

# LACTOBACILLUS PARACASEI SUBSP. PARACASEI F19 FOR THE TREATMENT OF EOSINOPHILIC COLITIS: A CASE REPORT AND LITERATURE REVIEW

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**Abstract** – Eosinophilic colitis (EoC) is a rare gastrointestinal (GI) disease that is not fully understood. It presents with different manifestations depending on the stratum and gastrointestinal area affected. EoC is characterized by intestinal inflammation rich in eosinophils, without any known causes of eosinophilia. Colon biopsies are required to identify this condition. It is not entirely clear whether EoC is a colonic manifestation of inflammatory bowel disease (IBD). To date, treatment has been based on steroids for an indefinite duration, dietary modification, and in some cases sodium cromoglycate and leukotriene receptor antagonists. We report the case of a 57 years old male patient who was admitted to the emergency department with persistent chronic diarrhea, abdominal pain, and malabsorption. After unsuccessful therapy with steroids and mesalazine, he received *Lactobacillus Paracasei* subsp. *paracasei* F19, which improved symptoms, endoscopic pattern, laboratoristic parameters and general condition.

**Keywords:** Probiotics, Eosinophilic colitis, Lactobacillus, Microbiota.

## INTRODUCTION

Eosinophilic colitis (EoC) is a rare gastrointestinal (GI) disorder that affects neonates and young adults of both sexes<sup>1</sup>. Colon biopsies are the gold standard for diagnosis<sup>2</sup>. EoC, along with eosinophilic esophagitis and eosinophilic gastroenteritis, belongs to the “eosinophilic diseases” of the digestive tract<sup>3</sup>. The cecum and vermiform appendix of the colon usually contains the highest concentrations of eosinophils in the lamina propria<sup>4</sup>. They play an important role in protecting against pathogens, especially parasitic infections<sup>5</sup>. When activated, they release a large number of inflammatory mediators and cytotoxic proteins which are host defenses but are also responsible for inflammation and damage in the colon<sup>6</sup>. Factors leading to eosinophil activation include food allergens, parasite infections, certain drugs, or malignancies<sup>7</sup>. EoC is characterized by intestinal inflammation with GI symptoms (abdominal pain, bleeding, diarrhea, etc.) without a known etiology of eosinophilia. There are no standardized diagnostic criteria yet and prospective studies on treatment are still lacking<sup>8</sup>. Probiotics are live microorganisms that provide health benefits improving and re-



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storing intestinal flora through various mechanisms of action. Probiotics have been used in various gastrointestinal diseases, such as inflammatory bowel disease, chronic diarrhea, constipation, diverticular disease, and diverticulitis but never in eosinophilic gastrointestinal diseases<sup>9-14</sup>.

## CASE REPORT

We report the case of a 57-year-old man who was admitted to the emergency department (ED) because of persistent diarrhea, weight loss, and recurrent episodes of abdominal pain associated with meals. He had a history of gastroesophageal reflux and chronic gastritis. The patient had undergone esophagogastroduodenoscopy with gastric and duodenal biopsies that excluded both intestinal villous atrophy and the presence of eosinophilic infiltrates in the gastric mucosa. Anti-endomysium antibodies were negative. The patient also tested negative for food allergies. He was treated by a gastroenterologist for suspected Crohn's disease. The patient was evaluated for possible causes of eosinophilia and treated with proton pump inhibitors, steroids, and sodium cromoglycate for one month with no benefit. Then, his therapy was changed, and he started cholestyramine, diosmectite, and mesalamine (3200 mg/day) and high doses of steroids (methylprednisolone, 1 mg/kg/day). When he came to our observation, steroids were gradually discontinued, and other chronic therapies were suspended. On examination, the abdomen and vital signs were normal. No fever was noted. Blood tests revealed normal values for creatinine, glucose, transaminase, total and direct bilirubin, amylase, lipase, creatine kinase, lactate dehydrogenase, coagulation parameters, hemoglobin, white blood cells, eosinophils, and c-reactive protein. Cholesterol and triglycerides were slightly higher than normal. Stool samples were negative for *Clostridioides difficile*, *Salmonella spp*, *Shigella spp*, *Campylobacter spp*, protozoa, and other enteric pathogens, but positive for blood. Fecal calprotectin was 915 mcg/g (normal value < 50 mcg/g). Colonoscopy+ biopsy revealed small ileal erosions with evidence of chronic inflammation with eosinophilic granulocyte infiltrate. Therapy with *Lactobacillus paracasei* subsp. *paracasei* F19 (LP -F19) at a dosage of  $12 \times 10^9$  CFU/ml was administered in sachets three times daily for 30 days. No adverse effects were reported. The patient was examined after one month and reported improvement in his gastrointestinal symptoms and general condition. After 30 days of probiotic supplementation, he repeated fecal calprotectin, which showed normal findings, and colonoscopy+ biopsy, which showed normal ileal epithelium with resolution of erosions and absence of eosinophilic cells.

## DISCUSSION

EoC is a rare GI disorder estimated to occur in 3.3/100,000 people in the United States. More than 50 HPF (high power field) in the right colon wall or more than 35 in the transverse colon or more than 25 in the left colon wall characterize it<sup>14</sup>, although there are no standard histologic criteria or cutoff values for specific eosinophil count in colon tissue<sup>5</sup>. Two main forms are distinguished: primary and secondary eosinophilia when associated with allergies, gastrointestinal infections, inflammatory bowel disease, vasculitis, celiac disease, autoimmune diseases, drug reactions, and cancer<sup>15</sup>. Primary EoC can affect both children and adults. Eosinophils can typically infiltrate the lamina propria and spread through the muscularis mucosa and submucosa, with endoscopic evidence of edema, loss of normal vessels, erythematous changes, and often ulceration<sup>14-16</sup>. In the normal state, the small intestine is colonized by eosinophils, which play an important role in the response to intestinal pathogens (bacteria, viruses, parasites, etc.) and interact with the host microbiota. Moreover, eosinophils respond to cytokine signaling and promote local immunity and host defense<sup>17</sup>. The results of literature studies<sup>18</sup> suggest that eosinophils also maintain epithelial barrier function, but the mechanism remains to be elucidated. When excessive numbers of eosinophils are present in the intestinal wall, inflammation develops with the clinical presentation of diarrhea (with or without blood), abdominal



**Figure 1.** Beneficial gut-effects of the probiotic strain *Lactobacillus Paracasei* subsp. *paracasei* F19.

pain, weight loss, bloating, and nausea. Prospective randomized controlled trials on therapeutic approaches are lacking. Case reports and small case series suggest treatment based on elimination diets, steroids to inhibit eosinophil growth factors, such as IL-5, IL-3, and GM-CSF, immunomodulatory agents, such as azathioprine or 6-mercaptopurine, leukotriene D4 blockers, antihistamines, and sodium cromoglycate as a cell stabilizer<sup>19</sup>. Recent studies<sup>5</sup> demonstrate interest in the therapeutic properties of some probiotic strains in reducing intestinal inflammation and restoring balance in the composition of the gut microbiota. Some *Lactobacillus* or *Bifidobacterium* strains may even provide health benefits to the host by modulating the action of eosinophilic cells. Studies in the literature<sup>6</sup> show that eosinophils can respond to oral administration of probiotics, leading to improvement and resolution of gastrointestinal inflammation. In this regard, some probiotics<sup>20</sup>, such as *Lactobacillus Paracasei* subsp. *paracasei* F19 (LP -F19)<sup>21</sup> have shown beneficial effects in preventing some diseases such as atopic dermatitis<sup>22</sup>, which in some cases is characterized by increased numbers of eosinophils in the blood and tissue infiltrates, and in slowing the progression of necrotizing colitis in children<sup>23</sup>. Among the many other properties of LP-F19 revealed by Di Cerbo et al<sup>21</sup> are the genetic stability of this strain, clinical safety, benefits for intestinal motility, metabolic properties in activating lipid metabolism and balancing blood glucose levels, and the ability to elicit a Th1 response and suppress a Th2 response (and thus correlate with eosinophil activity and cytokine production) (Figure 1). Further studies on the benefits of this probiotic for gut health are ongoing.

## CONCLUSIONS

Supplementation with LP-F19 effectively improved gastrointestinal symptoms and histopathological patterns of EoC. Further studies with more patients on dosing, timing, and possibly other probiotic strains are needed to better define these issues.

## Conflict of Interest

The authors declare no conflict of interest.

## Informed Consent

The patient gave informed consent for the publication of this case report.

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