

SOUTH BAYLO UNIVERSITY

The Effectiveness of Acupuncture on Chronic Fatigue Syndrome: A Literature Review

By

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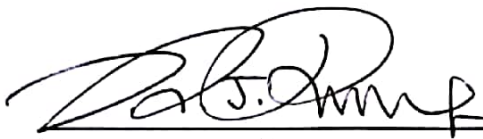
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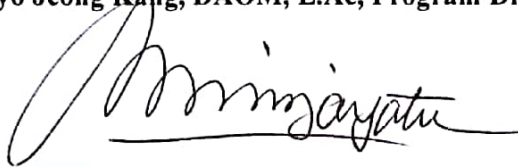
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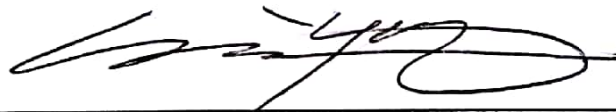
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The Effectiveness of Acupuncture and Moxibustion on Chronic Fatigue Syndrome: A Systematic Review

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ABSTRACT

Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is characterized by unexplained fatigue for at least 6 months by a diverse but consistent set of symptoms. There is no cure or standard treatment for CFS/ME in conventional Western medicine. Patients are seeking complementary and alternative medicines which include acupuncture and moxibustion for relieving symptoms. The objective of this study was to evaluate the use and effectiveness of acupuncture and moxibustion treatments on CFS/ME patients.

PubMed, Medline, Google scholar and EBASCO were systematically searched from 2001 up to March 2018. All studies on chronic fatigue syndrome treated with acupuncture and moxibustion with randomized control trial were included.

Seven studies that met the inclusion criteria were included. After analyzing the acupuncture points that were used in the included studies ST 36 and GV 20 were utilized the most. Body acupuncture had a significantly greater effect in reducing fatigue symptoms ($p < 0.001$) when compared to no acupuncture treatment. Acupuncture treatment when compared to sham acupuncture treatment, both showed improvement in fatigue symptoms and there was no significant difference between the two groups.

Acupuncture when compared to herbal treatment showed no significant difference in anxiety therapy. However acupuncture plus cupping treatment had a greater therapeutic effect than herbal treatment ($p < 0.05$). Acupuncture when compared to tuina, both treatment groups showed significant decrease in fatigue levels ($p < 0.05$). However, when comparing acupuncture treatment to tuina plus moxibustion treatment, the tuina plus moxibustion had a higher effective rate (93.3%) as compared to acupuncture (76.7%). Furthermore, acupuncture treatment compared to moxibustion treatment alone showed a greater decrease in levels of fatigue ($P < 0.05$). Thus, from the analyzed results moxibustions serves as a better TCM treatment for individuals with CFS than acupuncture or any of the combined treatments.

The results indicated that acupuncture and moxibustion have a high potency for being a principal therapy for patients with chronic fatigue syndrome. However, more future well-designed RCT studies are needed to confirm the efficacy of acupuncture and moxibustion in the treatment of CFS/ME. Fatigue-related symptoms will remain prevalent and are a target of treatment in TCM for future studies.

Keywords: Chronic fatigue syndrome, myalgic encephalomyelitis, moxibustion, acupuncture, Chinese medicine, and TCM.

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I. INTRODUCTION

Chronic Fatigue Syndrome (CFS) also known as Myalgic Encephalomyelitis (ME), is a complex and debilitating disease of unknown etiology affecting more than one million Americans and millions of individual worldwide^[10]. One report indicates that 84% to 91% of patients remain undiagnosed, and many individuals are ill for years before receiving the proper diagnosis^[13]. Recently, the Institute of Medicine released a report offering guidance to the medical field and Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis/ (CFS/ME) patients, redefining the illness with a new name, “Systemic Exertion Intolerance Disease” (SEID)^[10, 13], and new diagnostic criteria with the mission of promoting early detection^[22]. No objective tests have yet been established to identify these patients or provide fundamental information about the disruption that occurs in CFS/ME^[13]. CFS/ME is characterized by persistent or relapsing unexplained extreme fatigue that lasts for six months or more, that is not alleviated by rest^[16, 20, 26, 29, 39, 34, 38]. In CFS/ME patients, fatigue is one of multiple debilitating symptoms that include cognitive impairment, migraines, post-exertional malaise, myalgias, arthralgias, sore throats, lymphadenopathy, unrefreshed sleep, intolerance to certain food items, and hypersensitivity to noise and light^[1, 2, 12, 18, 20]. In 1980, the Center of Disease Control and Prevention first announced chronic fatigue syndrome as a disease^[26]. An individual is generally referred to be fatigue when they are exhausted and lack sufficient amount of energy after performing daily exercises^[19, 26]. Similarly the persistent and recurring characteristics of fatigue that continue for 6 months or more are classified as chronic fatigue^[19, 26].

CFS is prevalent in 1% of the total population and Idiopathic Chronic Fatigue (ICF) being a little more concurrent is prevalent in 10% of the population ^[19]. Furthermore, chronic fatigue syndrome and idiopathic chronic fatigue are described as forms of chronic fatigue that do not have any corresponding medical explanations ^[23, 27, 29].

Previous studies found that CFS/ME not only plays a significant role on daily functions, however, it also impacts clinical and psychological outcomes negatively; more so CFS/ME showed to significantly increase the risk of depression ^[9]. There are increasing number of studies racing to identify the cause of CFS/ME. Currently, Montoya et al., 2017^[25] reported that CFS/ME is an inflammatory disease and their study provide a solid basis for a diagnostic blood testing. Dr. Montoya's study found that variations in 17 cytokines are connected with the severity of the disease. Another study mentioned that sixteen different gene abnormalities have been identified with CFS patients some of which are responsible for the bodies immune and defense system ^[23].

In regards to previous treatment, research on pharmacology, physical exercise, cognitive behavior therapy, immunology, and antiviral were addressed in CFS/ME patients ^[26, 32]. None of the previously tested treatment options provided significant amount of results to be considered as treatment option ^[19, 32]. Nevertheless, western medicine is beneficial for diseases that have single cause, however does not serve well as a mean for treating diseases that have multivariable causes like CFS/ME. ^[2].

Likewise, CFS/ME patients have been considering other options of treatment such as complementary and alternative medicine ^[19]. Oriental medicine has been reported to be a useful treatment method in China, Korea, and Japan concerning CFS/ME patients ^[22,19]. Traditional Chinese medicine (TCM) is a style of Oriental medicine informed by modern medicine but built

on the foundation of more than 2,500 years of Chinese medical practice that includes various forms of herbal medicine, acupuncture, Tui Na massage, moxibustion, and Qigong exercise^[19, 4]. Acupuncture is the insertion of needles into different parts of the body, called acupoints, and moxibustion is the use of burning moxa which is made from special herb named argy wormwood leaf, to stimulate certain parts or points of the body ^[35, 29]. The selection of acupoints is based on the syndrome differentiation from the diagnosis according to TCM theory. Thus, the choice and number of acupoints are different from 1 patient to another. Previous systematic reviews have reported significantly positive effects of acupuncture and moxibustion as well as effects of TCM on CFS and ICF patients ^[19, 30], though the mechanism of CFS treated with acupuncture and moxibustion is not fully explained. The acupuncture and moxibustion treatment can adjust organ function of TCM, such as the zhang and fu, and have various ways by which they can be chosen depending on the characters of patients.

The purpose of this review was to evaluate the available current studies regarding the use of acupuncture and moxibustion in the management of chronic fatigue syndrome/maylgic encephalomyelitis patients. The study aimed to compare the effectiveness of acupuncture and moxibustion with other treatments and interventions. The review also targeted to provide information on the commonly used acupoints, the effectiveness of the treatment, and to integrate acupuncture and moxibustion in the management of Chronic Fatigue Syndrome.

II. LITERATURE REVIEW

2.1 How Chronic Fatigue Syndrome Came About

Outbreak of unknown illness began in 1984 in Lake Tahoe, Nevada. Further more the disease was recorded around the world, and the US Centers for Disease Control and Prevention (CDC) came in to help on the case of this unknown illness. The CDC tested individuals for a virus called Epstein-Barr, as it was known to cause severe fatigue. However results showed no signs of the virus and scientist were not able to draw firm conclusions. Later on, in 1987 the CDC reached consensus on the clinical characteristics of the illness. The team of researchers also recognized that CFS was been around for many years, however it was referenced to by many different names such as Myalgic Encephalomyelitis (ME) throughout the years and Systemic Exertion Intolerance Disease (SEID) being the most recent name.

2.2 Current Therapies for CFS

Many different therapies have been coined around with for many years to find the best possible intervention for CFS patients. Today the most utilized therapies include herbal therapy, cognitive behavioural therapy, self-management, and dietary management. In this study I analyzed several randomized control trials of these interventions to evaluate the effectiveness and identify which of the therapies resulted with positive outcomes. To serve as a background, two herbal therapy, two cognitive behavioural therapy, two self-management, and ten dietary management studies fit the criteria to be included (See appendix A for the included charts). After analyzing the therapies in the included studies, none showed a significant difference in managing/reducing the fatigue symptoms of CFS patients. However two studies conducted by

Fukuda and Castro-Marrero showed promising results about oral CoQ10 plus NADH and ubiquinol-10 serving as dietary management in CFS patients.

2.3 Chronic Fatigue Syndrome in TCM

CFS has no clear mechanism, with its complex symptoms. Acupuncture has been demonstrated to be effective worldwide in treating many disorders and endorsement. However, the lack of general mechanism brings considerable controversy for the acupuncture in evidence-based medicine.

The concept of multi-symptomatic syndromes that have fatigue as a main entity has been written about for over 200 years in Traditional Chinese Medicine (TCM). TCM takes into account the fact that environmental influences such as cold, wind or other negative exogenous factors can become internalized and damage the body either immediately or delayed and become later as disease. Negative influences such as viruses or other infectious agents, inoculations, environmental toxins, simple wind, cold and deleterious lifestyle can weaken the body and if they were to remain in the body they can manifest as chronic illness. The theory of deferred clinical indications brought on by an earlier insult to the human body has been reviewed and treated since the Inner Classic of the Yellow Emperor-Nei Jing (about 100B.C.) which includes the Su Wen (Simple Questions) and referred to as latent heat. It states “ if cold penetrates the body in winter, it will manifests as heat in springtime”. In TCM sometimes the exterior pathogenic factor is not felt by the patient, especially in weak and or physically or emotionally stressed, and then goes deeper into the body without creating symptoms only to manifest later as a serious disease.

In the article by Rui Chen et al., 2010 the Japanese researchers analyzed 600 books in the “Encyclopedia of Traditional Chinese Medicine”. The studies they analyzed served as an

overview of the ancient and current literature information on the treatment of CFS. Modern TCM is focusing on boosting the immune system, regulating abnormal activity of the hypothalamic-pituitary adrenal (HPA) axis.

Patient with CFS have classic qi and blood deficiencies. Studies have revealed the physiological effects of acupuncture: increased levels of endorphins, increased phagocytic activity, improved endocrine, hormonal functions, and immunological reactions, normal T-cell values, as well as increased numbers of white blood cells, activating the reticuloendothelial system.

III. MATERIALS AND METHODS

3.1 Search Methods to identify studies correlated to CFS

Literature search was conducted using eight electronic literature databases such as PubMed, EBASCO, Google scholar, EMBASE, cumulative Index to Nursing Allied Health Literature (CINAHL), Cochrane Library, Allied and Complementary Medicine Database (AMED) and MEDLINE for relevant studies from 2001 up to March 2018.

The using the following keywords: Chronic fatigue syndrome, myalgic encephalomyelitis, acupuncture, and moxibustion.

In the databases, PubMed, EMBASE, Cochrane Library the system of MeSH terms was used to conduct the searches. A similar method of searching was used in Medline. The MeSH terms were also combined along with the keywords as another search method. The references of the retrieved articles were further evaluated for additional possible references. The search was broad and no focus filters were applied. The aim of the search was to present all randomized control trial studies that were conducted on CFS/ME patients.

3.2 Inclusion Criteria for considering studies for review

Type of Studies

All studies included were randomized clinical trials (RCT). Studies that were included were...

1. Published in English.

2. Published from 2001 to March 2018
3. There was no restriction on studies with respect to blinding.
4. Patients in the study were diagnosed with CFS/ME according to the research criteria for CFS from the Centre for Disease Control (CDC), Oxford, and the Canadian CFS Guidelines for Clinicians.
5. Participants included in the review must have been diagnosed with CFS.
6. Participants were not restricted by gender, age, and severity of diagnosis, or ethnicity.

Type of Intervention

1. Studies involving all types of interventions which included acupuncture and moxibustion utilized in the treatment or management of CFS.
2. Also the studies needed to include treatment conditions as well as a use of a control procedure to compare to.
3. The control group consisted of either no treatment, placebo treatment, or a conventional standard of care (SOC) as recommended or guided in country of treatment.

The definition of TCM in this review is a broad terminology for the wide range treatment practices including but not limited to herbs, acupuncture, acupoint stimulation, moxibustion, tuina, cupping, etc.

Type of Measurements

1. The included studies measured fatigue by using a standardized or validated measurement tool such as the Chalder Fatigue Scale or Fatigue Severity Scale.

2. The fatigue score after treatment was then compared between the intervention and control groups.

3.3 Exclusion Criteria for considering studies for review

Studies will be excluded if:

1. They combined CFS/ME with other patient groups [e.g. CFS/ME and fibromyalgia (FM)]
2. Non-RCTs or duplicate publications;
3. Animal studies;
4. Uncontrolled trials or case studies
5. Case reports and reviews not meeting the above inclusion criteria will be excluded
6. Published in language other than English
7. Unpublished studies, cases, or trials.

Data Retrieval

The searches retrieved a total of 1345 potentially relevant citations, 658 were excluded because articles were duplicates. The 687 left articles were further screened; 569 records were excluded based on the Title and Abstract. 118 records were further evaluated based on diagnostic criteria, randomization, intervention, and data analysis. 111 studies were excluded because 18 studies were uncontrolled trials, 46 studies were not Randomized Controlled Trials, 27 were case studies, 13 studies were not conducted on CFS/ME patients, and 7 studies were reviews. After further investigation only seven RCT studies met the inclusion criteria. The included flow chart contains the process and number of included and excluded studies (Figure 1). Articles were

excluded if they were descriptive papers, animal studies, the methodology was poorly described and if not RCT. Seven RCT studies were included for further study in this systemic review.

Data Analysis

Relevant data such as first author, year of publication, study design, intervention of each group, diagnosis criteria, number of participants, outcomes, and treatment duration were extracted independently from all the included studies using the inclusion criteria. Key data from the included RCTs are summarized in Table 1 and 2 respectively.

The extracted data from the RCTs were analyzed and divided into five categories based on the treatment intervention for CFS with respect to acupuncture:

- (1) Acupuncture versus No Acupuncture
- (2) Acupuncture versus Herbs
- (3) Acupuncture versus Tuina
- (4) Acupuncture versus Sham Acupuncture
- (5) Acupuncture versus Moxibustion

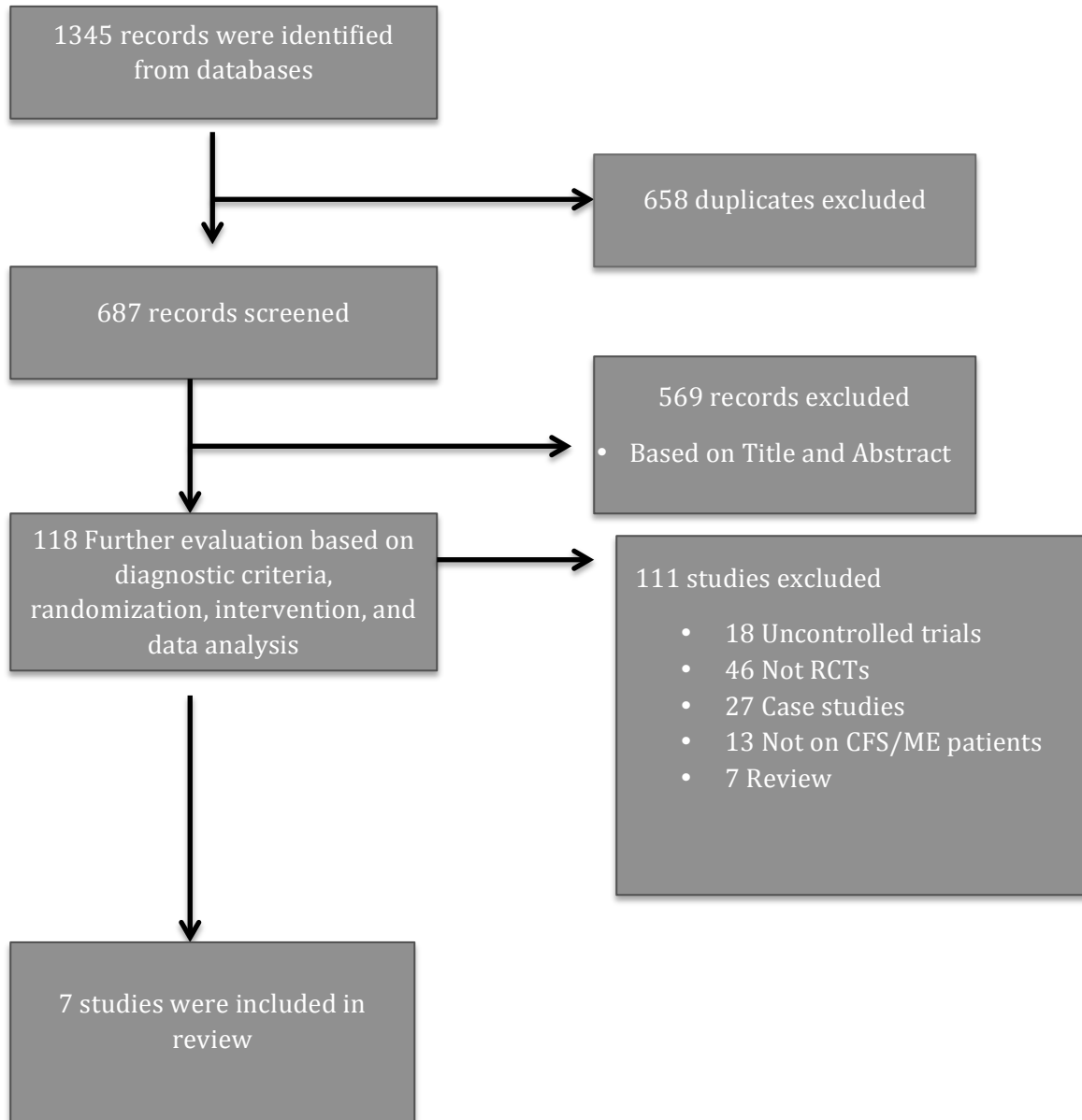


Figure 1- Flow chart of the trial selection process

Table 1. Data of RCT's of *Acupuncture and Moxibustion Management in CFS*

Reference/year	Diagnosis criteria	Sample size	Intervention/treatment	Control	Duration	Outcome	Results
Kim et al./ 2015		n=150	2 groups A&B (A) body acupuncture (GV20,GB2,BL11,BL13,BL15,BL18,BL20, BL23) & (B) Sa-am acupuncture (LU8,SP3,HT8,BL15, CV6)	No acupuncture treatment	4 weeks, 2-3 times per week total 10 sessions	Group A: FSS – (p=0.032) Group B: BDI – (P=0.007) Both intervention groups: SRI – (A, p=0.032;B, p<0.001), NRS – (A&B, P<0.001)	Suggests that body acupuncture for 4weeks or more may help improve fatigue in CFS/ICF patients
Ng et al./ 2013		n=99	3o minute acupuncture (DU20, ST36 bilateral, SP6 bilateral)	Sham acupuncture	4 weeks, 2 times per week	Chalder's fatigue scale – (p=0.040) Mental fatigue (GHQ-12) – (P=0.002) Improved physical score (SF-12)+ (p=0.031)	Even though control group showed + effect, the treatment group showed significant net-effect of physical and mental fatigue
Huanan et al./ 2013		n=77	Abdominal tuna	Acupuncture	4 weeks, 5 times per week	In both groups:FS-14, SAS, HAMD - (p<0.05) compared to baseline FS-14, HAMD - (p<0.05) No significant difference in SAS scores	Suggests that abdominal tuna provides a more effective treatment than acupuncture alone in CFS patients

Table 1. *Acupuncture and Moxibustion.* - (significantly lower in intervention group compared to control),+ (significantly high in intervention group compared to control). FS-14 (Fatigue Scale-14), SAS (Self-rating Anxiety Scale), HAMD (Hamilton Rating Scale for Depression). FSS(Fatigue Severity Scale), BDI (Beck Depression Inventory), EQ-5D (EuroQol-5 Dimension), SRI (Stress Response Inventory), SF-12 (health-related quality of life), GHQ-12 (general mental health), FAI (Fatigue Assessment Instrument), HRV (heart rate variability),SAS (self-rating Anxiety Scale)

Continued Table 1 . Data of RCT's of Acupuncture and Moxibustion Management in CFS

Reference/year	Diagnosis criteria	Sample size	Intervention/treatment	Control	Duration	Outcome	Results
Wei-hong et al./2006	CDC 1991	n=50	Needling points: GV14, GV9, BL15, BL17, GV4, BL23, GV1 Every other day, every 5 times 3 days rest	Chinese medicinal herbs, caili composition given orally (25ml) twice daily	12 weeks	Therapeutic effect was significantly different (p<0.05)	Acupuncture plus cupping serves as an effective method to treat CFS
Xing-hua et al./2012	Fukuda and Canadian criteria	N=90	Acupuncture therapy Points: ST9, GV16, GV20 Once every day	Medical therapy Shen mai injections intravenous once per week	2 weeks	SAS score decreased in both groups (p<0.05)	Both acupuncture and medicine treatments could improve the anxiety symptoms of CFS
Rui et al./2012	CDC 1994	N= 60	Tuina and thunder-fire moxibustion Points: BL 28, BL 13, CV4, CV8 Once every other day	Points: GV20, Ex-HN1, Ex-HN5, PC6, HT7, CV6, ST 36, SP6	4 weeks	Recovery rate and total effective rate was statistically significant (p<0.01)	Treatment of tuina and thunder-fire moxibustion have better therapeutic effect than regular acupuncture in treating CFS
Shu et al./ 2016		N=45	2 groups: (AG) Manipulation acupuncture (ST36& CV4) & (MG) indirect moxibustion treatment	Same treatment as acupuncture group	10 sessions (ever other day) 15mins each	FAI – in MG vs. AG AG more effective short term HRV, but MG more effective long term effect of HRV	Suggested both acupuncture and moxibustion improved fatigue in CFS, noxibustion more effective in long term treatment

Continued Table 1. Acupuncture and Moxibustion. - (Significantly lower in intervention group compared to control),+ (significantly high in intervention group compared to control). NRS (Numeric rating scale), VAS (visual analog scale), MDA (malondaldehyde), FSS (Fatigue Severity Scale), BDI (Beck Dpression Inventory), EQ-5D (EuroQol-5 Dimension), SRI (Stress Response Inventory), SF-12 (health-related quality of life), GHQ-12 (general mental health), FAI (Fatigue Assessment Instrument), HRV (heart rate variability), SAS (self-rating Anxiety Scale).

IV. RESULTS

Study Description

The analysis included a total of seven studies. To compare the studies, they were divided into five categories based on the type of intervention used on CFS/ME patients with respect to acupuncture intervention.

(1) Acupuncture versus No Acupuncture

(2) Acupuncture versus Herbs

(3) Acupuncture versus Tuina

(4) Acupuncture versus Sham Acupuncture

(5) Acupuncture versus Moibustion

- **Acupuncture Versus No Acupuncture**

Kim et al. (2015) conducted a three arm parallel, multicenter, nonblind, randomized controlled trial. The study was located in Daejeon, South Korea at the Institute of Oriental Medicine. The study collected one hundred-fifty patients that suffered from either Chronic Fatigue Syndrome or Idiopathic Chronic Fatigue, and were divided into three divided treatment groups. The first group received body acupuncture at GV20, GB2, BL11, BL13, BL15, BL18, BL20, and BL23. The second group received Sa-am acupuncture at LU8, BL15, SP3, CV6, and HT8. Treatment was 2-3 times a week for four weeks. The third group of patients did not receive any acupuncture treatment and only usual care. Outcomes were measured using the Fatigue Severity Scale, the Stress Response Inventory, the Beck Depression Inventory, the Numeric Rating Scale, and the EuroQol-5 Dimension. Outcome results showed that body acupuncture and Sa-am acupuncture had a significantly greater effect in helping reduce fatigue

symptoms ($p < 0.001$) as compared to No acupuncture treatment. (For data see Table 2 and Figure 2)

Table 2. Acupuncture Versus No Acupuncture: Kim 2015

Method value	# of Cases	Baseline		5 weeks		13 weeks		P
		Mean	SD	Mean	SD	Mean	SD	
Body Acupuncture	50	4.67*	1.27	3.39**	1.12	3.32***	1.17	<0.001
Sa-am (Korean) Acupuncture	50	4.75*	1.07	3.62**	1.13	3.58***	1.20	
No Acupuncture	50	4.48*	1.27	4.43**	1.19	4.24***	1.25	

* = Fatigue Severity Scale mean baseline score; ** = Fatigue Severity Scale mean score after five weeks of treatment; *** = Fatigue Severity Scale mean score after thirteen weeks of treatment; SD = standard deviation; P value is calculated with 95% confidence interval

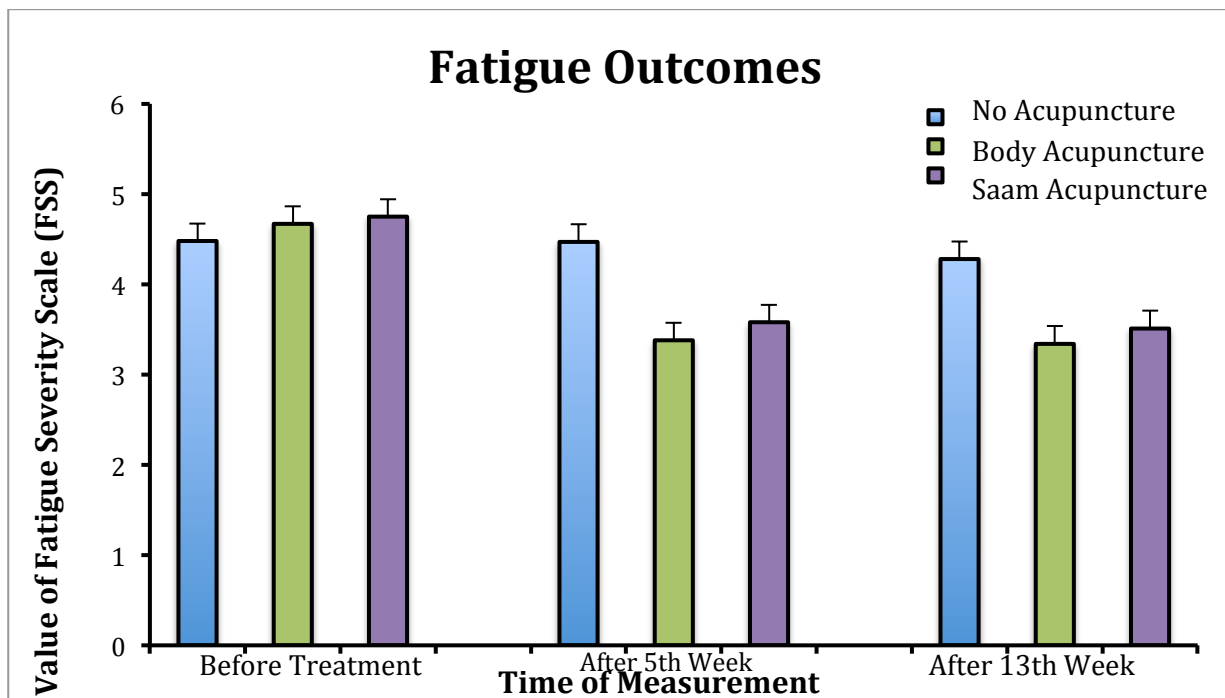


Figure 2. Fatigue Outcomes: Kim et al., 2015

- **Acupuncture Versus Herbs**

Xing hua et al. (2012) conducted a clinical study analyzing the anxiety levels of Chronic Fatigue Syndrome patients after acupuncture treatments as compared to an herbal treatment. The study took place in Guangzhou, China at the Guangzhou University of Traditional Chinese Medicine Hospital. Ninety patients with Chronic Fatigue Syndrome were included in the study. Forty-five of the patients were treated with acupuncture. Treatment was once daily for two weeks with one day break every seven days. ST9, GV16, and GV20 points were utilized. The other forty-five patients received medicine therapy. Shen mai injections were given intravenously once a week. To analyze the patients anxiety level, the Self-Rating Anxiety Scale was used before and after treatment. The scores showed a significant decrease in anxiety in both treatment groups ($p < 0.05$). As a conclusion both acupuncture and medicine treatment can improve anxiety symptoms of Chronic Fatigue Syndrome patients.

Wei-hong and his fellow research mates (2006) conducted a clinical case study to observe the combined treatment of acupuncture and cupping compared to herbal treatment on Chronic Fatigue Syndrome patients. The study took place in Shandong, China at the Traditional Chinese Medicine Hospital of Ju County. The study included fifty cases that were divided into two treatment groups. One group (25 patients) received acupuncture treatment by needling on points GV14, GV9, BL15, BL17, GV4, BL23, and GV1, followed by cupping. Treatment was for twelve weeks, every other day with every five treatments, 3 days break. The other group of patients (25 patients) were treated by orally ingesting Chinese medicinal herbs with Caili composition twice daily. After the twelve week treatment the therapeutic effect of acupuncture plus cupping was 92% and the therapeutic effect of the herbal treatment was 64%. Furthermore

the significant difference in the therapeutic effect between the 2 groups was ($\chi^2= 7.29, P<0.05$). Thus as a conclusion the intervention method of acupuncture plus cupping is a more effective treatment method for individuals with chronic fatigue syndrome than herbal treatment. (For data see Table 3, Table 4, Figure 3, and Figure 4)

Table 3. Acupuncture Versus Herbal Treatment for Anxiety

Author value	Method	# of Cases	Before *	After**	P
Xing Hua ^[8]	Acupuncture	45	48.6	42.91	<0.01
	Herbal	45	47.1	41.91	

* = SAS score before treatment; ** = SAS score after twelve weeks of treatment

Table 4. Acupuncture Plus Cupping Versus Herbal Treatment for Fatigue Symptoms

Author value	Acupuncture Plus Cupping		Herbal Treatment		P
	# of Cases	Total Effective Rate (%)	# of Cases	Total Effective Rate (%)	
Wei-Hong ^[33]	25	92.0%	25	64.0%	<0.05

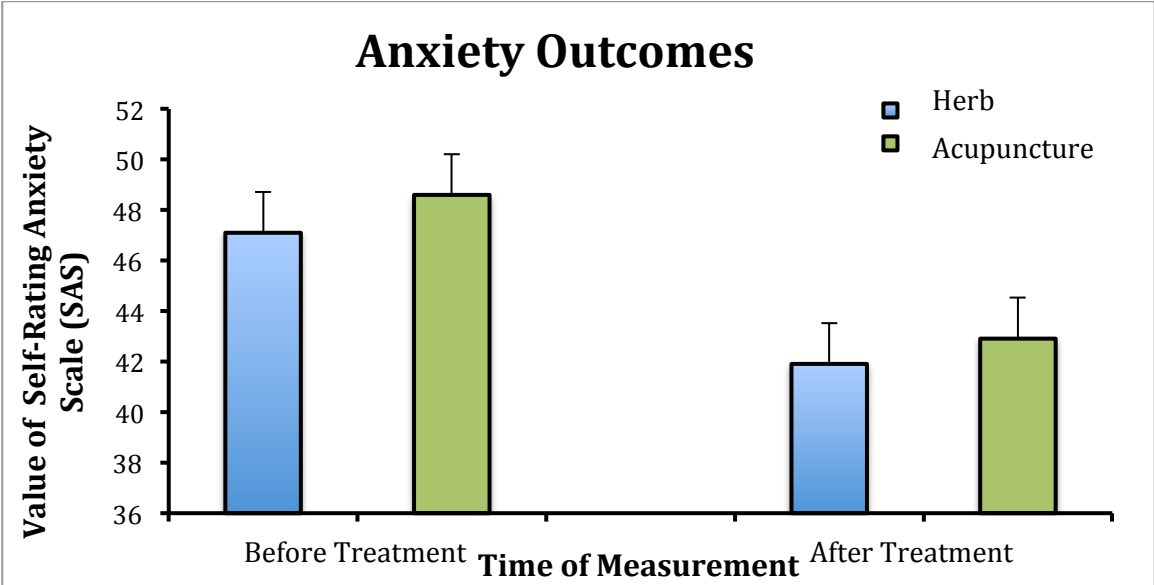


Figure 3. Anxiety Outcomes: Xing-hua et al., 2012

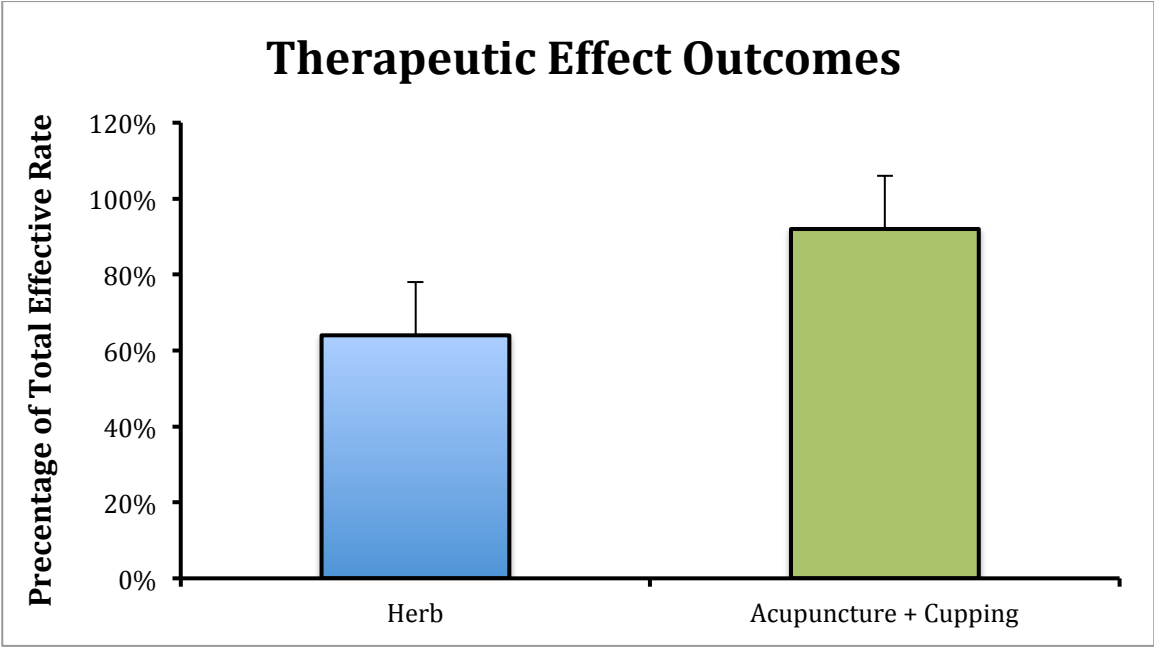


Figure 4. Therapeutic Effect Outcomes: Wei-hong et al., 2006

- **Acupuncture Versus Tuina**

Huanan et la. (2017) conducted a single assessor-blinded randomized clinical trial evaluating the effectiveness of abdominal tuina compared to acupuncture on chronic fatigue

syndrome patients in Tianjin, China. Eighty individuals participated in the study. The group of patients that were treated with abdominal tuina (40 patients) was treated with the following abdominal points CV4, CV6, CV12, CV8, and CV14. The other group that was treated with acupuncture, patients were needled on CV6, BL26, CV12, ST34, ST36, SP6, SP9, and SP10. Each treatment was done once daily for four weeks. Every five days there was two days break. To assess the effectiveness of intervention the Fatigue Scale-14, Self-Rating Anxiety Scale and Hamilton Rating Scale were used before and after treatment. In both treatment groups the scores of all the measured scales showed a significant decrease ($p < 0.05$). The Fatigue Scale-14 was used to measure fatigue and Hamilton Rating Scale for Depression.

Rui and Jun-liang conducted a study to depict the effect of tuina plus moxibustion as compared to acupuncture in treating patients with Chronic Fatigue Syndrome. The study took place in Guangdong, China at Dongsheng Hospital of Guangzhou. Sixty patients were included in the study. In one group (30 patients) were treated with tuina and thunder-fire moxibustion at points BL13, CV8, CV4 and BL28. Treatment was done three times a week, once every other day for four weeks. In the other group (30 patients) were treated with acupuncture on GV20, Ex-HN1, Ex-HN5, PC6, HT7, CV6, ST36, and SP6. Treatment was also done three times a week, once every other day for four weeks. After four weeks of treatment the group that was treated with tuina and moxibustion had a recovery rate of 36.7% and the total effective rate of 76.7%. The data showed statistical difference ($p < 0.01$) between the two intervention methods that were being assessed. As a conclusion, results of this study showed that the combined treatment of tuina and thunder-fire moxibustion serves as better treatment for patients with Chronic Fatigue Syndrome than acupuncture alone. (For data see Table 5, Figure 5, and Figure 6)

Table 5. Acupuncture Versus Tuina

Author value	Method	# of Cases	Results		P
Huanan ^[15]	Abdominal Tuina	40	9.3*	7.6**	<0.05
	Acupuncture	40	8.9*	6.6**	<0.05
Rui ^[38]	Tuina + Moxibustion	30	36.7% [^]	93.3% ^{^^}	
	<0.001 Acupuncture	30	16.7% [^]	76.7% ^{^^}	<0.01

* = Fatigue Scale-14 score before treatment; ** = Fatigue Scale-14 score after four weeks of treatment;

[^] = Recovery Rate after treatment; ^{^^} = Total effective rate

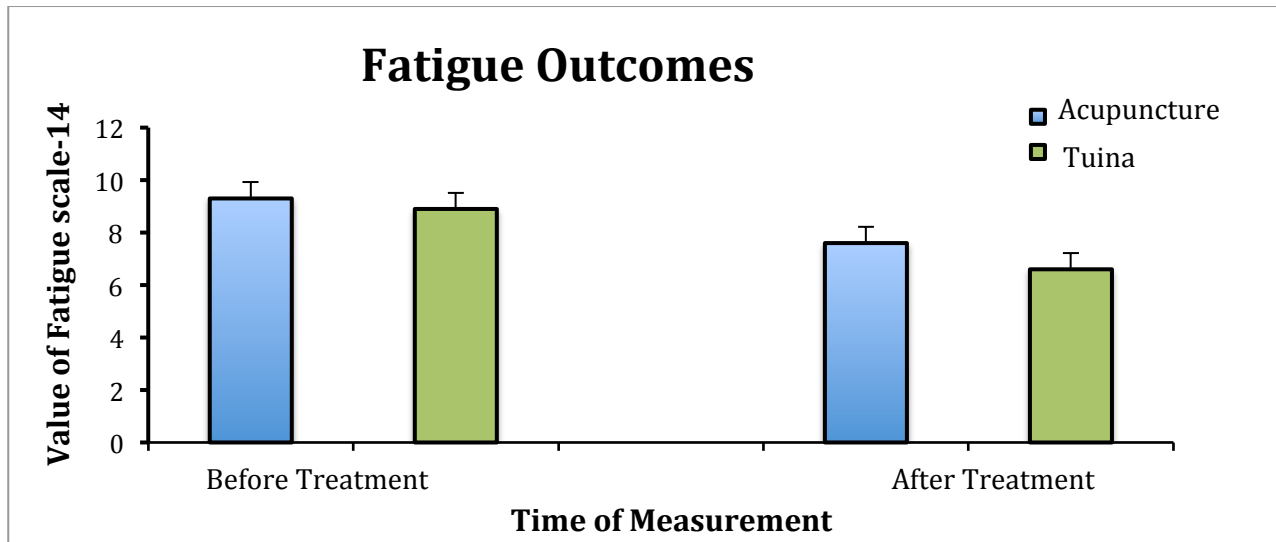


Figure 5. Fatigue Outcomes: Huanan et al., 2017

Therapeutic Effect Outcomes

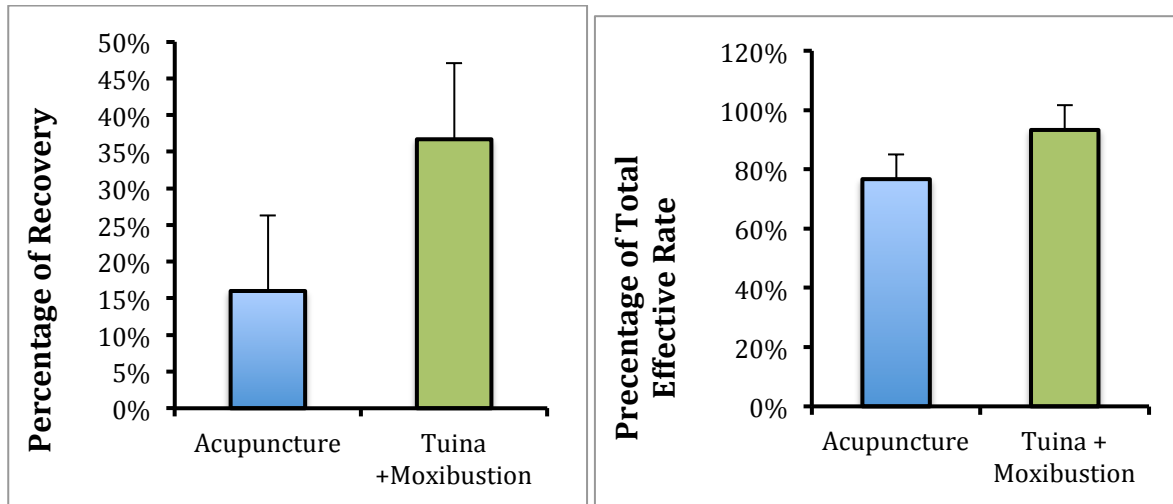


Figure 6. Therapeutic Effect Outcomes: Rui et al., 2012

- Acupuncture Versus Sham Acupuncture

Ng and Yia (2013) conducted a study to determine the efficacy of acupuncture for Chronic Fatigue Syndrome patients. The study was a two-arm randomized, controlled single blinded design. The study took place in Hong Kong, China at the University of Hong Kong. The study included ninety-nine participants. The Chalder's Fatigue Scale was used to measure fatigue, SF-12 to measure health-related quality of life and GHQ-12 to assess the general mental health. Acupuncture points used for both the experimental and control groups were DU20, ST36, SP6 (san yin jiao) and Bai hui (zu san li). However for the control group sham acupuncture was used where the tip of the needles were blunt. Treatment consisted of eight sessions of acupuncture two times a week for four weeks. In this study both the acupuncture and the sham

group had a large positive effect when evaluating the resultant effect sizes. The physical fatigue scale was 1.44 for the acupuncture group and 0.92 for the sham group therefore a net effect size of 0.52 which is measured with Cohen’s d. (For data see Table 6 and Figure 7)

Table 6. Acupuncture Versus Sham Acupuncture

Author value	Method	# of Cases	Results	P
Ng ^[26] <0.05	Acupuncture	50	30.67*	22.29**
	Sham Acupuncture	49	29.17*	23.7**

* = Chalder’s Fatigue Scale mean score before treatment; ** = Chalder’s Fatigue Scale mean score after four weeks of treatment

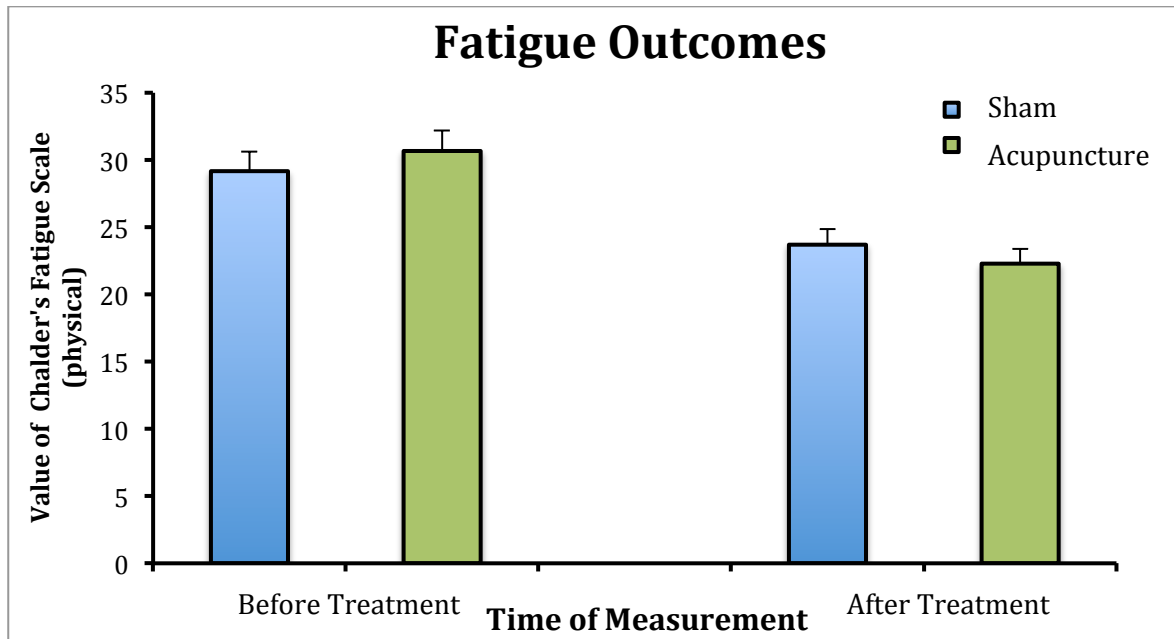


Figure 7. Fatigue Outcomes: Ng et al., 2013

- **Acupuncture Versus Moxibustion**

Shu et al. (2016) conducted a pilot controlled clinical trial to investigate the different effects of acupuncture and moxibustion on Chronic Fatigue Syndrome patients and alterations in the autonomic nervous system (regulation of HRV). Outcome measures were assessed by using the scores of the Fatigue Assessment Instrument (FAI), which reflects the level of fatigue and the influence of fatigue on quality of life as well. The FAI test was completed before and after the 4th and 10th treatment. Both acupuncture and moxibustion can improve fatigue of Chronic Fatigue Syndrome patients and the mechanism responsible for this effect may involve activating the vagus nerve. Moxibustion is more effective than acupuncture in treating Chronic Fatigue Syndrome in the long run as reflected by HRV indices. When comparing Acupuncture and moxibustion to analyze the therapeutic effect outcomes, two of the included studies were used in the evaluation (Rui et al., 2012; Shu et al., 2016). The study conducted by Rui et al, 2012 compared the acupuncture group to the treatment group, which consisted of tuina and moxibustion. Also the study directed by Shu et al., 2016 compared the two types of treatment groups, acupuncture and moxibustion. The results of both studies revealed that moxibustion served as a more effective treatment method than acupuncture. (For data see Table 7, Table 8, Table 9 and Figure 8)

Table 7. Acupuncture Versus Moxibustion on CFS patients: 4th Treatment

Author value	Acupuncture			Moxibustion			P
	# of Cases	Baseline	4 th Treatment	# of Cases	Baseline	4 th Treatment	
Shu ^[28] >0.05	15	150	145	15	144	130	

FAI score in all three groups decreased after treatment. However there was no significant difference in decrease in value after 4th treatment ($P > 0.05$)

Table 8. Acupuncture Versus Moxibustion on CFS patients: 10th Treatment

Author value	Acupuncture			Moxibustion			P
	# of Cases	Baseline	10 th Treatment	# of Cases	Baseline	10 th Treatment	
Shu ^[28] <0.05	15	150	98	15	144	118	

After the 10th treatment there was a greater decrease fatigue value in the group treated with moxibustion than the group of CFS patients treated with acupuncture ($P < 0.05$).

Table 9. Acupuncture on CFS Patients Versus Acupuncture on Healthy Patients

Author	Acupuncture on CFS Patients			Acupuncture on Healthy Patients			P
	# of Cases	Baseline	After Treatment	# of Cases	Baseline	After Treatment	
Shu ^[28]	15	150	98	15	110	80	
							<0.05

The group of CFS patients treated with acupuncture showed greater decreased value of fatigue as compared to the group of healthy patients treated with acupuncture (P <0.05).

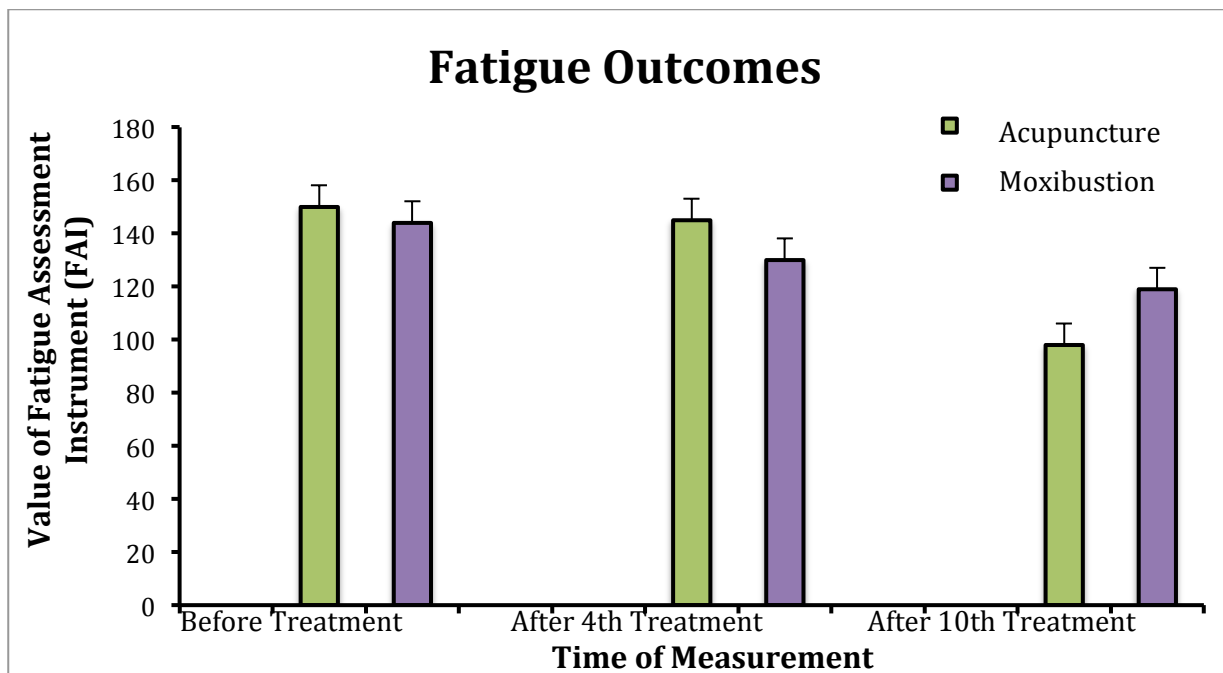


Figure 8. Fatigue Outcomes: Shu et al., 2016

Most Commonly Used Points

After analyzing the acupuncture points that were used in the included studies (Rui 2012, Shu 2016, Huanan 2017, Ng 2013, Xing-hua 2012, Kim 2015, Wei-hong 2006) ST 36

and GV 20 was utilized the most (see Chart 1). Second most used acupuncture points for treatment were SP 6, and CV6. The third most applied point in the studies was BL15. Other points include GV 1, GV 4, GV 9, GV 14, GV 16, CV 4, CV 12, SP 3, SP 9, SP 10, ST 9, ST 34, BL 11, BL 13, BL 17, BL 18, BL 20, BL 23, BL 26, LU 8, HT 7, HT 8, PC 6, GB 20, Si Chen Cong, and Tai Yang which were only used once (See Table 10 and Figure 9).

The most commonly used acupoint is stomach 36 (in chinese Zusan li) and GV 20. These acupoints enhance immune functioning and fatigue (yim y-k, lee h, Hong k-e, EBCAM 2007).

Table 10. Acupuncture Points Used by Each Study

	Ng ^[26]	Shu ^[28]	Kim ^[19]	Xing hua ^[8]	Wei-hong ^[33]	Huanan ^[15]	Rui ^[38]
GV 1					X		
GV4					X		
GV 9					X		
GV 14					X		
GV 16				X			
GV 20	X		X	X			X
CV 4		X					
CV 6			X			X	X
CV 12						X	
SP 3			X				
SP 6	X					X	X
SP 9						X	
SP 10						X	
ST 9				X			
ST 34						X	
ST 36	X	X				X	X
BL 11			X				
BL 13			X				
BL 15			X	X			
BL 17				X			
BL 18			X				
BL 20			X				
BL 23			X				
BL 26						X	
LU 8			X				
HT 7							X
HT 8			X				
PC 6							X
GB 20			X				
Si Chen Cong							X
Tai Yang							X

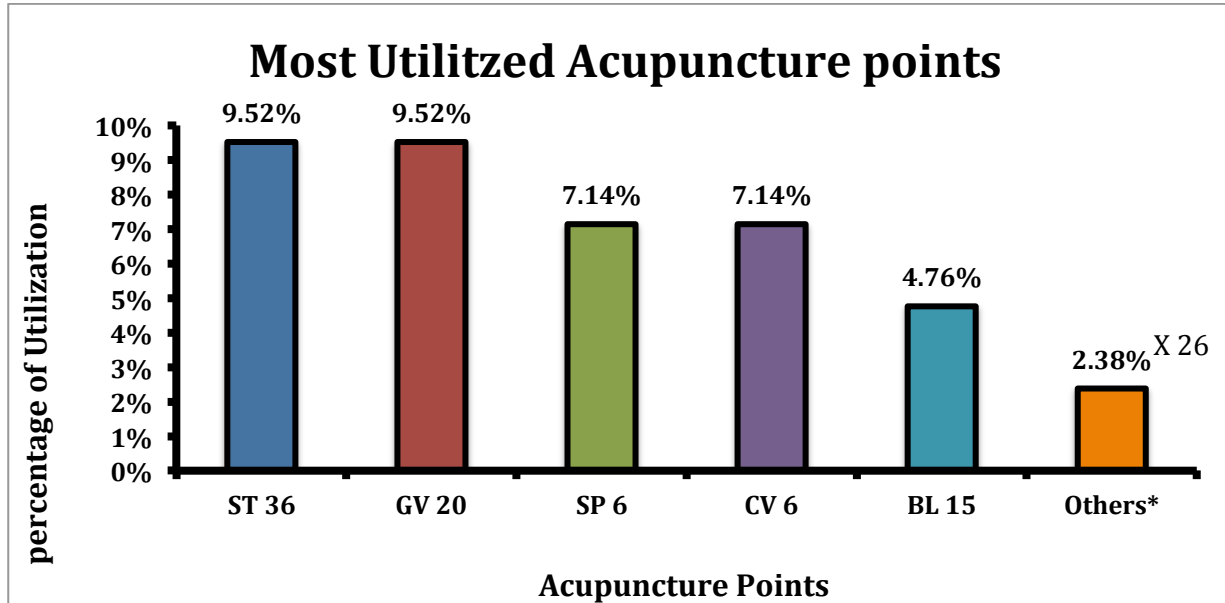


Figure 9. Most Utilized Acupuncture Points: within the studies analyzed for this review points ST 36 and GV 20 were the most utilized for treatment in studies (Rui 2012, Shu 2016, Huanan 2017, Ng 2013, Kim 2015). Second most used acupuncture points for treatment were SP 6, used by (Rui 2012, Huanan 2017, Ng 2013), and CV6 (Rui 2012, Kim 2015, Huanan 2017). The third most applied point in the studies was BL15, used by (Wei-hong 2006, Kim 2015). All other points that were used once were labeled as others. Points include GV 1, GV 4, GV 9, GV 14, GV 16, CV 4, CV 12, SP 3, SP 9, SP 10, ST 9, ST 34, BL 11, BL 13, BL 17, BL 18, BL 20, BL 23, BL 26, LU 8, HT 7, HT 8, PC 6, GB 20, Si Chen Cong, and Tai Yang.

* Each point was 2.38% as a total, the points labeled as *others* were 61.9%.

V. DISCUSSION

In this review, seven RCTs were identified. When comparing body acupuncture to no acupuncture, outcome results showed that body acupuncture and Sa-am acupuncture had a significantly greater effect in helping reduce fatigue symptoms ($p < 0.001$) as compared to No acupuncture treatment. When comparing acupuncture and herbal treatment groups the scores from the Self-Rating Anxiety Scale showed a significant decrease in anxiety in both groups ($p < 0.05$). Both acupuncture and herbal treatment can improve anxiety symptoms of Chronic Fatigue Syndrome patients. However after the twelve week treatment the therapeutic effect of acupuncture plus cupping was 92% and the therapeutic effect of the herbal treatment was 64%. Furthermore, the significant difference in the therapeutic effect between the 2 groups was ($P < 0.05$). Thus the intervention method of acupuncture plus cupping is a more effective treatment method for individuals with chronic fatigue syndrome than herbal treatment.

Evaluating the effectiveness of abdominal tuina compared to acupuncture on chronic fatigue syndrome patients, in both treatment groups the scores of the Fatigue Scale-14 showed a significant decrease ($p < 0.05$) in fatigue levels. In addition, after four weeks treatment the effect of tuina plus thunder-fire moxibustion as compared to acupuncture serves as better treatment for patients with Chronic Fatigue Syndrome. Patients treated with tuina and moxibustion had a recovery rate of 36.7% and the total effective rate of 93.3% as compared to acupuncture the recovery rate of 16.7% and the total effective rate of 76.7%. The data showed statistical difference ($p < 0.01$) between the two intervention methods that were being assessed.

When comparing acupuncture and the sham group, both had a large positive effect when evaluating the resultant effect sizes. The physical fatigue scale was 1.44 for the acupuncture

group and 0.92 for the sham group therefore a net effect size of 0.52 which is measured with Cohen's d. thus both interventions showed improvement in fatigue, there was no significant difference. When comparing Acupuncture (on CFS and healthy patients) and moxibustion to analyze the therapeutic effect outcomes, the Fatigue Assessment Instrument score in all three groups decreased after treatment. However there was no significant difference in decrease in value after 4th treatment ($P > 0.05$). After the 10th treatment there was a greater decrease in fatigue value in the group treated with moxibustion than the group of CFS patients treated with acupuncture ($P < 0.05$). Moreover the group of CFS patients treated with acupuncture showed greater decreased value of fatigue as compared to the group of healthy patients treated with acupuncture ($P < 0.05$).

Limitations

Many studies that include acupuncture and moxibustion interventions for CFS have been published and state that the studies are RCT. However when further analyzing the study, it was found that many of the studies were either not randomized or had no control. Moreover the main reason studies were excluded was because of the inappropriate terminology use of the word “randomized” or “controlled” to describe the method in studies. Thus, many studies were eliminated because they did not meet all the inclusion criteria. Therefore, it was not possible to achieve a complete review of all the evidence.

Although the studies matched the inclusion criteria of the review, the quality of methodology were poor and limiting to draw strong conclusions as to which treatment method is effective. The included studies showed positive results of acupuncture as a treatment method when compared to the control groups however it was not possible to combine results of the various studies and form conclusions about the practice of acupuncture and moxibustion as an effective treatment or not for patients with Chronic Fatigue Syndrome. Also the way the outcomes of the studies were reported and evaluated varied greatly from one study to another. For example several different methods and scales were used just to measure fatigue; like Chalders scale, Fatigue severity scale, Fatigue Assessment Instrument, and more. On another note, it was difficult to compare the studies as they all used different criteria, measured different outcomes and used different intervention methods. There remains to be a need for more RCTs on patients with CFS through acupuncture and moxibustion interventions.

Future Research

Future research studies should consider improving the methodological approach, the way in which the studies are being conducted. For example one study conducted by Huanan et al., 2017 for the experimental and control groups of the study they used two interventions, acupuncture and tuina. Also another study conducted by Wei-hong et al., 2012 for their control group they used herbs which is known to be a type of treatment in oriental medicine. Rather than conducting a study using two types of interventions that have not yet been proven to be an effective treatment, it would be more beneficial and a strong study if they used for the control a placebo or sham acupuncture or any other method to have a control as a baseline to compare to the experimental group in the study.

Furthermore, stronger studies on the treatment methods of Chronic Fatigue Syndrome is highly needed to be added to the current literature. To improve the level of reporting, strong well designed randomized controlled trials and clinical control trials are needed to insure that promising intervention methods like acupuncture have been assessed properly and were indeed found to be effective. All in all the included RCT/CCT have been conducted with relatively poor quality, thus high quality studies are needed to confirm the preliminary findings that have been found in the current literature.

Most studies on any given disease are done to be standardized. However, with chronic fatigue syndrome it is very difficult to standardize. For example some patients suffer from insomnia more than others while another patient suffers from headache more than the lassitude. The range of fatigue vary from one patient to the other.

II. CONCLUSION

As a conclusion, this systematic review provided an evaluation on the limited evidence for the use of acupuncture and moxibustion in treating patients with chronic fatigue syndrome. The total number of included RCTs that fit the criteria in the study were very little. Even though the included studies claimed that their results showed statistical significance, the studies have poor quality therefore the results that were extracted from those studies are not accurate. Thus drawing firm conclusions remains difficult. Hence higher quality RCTs are needed in the current literature to confirm the suggested preliminary findings in the studies.

Body acupuncture had a significantly greater effect in reducing fatigue symptoms ($p < 0.001$) when compared to no acupuncture treatment. However acupuncture plus cupping treatment had a greater therapeutic effect than herbal treatment ($p < 0.05$). Acupuncture when compared to tuina, both treatment groups showed significant decrease in fatigue levels ($p < 0.05$). However, when comparing acupuncture treatment to tuina plus moxibustion treatment, the tuina plus moxibustion had a higher effective rate (93.3%) as compared to acupuncture (76.7%). Furthermore, acupuncture treatment compared to moxibustion treatment alone showed a greater decrease in levels of fatigue ($P < 0.05$). Thus, from the analyzed results moxibustions serves as a better TCM treatment for individuals with CFS than acupuncture or any of the combined treatments.

The results indicated that acupuncture and moxibustion have a high potency for being a principal therapy for patients with chronic fatigue syndrome. However, more future well-designed RCT studies are needed to confirm the efficacy of acupuncture and moxibustion in the

treatment of CFS/ME. Fatigue-related symptoms will remain prevalent and are a target of treatment in TCM for future studies.

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Appendix A

Table 1. Data of RCT's of Herbal Therapy in management of CFS. Myelophil is an extract of Astragali Radix and Salviae Radix. Hyangsapyunweesan granules were prepared from Attactylodis Rhizoma, Citri Pericarpium, Cyperi Rhizoma, Auranti Immaturus Fructus, Pogostemonis Herba, Magnoliae Cortex, Amomi Fructus, Aucklandiae Radix, Clycyprhizae Radix

Reference/year	Sample size	Intervention/treatment	Control	Duration	Outcome	Results
Hartz et al./ 2004	n=76	Standardized powdered extract of Eleutherococcus senticosus (Siberian ginseng)	placebo	2 months, 2mg a day	Fatigue was reduced in both groups. No significant difference	The study did not present significant efficacy of Siberian ginseng
Cho et al./ 2009	n=36	2 groups: Low dose (1.5g of myelophil) high dose (3g of myelophil)	Placebo, Hyangsapyun weesan granules	4 weeks, 2 times per day	Low dose Myelophil – fatigue (p<0.05)	Myelophil had a pharmacological effect against fatigue. Study did not prov

Table 2. Data of RCT's of *Cognitive Behavioural Therapy in management of CFS*. CBT (Cognitive Behavioural Therapy), EAS (Education and Support), SMC (Standard Medical Care), SF-36 (Short Form with 36 items physical and mental health scales), CIS (Checklist Individual Strength).

Reference/year	Sample size	Intervention/treatment	Control	Duration	Outcome	Results
O'dowd et al./ 2006	n=153	2 groups CBT & EAS	SMC	6-12 months	SF-36 +(p=0.019) Chadler Fatigue scale -(p=0.027) Walking speed +(p=0.0013) CBT+EAS	indicated no significant improvement with CBT group
Prins et al./ 2001	n=278	CBT n=93 Support group	Natural course	8-14 months	CIS +(p=0.009) Karnofsky performance +(p=0.001) Self-related improvement +(p<0.0001) CBT+ Support groups *At 14 months	indicated significant improvement with CBT group

Table 3. Data of RCT's of *Self- management in CFS*. APSM (Activity pacing self-management), COPM (Canadian Occupational Performance Measure), CIS (Checklist Individual Strength)

Reference/ year	Diagnosis criteria	Sample size	Interventio n /treatment	Control	Duration	Outcome	Results
Pinxsterhuis et al./ 2017	Centers of Disease Control and Prevention research diagnostic criteria Clinical or research Canadian diagnostic criteria	n=137	Self-management	Usual care	6-12 months 8 meetings once every other week for 2.5 hours each	Fatigue severity -(p=0.039) Concerning self-efficacy +(p=0.039) Self-management=usual care	Indicated no significant improvement with intervention group
Kos et al./ 2015	Centers of Disease Control and Prevention research diagnostic criteria	N=33 *women only	APSM	Relaxation	60-90 min/wk for 3 consecutive weeks	COPM (p=0.03) Satisfaction +(effect size =0.74) CIS -(p<0.01)	Indicated significant improvement with APSM group

Table 4. Dietary Management. IGF (Insulin-like growth factor), SIP-8 (Sickness Impact Profile-8), CIS-fatigue (Subscale fatigue severity), IGFBP3/IGF1 (Insulin-like growth factor binding protein 3/ Insulin-like growth factor 1), GAA(guanidinoacetic acid), CIS-fatigue (Checklist Individual Strength Subscale fatigue severity), SIP-8 (Subscales of the Sickness Impact Profile) IL-1 (Interleukin-1)

Reference/ year	Diagnosis criteria	Sampl e size	Intervention /treatment	Control	Duration	Outcome	Results
Hobday et al./ 2008		n=52	Low sugar low yeast diet (LSLY) Diet excluded foods containing sugar and yeast, refined carbohydrates, alcohol, and caffeine	Healthy eating diet (HE) Consisted of foods high in fibre, fruit, and vegetables 5 portions a day Reduced fat and refined sugar intake Twice a week fish intake	24 weeks	Fatigue by Chalder Fatigue score QoL by Medical Outcomes Survey Short Form-36 Both showed no statistically significant differences	LSLY diet was not more efficacious concerning fatigue and QoL compared to HE diet
Witham et al./ 2014	Fukuda and Canadian criteria	N=50	100,000 units of oral Vitamin D3 every 2 months	Matching Placebo	6 months	25-hydrovitamin D levels increased in treatment group compared to placebo no effect of treatment on pluse wave velocity no improvement seen in other vascular and metabolic outcomes	High-dose of oral vitamin D3 intake showed no improvement on vascular health or fatigue in patients with CFS
Bleijenberg et al./ 2007	US CDC	N= 57	Accllydine	placebo	14 weeks	No difference in IGF status between CFS patients and control. Also accllydine treatment had no significant difference compared to placebo on CIS-fatigue , SIP-8, IGFBP3/IGF1	There was no difference in IGF1 status compared to control The results of study don't show any benefit on Accllydine over placebo for treatment of CFS
Rowe et al./2001	CDC and prevention	N=100	Fludrocortisone acetate titrated to	Matched placebo Contained	9 weeks	No difference in the treatment group was observed in SF-36,	Fludrocortison e as a monotherapy

	criteria		0.1mg/d Week 1: 1 capsule of 0.025mg/d Week 2: 2 capsules of 0.05mg/d Week 3-9: 4 capsules of 0.025mg/d	methylcellulose			Beck Depression inventory, Wood mental Fatigue inventory, profile of mood states questionnaire, Duke Activity Status Index as compared to placebo	for CFS patients was no more efficacious than placebo. Further studies need to be conducted on other medications
Castro-Marrero et al./ 2015	CDC Fukuda's criteria	N=73	Oral CoQ10 (200 mg/day) plus NADH (20mg/day) supplementation	placebo	8 weeks	Fatigue – (p<0.05) Also recovery of biochemical parameters: NAD+/NADH (P<0.001), CoQ10 (p<0.05), ATP (P<0.05), citrate synthase (p<0.05) were + and lipoperoxides (p<0.05) were -	Oral CoQ10 plus NADH supplementation could be potential therapeutic benefits for individuals with CFS. However study on its own does not prove sufficient information. A study with a larger sample group should be conducted to confirm finding	
Ostojic et al./ 2016	CDC and prevention criteria	N=21	GAA (2.4 grams per day) orally	Placebo (cellulose) orally	3 months with 2 months wash out period	No effect of intervention was found on primary efficacy outcomes Participants receiving GAA treatment + in muscular creatine level (p<0.01) also muscular strength and aerobic power + (p<0.05)	Results indicated supplemental GAA can positively affect creatine metabolism in CFS, however GAA had no effect on main clinical outcome such as fatigue and musculoskeletal soreness	
Brouwers et al./ 2002	CDC criteria	N=53	Intake of Polynutrient supplement	Placebo 2x daily	10 weeks	No significant difference was found between the placebo	Study findings don't support the use of a	

			containing many vitamins, minerals and enzymes 2x daily			and treatment group on any outcomes: CIS fatigue score, CDC symptoms and SIP8 score	nutritional supplement in treating CFS related symptoms
McDermott et al./ 2006	CDC criteria	N= 64	Oral BioBran MGN-3 (2g 3x per day)	Equivalent placebo	8 weeks	Both groups should improve however no significant difference with regards to Chalder physical fatigue score	The finding of study do not support the use of BioBran as being helpful for patients with CFS
Fukuda et al./ 2016	CDC criteria	N=40	3 capsules of ubiquinol-10 (50mg each) daily after a meal	placebo	12 weeks	Chalder's fatigue scale showed no significant difference between the placebo and ubiquinol groups Center for Epidemiologic Studies Depression Scale	The results of the study suggests that supplementation contains ubiquinol-10 for 12 weeks is effective for improving several CFS symptoms
Roerink et al./ 2017	CDC criteria	N=50 women	Daily subcutaneous anakinra (100mg)	Placebo, mixture of sodium citrate, sodium chloride, and polysorbate	4 weeks	No statistically significant or clinically important difference between to placebo and intervention groups in CIS-fatigue seen	Peripheral IL-1 inhibition using anakinra of 4 week showed no significant results in reducing fatigue in women with CFS