Comparison of the Plant Plantago Major and the Drug Colofac on Clinical Symptoms in IBS Patients

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ABSTRACT

Background and Aim: Despite the frequency with which IBS is encountered in clinical practice, it remains an important medical problem for both health care providers and patients. Unfortunately, so far no single treatment option has been effective for managing IBS. Therefore we decided to Comparison of the plant Plantago major and the drug Colofac on clinical symptoms in IBS patients.

Method of investigation: This study was done as a double-blinded clinical trial in Aug 2014 until Nov 2014. 51 patients (male and female) were included in the study after considerations of inclusion and exclusion criteria. Diagnosis of IBS was based on Rome II Criteria and organic causes were ruled out. Patients were divided randomly into the two groups, A and B. In the first visit, all patients were observed for two weeks without any medication. Patients in group A were given a 4.5 g dose of powdered plantago plant per day in two administrations, (2 hours before eating lunch and dinner) in the form of an oral capsule. Patients in Group B received a Colofac capsule (200 mg) morning and night for 3 months. Patients in both groups were visited for an examination to evaluate their condition in terms of diarrhea, constipation, number of defecations. Visits and examinations were made every week in the first month and every two weeks in the second month plus one at the end of the third month. Data were further analyzed by SPSS-17 software and statistical test of chi-square was done, and a repeated measure.

Findings: Evaluations for number of days of diarrheal defecation per day show significant difference at each visit in repeated measurements; however, average of the descending trend for number of days of diarrheal defecation showed no significant difference between the two therapeutic methods. The effectiveness of plantago in reducing numbers of diarrheal defecations in a day was higher than that of Colofac. number of defecations per week showed no significant difference in relation to each of the visits in repeated measures. However, there was no significant difference between the two treatments in terms of the mean of descending trend of number of defecations during a week, although the effectiveness of plantago in for reducing the number of defecations per week was greater than that of Colofac.

Conclusion: The present study is the clinical trial to Comparison of the plant Plantago major and the drug Colofac on clinical symptoms in IBS patients. Our study demonstrated that two therapeutic methods are effective in the management of IBS symptoms, although the effectiveness of plantago was greater than that of Colofac.
sensitivity and abnormal bowel movements, bowel microbial factors, immune disorder and inflammation, genetic predisposition, abnormal gas handling in the bowel, psychosocial factors, bowel infection, the central nervous system, and serotonin are all factors associated with the development of IBS (2, 6, 7, 8, 9). Patients suffering from IBS have a poor quality of life (2, 10, 11) and research has shown that 37% of such patients develop depression as a result of the disorder. Furthermore, it is significant that 38% of those with IBS attempted suicide because of symptoms of the disease (12).

A variety of drugs are commonly recommended to treat the condition, they include tricyclic antidepressants (10), antispasmodics (12, 13), 5-hydroxytriptamin-3 receptor (5-HT3) antagonists, 5-HT4 agonists (14), antibiotics (15), probiotics (16), melatonin (17), selective serotonin reuptake inhibitor (11). Colofac is an antispasmodic drug, commonly indicated as a common therapy for IBS.

Involvement of numerous factors in the pathophysiology and evidence of the placebo effect means that treatment of this disease is highly complex (18), and considering the disappointing results of common treatments, alternative and traditional treatments are suitable options for many patients. So far, 11 to 43% of patients suffering from digestive disorders use alternative or complementary approaches. Although herbal medicine is used by many people to treat or prevent digestive disorders, there is little research available on the subject (19-21).

Plantago major is a durable plant from the Plantaginaceae family. Novel pharmaceutical research has indicated that this plant has been widely used all over the world to treat a number of diseases such as skin diseases, problems associated with the digestive system, respiratory, reproductive, and blood circulation system diseases; it is also used against infections and tumors and to mitigate pain and fever. It has traditionally been used to treat diarrhea in many parts of the world yet little research has been done on its effectiveness (22). The aim of this study was to compare the effect of the plant plantagel, a herbal plant with that medication in the form of Colofac capsules for treating diarrhea-predominant irritable bowel syndrome. Mebevirine hydrochloride, is marketed under the trade name of Colofac; it is an antispasmodic drug available in the form of a coated tablet (135 mg) and Cap Colofac Retard (200 mg). Mebevirine acts as a musculotropic antispasmodic that directly affects smooth myocytes in the digestive system and dispels spasm without affecting natural bowel movement or causing hypotony. Mebevirine is rapidly absorbed in the intestine. It is hydrolyzed in the body and secreted in the urine. It is recommended for treating IBS and similar conditions including chronic irritable colon, spastic constipation, mucous colitis and spastic colitis. In addition, Colofac is effective for treating other symptoms such as cramps and abdominal colic pain, non-specific diarrhea and bloating (12, 13). Recommended Colofac consumption is three times a day, 20 min before each meal. This medication has no common side effects. In rare cases, it has caused skin rash and hives and its potential side effects include dizziness, headache, bradycardia, nausea and vomiting.

**MATERIALS AND METHODS**

This study was done as a double-blinded clinical trial in the specialized clinic of liver and digestion in Rasul Akram Hospital between the beginning of Aug 2014 until Nov 2014. 80 patients with IBS were examined, and a total of 51 patients (male and female) were included in the study after considerations of inclusion and exclusion criteria. Diagnosis of IBS was based on Rome II Criteria and organic causes were ruled out. Diagnosis included the following symptoms: 1 - abdominal pain experienced during the previous 12 weeks, presented constantly or periodically over the previous 12 months. 2 - abdominal pain or discomfort that improved by defecation and when its onset presented itself as a change in the number of defecations or in stool consistency.

Conditions for inclusion in the study were as follows:

1. Diagnosis of IBS by ruling out organic causes using colonoscopy and stool tests.
2. Normal results of the last examination over the previous 5 years (colonoscopy in patients over the age of 55 and sigmoidoscopy in others).

Exclusion criteria included existence of any active digestive disease, major psychiatric disease (either in the past or present), pregnancy or breast-feeding, under any other treatment at the beginning of participation in the plan or during it, and any abnormal test laboratory results.

A written testimonial was taken from each patient included in the study. Each patient was identified by a code. Patients were divided randomly into two equal groups (plantago and Colofac) and thus each patient had a 50% chance of entry into either group. Patients were divided randomly into the two groups, A and B. In the first visit, all patients were observed for two weeks without any medication. The aim of this stage was to cancel out effects of any other medication recently consumed by the patient. Patients in group A were given a 4.5 g dose of powdered plantago plant per day in two administrations, (2 hours before eating lunch and dinner) in the form of an oral capsule. Patients in Group B received a Colofac capsule (200 mg) morning and night for 3 months. Patients in both groups were visited for an examination to evaluate their condition in terms of diarrhea,
constipation, number of defecations. Visits and examinations were made every week in the first month and every two weeks in the second month plus one at the end of the third month. The results were then recorded on the relevant forms. Data were further analyzed by SPSS-17 software and statistical test of chi-square was done, and a repeated measure. In this study, an evaluation of p<0.05 was considered as significant difference.

RESULTS

In this study, 80 cases were investigated. With respect to inclusion and exclusion criteria, 51 patients were enrolled and data related to 51 patients were subjected to statistical analysis. 25 patients from the group taking plantago and 26 patients from that taking Colofac where excluded from the plan, together with one patient from the plantago group and two patients from Colofac group due to lack of access to the patient during the course of treatment.

There were 24 persons in each group 31 (64.6%) of which were female and the rest were male. Means of age for each group were 36.1 ± 12.02 and 37.88 ± 8.9 for the plantago and Colofac groups respectively, indicating no significant difference (p value=0.535).

Mean duration of course of the disease was 7.3 years in patients in both groups with a standard deviation of 5.19. Furthermore, minimum and maximum ages of participants were 19 and 62 years, respectively, and the minimum and maximum numbers of years for duration of the disease were 1 and 20, years respectively.

Table 1. Shows demographic information on mean age and course of the disease based on each treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment group</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Plantago</td>
<td>36.1±12.02</td>
</tr>
<tr>
<td>Duration of being</td>
<td>Colofac</td>
<td>37.88±8.9</td>
</tr>
<tr>
<td>Deseased</td>
<td>P-Value</td>
<td>0.535</td>
</tr>
</tbody>
</table>

Table 2. Shows frequency for symptoms of diarrhea and constipation in both groups under treatment before intervention.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment group</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Yes</td>
<td>18(51/4)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6(25)</td>
</tr>
<tr>
<td>Constipation</td>
<td>Yes</td>
<td>9(37/5)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>15(62/5)</td>
</tr>
</tbody>
</table>

Table 3. Shows mean of dependent variables investigated at different stages of intervention.

<table>
<thead>
<tr>
<th>Variable</th>
<th>First visit</th>
<th>Second visit</th>
<th>Third visit</th>
<th>Fourth visit</th>
<th>Fifth visit</th>
<th>Sixth visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>The number of defecation days</td>
<td>Plantago</td>
<td>12.63</td>
<td>11.27</td>
<td>11.18</td>
<td>10.36</td>
<td>10.63</td>
</tr>
<tr>
<td>with constipation during a week</td>
<td>Colofac</td>
<td>7.77</td>
<td>7.66</td>
<td>8.00</td>
<td>7.88</td>
<td>7.77</td>
</tr>
<tr>
<td>The number of defecation times</td>
<td>Plantago</td>
<td>19.50</td>
<td>17.83</td>
<td>15.79</td>
<td>13.91</td>
<td>13.00</td>
</tr>
<tr>
<td>per week</td>
<td>Colofac</td>
<td>18.79</td>
<td>18.20</td>
<td>17.20</td>
<td>16.41</td>
<td>15.33</td>
</tr>
<tr>
<td>The number of diarrheal defecation times in a day</td>
<td>Plantago</td>
<td>3.45</td>
<td>3.00</td>
<td>2.12</td>
<td>1.95</td>
<td>1.54</td>
</tr>
<tr>
<td></td>
<td>Colofac</td>
<td>2.91</td>
<td>3.12</td>
<td>3.12</td>
<td>3.00</td>
<td>2.54</td>
</tr>
</tbody>
</table>

Diarrhea:
In the table above, mean of numbers of diarrhea defecation is shown per day, recorded on each of the 6 visits. Records are shown individually for each of the two intervention methods. Based on the Repeated Measure Test, evaluations for number of days of diarrheal defecation per day show significant difference at each
visit in repeated measurements \( p<0.001, F=23.1 \); however, average of the descending trend for number of days of diarrheal defecation showed no significant difference between the two therapeutic methods \( p=0.2, F=1.49 \). The effectiveness of plantago in reducing numbers of diarrheal defecations in a day was higher than that of Colofac.

The trend of diarrheal defecations per day, for plantago and Colofac therapeutic interventions was determined separately.

Similarly, the above table shows number of days with constipated defecation in a week recorded in each of the 6 visits for both interventions. According to the Repeated Measure Test, there was significant difference between each of the visits in repeated measures in terms of number of days with constipated defecation per week \( p=0.001, F=38.2 \). However, the mean of the descending trend of this number shows no significant difference between the two interventions \( p=0.3, F=1.06 \).

**DISCUSSION**

Despite high prevalence of IBS in societies, this disease has remains a challenge for health organizations and patients. Despite availability of various medications, each of which affects one symptom of the disease, these are sometimes ineffective and their consumption has not been continued because of increased cost or onset of serious side effects, patients have turned their attention to the use of herbal medicines (5).

In this study, the therapeutic effect of the plant plantago was compared with that of Colofac for treating symptoms of irritable bowel syndrome. In this comparison, it was observed that both of the mentioned medications effectively reduced number of defecations. Results show that plantago had a greater impact in terms of reducing the number of defecations and that difference between the two methods was significant. Moreover, significant difference was determined between the two treatments in terms of reducing the number of diarrheal defecation occurrences compared with pre-treatment conditions. However, the two treatments were determined as significantly different, although some diagrams indicated that plantago was the more effective. The present study has demonstrated that consumption of the plant plantago major was more effective than taking Colofac capsules to control symptoms of diarrhea in IBS patients.

The effect of various herbs has been investigated for treating this disease in other studies, but results are not in accordance with one another. In a study done in 2006 on Aloe Vera, no significant difference was observed in improving symptoms in patients compared with the placebo (23).
A study on the impact of Curcuma xanthorrhiza (24), Fumaria officinalis (24), and Curcuma longa (25), determined no significant difference in terms of reducing symptoms in patients under pharmaceutical treatment compared with the placebo.

However, studies on Cynara scolymus (26), Hypericum perforatum (27), Iberis amara (28), Maranta arundinacea (29), Menta piperita (30), and Plantago psyllium (31), determined significant difference in terms of reducing symptoms in patients under treatment with the tested plants in comparison with the placebo.

Tests have also been done on the therapeutic effect of some Chinese plants. In a clinical study conducted by Bensoussan, in three herbal health centers on 106 IBS patients, improved digestive symptoms were recorded in the group that consumed Chinese herbal medicines compared with the placebo group (32).

A double-blinded clinical trial on herbal medicines based on Ayurvedic medical doctrine; patients treated in three different groups of standard treatment (clindinium C, chlorodiazepoxide, and psyllium), Ayurvedic, and placebo during 6 weeks. Results showed improved symptoms of 78, 65, and 33% for standard, Ayurvedic and placebo treatments respectively (19).

In most other studies, patients have been considered according to generalized symptoms but in this study evaluation of symptoms was more specific and made in terms of number of defecations. This study is unique in that patients were investigated separately according to symptoms of either diarrhea or constipation. Note that in previous studies, most medications were compared with a placebo, but the value of this study is that improvement of symptoms in patients was compared with the medication Colofac, which is already accepted as an effective treatment for symptoms of IBS.

Based on the results of this study, Plantago major can improve symptoms in IBS patients with complaints of diarrhea or constipation at a lower cost and with more tolerance. Future studies considering a larger number of subjects and a follow-up period after discontinuation of the treatment is recommended so that if confirmed, this therapeutic approach could be used to help IBS patients.

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