PROBIOTICS: BOON OR A BANE IN CROHN’S DISEASE

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ABSTRACT

Crohn’s disease is one of the complex disease entity to treat. Though there are medication available for the therapy of this inflammatory bowel disease, few drugs are safe to be given on a longer run. There are hardly any studies and research work on probiotics which is presumed to have a role in the therapy of crohn’s disease. Hence, we sought to review the available scientific resources to know the status of probiotics in the treatment of crohn’s disease.

KEYWORD: Probiotics; Crohn’s disease; Inflammatory bowel disease.

INTRODUCTION

The etiopathogenesis of Crohn’s disease (CD) is complex and consists of three interacting elements: environmental factors, genetic susceptibility and infectious agents. The most widely accepted theory is that this disorder is caused by an aggressive immune response to microorganisms of the intestinal microbiota in genetically predisposed individuals. Numerous epidemiological studies, clinicopathological data, genetic and experimental evidence increasingly support an implication of microorganisms in CD pathogenesis. One of the three exclusive theories currently explored to explain the infectious etiology of CD is “dysbiosis”, i.e. a modification of intestinal microbiota composition with an imbalance between beneficial and harmful bacteria.¹

The human gastrointestinal (GI) tract contains $10^{14}$ microorganisms of more than 500-1000 different species, forming intestinal microbiota. The density of intestinal microbiota varies along the GI tract, going from $10^2$ colony forming units (CFU) per gram in stomach to $10^{12}$ CFU per gram in colon.² An imbalance of the intestinal microbiota, i.e. a modification of its...
composition, with decreased complexity of commensal bacterial profiles and higher numbers of mucosa-associated bacteria, has been reported in CD patients.\(^1\) Currently to summarize the drugs currently used for treating crohn’s disease are: folic acid antagonists, modulators of intestinal microbiota, corticosteroids, thiopurines, anti-TNF antibodies, anti-IL-12 antibodies, HSCT (hematopoietic stem cell transplantation), MSC (mesenchymal stromal cells) all of which have their different levels of efficacy and toxicities.\(^3\) Given that intestinal dysbiosis has been postulated to cause CD in genetically predisposed individuals, therapeutic strategies based on the use of probiotics to modulate the imbalance of intestinal microbiota observed in CD patients.

Probiotics are defined as “a living microbial food ingredient with a beneficial effect on human health”.\(^4\) Potential action mechanisms of probiotics include competitive interactions with enteropathogens, production of antimicrobial metabolites, influences on the epithelium, and immune modulation.\(^5\)

Current clinical evidence for probiotics usage in crohn’s disease

Table 1- Clinical trials on probiotics in active crohn’s disease and maintenance of remission.

<table>
<thead>
<tr>
<th>Active crohn’s disease</th>
<th>Design</th>
<th>Strain</th>
<th>Trial period</th>
<th>N</th>
<th>Results</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Open label pilot</td>
<td><em>Lactobacillus rhamnosus GG</em></td>
<td>6 mts</td>
<td>4</td>
<td>Improvement in clinical status</td>
<td>(^6)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td><em>Lactobacillus rhamnosus GG</em></td>
<td>6 mts</td>
<td>11(5)</td>
<td>No benefit of lactobacillus GG in inducing or maintaining remission in CD</td>
<td>(^7)</td>
</tr>
<tr>
<td></td>
<td>Open label</td>
<td>Synbiotic ((Bifidobacterium breve, Lactobacillus casei, Bifidobacterium longum) + (psyllium))</td>
<td>13 mts</td>
<td>10</td>
<td>Safe and effective for active CD</td>
<td>(^8)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td>Synbiotic (Bifidobacterium longum + (Oligofructose+Inulin))</td>
<td>6 mts</td>
<td>35(13)</td>
<td>Significant clinical improvement and increased histological scores</td>
<td>(^9)</td>
</tr>
<tr>
<td>Maintenance of remission in crohn’s disease</td>
<td>R</td>
<td><em>Saccharomyces boulardii</em></td>
<td>6 mts</td>
<td>32(16)</td>
<td>Useful in remission maintenance</td>
<td>(^10)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td><em>Lactobacillus rhamnosus GG</em></td>
<td>24 mts</td>
<td>75(39)</td>
<td>Not useful in maintenance</td>
<td>(^11)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td><em>Lactobacillus rhamnosus GG</em></td>
<td>12 mts</td>
<td>45(23)</td>
<td>No significant difference in recurrence rate compared to placebo</td>
<td>(^12)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td><em>Lactobacillus johnsonii LA1</em></td>
<td>6 mts</td>
<td>98(48)</td>
<td>No difference observed with placebo group</td>
<td>(^13)</td>
</tr>
<tr>
<td></td>
<td>DRPC</td>
<td><em>Lactobacillus johnsonii LA1</em></td>
<td>3 mts</td>
<td>70(34)</td>
<td>No difference observed with placebo group</td>
<td>(^14)</td>
</tr>
</tbody>
</table>
DRPC: Double blind randomized placebo controlled trials; R: Randomized; N: Total number of participants and actual number on probiotics in parenthesis; Mts: months; Ref: Reference

There is scarcity of clinical studies in CD. It is noted from the above table 1 that some strains used as probiotics has shown promise in the treatment of active CD and there should be no compunction in using them especially the symbiotic. Majority of the studies which employed probiotics to maintain the remission in CD is disappointing. Similarly, cochrane review regarding probiotics for maintenance of remission in CD by Rolfe et al.(15), found no benefits for the strains *E. coli Nissle* for reducing the risk of relapse compared to placebo, or for *Lactobacillus rhamnosus GG* after surgical or medically- induced remission. There was no benefit of probiotics for reducing the risk of relapse compared to maintenance therapy with aminosalicylates or azathioprine but found more adverse events in *Lactobacillus GG* treated patients.

CONCLUSION

It is observed from the available few clinical trials that very few patients were enrolled in studies as participants and in some of the studies probiotics were given with other drugs. This makes it hard to come to any reasonable conclusions. Nevertheless, the available evidence indicates probiotics can be used in active CD treatment and its use is not appropriate in maintenance therapy. Since CD is a complex entity, the efficacy of probiotics may depend on the part of gut involved, strains used and timing of administration with respect to course of the disease. Future clinical trials should be conducted in large number of patients and keeping all these in mind to make a acceptable conclusion on the status of probiotics use in CD.

Conflict of interest

None.

REFERENCE


Dis., 2007; 13(2): 135–42.