

## LEADING ARTICLE

## Complementary and alternative medicine for functional gastrointestinal disorders

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Patients suffering from functional gastrointestinal disorders are likely to search elsewhere when conventional therapies fail them. Enthusiasm for complementary and alternative medicine use and research is clearly growing. Studies of acupuncture and herbal therapy for functional gastrointestinal disorders in the Western literature have often been limited by poor study design but these interventions may have promise and are discussed here.

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Dissatisfied patients are likely to search elsewhere when conventional therapies fail them. This is often the case with patients suffering from functional gastrointestinal disorders (FGID), as our available treatment options have limited efficacy. Increasingly, more FGID patients are looking to alternative practitioners and non-conventional sources to manage their chronic symptoms.<sup>1</sup> In a UK sample, 26% of patients with gastrointestinal symptoms sought complementary and alternative medicine (CAM) therapy, and 48% of those with irritable bowel syndrome (IBS) used CAM.<sup>2</sup> Of these patients, almost half found their CAM therapy to work well.<sup>2</sup> Costs of CAM treatment are often significant, with Americans spending over 20 billion dollars on CAM in 1997.<sup>1</sup> Much of this burden is paid for by the patient, rather than by medical insurance. Patients appear willing to accept these costs, despite the lack of efficacy evidence for most CAM therapies. Patients are drawn to CAM treatments with long histories, such as traditional Chinese medicine (TCM), Ayurvedic medicine, and homeopathy, possibly associating longevity with efficacy. The choice of a “natural” rather than a “chemical” therapy is also a motivating factor as many patients equate “natural” products with safety. Due to the fact that technology has supplanted bedside manner, the deteriorating relationship between patients and physicians may also encourage CAM use, giving patients a sense of greater autonomy in their care. Given the substantial impact of CAM on both individual patients and society, it is crucial for us to gain a better understanding of the potential benefits and pitfalls of CAM.

To date, research on CAM in the English literature has been scarce, and most studies have been weakened by small sample size or poor study design. Interest in CAM research has been increasing, however, which has led to a number of unexpected issues in study design. Rigorous experimental designs by Western definitions often lead to a reductionist approach, which

may be inadequate to measure complex multi-modal therapies. Conventional concepts of valid clinical trial design, such as the double blind, randomised, placebo controlled trial, are well suited for studying single agent interventions but may not be ideal for some CAM therapies. Blinding the patient to CAM modalities can be challenging, particularly with acupuncture and other body based treatments. Additionally, many of the alternative therapies are rooted in the concept of individualised care, rather than disease based treatment. The choice of treatment for a single diagnosis may vary for patients with other comorbid symptoms, and may be repeatedly adjusted over time by the practitioner. The therapeutic relationship between patient and practitioner is considered essential, making standardisation across study subjects difficult. Choosing the outcome measures and a therapeutic regimen for CAM studies requires careful understanding of the expected role of a given therapy for a gastrointestinal disorder. For example, when used for IBS, a single CAM therapy such as acupuncture may be potentially useful for acute abdominal pain symptoms but not altered bowel habits. Thus a trial looking at global symptom reduction alone may not show benefit. Additionally, in the traditional practice of Chinese medicine, acupuncture would rarely be used alone for a patient with the symptom complex of IBS. It would generally be combined with herbal therapy, resulting in a variety of potential regimens used for individual patients. Additional concerns include the development of appropriate control conditions, adequate duration of treatment and follow up, and utilisation of practitioners with relatively uniform training.

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Numerous CAM modalities are used for medical symptoms. Major CAM categories include acupuncture/body based treatment, herbal/dietary therapy, and mind/body approaches. Most CAM research in FGID to date has studied the most common disorders, IBS and functional dyspepsia (FD). Probiotics, classified as a dietary supplement, appear to have promise in FGIDs.<sup>3,4</sup> They have often been included in discussions of CAM but have become increasingly prominent in

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**Abbreviations:** FGID, functional gastrointestinal disorders; CAM, complementary and alternative medicine; IBS, irritable bowel syndrome; TCM, traditional Chinese medicine; FD, functional dyspepsia

the mainstream of gastrointestinal research and will not be commented on here. While mind/body therapies such as mindfulness meditation, tai chi, and yoga are potential areas of interest in FGIDs, insufficient data exists regarding their usefulness. More commonly used mind/body modalities include cognitive behavioural therapy and hypnotherapy, both of which have been shown to be useful in FGIDs and have been well described in recent reviews.<sup>5-7</sup> Studies of acupuncture and herbal therapy for FGIDs in the Western literature have often been limited by poor study design but these interventions may have promise and will be discussed further below.

## ACUPUNCTURE FOR FGIDS

While FGID patients may be drawn to its ancient roots and the desire for non-pharmacological treatment, acupuncture has also been an attractive subject for FGID researchers. Alterations in pain modulation, motility, and autonomic function are likely mechanisms of FGID symptoms, which may have physiological responses to acupuncture. Several animal and human studies have shown acupuncture effects on gut motility, including improved gastric emptying and accommodation.<sup>8-9</sup> A logical extension of this research could include study of FD, functional bloating, and nausea. Pain and/or discomfort are requisite symptoms of both FD and IBS. Brain imaging studies have demonstrated two potential routes of pain modulation by acupuncture via deactivation of descending nociceptive pathways and by decreased limbic activity during acupoint stimulation.<sup>10-12</sup> Antinociceptive effects have been supported by animal studies. Both decreased pain and decreased autonomic nervous system response to visceral stimulation are seen when acupuncture is performed on dogs and rats undergoing colonic balloon inflation.<sup>13-14</sup>

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Human studies have shown varied results. In a small sample of healthy and IBS subjects, Rohrbock and colleagues failed to show altered rectal sensation with balloon inflation using electroacupuncture at two points in the S3 and S4 dermatomes.<sup>15</sup> However, two studies have shown increased rectal sensory thresholds in patients with diarrhoea predominant IBS after acupoint electrical stimulation.<sup>16-17</sup> The acupoints and stimulation techniques in these studies differed, precluding close comparison across studies. Interestingly, the acupoints used in the study with negative findings<sup>15</sup> are located in the dermatomal distribution of the lower abdomen, and are points which TCM may treat urogenital symptoms and haemorrhoids, but not for the common symptoms of IBS. Conversely, the Zusanli acupoint used in the two positive studies, which appeared to have benefit on visceral sensitivity, is commonly used for IBS-like gastrointestinal symptoms in the TCM paradigm and was also shown to be effective in reducing visceral sensitivity in rats and dogs.<sup>13-14-17</sup> While the studies differed in a number of ways, the dichotomy of results seen in the paradigm specific and non-specific use of acupoints provides an example of the potential complexities that exist in interpreting CAM study results, particularly for those not familiar with the underlying theoretical constructs.

A number of issues make interpretation of the existing acupuncture data for IBS treatment difficult. The wide variety of acupoint combinations used for treating pain or bowel symptoms and range of acupuncture styles (needling

technique, depth of insertion, use of electroacupuncture, acupressure) impair comparison across studies. The problem of adequate placebo in acupuncture trials has been problematic. Some studies have used needle insertion at “sham” acupuncture points near the true points. Others argue that the exact location of the needle insertion is less important than the technique of insertion. Shallow skin insertion, skin tapping without insertion, and telescoping needles which touch the skin but do not penetrate are also used as acupoint controls.

“Studies on the therapeutic value of acupuncture in treating specific FGIDs have been limited”

Thus far studies on the therapeutic value of acupuncture in treating specific FGIDs have been limited. Two pilot studies have shown improvement in IBS symptoms with acupuncture but had a number of flaws.<sup>16-18</sup> Both used only a few acupoints, atypical of general clinical practice; one was an open design and the other also included a rectal distension protocol, which may have altered responses. Three other small studies have shown lack of acupuncture efficacy over placebo in IBS,<sup>19-21</sup> including that of Schneider and colleagues<sup>21</sup> in the current issue of *Gut* (see page 649). Fireman and colleagues<sup>20</sup> used a poor study design with a single acupoint, which would not be expected to lead to symptomatic improvement. The study by Forbes and colleagues<sup>19</sup> is more convincing as it had a paradigm specific approach with acupuncture individualised to the patient’s TCM diagnoses, and an adequate duration of therapy. It was a small study and used a potential confounding control condition (needling at sham points) but suggests that acupuncture used alone for IBS has little, if any, effect on IBS symptoms. In this issue of *Gut*, Schneider and colleagues<sup>21</sup> employed a standard combination of eight points frequently used in TCM for IBS-like symptoms. While this does not perfectly model the practice of individualised acupuncture in TCM, it may be a reasonable compromise to achieve standardisation between subjects. The study used a good control technique and employed appropriate symptom, global outcome, and quality of life outcome measures. The similarity of response to true and placebo acupuncture in this study raises further questions about the usefulness of acupuncture in treating IBS patients. Given the numerous reports showing physiological gastrointestinal responses to acupuncture, its use in other functional disorders warrants further research.

## HERBAL THERAPY FOR FGIDS

The only rigorous English language study of herbal therapy in FGIDs to date examined the effects of Chinese herbal medicine in IBS.<sup>22</sup> This ambitious study not only used a paradigm specific approach within TCM, but also sought to test the TCM paradigm under which herbal combinations were individualised to patients’ global symptom patterns and adjusted at each visit as symptoms changed. IBS patients were treated with either a standardised combination herbal formula (all subjects received the same treatment regardless of specific symptoms), an individualised herbal formula, or placebo. Both treatment groups showed a substantial benefit over placebo after 16 weeks of therapy, and the individualised treatment showed continued benefit 14 weeks after treatment ended. Unfortunately, despite being widely cited, the study has not been replicated and the mechanisms of the herbal formula’s action on IBS symptoms are unknown. While herbal formulas appear to improve on most reported benefits from IBS pharmacotherapy, the findings have not translated into use in Western clinical practice, a sign of the difficulty of integrating CAM into the routine care of FGID patients.

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Single herb and fixed dose combination herbal therapies have also been described for IBS and FD and are more amenable to conventional trial designs. Peppermint oil has been studied for both disorders, showing improved abdominal pain, abdominal distension, and flatulence in IBS<sup>23–24</sup> and, in combination with caraway oil, has been shown to provide global symptom improvement for FD.<sup>25</sup> Its smooth muscle relaxant properties are mediated via calcium channel blockade, and it appears to act as an antispasmodic.<sup>26</sup> A meta-analysis of eight trials of peppermint oil for IBS showed improved symptoms, but the data were inconclusive due to methodological flaws in the analysed studies.<sup>27</sup> Overall, the data are encouraging and suggestive, but no large well designed trials have been completed.

Study of several other herbal compounds have been examined in FGIDs, and may hold promise in the future. Extract of artichoke leaf showed potential benefits in a randomised, placebo controlled trial for FD and a post marketing surveillance study for IBS.<sup>28–29</sup> A commercial compound of nine herbs, STW 5, improved abdominal pain and IBS symptom score, and may have potential for use in FD as well.<sup>30–31</sup> Increasingly, new herbal supplements and combinations of herbs are available to consumers with claims for generalised gastrointestinal health or specific symptoms. Data on long term side effects, drug interactions, and quality control for most herbal therapy are lacking.

### THE FUTURE OF CAM THERAPY FOR FGIDS

Enthusiasm for CAM use and research is clearly growing. Medline citations for alternative medicine have steadily increased from 69 citations in the 1970s to 423 citations since 2000. Unfortunately, a growing percentage of these articles are reviews, rather than original research (20% reviews since 2000 compared with 10% in 1970–1979). As the traditional prejudices against CAM therapies begin to decline, the major obstacle to these studies remains funding. The development of the National Center for Complementary and Alternative Medicine at the National Institute of Health has increased such funding in the USA, with a budget of over 100 million dollars in 2005. Other government and private foundations are increasingly investing in CAM research, although the proportion of gastrointestinal research funding dedicated to CAM is quite small. In addition to overcoming economic barriers, collaboration of gastrointestinal physiologists, researchers, and clinicians with experienced CAM providers internationally will be necessary, particularly in the areas of acupuncture, Chinese herbal medicine, Ayurvedic medicine, and other traditional practices.

“Enthusiasm for CAM use and research is clearly growing”

FGID patients are interested in CAM and will continue to use these modalities as long as medical therapy fails to relieve their symptoms. To optimise the care of our patients we must have further evidence of the potential benefits and safety of these treatments. Integration of CAM into Western medical practice will require more than selection of a few isolated herbs, acupoints, or yoga positions into our usual practice routine. A fuller understanding of the paradigm specific use of these techniques, mechanisms of action, and potential

pitfalls will be needed before we can take full advantage of what CAM has to offer.

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