

Evidence-based Study

Integrated traditional and Western medicine for treatment of depression based on syndrome differentiation: a meta-analysis of randomized controlled trials based on the Hamilton depression scale

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Abstract

OBJECTIVE: To systematically review the benefits of integrated traditional and Western medicine therapies based on the Hamilton depression scale (HAMD) following syndrome differentiation of depression.

METHODS: We searched six English and Chinese electronic databases for randomized clinical trials (RCTs) on integrated traditional and Western medicine for treatment of depression. Two authors extracted data and independently assessed the trial quality. RevMan 5 software was used for data analyses with an effect estimate presented as weighted mean difference (WMD) with a 95% confidence interval (CI).

RESULTS: Seven RCTs with 576 participants were identified for this review. All trials were eligible for the meta-analysis and were evaluated as unclear or having a risk of bias. Meta-analysis showed, compared with Western medicine alone, integrated traditional and Western medicine based on syndrome differentiation could improve the effect of treatment represented by the HAMD [WMD=-2.39, CI

(-2.96,-1.83), $Z=8.29$, $P<0.00001$]. There were no reported serious adverse effects that were related to integrated traditional and Western medicine based therapies in these trials.

CONCLUSIONS: Integrated traditional and Western medicine based therapies for the syndrome differentiation of depression significantly improved the HAMD, illustrating that combining therapies from integrated traditional and Western medicine for treatment of depression is better than Western medicine alone. However, further large, rigorously designed trials are warranted due to the insufficient methodological rigor seen in the trials included in this study.

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Key words: Syndrome differentiation; Depression; Integrated traditional and western medicine; Meta-analysis; Randomized controlled trials

INTRODUCTION

Depression is a form of mood disorder, where sufferers experience psychological and somatic symptoms^[1]. Incidence of depression has significantly increased in recent years, becoming a direct threat to the health of the young and elderly. Currently, drug therapy is the main treatment of this disease. The efficacy of these drugs has been proven, but drug dependence and side effects are a real risk when using these medications.

In traditional Chinese medicine (TCM), depression is categorized as depressive psychosis or depressive disease. Currently, TCM combined with Western medicine has been widely used as a treatment of depression in China. Thousands of clinical studies, ranging from

case reports and case series, to controlled and randomized trials, have reported the effectiveness of TCM for depression, but the conclusions from these trials are not consistent. Limited sample size is one of the main causes behind this ambiguity. The present meta-analysis of randomized controlled trials using the Hamilton depression scale (HAMD) as a measure of outcome, aims to evaluate the evidence for the effectiveness of using integrated traditional and Western based medicine on syndrome differentiation for the treatment of depression.

METHODS

Search strategy

Literature searches were conducted on the China National Knowledge Infrastructure (1999 – 2010), the VIP Database for Chinese Technical Periodicals (1999 – 2010), the Chinese Biomedical Literature Database (1999 – 2010), PubMed (1999 – 2010), Embase (from its inception until 2009), and the Cochrane Library (Issue 3, 2009). The reference lists in the retrieved papers were then browsed. All searches were accomplished by the end of March 2010. Search terms including "depression", "TCM", "Integrated traditional and Western medicine", "TCM combined with Western medicine", "syndrome differentiation", and "clinical trial" were used in various combinations, depending on the database searched. The bibliographies of included trials were searched for additional references.

Inclusion criteria

We included randomized clinical trials (RCTs) comparing integrated traditional and Western medicine versus Western medicine alone. All selected trials chose treatment based on syndrome differentiation. RCTs were the only study design chosen to minimize any potential bias where nonobjective or patient-reported outcomes were used. When more than one publication described a single study, we extracted data from the one providing the most detailed information. Non-RCT trials were excluded.

Assessment of methodological quality

The methodological quality of trials was assessed by examining: the generation of allocation sequence; the allocation concealment; baseline characteristics; blinding; and withdrawals/dropouts. Based on the "Risk of Bias" assessment tool on the Cochrane Handbook for Systematic Reviews of Interventions^[2], quality of the included trials was categorized as "low risk of bias", "high risk of bias", and "uncertain risk of bias".

Data extraction

The following study characteristics were tabulated

from the trials: design, participants and diagnosis, intervention and comparator, and clinical outcomes.

Statistical analyses

The statistical package, RevMan 4.3.2, which was provided by the Cochrane Collaboration, was used for data analyses. Due to sufficient similarity between the studies, data outcomes were measured as weighted mean difference (WMD), with 95% confidence interval (CI).

RESULTS

Description of included trials

In this review, 612 articles were selected from electronic and manual searches. Only 7 articles met the inclusion criteria^[3-9]. All studies were journal articles and published between 2001-2009. The exclusion criteria were: 1) repeat clinical trials; 2) non-randomized controlled trial^[10,13]; 3) therapy not based on TCM syndrome differentiation^[11,14,15,17,20]; 4) interventions not meeting the inclusion criteria; and 5) the HAMD score not used in the study^[12,16].

Test characteristics

Diagnostic criteria: Altogether, 576 cases were included in this study. Five trials used the Chinese Classification and Diagnostic Criteria of Mental Disorders Version 3 (CCMD-3)^[3,6-9], one trial used the Chinese Classification and Diagnostic Criteria of Mental Disorders Version 2 (CCMD-2)^[5], and one trial failed to identify the source of diagnostic criteria^[4]. After reading this article, it was found to meet the clinical diagnostic criteria.

Treatment programs: Two groups were included in all articles, the treatment group and the control group. Patients in the control groups only received Western medical treatment, while those in the treatment groups received treatment from Western medicine and Chinese herbs which were prescribed following a doctor's indication of syndrome differentiation. Eleven syndromes and 12 Chinese herbal decoctions were described in this study (shown in Table 1).

Outcome indicators: All seven studies used the HAMD (shown in Table 2).

Methodological quality of included trials

All 7 trials were described as randomized, but only one trial gave details of the methods used for generating the allocation sequence (i.e. random number tables). Given these findings, we evaluated that the randomization quality in one trial was adequate. The quality of the remaining trials was unclear.

All trials reported that baseline characteristics between the groups were comparable. No trials clearly described

the method used to generate allocation concealment. No trials mentioned who was blinded to treatment allocation. Only one trial reported withdrawal/dropout information. No trial provided information on intention-to-treat, or prior sample size estimation. Accordingly, the included trials had generally low methodological quality (with high risk of bias), and most of the studies fell into the uncertain risk of bias category (shown in Table 3).

Meta-analysis of Hamilton Depression Scale scores

The outcome of meta-analysis shows there is significant difference between treatment group and control group. WMD=-2.39, CI (-2.96,-1.83), Z=8.29, $P<0.00001$ (shown in Figure 1).

DISCUSSION

Syndrome differentiation is one of the basic characteristics of TCM theory. Based on syndrome differentia-

tion, a disease may have different types of syndromes. Therefore, a variety of therapies in TCM may exist, according to the patient's condition, for the treatment of the same disease^[12]. In this study, we found 11 syndromes involved in depression, including the syndrome of blood stasis due to deficient *Qi*, the syndrome of stagnation of liver *Qi* and spleen deficiency, the syndrome of stagnation of liver *Qi*, the syndrome of stagnation of liver *Qi* and endogenous heat due to *yin* deficiency, the syndrome of deficiency of both heart and spleen, the syndrome of disharmony between heart and kidney, the syndrome of stagnated liver *Qi* and disturbing phlegm, the syndrome of *Qi* depression transforming into fire, *Qi* stagnation and blood stasis, the syndrome of *yin* deficiency of liver and kidney, and the syndrome of kidney deficiency and stagnation of liver *Qi*. The most common syndrome seen in this study was the syndrome of stagnation of liver *Qi* and spleen.

Table 1 Syndromes and treatments found in the included trials

Included trials	Treatment group	Control group
Shaojing ³	Decoction benefiting <i>Qi</i> and relieving <i>Qi</i> stagnation with modification for syndrome of blood stasis due to deficient <i>Qi</i> , combined with Deanxit	Deanxit
Lihong ⁴	Xiaoyao powder for syndrome of stagnation of liver <i>Qi</i> and spleen deficiency, combined with fluoxetine hydrochloride	Fluoxetine hydrochloride
Jiangyouqian ⁵	Decoction of danzhi xiaoyao for syndrome of stagnation of liver <i>Qi</i> , decoction of Huanglian Wendan for syndrome of stagnation of liver <i>Qi</i> and endogenous heat due to <i>yin</i> deficiency, Guipi decoction for syndrome of deficiency of both heart and spleen, Liuwei dihuang pill and Jiaotai pill for syndrome of disharmony between heart and kidney, combined with fluoxetine	Fluoxetine
Niusuying ⁶	Chaihu shugan powder for syndrome of stagnated liver <i>Qi</i> and disturbing phlegm, decoction of Danzhi Xiaoyao for syndrome of <i>Qi</i> depression transforming into fire, Xuefu zhuyu decoction for syndrome of <i>Qi</i> stagnation and blood stasis, oral liquid of Zishui Qinggan for syndrome of <i>yin</i> deficiency of liver and kidney, Yueju pill for syndrome of stagnation of liver <i>Qi</i> and spleen deficiency, combined with paroxetine	Paroxetine
Zhangtao ⁷	Xiaoyao powder for syndrome of stagnation of liver <i>Qi</i> and spleen deficiency, Xiaoyao powder and Guipi decoction for syndrome of deficiency of both heart and spleen, Xiaoyao powder and Liuwei Dihuang pill for syndrome of <i>yin</i> deficiency of liver and kidney, combined with Seroxat	Seroxat
Qihaojun ⁸	Decoction of Bushen Jieyu for syndrome of kidney deficiency and stagnation of liver <i>Qi</i> , combined with fluoxetine	Fluoxetine
Liujiupeng ⁹	Chaihu shugan powder for syndrome of stagnated liver <i>Qi</i> , Xuefu zhuyu decoction for syndrome of <i>Qi</i> stagnation and blood stasis, Wendan decoction for syndrome of stagnated liver <i>Qi</i> and disturbing phlegm, Guipi decoction for syndrome of deficiency of both heart and spleen, combined with venlafaxine	Venlafaxine

Table 2 Hamilton depression scale score from included trials

Included trials	Treatment group			Control group		
	cases	Before treatment	After treatment	cases	Before treatment	After treatment
Shaojing ³	28	28.83±4.96	17.97±4.07	28	28.17±5.13	18.53±4.13
Lihong ⁴	41	30.80±3.80	9.70±1.80	39	30.90±3.70	11.50±2.10
Jiangyouqian ⁵	30	19.50±3.42	8.90±4.80	30	20.37±3.47	11.90±4.71
Niusuying ⁶	50	37.75±5.51	13.12±2.14	50	36.71±5.59	16.33±4.37
Zhangtao ⁷	60	32.06±6.91	12.02±5.86	40	31.63±7.86	15.36±6.08

Qihaojun ⁸	60	25.31±6.05	10.51±2.35	60	25.41±5.08	13.81±4.49
Liujinpeng ⁹	30	27.06±4.85	5.10±9.32	30	26.35±4.65	6.04±8.68

Table 3 Methodological quality of included trials

Included trials	Treatment duration(w)	outcome indicator	Random	Allocation concealment	Blind	Baseline	withdrawal s/dropouts
Shaojing ³	6	HAMD	unclear	unclear	unclear	Consistent	0
Lihong ⁴	6	HAMD	unclear	unclear	unclear	Consistent	2
Jiangyouqian ⁵	6	HAMD	unclear	unclear	unclear	Consistent	0
Niusuying ⁶	8	HAMD	random number tables	unclear	unclear	Consistent	0
Zhangtao ⁷	6	HAMD	unclear	unclear	unclear	Consistent	0
Qihaojun ⁸	6	HAMD	unclear	unclear	unclear	Consistent	0
Liujinpeng ⁹	6	HAMD	unclear	unclear	unclear	Consistent	0

Review: Chinese and western medicine on patients with depression
 Comparison: 01 traditional chinese medicine for the treatment of depression
 Outcome: 01 HAMD

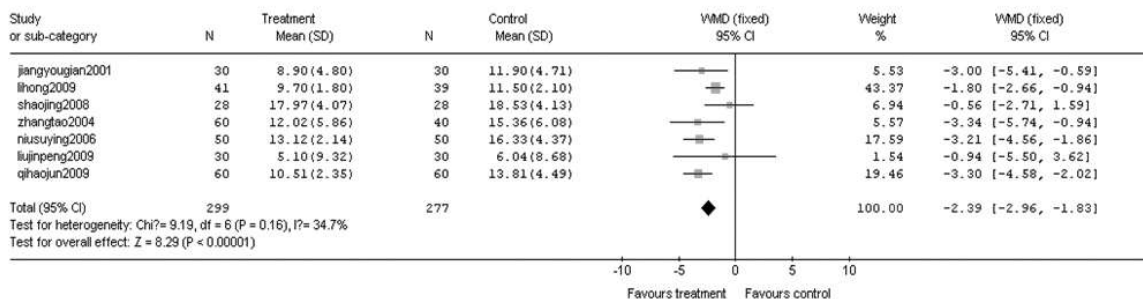


Figure 1 Meta-analysis of Hamilton depression scale scores.

Syndrome of stagnation of liver *Qi* and spleen deficiency is one of the common syndromes of depression. Excessive pressure from work or a poor emotional state will lead to the dysfunction of "liver controlling conveyance and dispersion" and the stagnation of liver *Qi* will result in spleen and stomach disorders. As a result, depression, anxiety, fatigue and other symptoms will occur. Therefore, further research between depression and stagnation of liver *Qi* and spleen deficiency should be conducted.

HAMD is a classic depression rating scale, which is most commonly used in clinical assessment of depression. It is also an objective scale to evaluate effectiveness of treatment. The meta-analysis on data from the HAMD showed a significant benefit of integrated traditional and Western medicine based on syndrome differentiation in the treatment of depression. Though the quality of all the included trials is generally low, the conclusions from a meta-analysis are more comprehensive and reliable than a single trail.

Based on the "risk of bias" assessment tool in the Cochrane approach, the quality of most included trials was categorized as "uncertain risk of bias". Proper randomization techniques need to be used, clearly described, and fully reported. An intention-to-treat principle and an appropriate method for including dropouts in data analyses are also important in the design of the trials. Considering there are insufficient high-quality

trials on integrated traditional and Western medicine based on syndrome differentiation treatment of depression, proof of the effectiveness of this mode of treatment will require further rigorous trials. Therefore, the authors suggest that the efficacy of TCM should be seriously evaluated according to the principles of evidence-based medicine and based on syndrome differentiation, even though abundant clinical experience, especially case reports, have been repeated and treatments have lasted for thousands of years^[19-21].

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Disclosure Statement

No competing financial interests exist.

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