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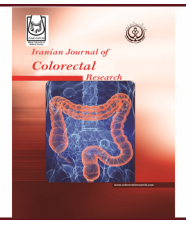

Difficulties in Irritable bowel syndrome: Disease Definition, Epidemiology, Pain Management and Treatment

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Abstract

The diagnosis and definition of irritable bowel syndrome are problematic. However, its existence as a disease entity has been recognized for at least a thousand years with both Rhazes and Avicenna discussing its constellation of symptoms. In recent times, attention has focused on the symptoms and symptom durations critical to the diagnosis. This work has been encapsulated in the reports of the Rome Foundation. The difficulties in disease definition have led to wide variations between reports on the condition's prevalence in both within and between countries. Nevertheless, it is clear that irritable bowel syndrome is common across all societies. It is consequently of concern that allopathic medications are of limited benefit, particularly in the management of pain, and this has generated a growing interest in traditional therapies as well as hypnotherapy and acupuncture. This review touches on these issues and will hopefully stimulate further research.

Keywords: History, Symptoms, Pain, Epidemiology, Alternative therapies

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Introduction

Irritable bowel syndrome (IBS) is a common gastrointestinal disease seen by both general practitioners and consultant gastroenterologists (1). It is characterized by bouts of recurrent abdominal pain and an irregular bowel habit, which may take the form of either diarrhoea or constipation. There are no specific diagnostic tests at present, and the diagnosis is a clinical one. In addition, there are no recognized "cures" for the condition, and many patients are told that they will simply have to live with it.

The rationale for this review was to identify and attempt to address some uncertain aspects pertaining to IBS. The absence of a clear definition of the disease entity limits comparisons between individual studies of disease frequency in various communities. It also has a direct impact on clinical trials and in separating case from non-case and so the recruitment of suitable patients. The absence of objective measures of disease activity makes any assessment of the benefits of any treatment subjective. Such subjective assessments are also affected by whether they are made by patients or external observers. It is such issues that have

limited the emergence of effective treatments for a condition with significant morbidity, affecting both employment and family life.

History

It has been suggested that the earliest description of irritable bowel syndrome (IBS) was made in 1820 by Powell (2). He described four cases with symptoms that could have been consistent with that diagnosis. Among the symptoms that he identified were occasional abdominal pain and flatulence, with some relief obtained by using laxatives, suggesting that the patient had IBS associated with constipation. However, the role of bloating as a cause of abdominal discomfort and its linkage to diet and lifestyle was recognized by Avicenna and Rhazes one thousand years ago (3, 4). During World War II Peters and Bargen noted an increased incidence of a similar symptom complex for which they coined the name "irritable bowel syndrome" (5). This term was readily taken up in preference to spastic colon or mucous colitis and similar terms. By 1947, Dr Phillip Brown of the Mayo Clinic recognized the role of intermittent or chronic diarrhoea, cramping and wind pains, and abdominal soreness (6).

Pathophysiology

The traditional view of IBS is that is the outcome of a combination of altered gastrointestinal motility against a background of visceral hyperalgaesia in people with a psychological predisposition (7). Recent work has suggested that elements of the gut microbiota may affect brain activity and behaviour so linking cerebral and gut function (8). The beneficial effect of faecal transplantation on IBS in a recent randomised double-blind placebo controlled trial gives added weight to the role of the microbiota (9). It is unclear how these various triggers might interact but such differences could explain the range of symptoms experienced by different people within the IBS diathesis.

Diagnosis

It was not until the 1970s that Manning and his colleagues attempted to establish clear diagnostic criteria for IBS by means of a questionnaire. They studied 33 patients with abdominal pain for whom an organic cause had been identified and compared them with 32 patients in whom no cause was found (10). Their study demonstrated the importance of chronic abdominal pain as a major diagnostic feature of IBS. In this study, relief of pain with a bowel movement, and more frequent and looser stools at the onset of pain were also identified as characteristic of IBS.

Subsequent to this work, an international movement towards developing a standardized definition of IBS emerged. It was based on the Rome Foundation in Raleigh, North Carolina. Between 1989 and 2016, four updates were published on the diagnostic criteria for functional gastrointestinal disorders. The criteria for IBS Rome IV are:

"Recurrent abdominal pain, on average, at least one day/week in the last three months, associated with two or more of the following criteria:

- related to defecation
- associated with a change in frequency of stool
- associated with a change in form (appearance) of the stool"

These criteria must be met for at least three months with an initial onset at least six months earlier (11). Essentially, they are a little different from the original criteria proposed by Manning et al (10) with pain as the dominant feature.

Pain and Associated Symptoms in IBS

The pain experienced in IBS is chronic and visceral pain, the stimulus for which is largely unknown (12). Stress and certain foods have been suggested as potential stimuli. Based on a questionnaire about patients' beliefs as to what causes flares of their IBS (13). Indeed, most studies on pain in IBS use either electronic or paper-based questionnaires to collect patient reported Outcomes (12). In a systematic review of 110 papers Mujagic et al found that many of the different tools used, have not been validated for cases IBS (12). They described two main methods for assessing abdominal pain in patients with IBS. The first approach was simply to document pain and the second was to provoke pain through techniques such as rectal distension. They suggested that the ten-point Numeric Rating Scale was probably the most appropriate for assessing the severity of abdominal pain and questioned whether provocation tests causing pain through rectal distension are relevant to chronic symptoms as they induced acute pain and are unrelated to natural stimuli that might cause IBS.

Recent work has linked sleep disturbance in IBS to pain, poor symptom control and reduced quality of life (14). Sleep deprivation may itself enhances visceral hypersensitivity with some support coming for this concept from a small exploratory study of 24 women with IBS (15). This study demonstrated that poor sleep was directly related to abdominal pain, but not to the other gastrointestinal disturbances seen in IBS. Such a finding is of direct relevance to the use of therapies such as acupuncture which can influence sleep patterns. Interestingly the role of stress in promoting IBS symptoms is far less clear (16). A systematic review of case-control studies indicated that patients with IBS had significantly higher levels of anxiety and depression than controls (17). To date,

there have been no published studies that have not found some form of link between stress and IBS. This is of importance as many complementary therapies, including acupuncture, are believed to impact this and other areas of health.

Epidemiology

Epidemiological studies on IBS have been limited by the absence of a clear definition, which also makes comparisons between patient groups and across borders even more difficult. Hillila and Farkkila's study from Finland illustrates this point (18). In a comparative study using the criteria proposed by Manning and two versions of the Rome criteria the prevalence of IBS in a community-based study of 5000 people was reported as 16.2%, 9.7%, 5.6%, and 5.1%. Such differences are also of considerable importance when selecting patients for treatment studies and may play a role in the differences in reported outcomes.

Significant differences between various studies can also arise as a result of whether a point or period prevalence is reported and the nature of the populations sampled. In the Wanoworie area of Pune, India a questionnaire survey of an urban population revealed that 33% of patients had symptoms consistent with Manning's criteria in the previous six months, but only 12% sought advice from a doctor (19). The outcomes of such surveys can be directly linked to whether they are completed by the subjects or by a field worker. Response rates are affected by questionnaire distribution and collection methods, with evidence that financial incentives may increase them, but could affect their accuracy. In general, most recent studies have based their diagnosis on the Rome II criteria. However, although there have been comparative studies of Manning and Rome criteria in reaching a diagnosis, there have been no studies comparing methods of collecting the data, such as subject or field worker completion. Interestingly, one of the lowest reported prevalences from the West was based on general practitioner (GP) diagnosis in Sweden (20). In many senses this group of patients reflects the more serious end of the disease where patients' symptoms were sufficiently severe for them to seek medical assistance.

In 2018 Zuckerman et al reported a four-fold difference in the frequency of IBS amongwomen (6.9%) compared with men (1.7%) using the Rome III criteria in a community- based study (Table 1) (21). This confirmed the general findings of Lovell & Ford (2012) in a meta-analysis of 56 studies including almost 200,000 subjects (22). However, their review did not identify any gender differences in earlier

Table 1: A Selection of Representative studies of Prevalence of Irritable Bowel Syndrome in Various Communities

Country	Criterion	Prevalence (%)	Age group	Number of Cases	Reference
Sweden	General Practitioner diagnosis	1.2%	Adults	10987	Waehrens et al (20)
Denmark	Rome lll	15.4%	18 – 50	920	Krogsgaaard et al (25)
Finland	Manning, Rome l & ll	5.6 - 9.7%	Adults	27 – 48	Hillila & Farkkila (18)
Germany	Rome lll	3.5%	Population cohort	4194	Schauer et al (26)
South-East China	Rome ll & lll	10.4%	Undergraduates	54	Dai et al (27)
South China	Manning & Rome ll	5.7 - 11.5%	Adults	238 - 240	Xiong et al (28)
China	Various	6.5%	Meta-analysis	?	Zhang et al (29)
Japan	Rome lll	6.1%	All ages	61	Satake et al (30)
Japan	Rome lll	18.6%	Adolescents	18305	Yamamoto et al (31)
Korea	Rome ll	11.1%	Adults	370	Yun et al (32)
Vietnam	Rome l	7.2%	Adults	53	Zuckerman et al (33)
Iran	Rome lll	1.1%	Adults. Face-to-face survey with validated questionnaire	98	Khoshkrood-Mansoori et al (34)
Iran	Not specified	3.1 – 3.6%	Interview	455	Massarrat et al (35)
Iran	Rome II	5.8%	Interviews with questionnaire	5492	Hoseini-Asl & Amra (36)
Iran	Rome II	10.9%	Questionairre	1978	Khademolhosseini et al (37)
Nigeria	Rome ll	31.6%	House to house visits (Adults)	443	Okeke et al (38)
India	1998	33%	Urban survey	307	Anand et al (19)
Chile	Rome ll	28.6%	Shoppers	437	Madrid-Silva et al (39)
Colombia	Rome lll	19.9%	15 – 60 year olds	558	Álvarez et al (40)
USA (Mexican Americans	Rome lll	5.6%	Colon Cancer Prevention program	464	Zuckerman et al (21)

studies from South America, South Asia or Africa. Such findings again have an impact on clinical studies of treatments. Should the population reflect the gender differences reported in many studies? Or should there be separate studies of men and women as there is no generally accepted explanation to account for the gender difference, suggesting different pathophysiology?

In 2016, a population-based study of 1 million people in Taiwan reported that IBS incidence increases three-fold between the ages of 20 and 80 (23). This confirmed similar findings from Olmsted County, Minnesota which were reported in 1995 by Talley et al (24). Again, should any trial ensure that the groups undergoing treatment reflect the increased incidence of IBS with age?

Current Therapy

The current allopathic treatments for irritable bowel syndrome are of limited efficacy and are directed at symptom control. For example, a Cochrane Review of 56 trials including bulking agents, antispasmodics and anti-depressants showed relatively limited benefit for anti-spasmodics with 58% of patients on such treatment experiencing improved pain control compared with a similar benefit in 46% of patients on placebo (41). The review demonstrated no benefit from bulking agents. Tricyclic anti-depressants did lead to pain reduction. Sub-group analysis of the anti-spasmodics confirmed the particular benefit of peppermint oil, as well as cimetropium/dicyclomine, pinaverium and trimebutine.

The emergence of peppermint oil as an effective allopathic treatment was a direct result of the limited effectiveness of drugs available in the latter part of the twentieth century. Rees et al (42) developed this traditional herbal remedy because conventional drugs were “often disappointing and their use limited by side effects”. The simple approach they adopted was to put concentrated peppermint oil in a delayed-release capsule, which was subsequently marketed as Colpermin. In 2016, enteric-coated anise oil (AnisEncap) was shown to be more effective (43).

Several other researchers took up this interest in traditional and complementary therapies. In 1984, Whorwell et al reported a comparative study in which 30 patients were randomly allocated to receive psychotherapy hypnotherapy (44). The patients who received hypnotherapy showed a highly significant improvement in their symptoms of abdominal pain, bloating, bowel frequency and general well-being which was maintained for the three months of follow-up. The role of biofeedback as a potential therapy also emerged at this time, although studies were small and used the feedback of bowel sounds through an electronic stethoscope to help patients gain control over large bowel contractions (45). A recent Cochrane review confirmed the need for larger and better controlled studies, indicating that the jury was still out as to whether this approach was effective (46).

Other psychologically-based interventions have been developed subsequently and a recent systematic review confirmed that cognitive-behavioural therapy was more effective than either relaxation therapy or hypnosis when daily functioning was assessed, although there was no specific analysis of pain experience (47). Recent studies have suggested similar benefits through yoga, although the pain was not specifically considered in a systematic review (48). The potential role of mindfulness-based stress reduction therapy has also come to the fore. In a randomized clinical trial of 24 patients with IBS based on Rome IV criteria, those who received mindfulness-based therapy showed a significant improvement in the severity of their bowel symptoms compared with those trained in emotional regulation and others who acted as controls without additional interventions (49).

Conclusion

Irritable bowel syndrome is a common condition found throughout the world, causing. Recurrent and frequent abdominal pain. It’s diagnosed based on clinical history. Its cause is unknown and at present there is no cure. Allopathic treatment is ineffective and as a result several complementary therapies have been investigated for their potential. Acupuncture and related therapies offer some benefits and are reviewed briefly in this study

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Authors' Contribution

A.F and J.F.M contributed to the conception, design, acquisition, writing the work, conception, design acquisition of the work and drafting and revising the work critically for important intellectual content. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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