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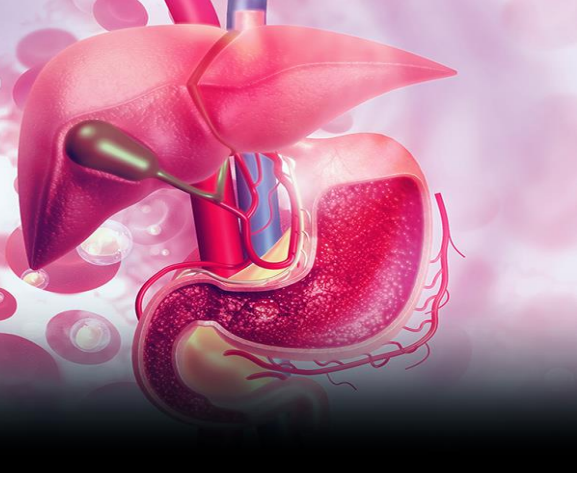

Bile Acids May Have Key Role in Refractory GERD

Studies have reported a new sequestrant of bile acid employed as an alternative to treatment with proton pump inhibitors greatly decreased reflux symptoms. According to the authors, the medication, which is currently under phase 3 testing, may benefit about 30 percent of patients with gastroesophageal reflux disorder who are not reacting adequately to PPIs.

"This is a medication that will resolve the lack of reaction to PPI treatment," said Ronnie Fass, MD, head of the Gastroenterology and Hepatology Section and Digestive Health Center's medical director at MetroHealth, Cleveland. "This medication is primarily designed for patients with proven gastroesophageal reflux disorder who do not respond to once - a-day PPI therapy." Dr. Fass and his colleagues presented their results in a recent issue of Gastroenterology (2020 Feb 21)

Some reports have indicated duodenogastroesophageal reflux (DGER) exists in around two-thirds of patients who, after taking PPIs, tend to suffer symptoms. Therefore, DGER in refractory GERD could be a significant underlying cause, and medications that target bile acids may play a role in the care of such patients.

The novel drug, IW-3718 (Ironwood Pharmaceuticals), is a bile acid sequestrant colesevelam gastric-retaining, extended-release formulation that binds bile acids in the stomach and may interact with bile acid reflux into the esophagus.

A multicenter, double-blind, placebo-controlled study from March 2016 to April 2017 to determine the effectiveness and protection of the IW-3718 as an alternative to PPI therapy. A total of 280 PPI therapy patients were randomly allocated to receive placebo or IW-3718 at one of three doses: twice every day, 500, 1,000 or 1,500 mg.

The primary result was the weekly increase in heartburn incidence from baseline to week 8 and the researchers also measured the percentage shift in regurgitation frequency per week.

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Looking forward to your valuable feedback
Best Regards,
Medical Team, Micro Labs Ltd

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The primary result was the weekly increase in heartburn incidence from baseline to week 8 and the researchers also measured the percentage shift in regurgitation frequency per week. In the weekly heartburn frequency score from baseline to week 8, a dose–response pattern was found among treatment classes, which was more prominent in the community that obtained the maximum dose of IW-3718 (P=0.02), according to the researchers. The score reduction in the placebo category was 46 percent, in the 500-mg category 49 percent, in the 1,000-mg group 55.1 percent, and in the 1,500-mg group 58 per cent. The difference in care between placebo and the IW-3718 dosage of 1,500 mg was 11.9 per cent (P=0.04), they recorded.

The study reported a 17 percent decrease in the condition among those taking the maximum dosage of IW-3718 relative to placebo, among the 276 patients with baseline regurgitation. "IW-3718 is tested only in tandem with PPIs, and not as a single medication," said Dr. Fass. Phase 3 clinical studies are ongoing but there are no details available.

"I would definitely testify to the reality that a large number of patients do not react to conventional proton pump inhibitor therapy— in the 30 percent range— and it will be helpful to provide an agent that we may utilize in this population to determine their reaction," said Samuel Giordano, MD, a gastroenterologist at Cooper University Health Care in Camden, N.J. "Based on the available evidence, the drug seems to be well absorbed except for a bit of constipation, and has proven secure."

Dr. Giordano said that one problem to look for in potential IW-3718 studies will be refractory patients with what is known as "bile acid reflux." This disorder happens as bile acids retrogradely invade the stomach from the small intestine which may contribute to reflux symptoms that often do not respond to conventional therapies.

"This form of reflux is more prevalent in patients that have their gallbladder extracted and I would be interested to know what number of patients that referred to in the refractory community It would be important to see what was the response rate in that group of patients."

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Efficacy and Safety of Peppermint Oil in Irritable Bowel Syndrome: PERSUADE study

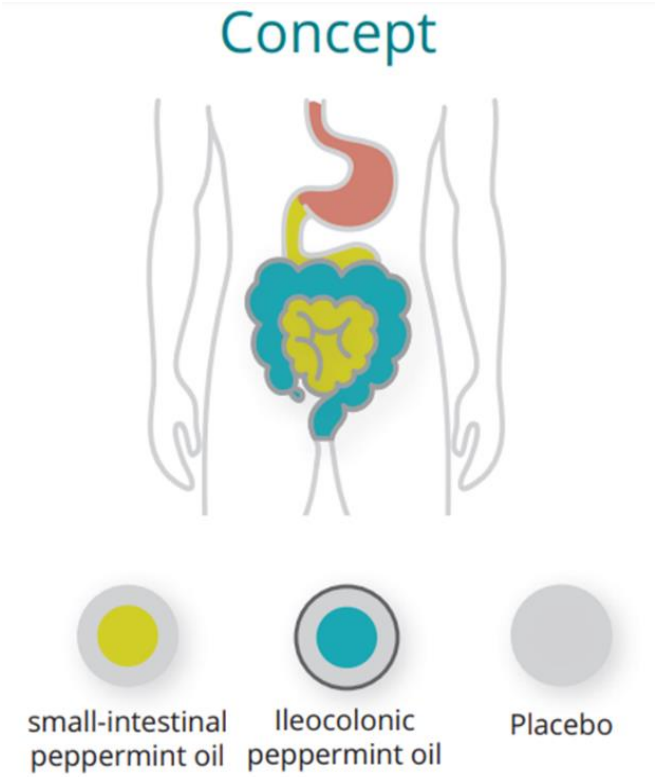
INTRODUCTION

Irritable intestine syndrome (IBS) is a gut-brain axis condition marked by persistent severe gastrointestinal discomfort and abnormal intestinal patterns. IBS is extremely prevalent with an average incidence of 5-6 per cent according to Rome IV guidelines in the general population.

IBS has a profound adverse effect on quality of living and bears a major socio-economic strain. Though the range of medical alternatives has recently increased, abdominal pain management remains difficult and is sometimes unsatisfactory.

The peppermint oil is one of the commonly utilized pharmacotherapeutic bodies. This herbal product has menthol as its key constituent and is believed to have many modes of action including intestinal smooth muscle relaxation, regulation of the transient receptor potential (TRP) system controlled visceral nociception, antagonism with 5-hydroxytryptamine, antimicrobial and antifungal impact and κ-opioid receptor agonism.

Enteric-coated capsules that produce peppermint oil in the small intestine are widely distributed in Europe as an over-the-counter (OTC) drug and in the USA and Canada as a natural food product branded as such.



Guidelines for the use of peppermint oil (small-intestinal release) in IBS care are primarily focused on recent trials showing very promising outcomes in terms of abdominal pain relief and global symptom improvement

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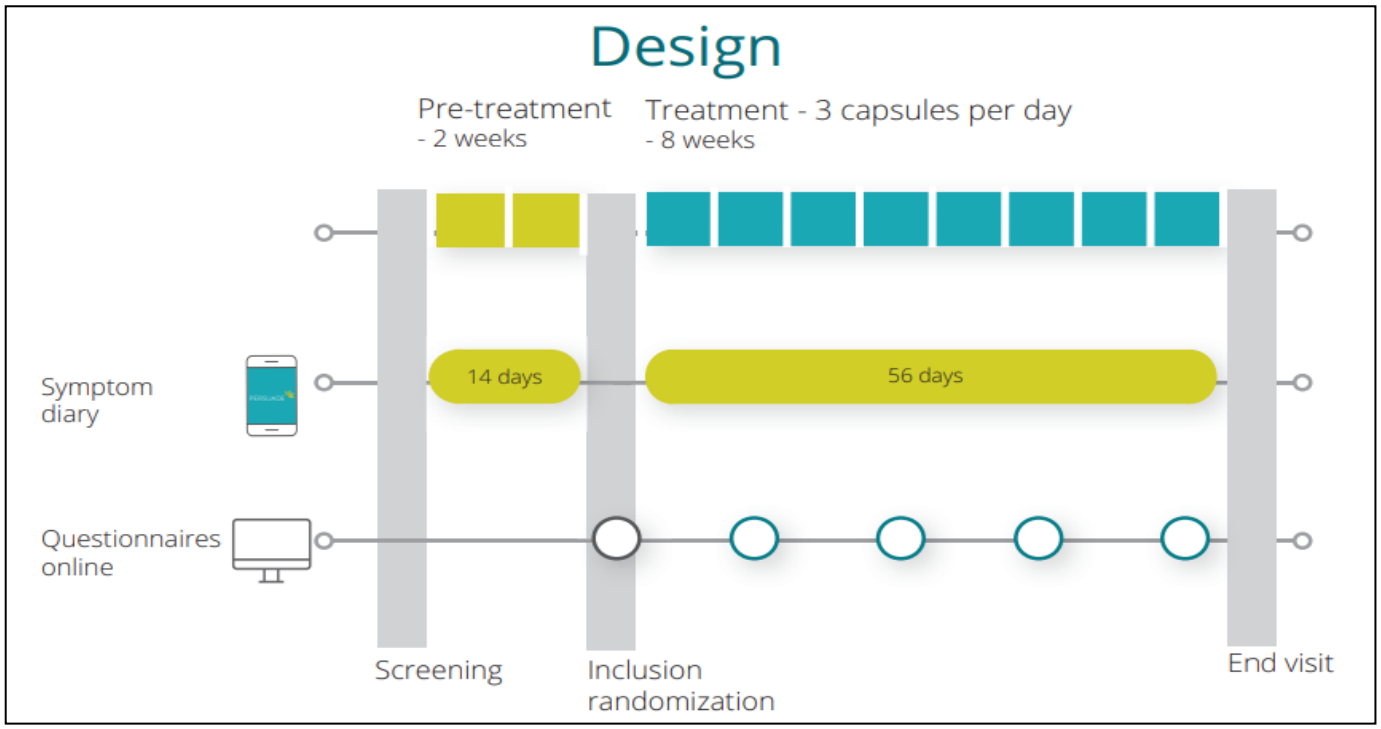
MATERIALS AND METHODS

This PERSUADE study was a randomized, double-blind, placebo-controlled trial

- Primary outcome: Abdominal Pain Response rate %
- Secondary outcomes, e.g.: IBS-symptom severity system (IBS-SSS)



RESULTS

The proportion of abdominal pain respondents did not vary substantially between groups: 46.8% in small-intestinal peppermint release oil (OR1.68; 95% CI0.80, 3.51; P=0.170; amount required to treat (NNT) 8.1) and 41.3% in ileocolonic peppermint release oil (OR1.39; 95% CI 0.66, 2.90; P=0.385; NNT 14.5), contrasted with 34.4% in placebo (Table 1)

The proportion of global relief respondents also did not vary substantially across groups: 9.7% in small-intestinal peppermint oil release (OR2.12; 95% CI 0.49, 9.17; P=0.317) and 1.6% in ileocolonic peppermint oil release (OR0.33; 95% CI 0.03, 3.35; P=0.351), contrasted with 4.7% in placebo (Table 2)

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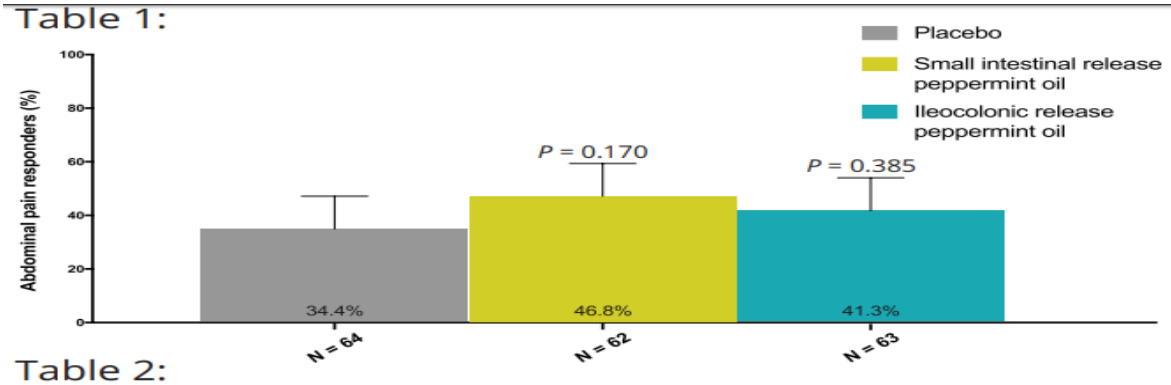
Table 1:



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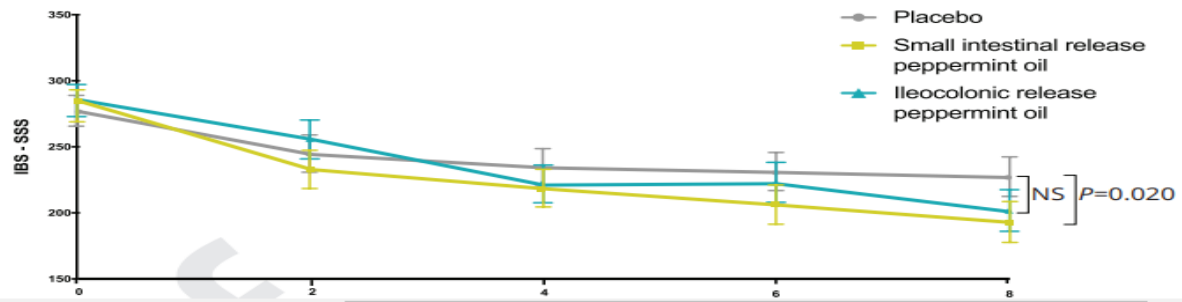

DISCUSSION

In this first randomized, double-blind, placebo-controlled, clinical trial of peppermint oil in patients with Rome IV-identified IBS, neither small-intestinal release nor ileocolonic peppermint oil release resulted in a statistically significant reduction in abdominal pain or an improvement in global relief based on the pre-specified primary outcome measures as described by the FDA and EMA guidelines.

However, small-intestinal peppermint oil, although not ileocolonic, has produced clinically meaningful increases in IBS symptom frequency, abdominal distress, and abdominal irritation exploratory secondary outcomes. In both peppermint oil groups AEs occurred more often than placebo, but were all mild and transient.

We had speculated that a guided ileocolonic release of peppermint oil would result in improved treatment effectiveness owing to a more central anti-nociceptive colonic impact based on recent experimental data indicating involvement of TRP channels on colonic sensory afferents.

Nonetheless, in the present research we find no proof that ileocolonic release peppermint oil has symptomatic advantages over placebo. Furthermore, while upper GI adverse effects significantly decreased relative to small-intestinal peppermint release oil, the novel formulation resulted in more serious abdominal cramping at the start of the treatment cycle.

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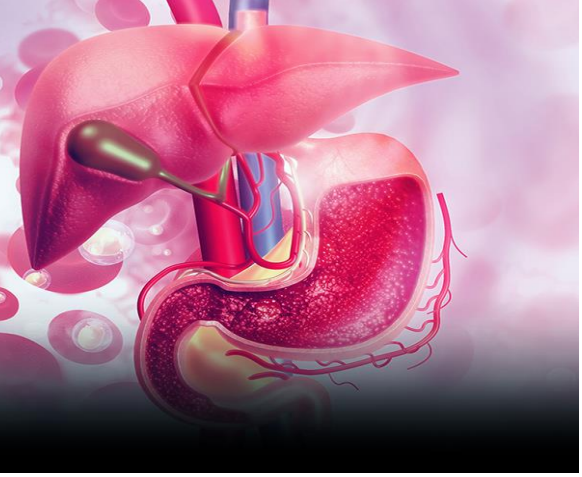

Consequently, our results, taken together, do not promote the usage or future production of this product for care of IBS patients. The explanation for increased incidence of abdominal cramps after ileocolonic release peppermint oil administration is uncertain and unexplained considering the agent's smooth muscle calming effects.

In respect to the effectiveness of peppermint oil, and relying on these observations, though, we conclude that the small intestine may be of greater value relative to the colon in terms of pain sensation development and IBS relief.

Therefore, considering the late onset of beneficial results, we postulate the presence of TRP channels on intestinal sensory afferents rather than a predominantly antispasmodic activity expected to appear more rapidly. From this viewpoint and in view of our observations, peppermint oil tends to be a desirable initial treatment source in IBS for the following reasons:

1) Peppermint oil is readily accessible as a low-cost OTC drug

2) Adverse effects are of a rather mild and intermittent nature

3) The usage of an herbal pharmacological agent without the possibility of severe adverse reactions may be appealing for patients

CONCLUSION

- By utilizing the pre-specified endpoint tests abdominal pain reaction and global relaxation of IBS symptoms based on FDA and EMA guidelines, peppermint oil relative to placebo was not better for patients with IBS.
- We find no benefits for the treatment of IBS from a guided Ileocolonic release peppermint oil formulation. However, traditional small-intestinal peppermint oil release enhanced secondary outcomes such as abdominal pain, gastrointestinal irritation, and frequency of IBS effects with a reduced adverse effect profile of 22 and good tolerability.
- Peppermint oil may therefore be deemed a beneficial therapeutic choice for the control of symptoms in IBS.