

## CASE SERIES

# Improvement in Gastroesophageal Reflux Symptoms From a Food-grade Maltosyl-isomaltooligosaccharide Soluble Fiber Supplement: A Case Series

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### Abstract

Gastroesophageal reflux disease (GERD) is a very common medical condition. Symptom improvement from ingested prebiotic soluble fiber has not been reported previously. In fact, a related soluble fiber, fructooligosaccharides, has been shown to worsen GERD. We report on a series of 24 patients with GERD, 88% of which improved after several weeks of daily consumption of a specific maltosyl-isomaltooligosaccharide (MIMO) fermented prebiotic soluble fiber. We also report on

2 proton pump inhibitor (PPI)-dependent patients with GERD who, after beginning daily MIMO, were able to eliminate PPI therapy. The hypotheses explaining the mechanism for GERD improvement with MIMO is discussed. To the best of our knowledge, these cases are the first time any prebiotic soluble fiber has been reported to improve or eliminate symptoms of GERD and enable patients with GERD to decrease or eliminate their PPI therapy.

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### Introduction

One of us (Peter Swann, MD) began receiving spontaneous, unsolicited reports from patients consuming a fermented maltosyl-isomaltooligosaccharides (MIMO) prebiotic. This product had never been marketed for gastroesophageal reflux disease (GERD) and the patients taking MIMO were doing so for other medical reasons. All patients reported a chronic history of symptomatic GERD with improvement or resolution, 2 to 8 weeks after daily ingestion of the MIMO prebiotic supplement. Because of these unsolicited reports, the database of customers taking this MIMO product was queried for their experience with GERD symptoms before and after taking MIMO prebiotic supplementation.

### Case Series

A total of 24 patients who had been previously diagnosed with GERD, who were taking daily MIMO for other reasons, responded to a standardized questionnaire. A total of 88% of these patients experienced GERD symptom improvement after MIMO supplementation. A total of 17% experienced complete symptom resolution.

### Case Reports

Because of the aforementioned case series results, and because MIMO is believed to be harmless, 2 additional patients with chronic GERD who wanted to decrease their proton pump inhibitor (PPI) use, were started on MIMO.

Patient 1 is a 73-year-old white female in good health. She has a 15-year history of postprandial substernal chest pressure, epigastric discomfort, and belching. Symptoms are generally worse after a large meal. She is a nonsmoker who has coffee each morning and drinks 1 glass of wine nightly with dinner. She has undergone upper endoscopy on 2 occasions and has uncomplicated GERD documented on biopsy. For the past 15 years, she has been maintained on a PPI, most recently esomeprazole 40 mg daily, with adequate symptom control. She has tried to decrease the dose of esomeprazole and/or substitute ranitidine and antacids due to her concerns about osteoporosis and other potential PPI side effects she has heard about. These changes in medication were without success due to return of symptoms. It was explained to her that there was no proof that any supplement (including MIMO) would help

her symptoms while reducing her PPI dose. She accepted that and was instructed to begin MIMO (ISOThrive prebiotic nectar, ISOThrive, Manassas, VA, USA) 1.4 mL once daily and taper off esomeprazole in the course of a 4-week period. During the 9 months subsequent to this, she has had no further use of PPI, H-2 antagonist, antacid or any supplement other than daily MIMO. She is asymptomatic except for mild bloating after a large meal. She continues coffee each morning and 1 glass of wine with dinner.

Patient 2 is a 45-year-old Korean female in good health. She has a 3-year history of substernal chest fullness with pressure and burning. She started adjusting her diet and ultimately could comfortably eat only a homemade porridge. She also developed hoarseness and sore throat. She could no longer sing in her church choir. Her primary care physician started her on esomeprazole 40 mg daily and had her evaluated by an ear, nose, and throat physician. Voice therapy did not help. She was next evaluated by a gastroenterologist approximately 18 months ago. An upper endoscopy revealed uncomplicated GERD by biopsy and 48-hour esophageal pH monitoring while off esomeprazole. She was asked to eat small frequent meals and not to lie down within 3 hours of eating, and her dose of esomeprazole was increased to 40 mg twice daily. She does not drink alcohol or smoke. At this dose, she was comfortable, and her voice and throat symptoms improved. She began reading and hearing about potential side effects of PPI and tried to reduce her dose of esomeprazole without success, due to worsening of symptoms. It was explained to her that there was no proof that any supplement (including MIMO) would help her symptoms while reducing her PPI dose. She accepted that and was instructed to begin MIMO (ISOThrive prebiotic nectar) 1.4 mL once daily and taper off her twice daily dose of esomeprazole in the course of a 4-week period. During the 6 months subsequent to starting MIMO, she has no further use of PPI, H-2 antagonist, antacid, or any supplement other than daily MIMO, except for PRN esomeprazole use, which occurs every 4 to 5 weeks if she overeats and feels chest pressure. She takes one 22-mg dose at that time. She is otherwise asymptomatic and has added foods back into her diet, such as chocolate, green tea, and tomato, which previously caused symptoms.

## Discussion

Our understanding of how GERD develops is evolving. Along with esophageal exposure to gastric acid, other factors involved in the pathophysiology include dysfunction of the lower esophageal sphincter (LES),<sup>1</sup> and variables that increase intragastric pressure such as gastric dysmotility,<sup>2</sup> hiatal hernia,<sup>3</sup> and body habitus.<sup>4</sup> Also important are additional characteristics of the refluxate, including the presence of pepsin, bile salts, *Helicobacter pylori*,<sup>5</sup> pancreatic juice,<sup>6,7</sup> swallowed toxins and irritants,<sup>8</sup> and genetic predisposition.<sup>9</sup>

Current proposals argue that the initial injury is not simply epithelial cell death caused by exposure to gastric refluxate. It is increasingly recognized that bacteria also play a role in the pathogenesis of GERD. Thus, recent discussions of the pathophysiology of GERD have addressed the importance of the microbiome intrinsic to the distal esophagus and LES.

Throughout the gastrointestinal tract there is a mucosal barrier that defends the local epithelium against local ambient aggressive factors. The nature of this barrier in the distal third of the esophagus, as well as in other areas of the gastrointestinal tract, is, in part, a product of the local microbiome.<sup>10</sup> Nearly 100 commensal species of bacteria reside in the distal esophagus.<sup>11</sup>

A contemporary proposed pathophysiology for GERD is as follows: multiple factors, including dietary changes and antibiotic use, alter the local microbiome from a symbiotic relationship to a dysbiotic, or potentially pathogenic, one. This dysbiotic state has been grossly characterized as a change in the esophageal microbiome from predominantly Gram-positive organisms to a majority of Gram-negative organisms.<sup>12</sup> This change alters the nature of the bacterial biofilm<sup>13</sup> altering, among other things, permeability. This, in turn, can negatively affect the maintenance of a robust mucosal barrier, exposing the esophageal epithelium to pathogenic bacteria, gastric refluxate, and swallowed bacterially produced toxins. Per Yang, in the GERD microbial dysbiotic state, the Gram-negative bacteria produce endotoxins that include lipopolysaccharides (LPS), which are located on the outer membrane of these Gram-negative organisms. These endotoxins are known to upregulate gene expression of proinflammatory cytokines<sup>14</sup> and are capable of triggering nitric oxide induced relaxation of the LES,<sup>15</sup> in effect, hindering its ability to sufficiently close and prevent gastric reflux.

LPS is also known to produce neuromuscular changes<sup>16</sup> in the LES that can result in decreased resistance to gastric pressure<sup>17</sup> and delayed gastric emptying,<sup>18</sup> both of which play a role in promoting esophageal reflux.

Orally ingested isomaltooligosaccharides have been shown to selectively increase populations of certain Gram-positive organisms in the colon, including *Bifidobacterium* and *Lactobacillus* species.<sup>19</sup> *Lactobacillus* species are also found in the mouth<sup>20</sup> and the distal esophagus<sup>21</sup> and are known to metabolize soluble fiber, including MIMO. MIMO thus may increase the populations of specific *Lactobacillus* species in the upper gastrointestinal tract and distal esophagus. The resulting increased number of Gram-positive organisms produce bacteriocins that can kill fungi and Gram-negative organisms such as *Listeria* species, as well as other pathogenic organisms.<sup>22</sup> For example, *Lactobacillus salivarius*, a common inhabitant of the human oral cavity, has been shown to produce a bacteriocin that inhibits *Campylobacter jejuni*,<sup>23</sup> a Gram-negative S-shaped rod. Macfarlane et al found

colonization of *Campylobacter* species in the distal esophagus of the majority of patients with Barrett's esophagus (BE) but none in controls.<sup>24</sup> Similarly, Blackett et al<sup>25</sup> found increased numbers of esophageal campylobacter in patients with GERD and BE.

## Conclusion

Improvement in GERD symptoms after ingestion of MIMO fermented soluble fiber was an unexpected outcome. The ability to decrease or eliminate PPI therapy in patients with chronic GERD by supplementing with a soluble fiber was also unexpected. This is especially true because oral ingestion of other molecular forms of soluble fiber, such as fructooligosaccharides, increases the rate of transient lower esophageal sphincter relaxations (TLESRs), and the number of acid reflux episodes, which increases the symptoms of GERD.<sup>26</sup>

This case series is the first-time a product containing soluble fiber has been reported to improve or eliminate symptoms of GERD. If there is a relationship between resolution of GERD symptoms and daily consumption of a supplement containing MIMO, then the mechanism likely involves either a change in the microbiome at the level of the LES, and/or is the result of a systemic response to a change in the intestinal microbiome due to MIMO. The proposed change involves local elimination of Gram-negative and other pathogenic bacteria, while increasing the numbers of Gram-positive bacteria. If the hypothesis is correct, MIMO would restore the protective symbiotic relationship at the LES.

Controlled studies comparing the action of various types of soluble fiber, including MIMO, should be conducted. If the resolution of GERD symptoms on daily consumption of indigestible soluble carbohydrates such as MIMO can be verified, then endoscopic studies should be done to correlate symptom control with healing. Ultimately, the mechanism, involving changes in the local microbiome, mucosal barrier, number of TLESRs, LES pressure, and gastric emptying may be elucidated.

## Author Disclosure Statement

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