Review of the Evidence for the Use of Probiotics in Gastrointestinal Disorders

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Abstract

The gut microbiota fulfils important metabolic and immunological tasks, and floral imbalance may lead to the development of dysbiosis and microbiota-related diseases. The most common illnesses associated with dysbiosis include infections, inflammatory bowel disease, Irritable Bowel Syndrome (IBS), colorectal cancer, and other gastrointestinal functional diseases which cause diarrhoea directly, or indirectly through treatment. In theory, every disorder associated with dysbiosis might benefit from modulation of the gut microbiota. We review the evidence for probiotics in prevention and treatment in these gastrointestinal disorders. We found probiotic efficacy was strain specific. They are well tolerated with minimal toxicity. There appears to be selective benefit of *Saccharomyces boulardii* and a mixture of *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Lactobacillus bulgaricus* and *Streptococcus thermophilus* probiotics as prophylaxis of travellers' diarrhoea. *S. boulardii* is useful in treating travellers' diarrhoea where other medical treatments have failed. For IBS, a mixture of bacterial strains including lactobacillus and bifidobacteria may be the most effective in IBS collective symptoms. Probiotics, especially those containing multiple strains can maintain remission in ulcerative colitis and also demonstrate efficacy in pouchitis. There is currently no evidence for probiotics in Crohn's disease. *Lactobacillus* species appear to be the most effective in preventing *Clostridium difficile* infections. For lactose intolerance there is most evidence for *Lactobacillus rhamnosus* and *bifidobacterium* usually in combination. Probiotics, in particular *Lactobacillus* and *Bifidobacteria* species have a beneficial role in the care of patients with diarrhoea associated chemotherapy and radiotherapy.

Keywords: Diarrhea; Probiotics; Dysbiosis; Inflammatory Bowel Diseases; *Bifidobacterium*; *Lactobacillus*

Introduction

The gastrointestinal tract naturally contains trillions of bacteria, which is estimated to account for 1-3% of total body mass [1] and collectively is known as the gastrointestinal microbiota. Most of the endogenous bacteria in healthy adults belong to just two phyla, *Firmicutes* and *Bacteroidetes*, which account for > 90% of the known phylogenetic categories of the human gastrointestinal tract [2]. They are important for maintaining not only gastrointestinal health, but they also impact

on the body's immune system [3]. The balance and mix of bacteria can be affected by many different factors, including antibiotics, aging, and illnesses such as Inflammatory Bowel Disease (IBD), following infective gastroenteritis, after cancer treatment or gastrointestinal surgery.

One way of boosting the natural beneficial bacteria in the gastrointestinal tract is by increasing the level of prebiotics in the diet. Prebiotics are forms of carbohydrate that only the gut bacteria can feed upon. Good sources of prebiotics in the diet include bananas, onions, garlic, asparagus, artichoke and chicory. These foods can cause unwanted side effects however e.g. bloating and increased bowel frequency, so some prefer to consume bacteria instead and thus take a probiotic product. Probiotic bacteria are live microorganisms that, when administered in adequate amounts, confer a health benefit to the host [4]. Probiotics may elicit immunomodulatory effects through direct interactions with the intestinal epithelium, especially in the small intestine, which is less densely populated by the commensal microbiota [5]. By contrast, probiotic immunomodulatory effects in the colon, where microbiota are densely populated, are more likely to occur via modulation of the endogenous microbiota [6].

There are a few possible mechanisms by which modulation of the gut microbiota specifically improves gastrointestinal disorders, although none of this is fully understood yet.

In Irritable Bowel Syndrome (IBS), probiotics and synbiotics (probiotic and prebiotic) can correct bacterial imbalances (dysbiosis) when increased intestinal permeability and barrier dysfunction exist [7]. A decrease in microbial biodiversity and increase in fungi has been found in mucosa and faeces of IBD patients; pre- and probiotics can modulate gut microbiota [8]. The leading hypothesis for IBD and pouchitis is that dysbiosis plays an active role in inducing and maintaining persistent inflammation. The dysbiosis in pouchitis patients is characterised by reduced diversity of the microbiota, which may lead to abnormal mucosal immune regulation triggering the inflammatory processes in genetically predisposed patients [9]. Thus treating the dysbiosis is considered a treatment. In cancer, dysbiosis in the human gut microbiota after chemotherapy may favour colonisation with

Clostridium difficile (*C. difficile*) and *Enterococcus faecium*, thus introducing competitive probiotic bacteria back into the gut may offer protection [10]. Unlike chemotherapy, it is not known which specific bacteria are involved in causing diarrhoea during pelvic radiotherapy, but there is evidence that dysbiosis occurs as a result of this treatment [11]. *C. difficile* is a bacterial infection in itself, resulting from gut microbiota dysbiosis. High numbers of protective bacteria, have been shown to reduce incidence of *C. difficile* infection as it is thought that some bacteria are better at competing than *C. difficile* [12]. Preventing dysbiosis is the key here, as modulating gut bacteria after infection proves difficult. In travellers' diarrhoea, the potential mechanisms by which balanced gut microbiota fights infectious diarrhoea include exclusion of pathogens by means of competition for binding sites and available substrates, lowering of luminal pH and production of bacteriocins, and promotion of the production of mucus [13]. Quite differently, in lactose intolerance, when some probiotics are introduced into the gut, they produce beta-galactosidase or lactase intracellularly that may assist in the digestion of lactose. These enzymes may alleviate clinical symptoms brought about by undigested lactose for other reasons (influence of colonic flora, the colonic pH), and hydrogen production [14].

There are many controversies regarding probiotics. Some of these are around which type of patients can benefit from their use, or even be put at risk from their use. For example, during immunosuppression and critical illness, fungemia is theoretically possible from yeast probiotics such as *S. boulardii*. Other controversy includes the difficulty in drawing conclusions from heterogeneity of probiotic studies (Table 1). Due to such uncertainty and limited evidence, the use of probiotics is confusing for both doctor and patient.

There are many different types of probiotics which are available, some in liquid form such as fermented milk drinks and yoghurts, as well as in supplements in the form of tablets, capsules or sachets. The most commonly used probiotics for diarrhoea disorders include: *Saccharomyces boulardii*, *Lactobacillus acidophilus* (*L. acidophilus*), *Lactobacillus brevis* (*L. brevis*), *Lactobacillus casei* (*L. casei*), *Lactobacillus rhamnosus* strains (*L. rhamnosus*/*L. rhamnosus GG*), *Bifidobacterium breve* (*B. breve*), *Bifidobacterium lactis* (*B. lactis*), *Bifidobacterium longum* (*B. longum*) and *Streptococcus thermophilus* (*S. thermophilus*). These probiotic bacteria have been used in relation to travellers'

diarrhoea, IBS, cancer, IBD, pouchitis, *C. difficile* and lactose intolerance. Undoubtedly, the combination of bacterial species and dose is important, however defining the most appropriate probiotic has been largely based more on marketing, rather than the best evidence.

Methods

Bibliographical searches were performed in Pubmed and Google scholar for the terms: travellers' diarrhoea, cancer, *Clostridium difficile*, inflammatory bowel disease, irritable bowel syndrome, pouchitis and lactose intolerance. The searches were combined with the generic terms; probiotic, *Saccharomyces*, *Lactobacillus*, *Bifidobacterium* as well as frequently used strains *Saccharomyces boulardii*, *Lactobacillus acidophilus*, *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus rhamnosus* strains including *rhamnosus GG*, *Bifidobacterium breve*, *Bifidobacterium lactis*, *Bifidobacterium longum* and *Streptococcus thermophilus*. For each gastrointestinal disorder, we excluded most *in vitro* and animal studies unless specifically relevant to the human conditions as noted above and prioritised meta-analyses, systematic (including Cochrane) reviews and randomised controlled trials (RCT's) where available. A final total of 70 papers were reviewed.

Results

Travellers' Diarrhoea

Travellers' diarrhoea is a common problem that affects 20-60% of travellers' who visit high risk parts of the world with contaminated food or water. Although cases of travellers' diarrhoea in returning residents continue to decrease on the whole, both *Campylobacter* and *Salmonella* are still the most common infections throughout the world [15]. Infections of *Shigella* spp, *Giardia* and *Entamoeba* spp is predominantly reported as having been associated with travel to lower income countries with less robust sanitation such as the Indian sub-continent, and Sub-Saharan and Southern Africa. For example, a study of London travellers' also found a predominance of *Giardia* cases in travellers returning from the Indian sub-continent, in particular Nepal [16].

Studies have demonstrated mixed results when administering probiotics to travellers. For example in a RCT study of travellers to Egypt, a mixture of *L. acidophilus*, *B. bifidum*, *L. bulgaricus*, and *S. thermophilus* or placebo, reduced the frequency of diarrhoea (43% versus 71% in the placebo) [17]. Oksanen et al. [18] compared *L. rhamnosus GG* with placebo in travellers' to Turkey, and found a reduction in diarrhoea (23.9% versus 39.5% in the placebo group) [18]. A double blinded placebo-controlled trial of *L. rhamnosus GG* in United States travellers' also showed a significant effect, with diarrhoea developing in 3.9% per day at risk compared with 7.4% in the placebo group [19].

However, other studies have failed to show a beneficial effect. In 50 travellers' to Mexico, prophylactic ingestion of a mixture of *L. acidophilus* and *L. bulgaricus* was not effective in reducing the frequency or duration of new-onset diarrhoea [20]. In a study of

Table 1: Limitations in concluding evidence from probiotic studies.

Number of colony forming units used/alive in dose
Form of product: powder/capsule/dairy drink or yoghurt
Single strain vs. multi strain doses
Inclusion of prebiotics in the dose or diet
Treatment duration
Type of patient population
Number of patients treated
Randomisation, controls and blinding of clinical trials

British soldiers who were deployed to Belize, participants were administered *Lactobacillus* there was no significant difference in the prevalence of diarrhoea between groups that received administered *Lactobacillus. fermentum* strain KLD, *L. acidophilus* or placebo. There were no significant differences in the incidence of diarrhoea between any groups after 3 weeks (23.8%, 25.7% and 23.8% respectively) [21].

A meta-analysis of 12 published RCT's which met inclusion and exclusion criteria and found that *S. boulardii* and a mixture of *L. acidophilus* and *B. bifidum* probiotics appear the best at preventing travellers' diarrhea [22].

A prospective study of 96 individuals returning from abroad with at least 11 days of travellers' diarrhoea already, were given 150-450mg *S. boulardii* which on average halted diarrhoea within 5 days. Sixty seven percent of these patients had previously tried anti-diarrhoeal agents or antibiotics, however only *S. boulardii* worked [23].

The problem with all the studies is knowing what should be the correct combination of bacterial species within a probiotic therapy and in what dose to prescribe them. Additionally, different types of travellers' diarrhoea from different countries may require different probiotic species.

Conclusion: There appears to be selective benefit of *S. boulardii* and a mixture of *L. acidophilus*, *B. bifidum*, *L. bulgaricus* and *S. thermophilus* probiotics as prophylaxis of travellers' diarrhoea. *S. boulardii* could be useful in treating travellers' diarrhoea where other medical treatments have failed.

Irritable Bowel Syndrome

IBS affects up to 20% of the world's population and accounts for a significant proportion of visits to primary and secondary care physicians. It is known that IBS patients have abnormal reflexes and perception in response to gastrointestinal stimuli and the individual symptoms may depend on the specific neural pathways affected. Several pathogenetic factors could cause these disturbances, including: genetic, early and environmental conditioning; cognitive/emotional adaptation; abnormalities in the composition of the gut microbiota; altered response to stress and inflammatory/post infectious processes in the gastrointestinal mucosa [24]. Hypothetically, probiotics may correct or counteract some of these underlying disturbances as specific probiotic strains may modulate gastrointestinal transit, visceral hypersensitivity, intestinal gas content, and inflammatory responses. IBS lacks effective drug management and the potential for probiotics is important. One IBS trial was unable to identify a mechanism of probiotic action but speculated that efficacy must result from factors other than the presence of induced microbiota itself (i.e. through action via direct interaction with the immune system rather than via interaction with the local bacterial colony) [25]. As previously mentioned, this direct action is more likely to occur in the small intestine where the microbiota density is lower [5].

It is however important to note that effects are strain specific

for each IBS symptom and one strain does not fit all [26]. Four review articles of probiotics in IBS [27-30] were subject to a meta-analysis which concluded that probiotics could improve the global IBS symptom score and reduce abdominal pain, but may not significantly affect specific IBS symptoms of diarrhoea, constipation, and/or bloating [31].

A Canadian systematic review of 19 RCT's concluded probiotics appear to be efficacious in IBS, but the magnitude of benefit and the most effective species and strain are uncertain [32]. Three studies of three probiotics evaluated diarrhoea as a secondary end point. Two studies reported no difference between specific probiotic treatments and placebo [33,34] and one study reported a significant increase of diarrhoea with the probiotic compared with placebo [35]. A review of 42 RCT's looked at the effect of lactic acid bacteria on IBS symptoms [36]. Thirty-four of these trials reported benefit in at least one of the end points studied, but only the VSL#3 mixture (*L. acidophilus*, *L. bulgaricus*, *L. casei*, *L. plantarum*, *S. thermophilus*, *B. breve*, *B. infantis*, *B. longum*) was found to reduce diarrhoea [37]. Another review of 16 RCT's found that 11 trials were not blinded well enough, were too short/small, and/or lacked intention to treat analysis [38], but they concluded that only *Bifidobacterium infantis* [39,40] showed significant improvements in bowel movements compared with placebo.

Most recently, a European Consensus Committee following systematic review of the literature and a Delphi process of consensus concluded specific probiotics help reduce overall symptoms burden and abdominal pain in some IBS patients. Symptom improvement includes reduced bloating, distension and improvement in bowel frequency and some probiotics improved quality of life [41].

Conclusion: A mixture of bacterial strains including lactobacillus and bifidobacteria may be the most effective in IBS collective symptoms with a good safety record and are thus appropriate for therapeutic trial in holistic IBS therapy.

Inflammatory Bowel Disease

Inflammatory Bowel Disease includes Crohn's disease and ulcerative colitis, with diarrhoea being a prevalent symptom in these patients. Patients often relapse with standard medical therapies (e.g. steroids and 5-amino-salicylic acid compounds). Given that an imbalance or a severe response to intraluminal bacteria seems to be involved in the pathogenesis of inflammatory bowel disease, including pouchitis [42], probiotic therapy to modify the bacterial flora is an attractive option.

Three studies using *L. rhamnosus GG* concluded no effects in Crohn's disease [43-45]. In addition, a meta-analysis on eight clinical trials looking at different probiotic strains confirmed this lack of benefit [46]. There is limited evidence that *S. boulardii* probiotic given in conjunction with mesalazine can increase remission time [47], and the British Dietetic Association 2013 guidelines concludes that there does not appear to be a benefit for probiotic use in Crohn's disease patients [48].

Using probiotics in Ulcerative Colitis (UC) can induce

remission [49]. Studies using preparations containing mainly bifidobacteria and commercial mixtures, including VSL#3 [50–56] revealed efficacy in the maintenance therapy of UC patients. In a meta-analysis of 23 RCT's only VSL#3 significantly increased the remission rates compared with controls in patients with active UC [57]. The most recent meta-analysis states that the same formulation is also safe and more effective than conventional therapy alone in achieving higher response and remission rates in mild to moderately active ulcerative colitis [58].

Up to 60% of patients following proctocolectomy and ileal-anal pouch formation develop an inflammatory condition often associated with bowel urgency and frequency, termed pouchitis. There appears to be a derangement in the pouch microbiome hence benefit has been shown for both antibiotics and probiotics.

Studies have tended to be small and of variable length. One study used the probiotic *L. rhamnosus* GG [59]; the other studies used combination of probiotics [60–64], including VSL#3. The comparison was made to placebo-treated control groups receiving maize starch or microcrystalline cellulose. The clinical efficacy of the probiotic intervention was evaluated based on clinical, histological, endoscopic and microbiological criteria, including the pouchitis disease activity index. The five studies using high dose probiotic mixture demonstrated clinical efficacy in pouchitis [60–64]. The study using *L. rhamnosus* GG alone observed alterations in intestinal microbiota but no other effects on clinical parameters [59]. In the most recent meta-analysis of 23 RCT's, only VSL#3 significantly reduced the clinical relapse rates for maintaining remission in patients with pouchitis [58]. Primary prevention of pouchitis and reducing the likelihood of relapse after successful antibiotic treatment has led to the highest possible rating, an 'A' recommendation [65].

Conclusion: Probiotics, especially those containing multiple strains can maintain remission in ulcerative colitis and also demonstrate efficacy in pouchitis. There is currently no evidence for probiotics in Crohn's disease.

***C. difficile* and antibiotic associated diarrhoea**

C. difficile is a major source of concern and infection in the hospital setting and is most frequently the result of broad spectrum antibiotic therapy. The cause is attributed to the reduction of the endogenous protective gastrointestinal microbiota [66]. *C. difficile* acquired diarrhoea causes 10–20% of all cases of antibiotic associated diarrhoea [67] and it can occur up to 8 weeks after antibiotic therapy [68]. A review of antibiotic associated diarrhoea in children found that *Lactobacillus* GG, *S. boulardii*, *B. lactis* and *S. thermophilus* reduced the risk of antibiotic-associated diarrhoea [69]. As evidence gathered for probiotics, it led to a Cochrane database of systematic review, evaluating their efficacy in acute infectious gastroenteritis [70]. There has also been significant interest to assess if probiotics can prevent *C. difficile* infection.

In a study of hospitalized patients, *L. acidophilus* alone or in combination with *L. casei* appears to prevent *C. difficile* infection

[71–74]. A dairy drink including *Lactobacillus casei*, *Lactobacillus delbrueckii subsp. bulgaricus* and *S. thermophilus* may also reduce rates of *C. difficile* infection [75]. A meta-analysis of 6 trials found the relative risk of getting antibiotic associated diarrhoea is significantly reduced while taking *L. rhamnosus* GG [76]. Despite the evidence, probiotics were considered insufficient to classify as the high grade 'A' recommendation in *C. difficile* associated diarrhoea [65].

In 2013, a more recent review and meta-analysis of 23 RCT's, including 4213 patients, suggests moderate quality evidence that probiotics are both safe and effective for preventing *C. difficile*-associated diarrhoea [77]. A further systematic review and meta-analysis of 16 studies found that probiotics were safe and effective for use in preventing antibiotic associated diarrhoea and *C. difficile* in inpatients requiring antibiotics [78]. They also conclude that *Lactobacillus* based products are slightly better than the others to prevent this type of diarrhoea and infection [78].

Conclusion: *Lactobacillus* species appear to be the most effective in preventing *C. difficile* infections, but more randomised trials need to be undertaken to identify whether a single strain or a mixture of probiotics work best.

Lactose intolerance

Lactose intolerance affects 70% of the world's population [79] and is mainly caused by lactase enzyme deficiency which leads to diarrhoea and nutrient malabsorption [82]. It could be possible to reduce the symptoms of lactose intolerance i.e. diarrhoea with the use of probiotics. The replacement of dietary milk with low-lactose and *L. rhamnosus* enriched dairy products has been shown to prevent the symptoms of lactose intolerance [80]. Another dairy drink (Yakult containing *L. casei* Shirota and *B. breve*), taken for four weeks, improved symptoms and decreased hydrogen production in lactose-intolerant patients. There was a lasting effect for at least 3 months after stopping probiotic intake [81].

In post infectious IBS, secondary lactase deficiency was detected in 59.4% of 138 patients, and all of those suffering secondary lactase deficiencies also had small intestinal bacterial overgrowth (SIBO) [82]. SIBO was confirmed using lactulose breath testing. A probiotic mixture of *B. longum* 107 and *Enterococcus faecium* 107 was administered as one capsule t.i.d. for 14 days. Restoration of eubiosis in the small bowel lumen was achieved in 70.8% of the patients, as shown by reduction in SIBO [82].

Conclusion: There is a benefit from taking probiotics in lactose intolerance. There is most evidence for *L. rhamnosus* and *bifidobacterium*, often in combination.

Cancer

Probiotics may be useful in reducing colorectal cancer risk [83], but the best evidence in human trials of colorectal cancer prevention involves synbiotics [84].

Components in our diet may affect the gut microbiota and

influence colorectal oncogenesis. Excess fat in the diet means that more bile will be produced and more bile acids will escape the enterohepatic circulation. In the colon, these can be metabolised to mutagenic components [85]. Probiotics such as *Lactobacilli* metabolise heterocyclic amines and are not fermented [86]. Meat cooked at high temperatures contains high levels of heterocyclic amines which have been found to be fermented by gut microbiota and the byproducts of this process can damage DNA and increase the risk of colorectal cancer [87]. There is a completed Phase 2 trial assessing the role of probiotics on gut microbiota and colorectal cancer but the results have not been published yet [88]. The role of the VSL#3 probiotic combinations in rectal cancer is being investigated in a phase 3 clinical trial and results are also due [89].

Some cancer therapies can be associated with gastrointestinal disturbance often including diarrhoea. The role of probiotics has been assessed in these patients. There is more information for patients with colorectal cancer [83], than other cancers at present. The theoretical risk of giving probiotics to potentially immunocompromised patients appears not to be substantiated in published studies although *S. boulardii* has been associated with fungemia [90-92]. In one randomised study of 150 patients diagnosed with colorectal cancer, half were given *L. rhamnosus GG* supplementation during 5-FU-based chemotherapy. *L. rhamnosus GG* was well tolerated and reduced the frequency of grade 3 or 4 diarrhoea (22% v's 37%) and abdominal discomfort related to 5-FU-based chemotherapy [93]. In another study, 398 men and women who were free from tumour but who had at least two colorectal tumours removed were given wheat bran and/or *L. casei*. It was found that *L. casei* prevented atypia of colorectal tumours [94]. A study of 31 subjects undergoing elective colorectal resection for cancer were given a mixture of *B. longum* and *L. johnsonii*. It was found that only *L. johnsonii* adhered to the colonic mucosa and affects intestinal microbiota by reducing the concentration of pathogens and modulates local immunity [95]. In a study of 37 high grade dysplastic /colorectal cancer patients, and 43 polypectomized patients were given a synbiotic preparation of oligofructose- enriched inulin, *L. rhamnosus GG* and *B. lactis*. The number of stool *Bifidobacterium* and *Lactobacillus* increased, stool *Clostridium perfringens* decreased, and there was a reduction of colorectal proliferation [84]. Additionally in another study, 50 patients with colorectal carcinoma scheduled for radical colectomy were given probiotics containing *Lactobacillus plantarum*, *L. acidophilus* and *B. longum*, for 16 days (six days preoperatively and ten days postoperatively). The treatment decreased the rate of postsurgical infection [96].

Patients undergoing radiotherapy may also benefit from probiotic use. Radiotherapy to the pelvic area often results in radiation-induced diarrhoea. In one study, *B. bifidum* and *L. acidophilus* significantly reduced both diarrhoea and use of anti-diarrhoeal agents in 32 women undergoing chemo (cisplatin) -radiation therapy for cervical cancer [97]. In a double blind

Table 2: Conclusions of probiotic use in gastrointestinal disorders.

Gastrointestinal Disorder	Conclusion
Travellers' Diarrhoea	A selective benefit of <i>S. boulardii</i> and a mixture of <i>L. acidophilus</i> , <i>B. bifidum</i> , <i>L. bulgaricus</i> and <i>S. thermophilus</i> probiotics as prophylaxis of travellers' diarrhoea. <i>S. boulardii</i> may be useful in treating travellers' diarrhoea where other medical treatments have failed.
Irritable Bowel Syndrome	A mixture of bacterial strains including lactobacillus and bifidobacteria may be the most effective in IBS collective symptoms with a good safety record and are thus appropriate for therapeutic trial in holistic IBS therapy.
Inflammatory Bowel Syndrome	Probiotics, especially those containing multiple strains can maintain remission in ulcerative colitis and also demonstrate efficacy in pouchitis. There is currently no evidence for probiotics in Crohn's disease.
<i>C. difficile</i> and antibiotic associated diarrhoea	<i>Lactobacillus</i> species appear to be the most effective in preventing <i>C. difficile</i> infections.
Lactose intolerance	There is benefit from taking probiotics in lactose intolerance. There is most evidence for <i>L. rhamnosus</i> and <i>bifidobacterium</i> , often in combination.
Cancer	Probiotics, mainly lactobacillus and bifidobacteria, have a beneficial role in the care of patients with diarrhoea associated with chemotherapy and radiotherapy.

placebo controlled trial of 251 bowel, rectal and cervical cancer patients undergoing adjuvant postoperative radiation therapy after surgery for sigmoid, rectal, or cervical cancer, 1 VSL#3 a day from the first day of radiation therapy had positive effects in the treatment group. This mixture of probiotics lead to significantly reduced number of bowel movements, much less grade 3 or 4 diarrhoea incidence (1.4% v's 55.4%), and also significantly increased the time until the patient had to use loperamide [98]. Other studies using single *L. acidophilus* found that even single probiotics improved the patients' status during pelvic radiotherapy and decreased radiation-induced diarrhoea [99].

Conclusion: Probiotics, mainly lactobacillus and bifidobacteria, have a beneficial role in the care of patients with diarrhoea associated with chemotherapy and radiotherapy.

Conclusions

The evidence has been concluded in Table 2. Undoubtedly diet will affect the endogenous gastrointestinal bacteria; however, taking a pragmatic approach, the addition of probiotics even without dietary change appears to be effective in diarrhoea associated disorders.

Defining the optimal dose and combination of probiotic species is a difficult task, especially when diet will also play an important factor. There is however good evidence for the role of

probiotics in diarrhoeal disorders and the development of well structured, RCT's are required.

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