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Comparison between herbal medicine and fluoxetine for depression: A systematic review of randomized controlled trials

Yi Ren[a,1], Chenjun Zhu[b,1], Jianjun Wu[c], Ruwen Zheng[d,**], Huijaun Cao[e,*]

[a] Department of Neurology, Dongzhimen Hospital, The First Affiliate Hospital of Beijing University of Chinese Medicine, Beijing 100029, China
[b] Department of Neurology, The Third Affiliate Hospital of Beijing University of Chinese Medicine, Beijing 100029, China
[c] Department of Respiration, The Third Affiliate Hospital of Beijing University of Chinese Medicine, Beijing 100029, China
[d] Department of Acupuncture and Moxibustion, Dongfang Hospital, The Second Affiliate Hospital of Beijing University of Chinese Medicine, Beijing 100029, China
[e] Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, China

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ABSTRACT

Objective: To evaluate the effectiveness and safety of Chinese herbal medicine (CHM) versus fluoxetine on depression.
Design: A systematic review of randomized controlled trials (RCTs).
Methods: RCT with two parallel groups that compared CHM and fluoxetine on treatment of depression with reported decreased Hamilton Depression Scale (HAMD) and adverse events during treatment were included after searching through six electric-databases. The methodological quality of RCTs was assessed according to the Cochrane risk of bias tool. Meta-analysis was conducted using RevMan 5.3 software with pooled mean difference (MD) or risk ratio (RR) and their 95% confidence interval (CI) if no significant heterogeneity was detected. A SOF table was generated using GRADEPro software to evaluate the overall quality of the evidence.
Results: Twenty-six trials with 3294 participants were included in the review. Most of them had high risk of bias during conducting and reporting. The results achieved weak evidence which showed CHM had similar effect to fluoxetine (20 mg/day) on relieving depression according to HAMD assessment (for primary depression: MD = −0.08, 95%CI −0.98–0.82; for secondary depression: MD = −0.36, 95%CI −1.55–0.83), but fewer incidences of adverse events than the drug (for primary depression: RR = 0.31, 95%CI 0.17–0.59; for post-stroke depression: RR = 0.04, 95%CI 0.00–0.25). No serious adverse event was found in neither CHM nor fluoxetine group.
Conclusions: Due to the poor quality of included trials and the potential publication bias of this review, no confirmed conclusion could be draw to evaluate the effectiveness and safety of CHM for depression compared with fluoxetine.

1. Background

Depression refers to a kind of mood disorder syndrome characterized by low spirits, retardation of thinking and decrease of interest, with great harmfulness, high modality and recurrence rate.[1] WHO pointed out the mental diseases would be the biggest health issue in twenty-first Century, of which depression was the top priorities.[2] The most serious consequence of depression is Dutch act. One research reported that suicide rate in China is 23.23/10 million, of which about 40% are caused by depression. Dutch act led to loss of 5,200 million Chinese dollars per year.[3]

Anti-depressant drugs, including tricyclics, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin-noradrenaline reuptake inhibitors and other agents are commonly used for depression. Among those drugs, fluoxetine (Trade name: Prozec, Yoko, etc.) — a kind of selective 5-serotonin reuptake inhibitor- is widely used in clinics in China.[4] However, the efficacy and safety of fluoxetine for depression were uncertain according to result of a Cochrane systematic review.[5] In Traditional Chinese medicine (TCM), depression could be diagnosed as “depression disease”, “lily disease”, or “hysteria”,[6] which mainly caused by

* Correspondin author.
** Corresponding author.
E-mail addresses: zrw123@sina.com (R. Zheng), huijuancao327@hotmail.com (H. Cao).
[1] These two authors contributed equally.

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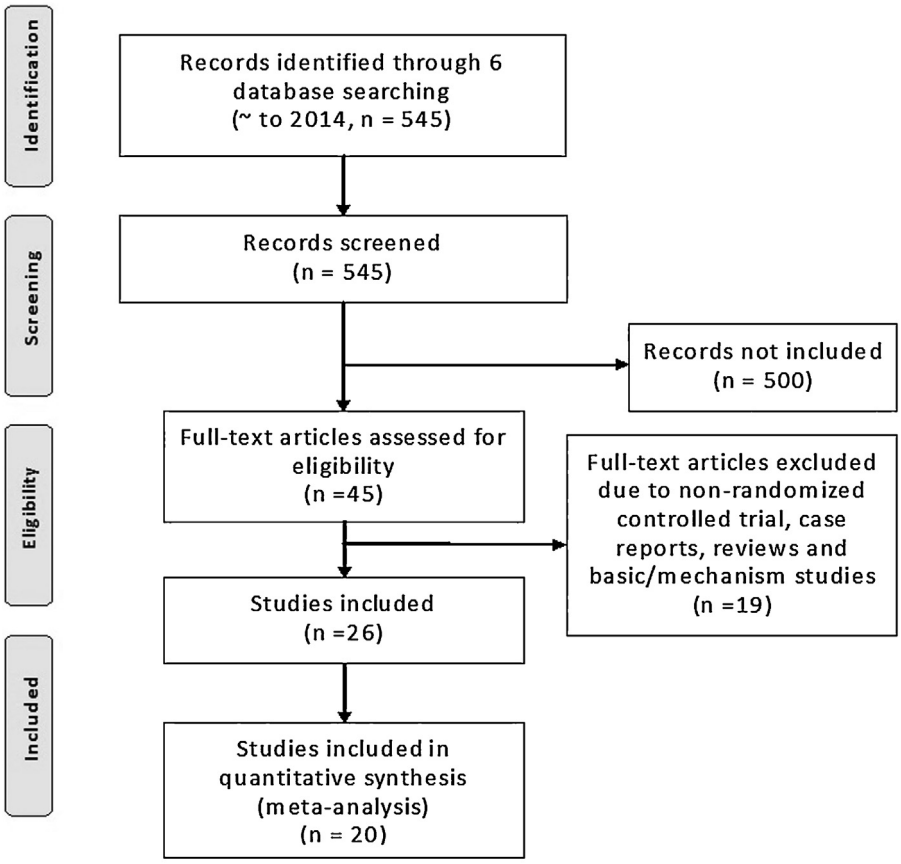

Fig. 1. Flow diagram.

dysfunction of liver and stagnation of qi (it refers to emotional problems and rage that impair the liver, or other pathogenic factors, impeding smooth flow of liver qi).[7] Chinese herbal medicine (CHM) has been widely applied in the treatment of depression, because of its potential effectiveness and less harmful.[8] Some studies[9–11] evaluated single specific herbal formula compared with antidepressants for depression, however, due to the obvious clinical or statistical heterogeneity among trials, meaningful meta-analysis could not be conducted to draw confirmed conclusions. Thus, we focused on CHM compared with fluoxetine on improving symptoms of depression, to systematically summarize the effectiveness and safety of CHM for this condition.

2. Objective

This systematic review evaluates the effectiveness and safety of CHM versus fluoxetine on depression.

3. Methods

3.1. Inclusion criteria of studies

Randomized clinical trials (RCTs) with two parallel groups that compared CHM and fluoxetine on treatment of depression were included. Depression should be diagnostic according to the recognized standard, regardless to the type of depression (primary/secondary). Outcome of Hamilton scale (HAMD)[11] had to be reported. There was no restriction on publication types or language.

3.2. Search strategy

The following terms were searched in PubMed, the Cochrane CENTRAL Database, China National Knowledge Infrastructure (CNKI), VIP Database, Chinese Biomedical Database (CBM), and Wanfang Database from inception to December 2014: ("herb" OR "herbal" OR "Chinese medicine") and ("fluoxetine") and ("depression"). Clinical trials were set as a limitation for searching. Details of searching strategy could be found as Supplementary information 1.

3.2. Study selection, data extraction, and methodological quality assessment

Two authors (CHJ and ZCJ) independently selected studies according to the below criteria and extracted data on patient characteristics, treatment details and outcomes. Consensus was reached by discussion with the third author (RY) in case of discrepancy.

Two authors (WJJ and ZCJ) independently assessed the methodological quality of the included trials. The methodological quality of RCTs was assessed according to the risk of bias tool described in the Cochrane handbook for systematic reviews of interventions.[12] Seven elements were assessed: random sequence generation, allocation concealment, blinding of participants/personnel; blinding of outcome assessors, incomplete outcome data, selective reporting and other bias. Disagreements were resolved by discussion with the third author (ZRW). Methodological quality of the studies may not affect the results of screening, which means all studies met the inclusion criteria would be included regardless to the level of their