% had mild symptoms. Nausea, present in 36% at the beginning, was present in only 4.68%. Vomiting, present in 6% before therapy, was present in 1.52% after therapy, which was mild occasionally. Heartburn, belching, flatulence and fullness of stomach was absent in all the patients. Abdominal distension was seen in only 1.75% (Table 1). These studies thus indicate that herbal preparations such as Himcocid can be a useful alternative medicine in patients with dyspeptic symptoms.

CONCLUSION
A promising finding, which emerges from this study, was that Himcocid appears to improve gastrointestinal sensitivity at the level of integration, which may involve the entire digestive tract. The use of Himcocid could offer a broader therapeutic option in the treatment of non-ulcer dyspepsia.

REFERENCES


