SOUTH BAYLO UNIVERSITY

LITERATURE REVIEW OF IRRITABLE BOWEL SYNDROM TREATED BY ACUPUNCTURE AND / OR MOXIBUSTION

By

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Literature Review of Irritable Bowel Syndrome treated by Acupuncture And/ Or

Moxibustion

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ABSTRACT

Irritable bowel syndrome (IBS) is a group of symptoms – including abdominal pain and changes in the pattern of bowel movements without any evidence of underlying damage. IBS patients have high rates of absenteeism from work and school. In the conventional medicine point of view, it is neither cure for nor untreatable. The medication Loperamide may be used to help with diarrhea while laxatives with constipation. Antidepressants may improve overall symptoms and pain. Bile acid binders including cholestyramine (Prevalite), colestipol (Colestid), or colesevelam (Welchol) can help some patients with IBS but can also cause bloating. However, prescribed medications often result in significant side effects, and many IBS sufferers do not improve. Instead of taking a variety of conventional medications, many have turned to taking traditional Chinese medicine for remedy.

Acupuncture and/or moxibustion therapy in traditional Chinese medicine usually administered together to achieve the optimal results. In the treatment of IBS patients and IBS rat models, the therapies have shown the effectiveness in relieving the syndromes. Research results indicated that acupuncture and/or moxibustion treatments for IBS can significantly regulate chronic visceral hypersensitivity (CVH), which was controlled by the Substance P (SP), Corticotrophi-releasing hormone (CRH), Hydroxy Tryptamine (5-HT), PK1 Prokineticin (PK1) and Prokineticin Receptor (PKR1). The frequent used acupuncture points for treating IBS are: ST25, ST36, ST37, RN6, bilateral were administered with true acupuncture or sham acupuncture; with moxibustion accompanied the acupuncture treatment or with acupuncture treatment alone were studied with the functional magnetic resonance image (fMRI) to determine the effectiveness. These results suggested that the acupuncture and/or moxibustion may relieve CVH by activating the receptors. The results of this study will help to provide reference for the future treatments of IBS.

TABLE OF CONTENTS

| I. | INTRODUCTION | 1 |
|------|--------------------|----|
| II. | MATERIAL & METHODS | 13 |
| III. | RESULTS | 14 |
| IV. | DISCUSSION | 22 |
| V. | CONCLUSIONS | 25 |
| VI. | REFERENCES | 26 |
| | APPENDIX | |

I. INTRODUCTION

Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder characterized by the presence of a cluster of symptoms and signs in adults or children that include cramping, abdominal pain, increased gas, altered bowel habits, food intolerance, and bloating (distention). IBS is a "functional" disorder. This term refers to the changes in the functioning of the digestive system that results in the collection of symptoms referred to as IBS, meaning that it is a problem with the movement (motility) rather than any damage to the tissues of the digestive system. The pathogenesis of IBS remains unknown. However, during recent years, pathophysiological research has increasingly indicated that multiple factors, such as genetic factors, psychological factors, diet, infections, immunity, and the brain-gut axis, can combine in a complex manner, leading to the visceral hypersensitivity and gastrointestinal dysmotility that are manifested by corresponding symptoms [1].

IBS negatively affects quality of life and may result in missed school or work. Disorders such as anxiety, major depression, and chronic fatigue syndrome, are common among people with IBS. The causes of IBS are not clear. Theories include gut–brain axis problems, small intestinal bacterial overgrowth, genetic factors, food sensitivity, and gut motility problems. Onset may be triggered by an intestinal infection, or stressful life event. IBS is a functional gastrointestinal disorder. Diagnosis is based on signs and symptoms in the absence of worrisome features. Worrisome features include onset at greater than 50 years of age, weight loss, blood in the stool, or a family history of inflammatory bowel disease. IBS negatively affects quality of life and may result in missed school or work. Disorders such as anxiety, major depression, and chronic

fatigue syndrome, are common among people with IBS. These symptoms occur over a long time, often years.

This review will examine the IBS treatment approaches in alternative treatment options in clinical practice for physicians who manage IBS. Furthermore, we believe that this assessment would also foster and facilitate potential areas of future research for more effective treatment models, thus providing IBS patients with better treatment outcomes while reducing the medical cost burden.

Conventional Western Medicine Categories of Irritable Bowel Syndrome

It's not known exactly what causes IBS, but a variety of factors plays a role. The walls of the intestines are lined with layers of muscle that contract and relax in a coordinated rhythm as they move food from one's stomach through intestinal tract to rectum. While when IBS is the case, the contractions may be stronger and last longer than normal, causing gas, bloating and diarrhea. Or the opposite may occur, with weak intestinal contractions slowing food passage and leading to hard, dry stools.

Stimuli that don't bother other people can trigger symptoms in people with IBS — but not all people with the condition reacting to the same stimuli. Common triggers include:

 Foods. The role of food allergy or intolerance in IBS is not yet clearly understood, but many people have more severe symptoms when they eat certain things. A wide range of foods has been implicated — chocolate, spices, fats, fruits, beans, cabbage, cauliflower, broccoli, milk, carbonated beverages and alcohol to name a few.

- Stress. Most people with IBS find that their signs and symptoms are worse or more frequent during periods of increased stress, such as finals week or the first weeks on a new job. But while stress may aggravate symptoms, it doesn't cause them.
- Hormones. Because women are twice as likely to have IBS, researchers believe that hormonal changes play a role in this condition. Many women find that signs and symptoms are worse during or around their menstrual periods.
- Other illnesses. Sometimes another illness, such as an acute episode of infectious diarrhea (gastroenteritis) or too many bacteria in the intestines (bacterial overgrowth), can trigger IBS. It may involve chemicals made by the body, such as serotonin and gastrin that control nerve signals between the brain and digestive tract.

It has been classified into three main types of IBS.

- IBS with constipation. This comes with stomach pain and discomfort, bloating, abnormally delayed or infrequent bowel movement, or lumpy/ hard stool.
- IBS with diarrhea. This comes with stomach pain and discomfort, an urgent need to move bowels, abnormally frequent bowel movements, or loose/watery stool.
- IBS with alternating constipation and diarrhea.

There are no specific lab tests that can diagnose IBS. Doctors will see if the symptoms match with the definition of IBS, and there may be tests to rule out conditions such as:

- Food allergies or intolerances, such as lactose intolerance and poor dietary habits Medications such as high blood pressure drugs, iron, and certain antacids.
- Enzyme deficiencies where the pancreas isn't releasing enough enzymes to properly digest or break down food.
- Inflammatory bowel diseases like ulcerative colitis or Crohn's disease.

The following tests to decide if you have IBS:

- Flexible sigmoidoscopy or colonoscopy to look for signs of blockage or inflammation in your intestines.
- Upper endoscopy if you have heartburn or indigestion.
- X-rays.
- Blood tests to look for anemia (too few red blood cells), thyroid problems, and signs of infection.
- Stool tests for blood or infections.
- Tests for lactose intolerance, gluten allergy, or celiac disease.
- Tests to look for problems with your bowel muscles.

The following types of drugs are used to treat IBS:

- Antispasmodics can control colon muscle spasms. They also have side effects, such as making drowsiness and constipation which make them a bad choice for some people.
- Antidiarrheal drugs, such as Imodium, may help with diarrhea.
- Laxatives can give short-term relief from constipation.
- Bulking agents, such as psyllium, wheat bran, and corn fiber, help slow the movement of food through the digestive system and may also help relieve symptoms.
- Antidepressants may also help relieve symptoms in some people.
- Linaclotide (Linzess) helps to relieve constipation by helping bowel movements happen more often. The drug's most common side effect is diarrhea.
- Lubiprostone (Amitiza) can treat IBS with constipation in women when other treatments have not helped. Common side effects include nausea, diarrhea, and belly pain. More

serious side effects may include, fainting, swelling of the arms and legs, breathing problems, and heart palpitations.

Traditional Chinese Medicine Categories of IBS

IBS negatively affects quality of life and may result in missed school or work. Disorders such as anxiety, major depression, and chronic fatigue syndrome, are common among people with IBS. Due to the increasing numbers of population suffering by the conditions of IBS, and the unknown causes, the effective therapeutic options are relatively limited in the contemporary western medicine; people start to seek the complementary or alternative approaches. Acupuncture has become increasingly popular in patients with various diseases, including IBS. Several recently published studies of acupuncture showed improvement in quality of life, regardless of whether it was traditional or sham acupuncture. Acupuncture for IBS provided an additional benefit over usual care alone. A meta-analysis of randomized controlled trials to assess whether there was any benefit of acupuncture in improving symptoms or health-related quality of life in patients with IBS.

The original Chinese term for what we today routinely call acupuncture is ZhenJiu, which refers to needling (针 Zhen) and moxibustion (灸 Jiu), two techniques understood to be essential parts of one fundamental approach to treating disease and maintaining health. Nonetheless, compared to acupuncture, moxibustion is usually deemed a secondary practice. Huang Di Nei Jing, which is (comprised of the SuWen and the LingShu), is the textual basis of ancient and modern concepts about acupuncture and moxibustion treatments. Chapter 73 of the LingShu states: 'A disease that may not be treated [is not successfully treated] by acupuncture may be treated by

moxibustion.' In Introduction to Medicine [1575 A.D.], it says: 'When a disease fails to respond to herbs and acupuncture, moxibustion is suggested.' [2].

In China, acupuncture, a therapy that involves inserting the tips of thin, stainless steel needles through the skin at specific points, has been widely used in clinical practice to treat various diseases and physiological disorders. The procedure can be accomplished by manual manipulation or electrical stimulation. Manual acupuncture involves the manipulation of the inserted needles by hand, such as lifting, thrusting, twisting, twirling, or other complex combinations. In principle, acupuncture is a method by which Yin and Yang can come into balance with one another and qi can flow harmoniously throughout the body. In addition, De-qi, a composite of unique needle sensations in patients, including soreness, numbness, heaviness, fullness, warmth, coolness, tingling, and dull pain, is an efficacy predictor and parameter for assessing clinical effectiveness of acupuncture [3].

Acupuncture-moxibustion is a crucial part of TCM, comprising both acupuncture and moxibustion methods. As external treatments of TCM, acupuncture and moxibustion act by stimulating acupuncture points to unblock the meridians and collaterals, regulating the function of qi and blood, supporting health and expelling pathogens.

Although IBS is not specifically mentioned in the classical books of Chinese medicine, the characteristic symptoms of IBS are described. According to TCM theory, IBS can be classified as "diarrhea" or "constipation" and treated as such with TCM treatment methods. In Traditional Chinese Medicine (TCM), IBS is considered to be primarily a disorder of the Qi pertaining to the Liver and Spleen Zang Organs. As the primary factors involved in IBS are related to the Qi of the Liver and Spleen, TCM diagnostic categories focus on these two Zang Organs and the relationship between them:

Psychological factors, such as certain depressive and anxiety disorders, play a role in the pathophysiology of IBS. Patients with IBS are more likely to have depression and anxiety. In IBS patients, feelings of frustration, inadequacy and powerlessness in dealing with medically unexplained symptoms can also adversely affect both medical decision making and the physician-patient relationship. Psychotherapies have been evaluated for their potential application in IBS. During periods of emotional turmoil or disharmony, the Liver Zang's Qi, which is responsible for the free flow of Qi in the body, may become stagnant. This stagnation may cause constipation, abdominal pain, and cramping, which is considered to be an intestinal Wind. Factors such as overwork, poor diet, insufficient rest, or excessive worry may cause the Spleen Qi to become weakened, which can lead to diarrhea, abdominal pain, and distention. Either of these factors can contribute to the symptoms of IBS. When the Liver Zang's Qi is stagnant or the Spleen Zang's Qi is weak, it is commonly said that the Liver Qi will invade and overwhelm the Spleen Qi, leading to a combination of alternating diarrhea and constipation, accompanied by the other symptoms that characterize IBS.

Likewise, the Qi Stasis and Qi Deficiency that underlie these symptoms can generate Dampness or Damp-Heat, which can cause mucus in the stools:

- Liver Qi Stasis: Symptoms include abdominal pain and distention, constipation (frequently with small stools), frustration, a high stress level, and irritability. There also may be hypochondriacally discomfort. The tongue usually is normal to dusky in color with distended sublingual veins and the pulse is wiry [4].
- Spleen Qi Deficiency: Symptoms include abdominal distention and discomfort, diarrhea or loose stools, tendency to worry, fatigue, and poor appetite. The tongue usually is pale and may have teeth marks on the side. The pulse usually is weak [4].

- Liver Invading the Spleen: Symptoms for this presentation include all those listed under Liver Qi Stasis and Spleen Qi Deficiency, with alternating diarrhea and constipation. The tongue usually is pale and dusky with a thin white coat. The pulse is wiry and weak, sometimes wiry on one side and weak on the other. If there is mucus in the stool in any of these Patterns of Disharmony, Dampness or Damp-Heat has been generated from Qi Stasis and/or Qi Deficiency [4].
- In the case of Dampness, the tongue has a greasy white coating and the pulse has a slippery quality [4].
- In the case of Damp-Heat, the greasy coating is yellow and the pulse has a slippery-rapid quality [4].

The basic treatment principle for IBS is to relieve the Liver Qi Stasis, strengthen the Spleen Qi, harmonize the Liver and Spleen Zang, and eliminate the Dampness or Damp-Heat [4].

Functions of Acupuncture Points for IBS

Acupuncture-moxibustion involves warm stimulation by moxa combustion at acupuncture point areas. This form of acupuncture is also a therapy for treating certain disorders in the clinic. Moxibustion includes suspended moxibustion (also named mild moxibustion), scarring moxibustion and herb-partition moxibustion have indicated that it has a beneficial effect on IBS.

Acupuncture treatment procedures were conducted in both sham acupuncture and true acupuncture to obtain and distinguish if acupuncture provides greater relief of IBS symptoms. Streitberger needles, a validated sham acupuncture device, has been shown to be indistinguishable from an actual acupuncture device. The 'needle' does not pierce the skin but create the illusion of doing so as it retracts into a hollow handle and true acupuncture needles were applied for an identical period of time. To avoid acupuncture pressure effect, sham needles were placed over predetermined 'non-acupuncture' points in the relative vicinity of the genuine points [5].

Acupuncture-moxibustion therapy has been shown to regulate the concentration of 5hydroxytryptamine (5-HT, serotonin), P-substance, PKR1 and corticotropin releasing factor (CRF) both locally and in the central nervous system. These substances are responsible for transmitting abdominal pain [6]. For this study an acupuncture protocol that used acupuncture points could be applied based on the participant's Chinese medicine diagnosis. The key results showed that acupuncture-moxibustion therapy was 76.92% effective for IBS symptoms when used on acupuncture points ST25 (TianShu), ST36 (ZuSanLi), and ST37 (ShangJuXu). Moxibustion applied to all these points are effective in treating IBS.

ST25(TianShu) is one of the most empowering points for the treatment for IBS that is located two-thumb width away from the belly button on either side. Needling these points 1 to 1.5 Cun perpendicularly can help in treating all kinds of intestinal disorders such as IBS, constipation and diarrhea. ST25 is the front Mu point of the large intestine, which can directly adjust the function of the large intestine and cure patients with IBS. Suspended moxibustion at ST25 significantly decreased visceral sensitivity to colorectal distention in a chronic visceral hyperalgesia rat model which involved in the analgesia using suspended moxibustion in rats with chronic visceral hyperalgesia [7].

ST36 (ZuSanLi) or the Three Mile Point is one of the vital acupuncture points for IBS that is situated four finger widths below on the edge of the knee cap and one thumb's width to the outside of the shinbone. Insertion perpendicularly 1 to 2 Cun is helpful in strengthening the whole body and relieving problems of indigestion and IBS. Moxa can facilitate the movement of

qi. ST36, the stomach He-Sea point, moderates the transporting function of the large intestine, stomach and spleen. As ST36 not only promoted gastric peristalsis, but also inhibited the acceleration of stress-induced colonic transit due to restraint, improved postprandial gastric dysrhythmia, and delayed gastric liquid emptying via the enhancement of vagal activity, which indicated that the accelerative effect of acupuncture on gastric motility might be blocked after a vagotomy. Acupuncture at the acupoints in the limb promoted gastric motility via a supra-spinal reflex that activated the vagal nerve fibers, while the same stimulus to the abdomen resulted in the reverse effect via a spinal reflex that activated sympathetic nerve fibers. Moreover, needling at ST36 has been found to enhance gastric motility via the efferent parasympathetic pathway. Also, needling at ST36 aided in the repair of the stomach mucosa by increasing the concentration of epidermal growth factor in gastric mucosal tissue [7].

ST37 (ShangJuXu) or the Upper Great Hollow, is the lower He-Sea point of the large intestine, it strengthens the transporting function of the spleen and stomach. This point is located on the anterior aspect of the lower leg, four finger widths below the kneecap ST36 (ZuSanLi). Insertion in this point perpendicularly 1 to 2 Cun is especially helpful in clearing damp heat and alleviates diarrhea and dysenteric disorder. ST37 activates the channel and alleviates pain, regulates the spleen and stomach, relieving acute appendicitis, abdominal pain, distension, borborygmus, dysentery, constipation, enteritis, diarrhea, constipation, symptoms of IBS, regulates the intestines and transforms stagnation [7].

SP4 (GongSun) also known as the Grandfather Grandson is one of the functional acupuncture points that have several benefits for health. This point is located at the middle aspect of the inner foot, right above the depression of the foot. Needling this point .5 to 1.5 Cun perpendicularly helps in relieving IBS, gastric pain, poor appetite, diarrhea and bloody stool. This Luo-

Connecting point of the Spleen Meridian can communicate with two meridians Chong Mai Vessel (couple with PC 6). They treat diseases of the collaterals and can be used to treat acute gastric pain, gastric distention and stuffiness, poor appetite, pain around the umbilical region, diarrhea, bloody stools, epigastric pain, chest congestion, distention in the hypochondrium, especially chronic diseases of the Zang-Fu organs [7].

UB25 (DaChangShu) also known as the Large Intestine Back Shu point that is located at the back, 1.5 Cun lateral to the lower edge of the 4th lumbar vertebra. Insertion 0.5 to 1 Cun perpendicularly at this point is especially useful for treating IBS along with abdominal distension, dysentery, colitis, constipation, hemorrhoids, diarrhea, lumbar pain and Urticaria [7].

LV3 (TaiChong) is a Liver Shu-Stream point, which located on the dorsum surface of the foot, in the angle between the first and second metatarsal bones. It pacifies and re-adjusts Liver Qi stagnation so that Liver Qi flows smoothly again, regulates the circulation of Qi and Liver Blood, especially in the lower abdomen and the chest, calms the mind, sedates and reduce or stop pain, clears dampness especially associated with Live Qi stagnation [7].

Acupuncture treatment varies according to the extent to the pattern of Disharmony is involved [8]:

- Liver Qi Stasis might be treated with points such as LV3 (TaiChong) and LI4 (HeGu), which also alleviates intestinal Wind caused by the constrained Liver Qi.
- Spleen Qi Deficiency may be treated with points such as ST25 (TianShu) and SP4 (GongSun). A combination of these points may be used if the Liver is Invading the Spleen. Likewise, points on the abdomen, such as ST25 (TianShu) and SP15 (DaHeng), may help balance symptoms of diarrhea and constipation.

- PC6 (NeiGuan) might be useful as well, PC6 inhibited the excessive GI motility induced by mosapride citrate, and enhanced the suppression of loperamide-induced conditions, as it affects the Liver and Stomach (which is paired with the Spleen) and helps balance the emotions and relieve stress.
- If there is Dampness or Damp-Heat, SP9 (YinLingQuan) may be added to the point formula.

II. MATERIALS & METHODS

Research Sites

The search strategy, research questions, inclusion and exclusion criteria and data extraction and analysis were predefined in this research. The systemic searching of PubMed Central Journals database and Internet Sites for literatures published from the year 1998 available up until September 2014, had included all studies to investigate the effect of results of the IBS syndromes treated by acupuncture and/or moxibustion. 198 papers were identified, 58 related to the clinical research for IBS. 15 met the inclusion criteria for the descriptive analysis. Studies meeting the following criteria were included: acupuncture-moxibustion treatments of IBS with clinical research RCT (Random Control Treatment).

• Acupuncture-Moxibustion mechanism with RCT.

Studies meeting the following criteria were excluded:

- Duplication (the same data of with the same authors published in different journals).
- Studies not meeting the inclusion criteria.

Keywords

Acupuncture, Moxibustion, Irritable Bowel Syndrome, Visceral hypersensitivity, Brain-gut relations, True Acupuncture, Sham Acupuncture

III. RESULTS

Despite the wide range of available medications and the continuous development of new drugs, the management of IBS remains a challenge, and to date, no completely effective remedy is available. The additional options in the use of TCM acupuncture and moxibustion, to the conventional medicines available to treat IBS based on the individual symptoms presented in each IBS patient. These strategies have produced beneficial effects, with lower adverse effects and lower reoccurrence rates. These additional treatment approaches may provide good options for the best symptom relief and highest quality of life to IBS patients. The integration of TCM with conventional Western medicine appears rather promising.

As acupuncture-moxibustion treats the body as a whole system through acupuncture points, its action mechanisms for the treatment of IBS could involve multiple segments, layers, and targets. Indeed, the current literature supports this perspective. Meanwhile, separate from medications, acupuncture-moxibustion is efficacious because it stimulates acupuncture points on the surface of body. Current studies have mainly focused on the regulation and mechanisms of the target organs after acupuncture-moxibustion has stimulated the appropriate acupuncture points. However, the precise action mechanisms of acupuncture-moxibustion used to stimulate the acupuncture points and the pathways through which IBS can be managed remain unknown. These questions still require further research to properly address them. Furthermore, both acupuncture and moxibustion, either in combination or alone, are effective in attenuating the symptoms of IBS.

This paper is expected to study the following aspects:

Effectiveness of Acupuncture-Moxibustion in Relieving Symptoms of IBS

Acupuncture-moxibustion relieves symptoms functional dyspepsia (FD) in IBS, a disorder of the large intestine often involving abdominal pain, cramping, diarrhea, constipation, bloating, and gas. Acupuncture and/or moxibustion has shown superior results including positive patient outcomes for reductions in stomach bloating and pain, diarrhea, and mucus in the stool.

Acupuncture effectiveness on FD was evaluated based on subjective and objective outcomes. Ji-Liang Fang et al [9] had found out that subjective outcomes included dyspeptic symptoms, quality of life, and mental status; objective outcomes included fasting serum gastrin concentration, height of gastric fluid retention, and frequency and propagation velocity of gastric slow wave measured by the barium swallow test. Subjective outcomes were measured in patients with FD before and after one month of acupuncture treatment; objective outcomes were measured in healthy adults as well as in patients with FD before and after one month of acupuncture treatment. Before treatment, patients with FD demonstrated lower levels of fasting serum gastrin concentration and frequency and propagation velocity of gastric slow wave than healthy adults. Before acupuncture treatment, patients had gastric significant fluid retention; after the treatment, no patient demonstrated measurable gastric fluid retention.

Siyuan Zhou et al [10] concluded that acupuncture exhibits clinically and statistically significant control of IBS symptoms. It is noted that acupuncture improves the symptoms of IBS, including abdominal pain and distension, sensation of incomplete defecation, times of defecation per day, and state of stool. Possible mechanisms of acupuncture's therapeutic actions showed that improvement in pain in IBS was positively associated with increased parasympathetic tone in the acupuncture treatment. Acupuncture and/or moxibustion produces better patient outcomes than

drug therapy. Acupuncture and/or moxibustion for IBS is better than the conventional western medication treatment.

| Author | Evaluation | Number | Res | P Value | |
|------------------|------------|-------------|-------------------|-----------------|---------|
| | Method | Of Patients | Before Treatment | After Treatment | |
| | | | | | |
| JiLiang Fang [9] | SDS & SAS | 30 | 61.88 ± 11.68 | 44.00 ± 8.64 | P<0.05 |
| Sizuro Zhou [10] | Defection | 20 | 16 17 + 5 29 | 0.78 + 2.75 | |
| Siyuan Zhou [10] | Frequency | 30 | 10.17 ± 5.28 | 9.78 ± 5.75 | P<0.001 |

Table1. Effectiveness of Acupuncture and/or moxibustion on IBS

FD = Functional Dyspepsia, SDS = Self-Rating Depression Scale, SAS = Self-Rating Anxiety Scale

Effectiveness of Acupuncture and/or Moxibustion in Treating Visceral Hyperalgesia

There were 5 experiments conducted on human and rats to realize the brain-gut interaction and multiple neural transmitters' relationship. It is known that the brain-gut peptides work extensively to regulate the gastrointestinal activities and which is closely related to IBS.

(1) Acupuncture and/or moxibustion relationship to SP receptor

Substance P (SP) is closely related with the pathological change in IBS, which plays a role in stress, intestinal infection and visceral hypersensitivity in the development of IBS. Meanwhile, SP is a gastrointestinal peptide hormone existing in the central nervous system and gastrointestinal tract, and a signaling molecule connecting the nervous system to the immune system. The expression of SP in the enteric and central nervous systems suggesting that abnormal changes in SP may be involved in the pathogenesis of IBS, and SP containing the neural pathway may be one of the neural pathways that play an important role in the regulation of gastrointestinal function.

SP in the intestinal tract is mainly produced by nerve terminal and endocrine cells. In the enteric nervous system which can increase gastrointestinal motility, promote contraction of alimentary tract smooth muscle, and stimulate water and electrolyte secretion in small intestine and colon. In the study by Xiao-Peng Ma et al [1], 21 rat models were divided in 3 groups and received treatments at ST25 and ST37 once a day for 7 day to evaluate the improvement in visceral hypersensitivity and the change in SP. After the trail was completed, the visceral sense was significantly decreased between the model group and the EA treatment group (P<0.005).

(2) fMRI of brain imaging observation of visceral pain

Yi Zhu et al [11] has conducted a study of functional Magnetic Resonance Image (fMRI) of brain imaging of visceral pain of 80 patients, 40 patients were each divided into a moxibustion group and sham moxibustion group, each patient received 2 courses of treatment. A treatment course on the ST25, RN6 and RN12 with 1 moxa cone for each treatment, 3 times per week for 2 weeks, and the sham group was administered as the moxibustion group. The changes in the brain imagine of IBS patients undergone the fMRI before and after moxibustion during the rectal balloon distention in either group, the decrease in pain threshold score were remarkable (P<0.01).

| Author | Subject | Group | Method | Before | After | P Value |
|--------------|-----------|----------|------------------|--------------------------|--------------------------|---------|
| Xiao-Peng Ma | [1] SP | 10 10 | N(A&M) W(A&M) | 15.50±3.25 21.81±1.93 | 57.95±5.45 63.23±6.24 | P<0.05 |
| Yi Zhu[11] | fMRI | 40 40 | N(A&M) W(A&M) | 27.38±3.95 28.27±3.64 | 21.4±4.31 9.00±4.05 | P<0.01 |

Table2. Pain Threshold in Visceral Hyperalgesia with A&M (Human)

SP = Substance P, fMRI = functional Magnetic Resonance Image, N(A&M)=No(Acu&Moxa), W(A&M)=With(Acu&Moxa)

(3) CRH relationship to the IBS

Corticotropin-releasing hormone (CRH) plays an important role in the pathophysiology of IBS and regulates the stress response through two CRH receptors (R1 and R2). Corticotropinreleasing hormone (CRH) is a major mediator of stress response in the brain-gut axis. IBS is presumed to be a disorder of the brain-gut link associated with exaggerated response to stress. This response was significantly suppressed in IBS patients. Evidence supporting the concept that peripheral CRH and CRH-R1 play important roles in brain-gut sensitization is increasing. Several studies have suggested the major role of CRH in stress-related pathophysiology of IBS and possibly in inflammation of the intestinal mucosa.

Electrical acupuncture induced significantly higher motility indices of the colon in IBS patients than in the control group.

Hui-Rong Liu et al [12] in the experiment of 6 litters of rats indicated that CRH protein levels in the peripheral colon were involved in modulation of visceral pain by electro-acupuncture. Therefore, they measured the expression of CRH protein in the spinal cord and hypothalamus. Compared with the rats in normal group (NG), the content of CRH in the spinal cord of the rats in modal group (MG) rats was significantly enhanced (P < 0.01). Compared with MG rats, the content of CRH in the spinal cord in the rats in EA was significantly reduced (P < 0.01).

(4) Acupuncture and/or moxibustion and the regulation of 5-HT

The interaction between the central nervous system (CNS) and enteric nervous system (ENS) through various neurotransmitters and hormones composes a complex bidirectional signaling system called brain-gut axis. 5-HT (Hydroxy Tryptamine), as one of the brain-gut peptides locating in both CNS and ENS, plays a predominant role in the pathophysiology of IBS which

involved in the regulation of intestinal movement and perception. Through interaction with different receptors, 5-HT controls the intestinal motility and secretion. Abnormalities in 5-HT signaling system may affect the sensory, motor, and secretory function of the digestive system, result in gastrointestinal dysmotility, visceral hypersensitivity, and infection, and further influence patients' mental condition [13].

In a clinical study by Yin Shi et al [14], there were 10 patients with D-IBS and 10 healthy controls received acupuncture at ST36, ST25, PC6, and were observed for the changes in their condition after the acupuncture intervention. The results were significantly downregulated to (P<0.01) which indicated that acupuncture can regulate the D-IBS condition instantly to lower the liver- intestine qi stagnation. The study has indicated that with the implementation of either acupuncture and/or moxibustion at the specific acupuncture points can significantly reduce the 5-HT which in turn has been showm to downregulate the concentration of 5-HT.

(5) PK1 and PKR1 relationship to IBS

It is known that the spinal cord is important for transmitting sensation and motor neuron impulses. Nerve impulses transmit into the dorsal root ganglion, which in turn transmits to the brain through the spinal cord. Neurophysiology of somatesthesia and visceral sensation states that dorsal horn neurons interact with the peripheral tissues or descending system of the brain stem when the dorsal horn neurons are over-excited. This mechanism plays a crucial role in the occurrence and development of gastrointestinal chronic hyperalgesia in humans. Research studying the harmful exion reflex in IBS patients has demonstrated that hyper-excitability existed in the spinal cord of this population.

PK (Prokineticin)1 and PKR (Prokineticin Receptor)1 are new members of a peptide family newly identified in mammals, which have been proven to be closely related with transmission of pain signals. This peptide is widely expressed in the brain, spinal cord, dorsal root ganglion and enteric plexus. PKR1 signaling was a requirement associated with activation and sensitization of primary afferent fibers. Blockade of PKR1 may present a novel strategy which can diminish the activation and sensitization of primary afferent nociceptors.

Chen Zhao et el [15] in the CRT of 22 rats each in the normal group and the model group receiving suspended moxibustion treatments for the evaluation of visceral hyperalgesia. AWR (abdominal withdrawal reflex) shown significant decreased after the treatment compared with the model group (P<0.01).

| Author | Subject | Group | Method | Before | After | P Value |
|--------------|----------------|----------|------------------|----------------------------|----------------------------|---------|
| Hui-Rong Liu | [12] | 6 | N(A&M) | 33.35±1.17 | 35.45±2.25 | |
| | CRH | 6 | W(A&M) | 35.15±1.25 | 35.53±2.45 | P<0.01 |
| Yin Shi [14 |] | 10 | N(A&M) | 204.37±61.97 | 122.13±50.09 | |
| | 5-HT | 10 | W(A&M) | 198.93±65.30 | 123.13±50.06 | P<0.01 |
| Chen Zhao [1 | 5] PK1 PKR1 | 22 22 | N(A&M) N(A&M) | 300.10±074.26 1.89±0.84 | 055.93±111.09 0.77±0.39 | P<0.01 |

Table 3. Pain Threshold in Visceral Hyperalgesia with A&M (Rats)

CRH = Corticotropin-releasing Hormone, 5-HT = 5 HydroxyTryptamine, PK = Prokineticin, PKR = Prokineticin Receptor, N(A&M)=No(Acu&Moxa), W(A&M)=With(Acu&Moxa),

Frequent Used Acupuncture Points for IBS

For this study there were fixed numbers of always used acupuncture points and there were optional points that could applied based on the participant's Chinese medicine diagnosis. The optional points provided the reproducibility and flexibility which were essential for the treatment of IBS. Ji-Ling Fang et al [9] [16] [17] [18] [19] [20] [21] [22] had chosen 6 main fixed acupuncture points: ST25, ST36, LV3, SP4, PC6, ST37 and 11 optional points: LI4, LI11, UB25, RN6, RN12, KD3, GB21, GB41, HT7, SI14, ST34, as the therapeutic intervention to perform, and was proven an effective form of treatment.

| Author | ST25, ST36, ST37, LI4, RN12, PC6 | | | | | | |
|--------------------|----------------------------------|---|---|---|---|---|--|
| Ji-Ling Fang [9] | | * | | | | * | |
| Wing-Wa Leung [16] | | * | | * | | * | |
| Z. J. Weng [17] | * | | * | | | | |
| Chun-Hui Bao [18] | * | * | | | | | |
| Hui Zheng [19] | * | | * | | | | |
| Yi Zhu [20] | * | | | | * | | |
| Ga-Jin Han [21] | | * | | * | * | * | |
| Hui Li [22] | | * | | * | * | * | |

Table4. Frequent Used Acupuncture Points for IBS

IV. DISCUSSION

IBS is defined as abdominal pain or discomfort that occurs in association with altered bowel habits over a period of at least 3 months. The diagnosis of IBS, a highly prevalent functional gastrointestinal disorder, is currently based on the presence of a characteristic symptom profile as abdominal pain/discomfort, bloating/distension, alterations in defecator function, in the absence of a demonstrable organic disease of the gastrointestinal tract. The burden of IBS is significant enough to contribute to considerable impairment of quality of life. Patients with IBS have higher healthcare resource utilization than non-IBS patients in terms of more frequent physician visits, more tests, greater medication use, and increased rates of unnecessary surgery. Although IBS is common, its pathophysiology is not completely understood, which poses problems in the search for effective therapeutic approaches.

Although the pathogenesis of IBS is not fully known, a multifactorial involvement of diet, gene mutations, psychosocial factors, and immune-mediated processes is hypothesized. Visceral hypersensitivity and dysregulation of central pain perception in the brain-gut axis are considered to play a pivotal role in the pathophysiology of IBS. One theory regarding the pathophysiology of IBS involves interference of neurotransmission between the central nervous system and the intestines.

IBS can be classified as either diarrhea predominant, constipation predominant, or a mixed form. Due to the wide range of symptoms that may be experienced, the available pharmacological treatments are mainly targeted at symptom reduction. Effective treatments for IBS are needed to relieve symptoms, improve quality of life, and reduce healthcare utilization. However, acupuncture, a 3000-year-old traditional Chinese medical practice, is receiving increasing

acceptance in the world of western medicine for treating certain medical conditions. In addition to gastrointestinal symptoms, IBS is also closely associated with anxiety and depression. IBS-related gastrointestinal symptoms and psychological conditions can severely affect patients' quality of life. The results have indicated that populations with high anxiety and depression scores had a higher incidence of IBS compared with other populations. There are also correlations among the severity of gastrointestinal symptoms, the severity of psychological conditions, and the abnormal activation of certain brain regions in IBS patients; once patients' emotional states improved, this abnormal activation of brain regions diminished. These results provided objective evidence that psychological factors influence the pathogenesis of IBS. Studies also found that in clinical practice, mild emotional stimuli can aggravate or induce gastrointestinal symptoms in IBS patients. This phenomenon occurred repeatedly; as a result, a considerable percentage of IBS patients treated in a clinical context had conditions accompanied by various degrees of anxiety, depression, and other psychological symptoms [17].

Acupuncture and/or moxibusion for IBS provided an additional benefit over usual care alone. The magnitude of the effect was sustained over the longer term. Acupuncture and/or moxibustion should be considered as a treatment option to be offered in primary care alongside other evidenced based treatments.

Despite the wide range of available medications and the continuous development of new drugs, the management of IBS remains a challenge, and to date, no completely effective remedy is available. Compared to treatment options available to physicians in other countries, physicians from China have the additional options in the use of TCM, including Chinese herbal medicines and acupuncture, in addition to conventional medicines available to other countries to treat IBS based on the individual symptoms presented in each IBS patient. These strategies have produced

beneficial effects, with lower adverse effects and lower reoccurrence rates. These additional treatment approaches from China may provide good options for the best symptom relief and highest quality of life to IBS patients. Among these, the integration of Chinese herbal medicine with conventional Western medicine appears rather promising.

V. CONCLUSIONS

Acupuncture and/or moxibustion can improve symptoms and quality of life in IBS patients. As acupuncture and/or moxibustion treats the body as a whole system through acupuncture points, its action mechanisms for the treatment of IBS could involve multiple segments, layers, and targets. Indeed, the current literature supports this perspective. These mechanisms were studied from various disciplinary perspectives and the variety of acupuncture-moxibustion methods. Meanwhile, separate from medications, acupuncture and/or moxibustion is efficacious because it stimulates acupuncture points on the surface of body. Furthermore, both acupuncture and/or moxibustion, either in combination or alone, are effective in attenuating the symptoms of IBS.

VI. REFERENCES

[1]. Xiao-Peng Ma, Jue Hong, Cai-Ping An, et al. Acupuncture-moxibustion in treating irritable bowel syndrome: How does it work? World J Gastroenterol. 2014, 20(20): 6044–6054.

[2]. HuangDi NeiJing (comprised of SuWen and the LingShu 214-282 A.D.)

[3]. Hui Li, Tian He, Qian Xu, et al. Acupuncture and regulation of gastrointestinal function World J Gastroenterol. 2015, 21(27): 8304–8313.

[4]. Publication Review By: Stanley J. Swierzewski, III, 2015.

[5]. En-Hua Zhou, Xiao-Mei Wang, Guang-Hong Ding, et al. Suspended moxibustion relieves chronic visceral hyperalgesia and decreases hypothalamic corticotropin-releasing hormone levels World J Gastroenterol. 2011 17(5): 662–665.

[6]. Ji-Meng Zhao, Lu-Yi Wu, Hui-Rong Liu, et al. Factorial study of moxibustion in treatment of diarrhea-predominant irritable bowel syndrome World J Gastroenterol. 2014; 20(37): 13563–13572.

[7]. Acupuncture Points Database – Locations, Functions and Clinical Usage Yin Yang House Chinese Medicine Theory Site.

[8]. Guan-Qun Chao and Shuo Zhang. Effectiveness of acupuncture to treat irritable bowel syndrome: A meta-analysis World J Gastroenterol. 2014 21; 20(7): 1871–1877.

[9]. Jiliang Fang, Danhong Wang, Qing Zhao, et al. Brain-Gut Axis Modulation of Acupuncture in Functional Dyspepsia: A Preliminary Resting-State fcMRI Study Evident Based Complement Alternative Med. 2015; 2015: 860463.

[10]. Siyuan Zhou, Fang Zeng, Jixin Liu, et al. Influence of Acupuncture Stimulation onCerebral Network in Functional Diarrhea Evident Based Complement Alternative Med. 2013;2013: 975769.

[11]. Yi Zhu, Zhiyuan Wu, Xiaopeng Ma, et al. Brain regions involved in moxibustion-induced analgesia in irritable bowel syndrome with diarrhea: a functional magnetic resonance imaging study. BMC Complement Alternative Med. 2014; 14: 500.

[12]. Hui-Rong Liu, Xiao-Yi Fang, Huan-Gan Wu, et al. Effects of electroacupuncture on corticotropin-releasing hormone in rats with chronic visceral hypersensitivity World J Gastroenterol. 2015. 21(23): 7181–7190.

[13]. Linying Tan, Tiffany Smith. The Role of Warm Moxibustion in IBS Treatment Acupuncture Today). 2014, Vol. 15, Issue 02.

[14]. Yin Shi, Yue-Hua Chen, Xiao-Jun Yin, et al. Electro-acupuncture versus Moxibustion for Irritable Bowel Syndrome: A Randomized, Parallel-Controlled Trial Evident Based Complement Alternative Med. 2015; 2015: 361786.

[15]. Chen Zhao, Li Qi, Luyi Wu, et al. Suspended moxibustion at TianShu (ST25) inhibits prokineticin 1 and prokineticin receptor 1 expression in the spinal cord of rats with chronic visceral hypersensitivity Neural Regen Res. 2012; 7(15): 1145–1150.

[16]. Wing-Wa Leung, Alice YM Jones, Simon SM Ng, et al. Acupuncture transcutaneous electrical nerve stimulation reduces discomfort associated with barostat-induced rectal distension: A randomized-controlled study. World J Gastroenterol. 2013; 19(3): 381–388.

[17]. Z. J. Weng, L. Y. Wu, C. L. Zhou, et al. Effect of electro-acupuncture on P2X3 receptor regulation in the peripheral and central nervous systems of rats with visceral pain caused by irritable bowel syndrome. Purinergic Signal. 2015; 11(3): 321–329.

[18]. Chunhui Bao, Jingzhi Zhang, Jinmei Liu, et al. Moxibustion treatment for diarrheapredominant irritable bowel syndrome: study protocol for a randomized controlled trial. BMC Complement Alternative Med. 2016; 16: 408.

[19]. Hui Zheng, Ying Li, Wei Zhang, et al. Electro-acupuncture for patients with diarrheapredominant irritable bowel syndrome or functional diarrhea. 2016; 95(24): e3884.

[20]. Yi Zhu, Zhiyuan Wu, Xiaopeng Ma, et al. Brain regions involved in moxibustion-induced analgesia in irritable bowel syndrome with diarrhea: a functional magnetic resonance imaging study. BMC Complement Alternative Med. 2014; 14: 500.

[21]. Ga-Jin Han, Seok-Jae Ko, Jae-Woo Park, et al. Acupuncture for functional dyspepsia: study protocol for a two-center, randomized controlled trial. 2014; 15: 89.

[22]. Hui Li, Tian He, Qian Xu, et al. Acupuncture and regulation of gastrointestinal function.World J Gastroenterol. 2015; 21(27): 8304–8313.