



Holistic Treatment of Functional Irritable Bowel Syndrome with a Spotlight on Medical Acupuncture: A Narrative Clinical Update!

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is a common recurrent functional disorder without organic pathology. IBS mostly afflicts females often presents in different forms with abdominal and extra-abdominal symptoms, and impacts quality of life of patients around the world.

Objective: This update aims to critically describe the salient clinical features of IBS along with brief snapshots of complementary, conventional and integrative therapeutic approaches with a special focus on medical acupuncture.

Methods: A selective e-searches of relevant literature were carried out using keywords and Boolean operators, and finally 65 articles were retained for this critical clinical update.

Results: The main clinical manifestations of IBS include diarrhoea, constipation, abdominal pain, bloating and flatulence in the absence of "red flag" signs. Its several types (IBS-diarrhoea/constipation/mixed) affect approximately 15% to 40% of the general population. A variety

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of risk factors including gut-brain and biopsychosocial interactions contribute to the pathogenesis of this multifaceted gastrointestinal disorder that is reported to comorbid with other psychiatric disorders and physical diseases. A typical patient with IBS may require holistic customised intervention that will include complementary and integrative medicine modalities and conventional drug interventions with variable therapeutic results. Acupuncture is increasingly used globally and frequently combined with other Traditional Chinese Medicines (TCM) such as moxibustion, cupping therapy (Hijamah), medicinal herbs, mind-body-spirit therapies, and dietary modifications such as prebiotics and probiotics and life style changes for the successful management of patients with IBS.

Conclusion: IBS is a multidimensional disorder and needs comprehensive clinical and diagnostic workup for making a precise diagnosis and personalised-treatment intervention. Medical acupuncture alone or combined with other holistic therapies produces good cost-effective results and improves quality of life of patients with IBS. This update calls for rigorous basic research to further explore the underlying pathophysiology of IBS along with mechanism of actions and effects of acupuncture in future.

Keywords: Irritable bowel syndrome; acupuncture; moxibustion; dietary supplements; acupoints; probiotics.

1. INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic debilitating functional gastrointestinal disorder (GIT) with no life-threatening consequences. IBS presents recurrently with a variety of abdominal and extra-abdominal symptoms of diverse biopsychosocial pathologies [1,2]. Common symptoms of IBS with no organic pathology include abdominal pain relieved or worsen by defecation, diarrhoea, constipation and bloating with flatulence that affect the patients' quality of life and further incur greater burden of illness including unnecessary surgery [3]. In addition, patients with IBS tend to increasingly use healthcare services (shopping around), impact health of caregivers and close family members, develop poor therapeutic relationship, and physical and psychiatric co-morbidities [2-4]. Two or more aforesaid symptoms should occur 3 days per month in last 3 months for making a diagnosis of IBS [5]. "Red flag" symptoms, which are rectal bleeding, nocturnal or progressive abdominal pain, weight loss, family history of colon cancer, past use of antibiotic, age above 50, and laboratory abnormalities in terms of anaemia, elevated inflammatory markers, or electrolyte disturbance tend to exclude the diagnosis of IBS. However, the "Red Flag" symptoms may indicate the diagnosis of inflammatory bowel disease (IBD) or colon cancer or malabsorption syndrome [6-8]. IBS (when its subtypes are not considered but Rome II criteria and age were used) affects 7%–23% of the general population (in Europe and Latin America, 10% to 15% and 26% and global prevalence in general population, 5% to 20%)

and has impact on quality of life (QOL) as well as social domains including sexual behavior; and is associated with a greater work load on healthcare services [2,4]. Besides diagnostic Rome criteria I, II & III, age and gender, study settings such as outpatient clinic versus community-base versus academic also impact prevalence of IBS. The prevalence and risk factors of IBS types are highly variable globally: IBS- diarrhoea (40.0%); IBS- constipation (35.0%); and IBS-mixed (23.0%) [9]. Rome III criteria support a symptom-based approach and classify IBS into 3 sub-categories: (1) IBS-C; (2) IBS-D; (3) IBS-M. Other recognised subtypes of IBS are postinfectious-IBS [10] and unsubtyped IBS (IBS-U) [11]. Being a functional complex disorder, IBS may co-occur with other psychiatric disorders including anxiety disorders, post-traumatic stress disorder, depression and schizophrenia [12]. Overall, precise diagnosis and elucidation of risk factors of IBS are two core components for guiding its successful management in clinical settings.

2. DETERMINANTS AND CRITICAL VIEWS

Evidently, multiple determinants [4,9] including dysbiosis of the gut microbiome, gene mutations, diet and immune-mediated processes including inflammation are involved not only in the pathogenesis of IBS but also inflammatory bowel diseases (IBD) including celiac disease and ulcerative colitis. In addition, some extraintestinal disorders, such as, asthma, allergy, cardiovascular disease, metabolic syndrome, diabetes mellitus, and obesity are also caused by

aforesaid similar gut-brain dysfunctioning [2,13-15]. The related underlying pathophysiological alterations in IBS include, but not limited to, the intestinal permeability, innate gut immune response, GIT motility, visceral sensation and sensitivity, nutrient absorption, pain perception (hyperalgesia), various neurotransmitters including serotonin, dopamine, epinephrine, and norepinephrine regulation, small-intestine bacterial (over) growth, food sensitivity, lactose absorption, sex hormones, enterochromaffin (EC) cells functions, hypopituitary adrenal (HPA) axis modulation, enhanced perception of visceral stimuli and brain-gut (enteric somatic nervous system including vagus nerve) interactions [2,4,10,12-18]. With special reference to serotonin neurotransmitter, various studies including meta-analyses have reported serotonin transporter gene-linked polymorphism regions (5-HTTLPR), tandem repeats (STin2) and single nucleotide polymorphism (SNP, rs25531) in gut-brain interactions underlying IBS [19-24]. Presumably, genetic studies concerning neurotransmitters in IBS may lead to précised individualised therapy which may include acupuncture and other integrative therapies [25]. To some extent acupuncture-moxibustion and electro-acupuncture (at ST25 and CV12 and other acupoints) improve these aforesaid abnormalities in IBS through various action mechanisms [26], also shown in experimental studies concerning post-inflammatory IBS associated with visceral hyperalgesia [17,27,28]. In addition, psychosociocultural milieu especially external stress (external factors) and genetic vulnerability (internal load) contributes to the development of functional IBS [12,29,30] and, hence, IBS patients need specific holistic therapies such as acupuncture, cupping (Hijamah), stress management approaches, and genetic counselling. Newer pharmacotherapies that include tegaserod, alosetron, lubiprostone, linaclotide, asimadoline, eluxadoline, and rifaximin may be used alone or combined with CAM modalities including clinical acupuncture. However, these therapies need further comparative trials to optimise their safe use as these medications have restricted use in males, prescribed off-label and some of them not approved by FDA cause potentially serious adverse effects including deaths [31-33].

Notably, aforesaid microbial intestinal-brain interactions disorders have overlapping symptoms and, hence, present diagnostic and therapeutic challenges [34,35]. Nevertheless, clinical acumen complements results of

endoscopy, colonoscopy, and a battery of laboratory tests, including fecal lactoferrin and calprotectin, in the differentiation of IBD from IBS and also helps in monitoring therapeutic responses and relapses together with detection of IBS or IBD in asymptomatic patients [34-37]. Overall, IBS is a multifactorial functional disease and needs holistic and multidisciplinary approach for its successful management [38].

3. CLINICAL SETTING

A typical patient with multi-faceted IBS needs a detailed history workup, physical and systemic examination, pertinent laboratory investigations, differential diagnosis and comprehensive treatment plan: prevention strategies such as use of prebiotics and probiotics to promote growth of beneficial GIT bacteria, i.e., gram negative bacteroides, dietary supplements including medicinal herbs and lifestyle modifications, and stress reduction through the lens of evidence-based conventional and complementary and integrative medicine (CIM) therapies [2,4,31-33,37-40]. Of note, acupuncture approaches (manual, electroacupuncture, acupressure, Pi acupuncture, laser acupuncture, etc) are increasingly used with variable effectiveness in IBS around the world [41-43]. Acupuncture is reported to be more effective than pharmacotherapies in patients with IBS [44-46]; however, studies' limitations such as small sample size and lack of rigor assessment tools and reported side-effects call for further comparative research concerning the therapeutic role of acupuncture in IBS. In a nutshell, IBS is a very complex clinical dilemma. However, in particular, Traditional Chinese Medicine (TCM) differentiates diarrhea, constipation and abdominal pain which are primary symptoms of IBS subtypes (Table 1) [8].

IBS preferentially afflicts females and is a multidimensional disorder [38], often presents differently in each individual and can be managed better with evidence-based patient-centered holistic-integrative approaches. A judicious combination of pharmacotherapy with complementary and alternative medicine (CAM) therapies including acupuncture is evidenced to produce cost-effective and best outcomes for patients with IBS compared to placebo [2,4,47-55]. Pharmacotherapies needing comparative research, and used relatively more in IBS-D include, but not limited to, antispasmodics, low-dose tricyclic antidepressants and specific serotonin reuptake inhibitors (SSRI), 5-HT-3 and

Table 1. TCM differential diagnosis of diarrhoea, constipation and abdominal pain [8]

Diarrhoea/loose stool	Constipation	Abdominal pain
1.Spleen qi xu	1.Large intestine qi xu	1.Stomach food stagnation
2.Spleen yang xu	2.Large intestine jinyexu	2.Cold, damp, or heat attacking the stomach
3.Large intestine damp heat	3.Stomach qi xu	3.Rebellious stomach qi
4.Kidney qi or yangxu	4.Stomach heat [shi]	4.Stomach qi deficiency with stagnation
5.Stomach food stagnation	5.Stomach yin xu	5.Qi and blood stagnation in the st channel
6.Stomach fire	6.Kidney yin xu	6.Small intestine qi stagnation
7.Stomach dampness	7.Liver overacting on the bowels	7.Cold, heat or phlegm obstruction in the bowels
8.Stomach cold	8.Liver overacting on stomach	8.Constrained liver qi
9.Stomach qi deficiency	9.Blood deficiency	9.Dai mai dysfunction
10.Liver overacting on the spleen	10.Lung qi xu	10.Stagnation in the yin chiao and/or yin wei mai
		11.Stagnation in the chong mai
		12.Retention of cold, cold damp or damp heat in the st divergent channel

-4 receptor antagonist and agonist, probiotics, melatonin, bulking agents, laxatives, selective C-2 chloride channel activators, and non-absorbable antibiotics such as neomycin and rifaximin [25]. On the other hand, CAM therapies include psyllium (*Plantago* spp.) fiber, peppermint (*Mentha X piperita*) oil, Chinese Geshanxiaoyao formula and six of Six Gentlemen Decoction, exercise, meditation, t'ai chi, progressive relaxation techniques, hypnotherapy and gut-directed hypnosis, energy therapies, and mindfulness-based stress reduction approaches and others. In addition, patients with IBS need to reduce raw foods and eliminate fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) for the improvement of their symptoms [54,56]. Furthermore, the use of multistrain probiotics (for correcting small intestine bacterial overgrowth) and herbal adaptogens and nervines also improve symptoms of IBS [54,57]. Patients with IBS need holistic treatment that more often prevent development of various complications such as depression and anxiety, poor quality of life, pregnancy complications, bladder problem, hemorrhoids, malnutrition, food intolerance, impacted bowel and dehydration [2-4,12,45, 56,58]. Evidently many CIM approaches are available for the treatment of IBS with good results and this clinical update will enhance the knowledge of CIM practitioners around the world.

Clinical acupuncture is a CAM modality and very often combined with other CIM therapies in the successful management of irritable bowel syndrome.

4. ACUPUNCTURE

Among CAM and integrative medicine approaches, medical acupuncture, more than 3000-year old TCM therapy in Chinese traditional practice is commonly used either alone or combined with moxibustion or electro-acupuncture or cupping (Hijamah) therapy or medicinal herbs in the treatment of IBS with better outcomes [2,4,26,48,59]. In a randomized clinical trial (RCT), Ling Gui Ba Fa Time-based acupuncture (eight magic turtle techniques) was compared with ordinary acupuncture (manual), and was found to be more effective in IBS-D [60]. In a systematic review, Manheimer found weak evidence supporting the effective use of acupuncture in improving IBS symptoms or patients' QOL [44]. Nonetheless, in another review acupuncture was more helpful than either pharmacotherapy or no specific therapy and reported adverse effects were syncope, dizziness, bruising, infection, and bleeding [45]. In a network meta-analysis, acupuncture was ranked as the most effective therapy with no adverse effects in patients with IBS-D: drug rifaximin (vs. Pinaverium bromide) was associated with severe adverse effects and the

common acupoints used were ST25, ST36, ST37, SP6, GV20, and EX-HN3 [46]. Notably, in RCTs, systematic reviews (SR) and meta-analyses (MA), placebo response up to 40% mainly in women determined by baseline pain symptoms, severity of baseline symptoms, early improvement of abdominal pain and other critical factors needs to be taken into consideration while reporting weak or strong effectiveness of acupuncture in IBS with different subtypes [61]. For a critique of recent studies concerning TCM and IBS, see this important source [8].

One method called OMD's balance, a derivation of Richard Tan, stands better than other acupuncture techniques in clinical settings. Acupuncturists needle one side of the patient's body at these acupoints; ST 36 (*Zusanli*), GB 34 (*Yanglingquan*), PC 6 (*Neiguan*), and LU 7 (*Lieque*). The other side of the patient's body is needled at LV 8 (*Ququan*), SP 9 (*Yinlingquan*), LI 4 (*Hegu*), and SJ5 (*Weiguan*) acupoints (Fig. 1).

According to this method, the stomach and spleen followed by the gall bladder and large intestine channels are of prime importance in digestion and digestive disorders whereas the liver and pericardium channels focus on

emotions [63], and gut-mind (enteric nervous system-central nervous system) interactions through the prism of stress certainly affect the GIT organs and involved in physiopathogenesis of IBS [64]. As there are numerous acupoints (Table 2), the selection of specific acupoints for needling is highly important among patients with IBS. Needling of SJ5 and LU7 tend to balance the flow of energy concerning other involved acupoints. Acupoints LI 11 (*Quchi*) and ST 44 (*Neiting*) need to be needled to drain heat for improving the burning pain in the patient's bowels. Sometimes, ST 25 (*Tianshu*), SP 15 (*Daheng*), and CV 6 (*Qihai*) need to be needled when patients present with symptoms of IBS-D or mixed type. In general, the needles are retained in place for 30 minutes and moved manually (ordinary/traditional acupuncture) or by electronic/laser means. The number of acupuncture treatments and needling varies in accordance to the nature and type of IBS but mostly once per week using 4 to 7 needles. The frequency of acupuncture treatments decreases as the clinical condition of the patient improves that may take about 6 weeks or so. The acupuncturists need to know that patients in remission may recur with IBS often attributed to overwhelming stress and then may again require it or electropuncture.

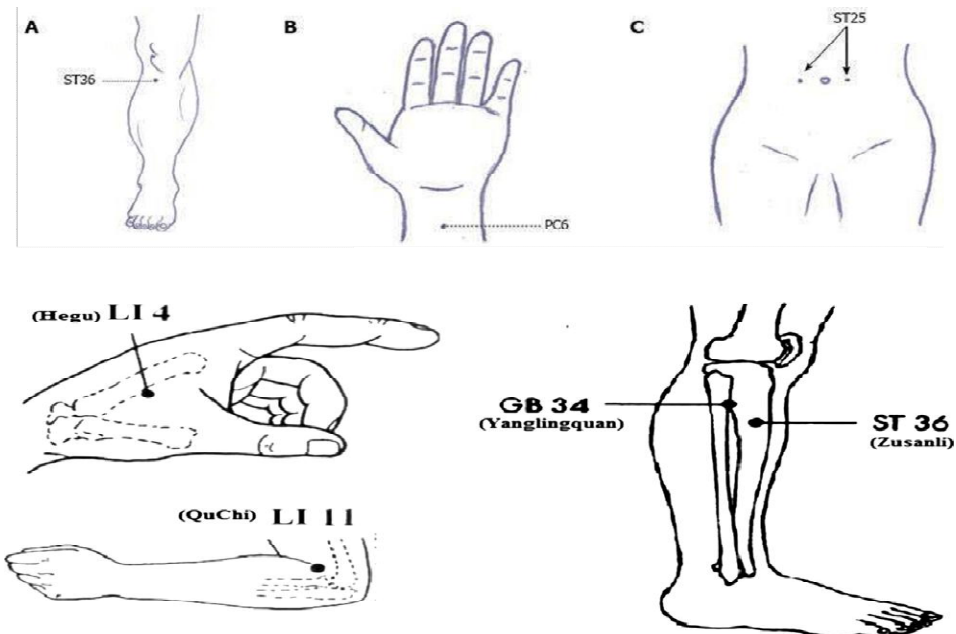


Fig. 1. Some important acupoints used in IBS and trigger finger [26,62]

Table 2. Acupoints used in IBS, humans and nonhumans [27,46,60,65]

Acupoints	Remarks
ST 36 (Zusanli),	One side of the patient's body, use in IBS-D
GB 34 (Yanglingquan)	-Do-
PC 6 (Neiguan),	-Do-, also used in IBS-D
LU 7(Lieque)	-Do-, also to balance other acupoints
LV 8 (Ququan),	Other side of the patient's body
SP 9 (Yinlingquan),	-Do-
LI 4 (Hegu),	-Do-
SJ5 (Weiguan)	-Do-, also to balance other acupoints
LI 11 (Quchi)	Burning sensations in the bowels (large intestine)
medical acupuncture and stress reduction strategies [63,64]. ST 44 (Neiting)	-Do-
ST25 (Tianshu),	Used in IBS-D (In rats with induced IBS)
ST37 (Shangju xu)	Used in IBS-D
SP15 (Daheng)	Used in IBS
CV 6 (Qihai)	Used in IBS
CV 12	Used in rats with induced IBS
SP6,	Used in IBS -D
GV20,	Used in IBS-D
EX-HN3	Used in IBS-D
SP4 (Gongsun)	Used in IBS
BL25 (Dachangshu)	Used in IBS
ST40 (Fenglong)	Used in IBS
BL20 (Pishu)	Used in IBS

Note: these acupoints are also used in other diseases and, hence, they are not specific concerning IBS.

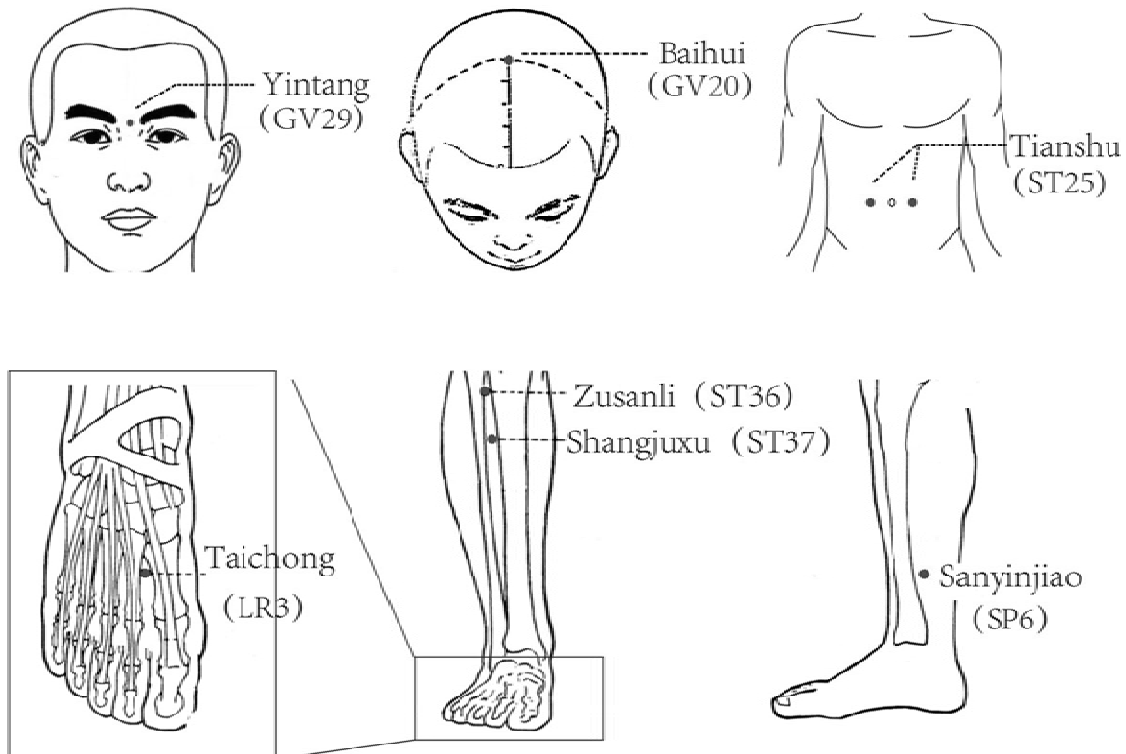


Fig. 2. Acupoints used in patients with IBS [58]

From acupuncture research perspective, Pei et al (2018) developed a multicenter RCT protocol concerning IBS and described succinctly the brain-gut axis in terms of TCM notions that represents primarily the interaction between the Shen (mind) and the Spleen, the latter is responsible for digesting food along with generating energy for the whole body. Accordingly, spleen deficiency frequently associated with IBS is characterised by abdominal pain, diarrhoea or constipation, and fatigue. Correcting spleen deficiency and regulating the Shen concerning mental or emotional problems are the two core principles that work in tandem with the treatment of IBS. Notably, a disturbance in Shen affects adversely the functioning of Spleen as evidenced by a close relationship between the Spleen and Shen, and reflected by high prevalence of anxiety-depression among IBS patients compared to the healthy population, and, hence, both need to be addressed in treating IBS using specific acupoints (Fig. 2) [58].

5. DISCUSSION

This study critically updates on Irritable bowel syndrome and its holistic treatment with a special focus on acupuncture, a TCM modality used since ancient times in Eastern world especially in Chinese culture. Currently, electroacupuncture (EA) is also increasingly used in many physical and psychological disorders in the Western world [41-43,66]. This is because of IBS patients never recover fully with modern conventional medications which are relatively more expensive and have significant adverse side-effects including cardiovascular events and ischemic colitis. Overall, researchers are not very optimistic about effectiveness of modern drugs among patients with all types of IBS [67]. IBS is a functional psychiatric disorder without any organic pathology. IBS is classified mainly into three types based on predominant GIT symptoms. It is multifactorial in nature and caused by various biogenetic, psychosocial and environmental stressors. IBS involves primarily abnormal gut-brain interactions along with spleen and Shen imbalance in the body [1-5,9-18,58]. Nonetheless, the pathophysiology of IBS is not fully understood and, therefore, basic pertinent researches are further needed in future [17,19-23]. Similarly, converging evidence suggests that acupuncture alone or combined with other CAM and conventional therapies is reported to produce beneficial effects in IBS through a variety of mechanism of actions [2,12,17,26-30,

45,46]. Again basic translational researches are needed to fully know the underlying mechanism of actions and effects concerning acupuncture not only in IBS but also other psychophysical disorders as these mechanisms are yet to be fully understood across the world. IBS more often posits several clinical challenges including diagnostic, mechanistic and theoretical, adverse effects, complications and therapeutic; prior or subsequent to its management with diverse CAM therapies, holistic approaches and integrative modalities [12,34-38,44-46,58]. Despite tremendous advances, acupuncture tends to produce certain adverse effects in IBS patients but these are not potentially life-threatening [45]. In addition, patients with IBS might develop a number of complications, poor quality of life, economic losses related to increasingly use of healthcare visits-services (shopping around) and expensive investigations, burden on family members, and somatic and psychiatric comorbidity (pain syndromes, overactive bladder and migraine, and anxiety and depression) on longterm basis. These complications tend to emerge in case IBS is not diagnosed early and managed properly using available resources including acupuncture with good followup and adherence to other prescribed holistic therapies [2-4]. Overall, patients with IBS need decision-shared multidisciplinary therapeutic approach associated with better outcome, and evidently acupuncture alone or combined with CAM therapy and modern medications is one of them [38].

According to various RCT, SR and MA, acupuncture (manual, electro, laser and other types combined with other CAM or modern therapies) using multiple specific acupoints is reported to have variable efficacy in IBS-D, IBS-C and IBS-mixed types across the board [44-46,60]. The inconsistent efficacy of acupuncture is reported in most SR and MA studies on IBS. Therefore, multiple protocols are developed to uniformly assess the efficacy of electroacupuncture in IBS and other GIT disorders [58,67-70]. However, results concerning acupuncture application in IBS were better than placebo, conventional medicines and sham acupuncture [41-46,71]. Electroacupuncture (EA) has positive effects on modulating pain sensations by altering the activation of neural pathways in IBS [71]. Of note, EA by stimulating heterotopic (ST36 and ST37) and homotopic (ST25 and ST26) acupoints, in terms of activated large (A β) and small (A δ -and/or C-fibers) pain fibers, produces

segmental (spinal cord) and extrasegmental analgesia through diffuse noxious inhibitory control (DNIC). DNIC is critical for chronic pain prediction and treatment of various conditions associated with pain including IBS. Efficient DNIC mechanisms are important for the treatment of IBS and other similar conditions with pain [68]. Another mechanism of EP may be through the down regulation of CNS serotonergic pathways in gut-brain axis resulting in attenuated pain in IBS as shown in experimental studies [72]. EA is also reported to attenuate visceral pain, and relaxes distended muscles and reduces intestinal motility in animal studies through acting on specific acupoints (PC6 and BL 27) and purinergic receptors found in peripheral and CNS [27,28,73]. Despite all this, further comparative multicenter research and SR of RCTs that focused on EA in English literature need to be pursued with large sample size, rigor assessment tools, and longer followup [69]. Notably, most of these studies have reported methodological limitations in particular small sample size, weak assessment tools and lack of high quality-rigor methods [44-46,58] in a nutshell, acupuncture is found to be effective in patients with all types of IBS in most studies as it is cost-effective, easily accessible and improves economy and quality of life not only of patients but also their caregivers. Regarding limitations, this clinical update is not comprehensive because of publication and selection biases. Huge literature exists on IBS and acupuncture in Chinese language. Currently western world also producing related data especially after launching a journal "The Medical Acupuncture". To include all published articles on several aspects of IBS including its greatly variable prevalence [74] and efficacy of electroacupuncture and other CAM therapies [75] is beyond the scope of this critical review. This clinical update is important as it might bridge the knowledge gaps of CAM practitioners especially acupuncturists globally.

6. CONCLUSION

In sum, IBS, a multi-faceted complex clinical dilemma, preferentially afflicts females and needs customised holistic approach in its management. Medical acupuncture either alone or combined with evidence-based CAM modalities or conventional medications that target the underlying pathophysiological processes of irritable bowel syndrome tend to be the effective treatment intervention for patients with variegated symptoms of irritable bowel

syndrome. This clinical update calls for rigorous basic research to further explore both the underlying pathophysiology of IBS and action mechanisms of electroacupuncture in IBS in future.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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