Improvement in Symptoms of Patients with Irritable Bowel Syndrome with Constipation Administered an Extract of Quebracho, Conker Tree, and *M. balsamea Willd*

(Atrantil™)

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Abstract

Aim: To observe the effects of a new dietary supplement, Atrantil™, composed of Quebracho, Conker Tree and *M. balsamea Willd* extracts on reductions in bloating, constipation and abdominal discomfort in IBS-C patients in a real-world setting.

Methods: Twenty-four IBS-C patients from a community office practice were administered the combination Quebracho (150 mg), Conker Tree (470 mg) and *M. balsamea Willd* (50 mg) for 2 weeks. Patient response to the extract for abdominal pain, constipation and bloating were assessed by visual analogue scale (VAS) at baseline and End of Study (EOS) at 2 weeks. Paired t-tests were used to compare changes over time. Significance was defined as $p<0.05$.

Results: Twenty-one of 24 individual patients responded to the extract for overall relief of abdominal discomfort, bloating and constipation symptoms (88%). There was also significant improvement in abdominal discomfort (<0.001), bloating (<0.001) and constipation (<0.001) scores from baseline to EOS with no reported side effects. Twenty-one patients expressed improved Quality of Life while on the extract compared to baseline.

Discussion: This real-world analysis supports a recent placebo-controlled study where the extract demonstrated significant improvements in the average constipation, bloating and constipation plus bloating scores compared to placebo. Therefore, the use of Quebracho, Conker Tree and *M. balsamea Willd* extra should be considered as an option in IBS-C patients.

The Problem

- One third of diagnosed irritable bowel syndrome in the US is constipation predominant (IBS-C) [1].
- Women experience IBS symptoms more frequently than men [2].
- IBS-C has a huge impact on quality of life and productivity especially in women [3].
- Gas (hydrogen, methane), bloating and constipation in IBS-C patients have been linked to the presence of methogenic archaebacteria [4,5].
- Methane production is associated with delayed transit time [6,7].
- It has also been found that individuals with a small intestinal bacterial overgrowth (SIBO) produce more hydrogen and methane which can lead to abdominal pain and constipation [8].
- Fiber supplements [9] and probiotics [10] as well as drugs like rifaximin, neomycin [11], laxatives [12,13], lubiprostone [14], linaclotide [15] all have variable effects in patients with IBS-C.
- There is still a need for safe agents to support GI health in patients with IBS-D.

The Solution

- Atrantil™, composed of Quebracho, Conker Tree and *M. balsamea Willd* extracts, has been shown against placebo to statistically improve constipation and bloating in IBS-C subjects [16].
- Quebracho extract contains tannins which are large delocalized flavonoid structures that have been used safely in wine for decades [17]. Tannins potentially have dual function [18]: they act as molecular

"sponges" for excess hydrogen and methane [19] as well as disrupt and destroy bacterial lipid bilayers.

- Conker Tree extract contains escins, also known as saponins. Saponins act as antimicrobial agents, promote intestinal motility [20] and directly reduce methane production/emission[21,22].
- *M. balsamea Willd* extract contains peppermint which has been shown to reduce abdominal discomfort [10].
- Atrantil™ represents a new, safe and effective way of supporting GI function in patients with gas, bloating, abdominal discomfort and constipation caused by IBS-C and SIBO.

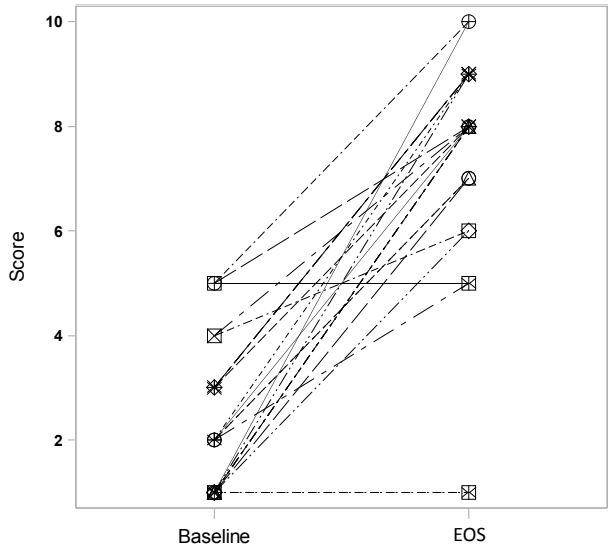
Observational Study Design

This was an observational study of 24 IBS-C patients who agreed to take a new dietary supplement Atrantil [Quebracho (150 mg), Conker Tree (470 mg) and *M. balsamea Willd* (50 mg) extracts] after experiencing incomplete management with other therapies. All patients consented to have their data published. Patients were previously on the FODMAP diet, probiotics and traditional drug treatments. Atrantil was administered for two weeks. Patient response to the combined extract was assessed by visual analogue scale (VAS) at baseline (before administration) and after two weeks [End of Study (EOS)] for abdominal pain, constipation and bloating. Paired t-tests were used to compare changes over time. Significance was defined as $p<0.05$. Side effects were noted at EOS. Changes in therapy for rescue due to symptoms were also noted.

Results

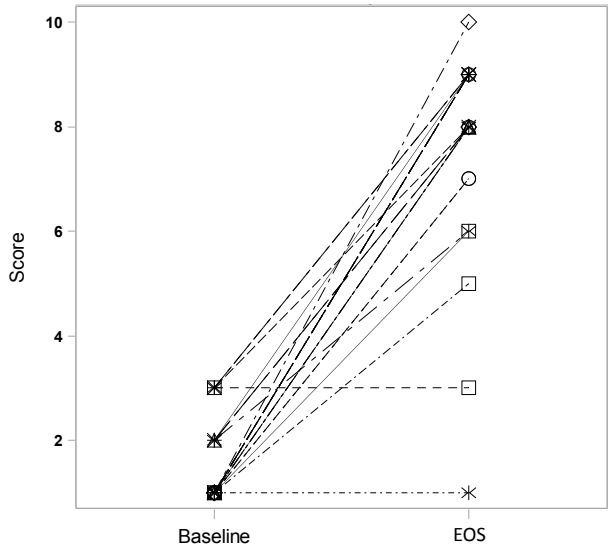
Patients were not taking any other therapies for IBS-C or SIBO when they were first administered Atrantil. By EOS, 21 out of 24 patients had responded with improved VAS scores for abdominal discomfort (Fig. 1), bloating (Fig. 2) and constipation (Fig 3). Overall, 88% of this real-world population which had incomplete relief with traditional therapies responded to therapy.

Figure 1. Improvement in Abdominal Discomfort



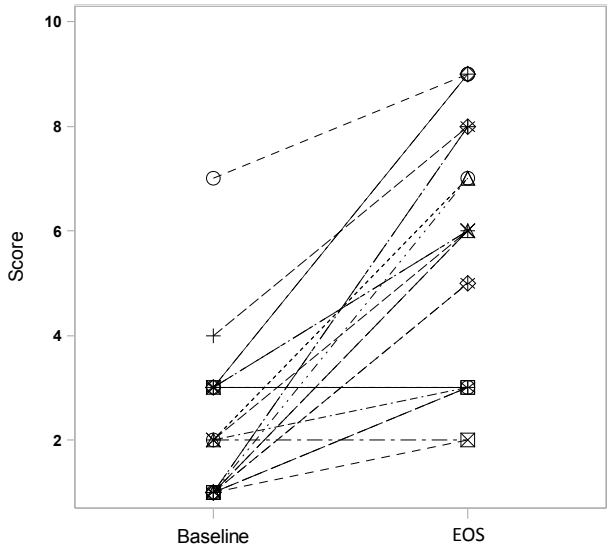
VAS for abdominal discomfort (0= extreme discomfort, 10= no discomfort)

Figure 2. Improvement in Bloating



VAS for bloating (0= extreme bloating, 10= no bloating)

Figure 3: Improvement in Constipation



VAS for constipation (0= extreme constipation, 10= no constipation)

A comparison of mean VAS scores for abdominal discomfort, bloating and constipation between baseline and EOS showed a significant improvement in all three symptoms over time for the entire population while on the combined extract (Table 1).

Table 1

Symptom	Baseline Mean (SD)	EOS Mean (SD)	EOS-Baseline Mean (SD)	p-value
Constipation	2.17 (1.40)	5.83 (2.37)	3.67 (2.24)	<0.001
Bloating	1.50 (0.78)	7.58 (2.10)	6.08 (2.28)	<0.001
Abdominal Discomfort	2.29 (1.43)	7.25 (2.35)	4.96 (2.49)	<0.001

EOS= End of Study (2 weeks); SD= Standard Deviation

No rescue medication was needed during the 2 week course of the observation and there were no reported adverse events.

Discussion

Over 90% of IBS patients suffer from bloating which is directly linked to abdominal pain and distention [23]. These symptoms may be caused by SIBO or dysbiosis. No matter the cause, current therapeutics are not meeting the needs of patients. In a 10 week study of rifaximin (550 mg TID) *vs* placebo, the overall response rate was 40.8% versus 31.2% for placebo (p = 0.01) [24]. In a similar construction to this observational study, rifaximin and neomycin were studied in a retrospective chart review of lactulose breath test responders with IBS [25]. There was a 69% response rate for rifaximin for reduction in symptoms compared to 44% for neomycin. Another study found that patients who had an abnormal lactulose breath test when treated with neomycin had a 75% response rate [26]. Even with the success of antibiotic treatment, relapse remains a significant problem in SIBO patients [27]. Other treatment agents are also used for constipated patients.

In an open-label extension study of lubiprostone (n = 522), a locally acting chloride channel activator, demonstrated a response rate of ~40%, but ~32% of participants in the extension part of the study required a rescue medication [28]. Adverse effects for lubiprostone include dose-related nausea and dyspnea with chest tightness. For idiopathic constipation, lanaclotide has demonstrated ~50% response rate for pain and increase in stool frequency compared to placebo responses of ~35% and ~25%, respectively [29,30]. About 20% of patients on lanaclotide experience diarrhea compared to ~3% in the placebo groups.

Nutritional approaches to IBS-C and SIBO include dietary fiber, the FODMAP (Fermentable oligosaccharides, disaccharides, monosaccharides

and polyols) diet and probiotics. Fiber can be effective in managing constipation, but bloating, distension, flatulence and cramping may limit the use of insoluble fiber. Water intake with fiber is very important. In patients with IBS, soluble fiber, such as psyllium may be effective, but insoluble fiber can exacerbate symptoms [10,32]. The FODMAP diet has been found to decrease abdominal pain and bloating, but adherence to the diet can be a problem [33]. Probiotics containing *Bifidobacterium lactis* DN-173 010, *Lactobacillus casei* Shirota, and *Escherichia coli* Nissle 1917 demonstrate favorable data on defecation frequency and stool consistency [34].

Patients administered Atrantil™ had a 2.7-fold improvement in constipation, a 5.1-fold improvement in bloating, and a 3.2-fold improvement in abdominal discomfort with an overall response rate of 88%. This observational data backs up a randomized double-blind, placebo-controlled trial in which Atrantil™ demonstrated significant improvements in average constipation ($p = 0.0034$), bloating ($p < 0.001$) and constipation plus bloating scores ($p < 0.001$) compared to no improvement for the placebo arm [16]. Based on these consistent results, this safe, new dietary supplement should be considered for patients with IBS-C and SIBO.

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