Acupuncture for vascular mild cognitive impairment: a systematic review of randomised controlled trials

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ABSTRACT

Background Vascular mild cognitive impairment (VMCI) is the most common type of vascular cognitive impairment induced by cerebrovascular disease. No effective medicines are currently available for VMCI.

Objective To assess the effectiveness and safety of acupuncture for VMCI.

Methods Seven electronic databases were searched for randomised controlled trials which investigated the effects of acupuncture compared with no treatment, placebo or conventional therapies on cognitive function or other clinical outcomes in patients with VMCI. The quality of the trials selected was evaluated according to the 'risk of bias' assessment provided by the Cochrane Handbook for Systematic Reviews of Interventions. RevMan V.5.1 software was employed for data analysis.

Results Twelve trials with 691 participants were included. The methodological quality of all included trials was unclear and/or they had a high risk of bias. Meta-analysis showed acupuncture in conjunction with other therapies could significantly improve Mini-Mental State Examination scores (mean difference 1.99, 95% CI 1.09 to 2.88, random model, p<0.0001, 6 trials). No included trials mentioned any adverse events of the treatment.

Conclusions The current clinical evidence is not of sufficient quality for wider application of acupuncture to be recommended for the treatment of VMCI, and further large, rigorously designed trials are warranted.

INTRODUCTION

The symptoms of vascular cognitive impairment (VCI) range from mild cognitive impairment to dementia. Risk factors for VCI include hypertension, diabetes mellitus, hyperlipidemia, localised cerebrovascular disease (including cerebral infarction and cerebral haemorrhage) and diffuse cerebrovascular disease (such as leukoaraiosis and chronic cerebral ischaemia). Vascular mild cognitive impairment (VMCI) is the most common type of VCI induced by cerebrovascular disease and does not meet the diagnostic criteria for dementia. The symptoms of VMCI range from cognitive function decline including partial memory loss, decreased concentration, reduced planning ability, impaired decision-making, and slowed action and data management, to psychological symptoms such as depression and anxiety.[1]

Currently, no effective medicines are available for the management of VMCI. Basic actions to prevent VMCI include actively identifying and controlling the various risk factors in order to reduce cognitive function impairment: early diagnosis, early intervention and early treatment; mental and psychological treatment; treatment of complications and rehabilitation.

Mild cognitive impairment and vascular dementia are categorised as 'dementia' (*chi dai*) or 'stroke' (*zhong feng*) in traditional Chinese medicine (TCM). It is suggested they are closely related to dysfunction of the heart, brain and kidney. The principal TCM treatments for VMCI include tonifying the kidney and promoting blood circulation.[2]

A number of studies[3][4] demonstrated that acupuncture techniques that tonify the kidney and nourish the marrow (in PC6, GV20, GB20, etc) may be effective for improving intelligence, stimulating consciousness and enhancing memory. These effects may result from activation and/or stimulation by acupuncture of the

regions responsible for cognition and memory. Scalp acupuncture, which involves stimulation of acupuncture points on the surface of the head using acupuncture needles, electroacupuncture or acupuncture with electrical stimulation, is the most commonly used acupuncture technique for vascular mental disease. Some published studies[5][6] also demonstrated that acupuncture may be able to promote the proliferation and differentiation of neural stem cells in the brain, accelerate angiogenesis and inhibit apoptosis.

Although acupuncture has been commonly used in clinical practice in China for VMCI for years, no systematic review has been performed to evaluate the effectiveness of acupuncture for the condition. Thus, the aim of the current systematic review is to assess the effectiveness and safety of acupuncture for VMCI.

METHODS

Inclusion criteria
Randomised controlled trials (RCTs) that compared acupuncture for the treatment of VMCI (without vascular dementia) to no treatment, placebo or conventional therapy (such as cognitive function training (CFT)) were included. RCTs that evaluated the use of acupuncture as an adjunct to existing conventional therapies for VCI were also included. Outcome measures for cognitive assessment had to include at least one of the internationally recognised scales such as the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Modified Barthel Index (MBI), Wechsler Memory Scale (WMS) or similar. There were no limitations on language of publication or publication type.

Identification and selection of studies
We searched the China National Knowledge Infrastructure (1979–2012), Chinese Scientific Journal Database (1989–2012), Wan Fang (Dissertation and Conference Articles) Database (1985–2012), PubMed (1966–2012) and the Cochrane Library (Issue 12, 2012). All searches were completed in December 2012. The search terms included 'VCI', 'VMCI', 'vascular dementia', 'acupuncture', 'meridian', 'three edged needle', 'triangle-edged needle', 'electroacupuncture', 'randomised' and 'randomisation'. Eligible studies were selected and checked independently by two authors (LZ and HC).

Data extraction and quality assessment
Two authors (HC and YW) independently extracted the data from the selected reports. The extracted data included the author names and title of the study, year of publication, diagnostic criteria, study size, age and sex of the participants, methodological information, type of acupuncture, treatment process, control interventions, outcomes and adverse effects.

The trials included were reviewed and assessed independently by two authors (YW and HC). Quality assessment was conducted according to the 'risk of bias' assessment table provided by the Cochrane Handbook for Systematic Reviews of Interventions.[7] The following types of bias were assessed: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting) and other bias.

Data analysis
RevMan V.5.1 software was employed for data analysis. Data were summarised using relative risk with 95% CI for binary outcomes or mean difference (MD) with 95% CI for continuous outcomes. Meta-analysis was used if the trials had good homogeneity for study design, participants, interventions, controls and outcome measures. Publication bias was explored by funnel plot analysis.

RESULTS

Description of studies
A total of 1223 articles were identified by the initial search and 124 studies with accessible full text were retrieved. However, the majority of these studies did not meet the inclusion criteria and were therefore excluded. Consequently, 12 trials including five publications[8–12] and seven unpublished dissertations[13–19] were included in this review (figure 1 gives details of the included and excluded studies). The characteristics of the included trials are listed in table 1.

A total of 691 participants (average age 61 years old) with VMCI were enrolled in the studies. Time from diagnosis ranged from 22 to 180 days and all trials used Chinese or international diagnostic criteria. The interventions included scalp acupuncture, body acupuncture and electroacupuncture, while the control groups received oral medicine and cognitive rehabilitation. Treatment duration lasted between 28 days and 6 months. All included trials used internationally recognised outcome measures to evaluate cognitive function, including the MMSE, MoCA, MBI and WMS. No trial reported whether adverse events had occurred during the intervention.

Methodological quality
In accordance with the quality evaluation criteria, all included trials clearly described participant characteristics, the study design, the intervention and the controls, and used appropriate methods for statistical analysis. There were 18–40 participants in each group, with an average of 29 patients per group. Sample size calculation was not reported. Eight trials[8][11][13–18] described randomisation procedures, including central randomisation and the use of random number tables and computer software. Five trials[11][13][14][17][18] used opaque envelopes for allocation concealment. Three trials[13][14][17] reported the
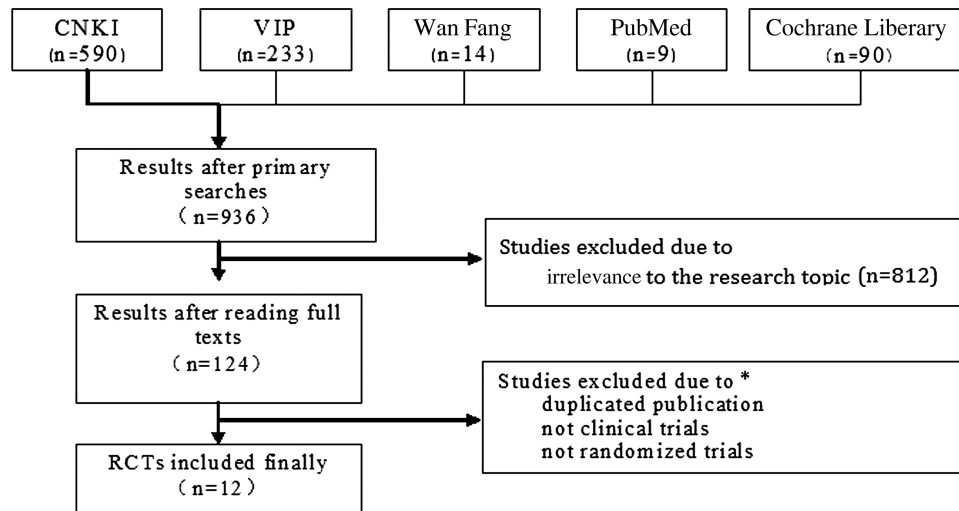
Figure 1 Details of the included and excluded studies of acupuncture in the treatment of vascular mild cognitive impairment (VMCI). CNKI, China National Knowledge Infrastructure; VIP, Chinese Scientific Journal Database; RCT, randomised controlled trial. *The numbers in each category are not recorded.

procedure for blinding the assessor, two[17] [18] stated that there was no blinding of participants or study personnel, and the other failed to report participant blinding. Four trials[13] [14] [17] [18] indicated there were no dropouts, two[11] [12] reported dropouts, and none used intention to treat analysis. Therefore, with the exception of four trials[11] [12] [17] [18] judged to have a high risk of bias, the remaining eight trials were judged to have an unclear risk of bias.

Effect estimates
Table 2 summarises the results from the included studies. Only one meta-analysis was conducted with a forest plot as shown in figure 2.

Acupuncture in conjunction with conventional therapy versus conventional therapy alone
Nine trials[8–10] [12–15] [17] [18] compared acupuncture as an adjunct to the existing therapy. Of these, four trials[10] [13] [14] [17] compared electroacupuncture in conjunction with CFT to CFT alone, two[8] [18] assessed body acupuncture in addition to CFT, two[12] [15] evaluated electroacupuncture in conjunction with pharmaceutical treatment, and one[9] assessed body acupuncture in addition to pharmaceutical treatment.

Six trials[8] [9] [13–15] [17] reported MMSE scores after treatment. Meta-analysis suggested that acupuncture (MD 1.99, 95% CI 1.09 to 2.88, p<0.0001, 6 trials) in conjunction with CFT/donepezil (0.25 mg daily) improved MMSE scores compared to CFT/donepezil alone.

One trial[15] reported cognitive assessment scores using MoCA; however, no significant difference was found between electroacupuncture in combination with donepezil and donepezil alone (MD 1.37, 95% CI −0.21 to 2.95, p=0.09, 1 trial).

Two trials[12] [18] reported MBI scores. One trial[18] suggested that electroacupuncture in combination with CFT was superior to CFT alone (MD 10.73, 95% CI 6.25 to 15.21, p<0.00001, 1 trial), and the other trial[12] showed that electroacupuncture in conjunction with nimodipine (90 mg daily) was also superior to nimodipine (90 mg daily) alone (MD 10.57, 95% CI 8.64 to 12.50, p<0.00001, 1 trial).

Acupuncture versus other interventions
Three trials[11] [12] [16] compared acupuncture to oral medicine, including electroacupuncture versus nimodipine (90 mg daily), body acupuncture versus nimodipine (90 mg daily), and body acupuncture versus enteric-coated aspirin tablets (100 mg daily). A significant difference was found in MMSE scores in all three trials (table 2).

Two trials[16] [19] reported changes in MoCA scores after treatment, and a statistical difference was found between acupuncture (alone or in conjunction with CFT) and nimodipine (in conjunction with CFT, 90 mg daily)/aspirin (100 mg daily) (table 2).

One trial[18] reported that electroacupuncture effectively increased MBI scores compared to nimodipine (90 mg daily) (MD 7.99, 95% CI 6.29 to 9.69, p<0.0001, 1 trial).

Adverse events
No trials mentioned whether adverse events had occurred in the treatment or control groups.

Funnel plot analysis
Funnel plot analysis could not be conducted due to the insufficient number of trials (less than 10) in the meta-analysis.

Table 1 Characteristics of RCTs of acupuncture in the treatment of vascular mild cognitive impairment

Included studies	Participants, male/female		Mean age, years		Diagnostic criteria	Intervention		Duration of treatment, weeks	Outcome measure
	T	C	T	C		T	C		
Huang et al (2008)[8]	21/19	20/20	59.2	61	GC	Body acupuncture, 30 min, daily, 6 times/week, plus CFT	CFT	4	MMSE, CDT, BDT
Sun and Wu (2011)[9]	24/12	25/11	63.6	64.1	GC	Scalp acupuncture, 30 min, daily, 6 times/week, plus donepezil 0.25 mg, daily	Donepezil 0.25 mg, daily	4	Effective rate, MMSE, MBI
Xie et al (2007)[10]	24/17	22/17	53.0	56.5	GC	Scalp acupuncture, 30 min, daily, 10/course, plus rehabilitation, daily	Rehabilitation, daily	12	ERP (P_{300}), WAIS
Yu and Han (2007)[11]	16/15	17/16	67.2	67.0	IC	Body acupuncture, 30 min, daily, 5 times/week	Nimodipine 30 mg, 3 times daily	12	MMSE, BBS
Yu et al (2007)[12]	14/11	15/11	63.3	57.7	GC	Body acupuncture, 20–30 min, daily, 5 times/week, nimodipine 30 mg, 3 times daily	Nimodipine 30 mg, 3 times daily	24	MMSE, MBI, WMS
Jiang (2011)[13]	12/8	10/10	62.9	61.8	GC	Body acupuncture, 30 min, daily, 7 times/week, plus CFT	CFT, daily, 7 times/week	8	ERP (P_{300}), MMSE
Kang (2011)[14]	17/17	15/9	60.7	62.7	GC	Body acupuncture, 30 min, daily, 7 times/week, plus CFT	CFT, daily, 7 times/week	8	ERP (P_{300}), MMSE
Li (2011)[15]	14/16	15/15	Unavailable		IC	Body acupuncture, 30 min, daily, 6/week, plus donepezil 5 mg, daily	Donepezil 5 mg, daily	12	MMSE, MoCA
Yan (2009)[16]	14/16	9/21	61.8	62.9	IC	Body acupuncture, 30 min, daily, 6 times/week, plus CFT, 5 times/week	Nimodipine 30 mg, 3 times daily, plus CFT, 5 times/week	12	MoCA, MMSE, WMS
Yang (2011)[17]	11/9	10/10	59.0	59.3	GC	Scalp acupuncture, 30 min, daily, CFT daily, 7 times/week	CFT daily, 7 times/week	8	MMSE, ERP (P_{300})
Yang (2006)[18]	10/8	11/7	62.3	63.8	GC	Body acupuncture, 30 min, daily, 6 times/week, plus CFT daily	CFT daily	4	NCSE, MBI, Fugl-Meyer
Zhao (2011)[19]	13/17	14/16	65.8	67.2	IC	Body acupuncture, 30 min, daily	Enteric-coated aspirin tablets, 100 mg, daily	12	MMSE, MoCA

BBS, Blessed-Roth Behavior Scale; BDT, block design test; C, control; CDT, clock drawing task; CFT, cognitive function training; ERP, event-related potentials; Fugl-Meyer, Fugl-Meyer Assessment of Sensorimotor Recovery after Stroke; GC, government criteria in China; IC, international criteria; MBI, Modified Barthel Index; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NCSE, non-convulsive status epilepticus; RCT, randomised controlled trial; T, treatment; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale.

Table 2 Summary of the individual studies included in the review

Included studies	Comparison	No. of patients	Week of assessment	Outcome measure	Results, MD (95% CI)
Huang (2008)[8]	Acupuncture plus CFT vs CFT	80	4	MMSE	3.26 (1.69 to 4.83)
				CDT	0.61 (0.39 to 0.83)
				BDT	3.57 (1.87 to 5.27)
Sun and Wu (2011)[9]	Acupuncture plus donepezil vs donepezil alone	72	4	MMSE	2.01 (0.27 to 3.75)
				MBI	−3.52 (−6.24 to −0.80)
Xie et al (2007)[10]	Acupuncture plus rehabilitation vs rehabilitation alone	80	12	WAIS	4.90 (0.76 to 9.04)
Yu and Han (2007)[11]	Acupuncture vs nimodipine	64	12	MMSE	2.41 (1.38 to 3.44)
				BBS	−1.08 (−2.15 to −0.01)
Yu et al (2007)[12]	Acupuncture plus nimodipine vs nimodipine alone	51	24	MBI	10.57 (8.64 to 12.50)
				WMS	
Jiang (2011)[13]	Acupuncture plus CFT vs CFT alone	40	8	MMSE	2.70 (0.71 to 4.69)
Kang (2011)[14]	Acupuncture plus CFT vs CFT alone	68	8	MMSE	0.54 (−0.71 to 1.79)
Li (2011)[15]	Acupuncture plus donepezil vs donepezil alone	60	12	MMSE	1.33 (−0.21 to 2.87)
				MoCA	1.37 (−0.21 to 2.95)
Yan (2009)[16]	Acupuncture plus CFT vs nimodipine plus CFT	60	12	MMSE	1.76 (−0.30 to 3.82)
				MoCA	1.95 (−1.55 to 5.45)
				MBI	7.99 (6.29 to 9.69)
				WMS	
Yang (2011)[17]	Acupuncture plus CFT vs CFT alone	40	8	MMSE	2.65 (0.99 to 4.31)
Yang (2006)[18]	Acupuncture plus CFT vs CFT alone	36	4	NCSE	5.89 (4.00 to 7.78)
				MBI	10.73 (6.25 to 15.21)
Zhao (2011)[19]	Acupuncture vs aspirin	60	12	MMSE	1.80 (0.23 to 3.37)
				MoCA	2.00 (0.11 to 3.89)

BBS, Blessed-Roth Behavior Scale; BDT, block design test; CDT, clock drawing task; CFT, cognitive function training; MBI, Modified Barthel Index; MD, mean difference; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NCSE, non-convulsive status epilepticus; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale.

DISCUSSION

Although the meta-analysis in the current review suggests that acupuncture could be effective as an adjunctive treatment with CFT or pharmaceutical therapies for VMCI, this result should be interpreted with caution as most of the trials had small sample sizes and poor methodological quality. Thus, no firm conclusion can be drawn on the efficacy of acupuncture for the treatment of VMCI.

A number of limitations were identified in this review. The overall quality of the studies included in this review was poor. The conclusions of most studies have potential bias due to missing information on randomisation concealment and the blinding procedure, and inappropriate methods for dealing with missing data. Funnel plot analysis could not be conducted due to the insufficient number of trials included in the meta-analysis; however, a high percentage of the trials conducted in China reported positive results, suggesting possible publication bias.

The participants involved in the trials were all diagnosed with MCI due to cerebral infarction, which limits the generalisability of the results. Another limitation was the variety of acupuncture treatments and controls used. Acupuncture techniques ranged from scalp acupuncture and body acupuncture to electroacupuncture, and so the acupuncture points selected differed greatly between studies. Various different
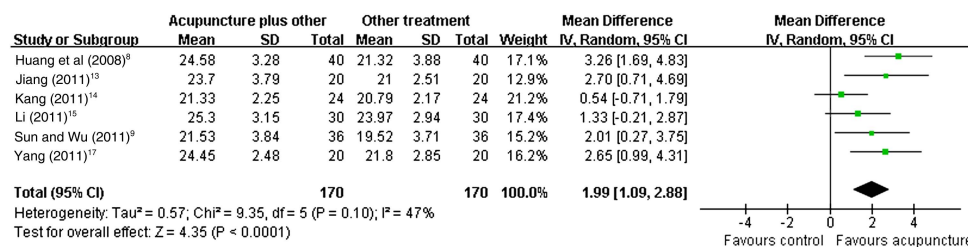

Figure 2 Forest plot of comparison: acupuncture plus other treatment versus other treatment alone. IV, inverse variance.

controls were used in these studies, which could affect the results of the meta-analysis due to clinical heterogeneity. Although statistical heterogeneity was not demonstrated by the I^2 test, variations in study quality, the characteristics of participants, types of interventions and outcome measures indicated some clinical heterogeneity among the included trials.

There are several ways the quality of future acupuncture trials in VMCI could be improved. Although it is difficult to blind practitioners and patients in acupuncture studies, implementation and measurement biases can be minimised if outcome assessors are blinded. Outcome measures used should be of international standard. Data analysis based on the intention-to-treat principle is critical, and clearly defined diagnostic criteria for VMCI should be used to improve comparability between trials. Finally, RCT reports should follow the Consolidated Standards of Reporting Trials (CONSORT) Statement,[20] which requires transparent and explicit descriptions of the trial processes.

In conclusion, acupuncture appears to be beneficial for the management of cognitive and memory function in patients with VMCI; however, further rigorously designed clinical investigations with larger sample sizes are needed to confirm the efficacy of acupuncture.

Summary points

▶ We reviewed the literature on acupuncture for mild cognitive vascular impairment.
▶ Twelve trials were identified, but their quality was too poor to allow conclusions; however, the results justify further studies.

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