Review

Probiotics in the Treatment of Irritable Bowel Syndrome in General Practice: A Real-World Narrative Review

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Probiotics in the Treatment of Irritable Bowel Syndrome in General Practice: A Real-World Narrative Review

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Abstract: Background Although the management of the majority of patients with IBS is dealt with by General Practitioners, randomized clinical trials and treatment guidelines are developed mostly in academic settings. Probiotics are one of the most investigated treatment modality for this condition. Scarce information is available as regards GPs attitude in this regard. Methods A literature search was performed to identify papers specifically dealing with probiotic treatment of IBS in the general practice setting. Moreover, the preliminary results of a survey on this topic conducted by the authors among general practitioners in a province in northern Italy are reported. Results Five papers specifically addressing probiotic treatment of IBS in general practice were found. The response rate varied from 4 to 100%. The prescription rate of probiotics by GPs in IBS varied from <10 to 46%, regardless of the patients' bowel habits. Physicians' satisfaction with this treatment varied from 20 to 93%. The variability of these results probably depends on factors such as differences in the interpretation of the available data on probiotics use in IBS and traditional/ cultural differences. Moreover, compliance with patient satisfaction, may play a role. Conclusions The reported data on the treatment of IBS with probiotics in general practice is scarce and inhomogeneous, thus it does not allow firm conclusions. It is suggested that the involvement in research on the use of probiotics in IBS of physicians working in general practice would be useful in order to pursue more reliable and useful results, since the majority of the IBS population is followed in general practice and may differ from the one represented in academic clinical trials.

Keywords: irritable bowel syndrome; probiotics; general practice

Introduction

Irritable Bowel Syndrome (IBS) is a common, chronic and disabling gastrointestinal disorder characterized by altered bowel movements and abdominal pain, often associated with abdominal bloating and/or distention [1], which belongs to the category of the Disorders of Gut-Brain Interaction (DGBI), formerly known as Functional Gastro-Intestinal Disorders (FGID).

The prevalence of IBS varies widely among countries, with an average prevalence of 4% according to a recent international survey of the Rome Foundation [2]. It significantly impacts both on the quality of life of the affected patients and on health services, even more than organic disorders, not to mention the costs due to absenteeism [3]. IBS is diagnosed positively by means of the objective criteria proposed by the Rome Foundation ([1] since there are no laboratory or imaging markers available.

Multiple mechanisms have been proposed to explain the pathophysiology of IBS, such as intestinal dysmotility and/or hypersensitivity, low-grade mucosal inflammation, increased permeability of the intestinal epithelium [4]. The etiology of this syndrome is still obscure: psychological, genetic and environmental, in particular dietary and infectious, factors have been proposed [4]. As regards the latter, since at least 10% of IBS patients report the beginning of their symptoms after an acute intestinal infection [5] it has been hypothesized that alterations in the

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composition of the colonic microbiota may play a role in the etiology of this syndrome [6], and in fact there is evidence of an altered intestinal microbiota in IBS patients compared to healthy subjects [7].

As a consequence of these latter findings, a manipulation of the microbiota has been proposed decades ago as a useful tool in the treatment of IBS [8] and growing evidence supports the effect of probiotics, that is "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (well-known even before the pioneering studies of Elia Metchnikoff at the beginning of the 20th century: see for example Deuteronomy 32:14 where fermented milk is cited as a beneficial food given by God to humanity) in this regard [9–11]. Moreover, research on probiotics has been recently enclosed in the 10-item list of top research priorities in IBS [12] and in fact controlled clinical trials, meta-analyses and reviews regarding the efficacy of probiotics in IBS abound in the literature [13–17]. These are truly powerful research tools, but their results do not always reflect what happens in the real world both because they are derived from a minority of the IBS population since the majority is cared for in primary care [18,19] and because their effects may not influence the prescribing attitudes of general practitioners [20].

Aim of our narrative review was thus to evaluate the available data regarding the prescription of probiotics in IBS by general practitioners (GPs). Moreover we report the preliminary results of a survey on probiotic use in IBS conducted among the GPs of a province in northern Italy.

Methods

Literature search

PubMed and Cochrane Library were searched by the authors in October 2023 using the following key words "IBS treatment general practice", "Probiotic use general practice", "Probiotics IBS general practice" to identify papers dealing with the prescribing attitudes of GPs as regards probiotics in patients with IBS. Moreover, a manual search of the bibliographies of the articles identified was performed by one of the authors (GM).

Survey

A questionnaire regarding the attitudes of GPs as regards probiotics in IBS was emailed in December 2023 to the 235 GPs in activity in the province of Mantova (northern Italy, population 412.292 as of 2019). A reminder is scheduled to be sent in spring 2024.

Demographic information included sex, age and years in practice as a GP. Rome IV criteria were included to identify patients with IBS. The five questions included in the questionnaire addressed the prescribing patterns of probiotics in IBS:

1) How do you rate your knowledge of the intestinal Microbiota?

- Adequate
- Scarce
- None

2) If you answered "scarce" or "none" to question n. 1, would you be interested in increasing your knowledge of the intestinal Microbiota?

- Yes
- No

3) In your experience are probiotics useful in the treatment of IBS?

- yes
- no
- don't know

4) In which percentage of patients with IBS do you prescribe probiotics?

- never
- rarely (1-25%)
- occasionally (26-50%)
- often (51-75%)
- very often (76-100%).

5) In which of these subgroups of IBS patients do you prescribe probiotics?

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- diarrhea
- constipation
- alternating diarrhea and constipation
- all of the aforementioned

Results

The literature search yielded 5 papers specifically addressing probiotic treatment of IBS in general practice; one more paper mentioned this treatment approach in general practice grouped together with other modalities such as phytotherapy, dietary advice and homeopathy [21].

Bellini et al.'s study [22] was based on 35 randomly selected GPs in the province of Pisa (central Italy). These physicians were previously contacted by phone, then they were sent a questionnaire on diagnostic criteria, management and treatment of IBS. The response rate was 80% (n. 28). Probiotics were prescribed in 29.8% of the respondents' IBS patients with a non-significant preference for diarrheal vs constipated patients.

Shivaji and Ford [23] employed an 18-item online questionnaire on IBS sent to 275 GPs in the Leeds area (UK) with a response rate of 37.1% (n. 102). Only 20% of these physicians were convinced of the efficacy of probiotics in IBS and <10% prescribed them often or always in this setting.

Austhof et al. [24] assessed knowledge and treatment of GPs as regards post-infectious IBS. The study was based on an online 40-item questionnaire sent to 50 physicians spanning the territory of the USA. The response rate was 100%. Probiotics were the first treatment modality employed in this setting by 66% of the respondents.

von Madisch et al. [25] mailed a questionnaire on various aspects of IBS to 12.300 GPs spanning the territory of Germany, 487 of whom replied (response rate 4%). As regards the treatment of IBS, 37% of the respondents prescribed probiotics and 75% were satisfied with the effect of this treatment.

Jordan D et al. [26] mailed a questionnaire to 1500 health providers, i.e GPs, dieticians, practice and community nurses in the UK (response rate not reported). In 62.1% of the prescriptions of probiotics the reason was "symptoms of IBS".

As regards the preliminary results of our survey, out of 235 online questionnaires we received 30 responses (rate 12.7%), mean age: 62.4 years (range 36-70), mean years in activity as GPs: 30.2 (range 1-43), n. 4 females and 26 males. The majority (53.3%) of the respondents rated their knowledge of the intestinal Microbiota as "scarce", 40% as "adequate" and 6.6% as "none" (Table 1). Of the 18 respondents who rated their knowledge as "scarce" or "none" 88.8% were interested in increasing their knowledge about the intestinal Microbiota (Table 2). In the opinion of the majority (93.3%) of the respondents probiotics are useful in the treatment of IBS (Table 3); 53.3% of the respondents prescribe probiotics in 51 to 100% of their IBS patients (Table 4). Lastly, 86.6% of the respondents prescribe probiotics regardless of the bowel habits of their IBS patients (Table 5).

Table 1. "How do you rate your knowledge of the intestinal Microbiota?

Adequate	**12 (40,0)**
Scarce	16 (53,3)
None	2 (6,6)

Table 2. "If you answered scarce or none to question n. 1, would you be interested in increasing your knowledge about the intestinal Microbiota?".

Yes	16 (88,8)
No	2 (11.1)

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Table 3. "Are in your opinion probiotics useful in IBS treatment?".

Yes	**28 (93.3)**
No	2 (6.6)
Don't know	0

Table 4. "How often do you prescribe probiotics in your IBS patients (%)?".

Never	**0**
1-25	6 (20)
26-50	8 (26,6)
51-75	12 (40)
76-100	4 (13,3)

Table 5. "In which IBS variant do you prescribe probiotics?".

Diarrhea	**4 (13.3)**
Constipation	0
Alternate	0
All	26 (86.6)

Discussion

The results of the few studies that we found in the literature on the prescribing attitude of GPs about IBS treatment with probiotics are not homogeneous.

The response rate varied widely from 4% [25] to 100% [24]. The reason for this variability depends mainly on the way the questionnaire was proposed. Bellini et al.'s 80% response rate was probably due to the invitation by phone which preceded the questionnaire. As regards Austhof et al.'s study, the 100% rate was probably due to the financial incentive given to the participating physicians.

The frequency of GPs prescribing probiotics in IBS varied from <10% [23] to 37% [25]. Austhof et al.'s frequency of prescription (66%) cannot be compared with the other studies because of the specific subset of IBS (post-infectious) investigated; the existence of an infectious cause may in fact have influenced the prescribing physicians, as shown by the 28% frequency of prescription of antibiotics. Also Jordan D et al.'s results are difficult to interpret because of the presence in their survey of health providers other than GPs, in particular dietitians who might have been more prone to prescribe probiotics than GPs; moreover, since the survey was organized by a yoghurt manufacturer, a bias cannot be excluded. The percentage of GPs who prescribe probiotics often+very often in our survey might seem at first glance rather high (53.3%, Table 4) compared with the studies reporting the highest prescription rates [22,25]; this may be due to the way the question was formulated in our survey, that is as 4 increasing tiers of prescription rate. Moreover, as regards the satisfaction of the physicians with the efficacy of probiotics, the majority in Madisch et al.'s study (75%) and in our survey (93.3%, Table 3) were satisfied, whereas the same is not true in Shivaji and Ford's study (20%).

A reason for these variable findings may depend both on a different interpretation of the data in the literature, which is far from homogeneous: the AGA recommends probiotics only in the context of clinical trials [27] whereas seven gastroenterological societies in Italy more recently recommend them, as a group, to alleviate symptoms in patients with IBS [28]. Moreover, it has been shown that the attitudes and practices of physicians as regards IBS vary according to the clinical setting, that is among GPs, internists and gastroenterologists [29]. Other reasons may depend on longstanding habits which may vary among countries according to cultural and traditional factors. For example, complementary and alternative treatments are frequently prescribed in Germany [21] whereas the same may not be true for other countries such as the USA [30,31].

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Another reason for prescribing probiotics in IBS patients is to comply with their desire for a treatment devoid of adverse effects. In fact, data obtained from focus groups composed of patients with IBS and Inflammatory Bowel Diseases [32] shows that patients favour probiotics mainly because they are perceived as a more "natural" and low-risk treatment modality. Teasdale et al. [33] approached the same topic in a different manner, that is by evaluating two internet forums of IBS patients, with a total of over 800.000 posts. Probiotics were used very frequently and their effects often described enthusiastically:

I have had success by supplementing with PROBIOTICS. I will never take anything less than 100 billion and less than 10 strains. The one I'm currently taking is over 150 billion and has over 40 strains. My symptoms have improved significantly. (Discussion 67, participant 1, IBS forum 1).

It should be noted that, beyond the enthusiasm, the above-mentioned patient was well aware of the importance of the composition of probiotic products as regards both quantity and quality, reflecting her/his knowledge of the details of this treatment. The knowledge of the patients as regards the IBS is confirmed by many posts underlining that *probiotics are effective in IBS symptom resolution because IBS is caused by abnormal growth of bacteria (dysbiosis) within the gut*.

Our review has important limitations due to the scarcity of reports in the literature, to the low quality of some of them and to the low number of physicians participating both in the published surveys and in ours. These limitations preclude firm conclusions on the basis of our findings. However the involvement of GPs in clinical studies on IBS, as in Begtrup et al.'s study [34], could provide interesting data on the real-life management of this disorder, particularly since GPs and patients share similar perceptions on IBS [35] and the former are in a good position to judge the effects of probiotics and the clinical settings in which they should be prescribed [34–36]. This approach could be useful both to better define the role of this treatment modality in real-world patients and to increase the physicians' knowledge on this issue, an important unmet need in our survey as shown in Table 2, with positive effects on their prescribing patterns.

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Ethical Considerations: Since the survey did not involve neither patients nor their sensitive data no ethical consideration needs to be addressed (see the WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects as amended during the 64th WMA General Assembly, Fortaleza, Brazil, October 2013 as specified in the General Principles section, sentence n. 7: "Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights").

Data Deposit: The raw data supporting the conclusions of this article will be made available by the authors on request.

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Conflicts of Interest: Both Authors declare no conflicts of interest

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