INPLASY PROTOCOL

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Tuina for Chronic Fatigue syndrome: a protocol for systematic review and meta-analysis

Tang, C[1]; Fang, M[2].

Review question / Objective: Population(P): Patients With Chronic Fatigue Syndrome(CFS). Intervention(I): Tuina Therapy(Manual therapy of traditional Chinese medicine). Comparison(C): Any treatment without Tuina, such as drugs, health education, acupuncture, aerobic exercise, diet control, psychotherapy, etc. Outcomes(O): The primary outcomes are the efficacy evaluation indexes for chronic fatigue syndrome including fatigue rating scale (FAI), fatigue scale-14 (FS-14), self-rating anxiety scale (SAS) and self-rating depression scale (SDS). The secondary outcomes include short form-36 health survey(SF-36), somatic and psychological health report- "SPHERE", FMRI evaluation indicators, laboratory biochemical indicators related to CFS mentioned in various literatures, etc. Study design(S): Randomized Controlled Trails.

INTRODUCTION

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outcomes include short form-36 health survey(SF-36), somatic and psychological health report- "SPHERE", FMRI evaluation indicators, laboratory biochemical indicators related to CFS mentioned in various literatures, etc. Study design(S): Randomized Controlled Trails.

Condition being studied: Chronic fatigue syndrome (CFS) is a complex chronic disease with uncertain etiology, which is characterized by long-term extreme fatigue (fatigue after rest and sleep, accompanied by low fever (or conscious fever), pain in many parts of the body, poor memory, difficulty in concentration, sleep disorders and headache, anxiety or depression, cognitive impairment, intolerance of physical exertion,etc. Compared with other chronic diseases, CFS has a greater negative impact on the functional state and health of the human body, and is a severe challenge to the medical profession and society. Some previous studies reported that Tuina showed beneficial effects on depression and anxiety of patients with CFS. Although there are several reviews on TCM therapy in the treatment of CFS in recent years, little evidence proved the differences in efficacy and safety between Tuina therapies and other therapies. The purpose of this review is to systemically evaluate the efficacy and safety of Tuina in the treatment of CFS, in order to provide more theoretical support for the related research of CFS.

METHODS

Search strategy: The electronic databases (China Knowledge Resource Integrated Database, Wanfang Data, VIP Date, PubMed, Embase, Cochrane Library) will be searched from their inception to December 2020. Two sets of search terms will be used, as follows: (1) "chronic fatigue syndrome" or "idiopathic chronic fatigue" or "Royal Free Disease"or"unexplained chronic fatigue"and (2)"Tuina" or "massage" or "manual therapy" or "osteopathy" or "manipulation" or "chiropractic".

Participant or population: Chronic fatigue syndrome(CFS) patients with main clinical manifestations as follow:long-term extreme fatigue last for 6 months or more（fatigue after rest and sleep）, accompanied by low fever(or conscious fever), pain in many parts of the body, poor memory, difficulty in concentration, sleep disorders and headache, anxiety and depression, cognitive impairment, intolerance of physical exertion and abnormal visual status. If a patient has 4 or more syndromes described above, he or she will will be eligible to be included in this study.

Intervention: In this review, Tuina is a necessary intervention. The included study used Tuina manipulation in management of CFS. Tuina therapy include muscle/tissue manipulation (similar with massage therapy) and mobilising manipulation (similar with chiroparacic).

Comparator: Control interventions include drugs, health education, acupuncture, aerobic exercise, diet control, psychotherapy and any otther treatment without Tuina.

Study designs to be included: This study will include randomized controlled trails (RCTs) about Tuina for the treatment of CFS.

Eligibility criteria: Inclusion criteria: All randomized controlled trails (RCTs) concerns Tuina therapy for chronic fatigue syndrome that have published and can be obtained in English and Chinese. Exclusion criteria: Observational studies, case reports, and cross-sectional design studies will be counted out. The conference abstract or study protocol of RCTs will also be foreclosed if the corresponding author could not provide detailed information.

Information sources: The electronic databases (China Knowledge Resource Integrated Database, Wanfang Data, VIP Database, PubMed, Embase, Cochrane Library) will be searched from their inception to December 2020 to select articles that meet requirements above. If

the data are unreported, we will try to contact the authors to request the original data if it's necessary for the completion of the systematic review.What's more,if the studies which are published as a letter, reviews, abstract or conference poster will be excluded unless sufficient data can be acquired from the authors.

Main outcome(s): The main outcomes were efficacy evaluation indexes:fatigue rating scale (FAI), fatigue scale-14 (FS-14), self-rating anxiety scale (SAS), self-rating depression scale (SDS).

Additional outcome(s): The additional outcomes include short form-36 health survey(SF-36), somatic and psychological health report-"SPHERE", FMRI evaluation indicators, laboratory biochemical indicators related to CFS mentioned in various literature, etc.

Quality assessment / Risk of bias analysis: The quality assessment of the included studies will be independently conducted by two reviewers using the Physiotherapy Evidence Database (PEDro) scale. The PEDro scale is a tool developed to measure the methodological quality of RCTs of physiotherapy interventions, which developed by Delphi scale, covers 11 items to score the selected studies and assess their quality. Any different opinions will be resolved by counsulting a third reviewer.

Strategy of data synthesis: RevMan 5.3 software will be used for Meta analysis. Continuous data's change between baseline and the end of interventions will be used in the meta-analysis. The mean difference (MD) and 95% confidence intervals (CI) will be calculated. According to the recommendations of the Cochrane handbook for systematic reviews of interventions, the heterogeneity will be assessed using the I^2 statistic and Q statistic. Three levels of heterogeneity are $I^2 < 25\%$ (low heterogeneity), $I^2 < 50\%$ (moderate heterogeneity) and $I^2 > 75\%$ (high heterogeneity). It will be considered to be statistically significant when $P < 0.10$. An Egger's test was performed to examine publication bias, and publication bias will

be determined from a corresponding p-value less than 0.05.

Subgroup analysis: If considerable heterogeneity is found, subgroup analysis will be envisaged to perform to investigate probable sources of heterogeneity in accordance with the duration of treatment, sex, age, duration of CFS, etc.

Sensibility analysis: If the quality of studies is low, or the outliers that are numerically distant from the rest of the data, a sensitivity analysis will be required. We will use the iteratively removing one study at a time of ReveMan5.3 to finish the sensitivity analysis.

Language: The language of targeted article will be limited in English and Chinese.

Country(ies) involved: China.

Keywords: chronic fatigue syndrome; Tuina; traditional Chinese medicine; manual therapy.

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