Systematic Review and Meta-Analysis

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Clinical effectiveness of acupuncture on Parkinson disease

A PRISMA-compliant systematic review and meta-analysis

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Abstract

Background: Parkinson's disease (PD) is the second-most-common chronic and progressive neurodegenerative disease. The long-term use of levodopa leads to a loss of efficacy and to complications. Therefore, many patients with PD have turned to complementary therapies to help relieve their symptoms. Acupuncture is most commonly used as a complementary therapy in patients with PD. This paper presents a systematic review and meta-analysis of the effects of acupuncture for patients with PD. This study was performed to summarize and evaluate evidence regarding the effectiveness of acupuncture in the relief of PD symptoms.

Methods: Seven databases, namely, MEDLINE, EMBASE, the Cochrane Library, the China National Knowledge Infrastructure [CNKI], and three Korean medical databases, were searched from their inception through August 2015 without language restrictions. Randomized controlled trials (RCTs) were included if they contained reports of acupuncture compared with no treatment and conventional treatment alone or acupuncture plus conventional treatment compared with conventional treatment alone for PD symptoms. Assessments were performed with the unified PD rating scales (UPDRS) I, II, III, and IV and the total score, the Webster scale, and effectiveness rating. Methodological quality was assessed using the Physiotherapy Evidence Database (PEDro) scale and the Cochrane risk of bias (ROB).

Results: In all, 982 potentially relevant articles were identified; 25 RCTs met our inclusion criterion, 19 of 25 RCTs were high-quality studies (i.e., a score of 6 or higher). The included RCTs showed favorable results for acupuncture plus conventional treatment compared with conventional treatment alone in the UPDRS II, III, and IV and the total score. Acupuncture was effective in relieving PD symptoms compared with no treatment and conventional treatment alone, and acupuncture plus conventional treatment had a more significant effect than conventional treatment alone.

Conclusions: We performed a systematic review and meta-analysis to evaluate the use of acupuncture for relief of PD symptoms and found that acupuncture has significant positive effects. Acupuncture can be considered as a combination treatment with conventional treatment for patients with PD. Further studies on this topic should be carried out according to rigorous methodological designs in both the East and the West.

Abbreviations: PD = Parkinson disease, PEDro scale = The Physiotherapy Evidence Database scale, RCTs = randomized controlled trials, ROB = the Cochrane risk of bias, TCM = Traditional Chinese Medicine theory, UPDRS = the unified Parkinson disease rating scales.

Keywords: PEDro scale, randomized controlled trials, unified Parkinson disease rating scales, UPDRS, Webster scale

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1. Introduction

Parkinson disease (PD) is the second-most-common chronic and progressive neurodegenerative disease worldwide.[1] PD is caused by the loss of dopaminergic neurons in the substantia nigra and features motor symptoms including distal resting bradykinesia, tremor, rigidity, postural instability, gait disturbance, and nonmotor symptoms.[2,3] PD usually occurs after 60 years of age and has become widespread among the world's rapidly aging population.[4]

The use of levodopa and other dopaminergic treatments in progressive PD lessens the risks of dyskinesia and motor fluctuation.[5,6] However, the long-term use of levodopa leads to a loss of efficacy and to complications such as motor fluctuation and dyskinesia.[3] These complications are observed in 50% of patients after 5 years of levodopa use for PD and in 80% of patients after 10 years of levodopa use.[7,8]

Generally, with the exception of older patients, patients with PD tend to delay the timing of their levodopa doses. Young patients in the early stages tend to use levodopa when their symptoms are sufficiently severe to interfere with their daily life. Therefore, the delay of levodopa doses is an important key to survival.[9–11]

Acupuncture is most commonly used as a complementary therapy in patients with PD. Acupuncture has been reported to have possible therapeutic effectiveness for PD in clinical trials, as manifested by improvement in clinical symptoms such as tremor, a decrease in the dosage of antiparkinsonian drugs, a decrease in side effects, and improvements in daily life, such as improved sleep. Increasing evidence shows that acupuncture can alleviate the symptoms of PD, delay the progression of these symptoms, allow for a decrease in the dosage of antiparkinsonian drugs, and decrease side effects.[12]

Some previous meta-analyses have reported no significant effects of acupuncture due to conflicting results, whereas other meta-analyses have reported significant effects of acupuncture on PD symptoms.[12,13] However, evidence to support acupuncture for PD symptoms remains unclear or inconclusive due to low sample sizes. Meanwhile, new randomized controlled trials (RCTs) have been conducted since the previous meta-analyses. Therefore, we performed a systematic review and meta-analysis of RCTs to seek a firm conclusion about the effects of acupuncture on PD symptoms with a larger sample size.

2. Methods

2.1. Search methods for identification of studies

The search was performed without restrictions in the language or year of publication. We searched Medline, EMBASE, and the Cochrane Central Register of Controlled Trials from the database inception through August 2015. For Korean publications, we searched 3 Korean medical databases (the Research Information Service System, National Discovery for Science Leaders, and OASIS). For Chinese articles, we searched the China National Knowledge Infrastructure (CNKI). A manual search of relevant references from previous systematic reviews was conducted. The keywords used for the search were "Parkinsonism or Parkinson's disease" AND "acupuncture" in each database language. The search strategy was adjusted for each database.

2.2. Inclusion/exclusion criteria

Relevant clinical trials were included if the following criteria were met: patients received a diagnosis of PD; acupuncture (e.g., manual acupuncture, electroacupuncture, or scalp acupuncture) versus no treatment or conventional treatment (madopar or levodopa); acupuncture plus conventional treatment versus conventional treatment alone; and the study was an RCT. Trials were excluded if the study design did not allow for evaluation of the effects of acupuncture on PD symptoms; that is, studies were excluded if they compared different types of acupuncture; compared different types of intervention; or reported insufficient information.

2.3. Data extraction

Two reviewers (SHL and JYK) independently reviewed and extracted data from each paper using a standardized data extraction form and reached consensus on all items. Ethical approval and patient written informed consent are not required due to that this is a systematic review and meta-analysis of previously published studies. The extracted data included the authors, year of publication, sample size, interventions, main outcomes. The main outcomes used in this systematic review were the unified Parkinson disease rating scales (UPDRS) I (nonmotor experiences of daily living), II (motor experiences of daily living), III (motor examination), and IV (motor complications) and the total score,[14] the Webster scale (Webster developed a rating scale for patients with PD based on 10 clinical findings such as, bradykinesia of hands, rigidity, posture, upper extremity swing, gait, tremor, facies, seborrhea, speech, self-care. The scale indicates the severity of disease and the clinical impairment), and effectiveness rates.[15] We also considered measures of general safety reported for acupuncture as a treatment.

2.4. Quality assessment

Evaluation of the methodological quality of the included studies was based on the Physiotherapy Evidence Database (PEDro) scale and the Cochrane risk of bias (ROB) for quality of studies in meta-analyses. Studies with PEDro scores of 9 or 10 were considered to be of "excellent" quality, those with scores of 6 to 8 were considered to be of "good" quality, and studies with scores of 4 or 5 were of "fair" quality. For this study, we considered a study with a score of 6 or higher on the PEDro scale to be a high quality study. The ROB of the included studies was determined according to the ROB tool in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.0.2). This instrument consists of 6 domains: random sequence generation; allocation concealment; blinding of patients, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias. The tool ranks evidence from research studies as having "high," "low," or "unclear" levels of bias; it is also appropriate for evaluation of the methodological quality of RCTs. Disagreements between the reviewers were resolved.

2.5. Statistical analysis

All statistical analyses were performed with Reviewer Manager Software (version 5.3; Cochrane Collaboration, Oxford, UK). Summary estimates of the treatment effects were calculated with a random-effects model. The effect of acupuncture on dichotomous data was expressed as the risk ratio; for continuous outcomes, the mean difference was calculated with a 95% confidence interval (CI). We assessed the clinical and methodological heterogeneity of the enrolled studies according to subgroup analysis. The statistical heterogeneity in the subgroups was analyzed with the I^2 test and was considered to be significant when the I^2 value was

greater than 50%. A random-effects model was applied even when low heterogeneity was detected because the validity of tests of heterogeneity can be limited with a small number of component studies.

3. Results

3.1. Study characteristics

We identified 982 publications; screening of the titles and abstracts reduced the number to 630. After careful full-text screening, a further 549 articles were rejected due to the reasons listed in Fig. 1. The remaining 81 articles were entered into the qualitative synthesis procedure. Of these 81 articles, 44 were not RCT studies, 3 compared different types of acupuncture, and 7 compared different types of intervention. Finally, 25 RCTs were included in the quantitative synthesis procedure (Fig. 1). The interventions in the included studies were acupuncture or acupuncture plus conventional treatment and the control interventions included placebo, no treatment, or conventional treatment (madopar or levodopa). The identified studies were conducted in the Republic of Korea and China between 2000 and 2014 and included 1616 subjects. One pilot RCT in our initial sample was conducted in the West, but it was excluded because it reported insufficient outcome data. The language of publication was English, Chinese, or Korean. The following standardized headings were extracted: author (year), time since diagnosis (years), sample size, intervention group, control group, and main outcomes (Table 1).[16–40]

3.2. Study quality

Table 2 summarizes the methodological quality of the studies included in the final analysis. The quality scores ranged from 5 to 7 on the PEDro scale, and the average score was 6. Nineteen studies were high-quality studies (i.e., a score of 6 or higher), and 4 were low-quality studies (score of less than 6). The results of the Cochrane ROB analysis varied widely. With regard to random sequence generation and allocation concealment, 5 studies had a low ROB, 17 studies had an unclear ROB, and only 1 study had a high ROB. All of the studies had an unclear ROB with regard to the blinding of patients and personnel and outcome assessment. Twenty-one studies had a low ROB with respect to incomplete outcome data and selective outcome reporting. Seven studies had a low ROB with respect to other sources of bias (Table 2).

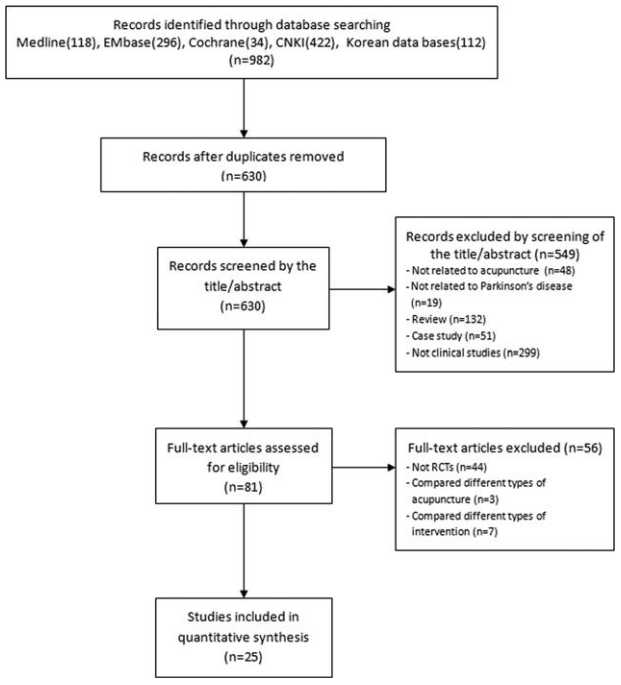

Figure 1. Flowchart of the trial selection process.

3.3. Acupuncture treatment

In all, a total of 65 acupuncture points were used across the 25 trials, with each using between 1 and 11 times in various combinations. The acupuncture point used most often for PD treatment was LR3, which was used in 11 RCTs, followed by GB34, GV20, EX-HN1, GB20, LI11, ST36, and KI3. Patients with PD were treated using 2 to 17 acupuncture points in all of the trials analyzed. Meta-analysis of the data on the number of acupuncture points measured by the UPDRS total score revealed a significant effect for 2 studies using 10 or more points (weighted mean difference, 13.56; 95% CIs: 3.88–23.25; $P=0.006$; $I^2=0\%$; n=64; see Supplementary Fig. 1(1), http://links.lww.com/MD/B511) and for 5 studies using fewer than 10 (weighted mean difference: 10.55; 95% CIs: 8.13–12.97; $P<0.001$; $I^2=0\%$; n=361; see Supplementary Fig. 1(2), http://links.lww.com/MD/B511). Pooled meta-analysis of the data on the number of acupuncture points evaluated by total efficacy showed a significant effect for 5 studies using 10 or more points (weighted risk ratio: 1.38; 95% CIs: 1.14–1.66; $P=0.006$; $I^2=34\%$; n=268; see Supplementary Fig. 2(1), http://links.lww.com/MD/B512) and for 9 studies of fewer than 10 points (weighted risk ratio: 1.22; 95% CIs: 1.05–1.42; $P=0.01$; $I^2=76\%$; n=763; see Supplement Fig. 2(2), http://links.lww.com/MD/B512).

3.4. Effects of acupuncture according to UPDRS

We conducted a meta-analysis of the study results based on the UPDRS used to the effects of acupuncture plus conventional treatment versus conventional treatment alone (Fig. 2). UPDRS I had no significant effect on PD symptoms in two studies (weighted mean difference, 0.27; 95% CIs, −0.17 to 0.72; $P=0.23$; $I^2=0\%$; n=228; Fig. 2(1)). UPDRS II had a significant effect on PD symptoms in 2 studies (weighted mean difference, 3.59; 95% CIs, 2.55–4.63; $P<0.001$; $I^2=0\%$; n=228; Fig. 2(2)). UPDRS III had a significant effect on PD symptoms in 5 studies (weighted mean difference, 4.46; 95% CIs, 3.53–5.39; $P<0.001$; $I^2=0\%$; n=366; Fig. 2(3)). UPDRS IV had no significant effect on PD symptoms in 2 studies (weighted mean difference, 1.36; 95% CIs, −0.57 to 3.29; $P=0.17$; $I^2=93\%$; n=228; Fig. 2(4)). In 7 studies that used the UPDRS total score to compare the effects of acupuncture plus conventional treatment versus conventional treatment alone, it was seen that combined treatment had a significant effect on PD symptoms (weighted mean difference, 10.73; 95% CIs, 8.38–13.07; $P<0.001$; $I^2=0\%$; n=425; Fig. 2(5)).

3.5. Effects of acupuncture according to Webster scales

Meta-analysis of the data on using the Webster scales (Fig. 3), 2 studies used a Webster scale to compare the effects of acupuncture versus no treatment and found that acupuncture had a significant effect on PD symptoms (weighted mean difference, 7.36; 95% CIs, 5.58–9.14; $P<0.001$; $I^2=0\%$; n=74; Fig. 3(1)).

Table 1

Summary of randomized controlled trials assessing of acupuncture for Parkinson disease.

Refs.	Time since diagnosis (y), sample size	Intervention group	Control group	Main outcomes
Park et al[16]	(A) 5.6, (B) 5.9, (C) 5.4 (13/21/12)	(A) AT (LR3, GB34, ST36; 2 times weekly for 4 wk, 15 min)	(B) Placebo AT, (C) Sasang-constitution AT	(1) UPDRS (I, II, III, IV, total)
Jung et al[17]	(A) 6.1, (B) 5.9 (16/21)	(A) AT (LR3, GB34; 2 times weekly for 4 wk, 15 min)	(2) Placebo AT	(1) UPDRS (I, II, III, IV, total)
Xu et al[18]	(A) 6.1, (B) 6.7 (21/10/23)	(A) AT (GB34, ST36, PC6, LR3, GV20; once every days for 15 d, 30 min)	(B) No treatment, (C) point injection	(1) Webster scale
Wang et al[19]	(A, B) 0.6–20 (29/14)	(A) EA (EX-HN1, GB13, GB20, GV20, LI4, SP6, LR3, EX6, LI11, TE5, GB34, ST36, ST40, EX21; once every 2 d for 3 mo, n.r., 40 min)	(B) No treatment	(1) Webster scale
Zhou and Zheng[20]	(A) 5.37, (B) 5.35, (C) 5.38 (30/31/31)	(A) Scalp EA + medication (GV20, EX-HN1, CTCA; 5 times weekly for 2 mo, 3 Hz, 30 min)	(B) Medication (madopar), (C) AT	(1) Webster scale
Huang et al[21]	(A) 5.4, (B) 6.4 (15/15)	(A) Scalp EA + medication (MS6, MS4, MS8, MS9, MS14; 6 times weekly for 5 wk, 100 Hz, 30 min)	(B) Medication (madopar)	(1) UPDRS total
Jiang et al[22]	(A) 5.4, (B) 6.4 (15/15)	(A) Scalp EA + medication (MS6, MS4, MS8, MS9, MS14; 5 times weekly for 6 wk, 100 Hz, 30 min)	(B) Medication (madopar)	(1) Webster scale, (2) UPDRS III, (3) Total efficacy
Yang et al[23]	(A, B) 0.67–6.08 (19/19)	(A) Scalp EA + medication (MS1, MS5, MS6, LI4, SI3, LI5, SI6, LI11, PC3, LU5, LR3, ST41, KI3, GB34, SP9, BL40, GB30, once every 2 d, 10 times, n.r., 30 min)	(B) Medication (madopar)	(1) UPDRS total (2) Total efficacy
Yang et al[24]	(A, B) 0.7–5.6 (13/13)	(A) Scalp EA + medication (MS1, MS5, MS6, LI4, SI3, LI5, SI6, LI11, PC3, LU5, LR3, ST41, KI3, GB34, SP9, BL40, GB30, once every 2 d, 10 times, n.r., 30 min)	(B) Medication (madopar)	(1) UPDRS total (2) Total efficacy
Wang et al[25]	(A) 2.6, (B) 2.2 (37/39)	(A) Scalp EA + medication (HN21–GB6, GV21–GB5, GV17–GV16, BL9–BL10, GB19–GB20, GB20–GB20, once every days for 30 d, n.r., 30 min)	(B) Medication (madopar)	(1) Total efficacy
Sun[26]	(A) 5.2, (B) 5.0 (32/32)	(A) Scalp AT + medication (GV20, CTCA, MA, LI11, TE5, LI4, SP10, ST34, ST36, LR3, SP9; 2 times weekly for 3 mo, n.r., 20–30 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy
Gu et al[27]	(A) 4.44, (B) 4.56 (23/25)	(A) Scalp AT + medication (MA, GB20, SP10, LI4, LR3, KI3, GB34; once every days for 36 d, 2 Hz, 20 min)	(B) Medication (madopar)	(1) UPDRS (I, II, III, IV, total) (2) Total efficacy
Yang and Chen[28]	(A) 4.6, (B) 4.8 (30/30)	(A) Scalp AT + medication (CTCA, MA, LMSA; once every 2 d for 3 mo, 30 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy
Zhang et al[29]	n.r. (32/32)	(A) Scalp AT + medication (MA, CTCA, once every 20 d/once every 5–7 d for 50 d, 5–10 min)	(B) Medication (levodopa)	(1) Webster scale (2) Total efficacy
Zhang et al[30]	(A) 4.96, (B) 5.17 (24/24)	(A) EA + medication (GV20, EX-HN1, GV24, LI11, PC6, SP6, KI3; 6 times weekly for 8 wk, 2 Hz, 60 min)	(B) Medication (madopar)	(1) UPDRS III
Chen et al[31]	(A) 5.4, (B) 6.4 (30/30)	(A) EA + medication (GV20, EX-HN1, EX-HN3; once every days for 6 wk, 2 Hz, 60 min)	(B) Medication (madopar)	(1) UPDRS III
Fu et al[32]	(A, B) 0.58–4.16 (36/28)	(A) EA + medication (GV23, GV24, GV20, EX-HN1, GV12, GV10, GV5, GV6, GV3, SP9; once every days for 15 d, n.r., 25 min)	(B) Medication (madopar)	(1) Webster scale
Zhuang and Wang[33]	(A, B) 0.25–18 (mean: 3.77) (29/24)	(A) EA + medication (EX-HN1, GB13, GB20, EX-HN1, LI11, TE5, GB34, ST36, ST40, GB13, GB20, GV20, LI4, SP6, LR3; once every 2 d, 3 mo, EA: 180/min, 15 min, AT: 40 min)	(B) Medication (levodopa)	(1) Webster scale
Liu et al[34]	(A) 6.67–3.16, (B) 1–2.83 (22/21)	(A) AT + medication (GV16, LR3; once every days for 30 d, 30 min)	(B) Medication (madopar)	(1) UPDRS total (2) Total efficacy
Han et al[35]	(A) 4.85, (B) 3.65 (22/21)	(A) AT + medication (PC6, GV26, LI4, SP6; once every days for 20 d, 60 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy
Chang et al[36]	(A) 3.4, (B) 3.6 (30/30)	(A) AT + medication (GV24, GV20, EX-HN1; once every days for 30 d, 30 min)	(B) Medication (madopar)	(1) UPDRS total (2) Total efficacy
Chen et al[37]	(A) 4.85, (B) 4.65 (30/30)	(A) AT + medication (CV12, CV10, CV6, CV4, KI13, KI17, ST24; once every days for 10 d, 30 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy
Ren et al[38]	(A) 1.5, (B) 2 (90/90)	(A) AT + medication (BL18, BL23, GB20, LI11, LI4, GB34, KI3, LR3; once every days for 30 d, 30 min)	(B) Medication (madopar)	(1) UPDRS (I, II, III, IV, total) (2) Total efficacy
Chen et al[39]	(A) 4.8, (B) 4.6 (40/40)	(A) AT (GB20, SI4, BL10, GV15; 3 times weekly for 10 times, 3 sessions, 30 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy
Wang et al[40]	(A) 0.67–10, (B) 0.83–8 (100/80)	(A) EA (HN21–GB6, GV21–GB5, GV17–GV16, BL9–BL10, GB19–GB20, GB20–GB20; once every days for 30 d, 1 Hz, 30 min)	(B) Medication (madopar)	(1) Webster scale (2) Total efficacy

AT = acupuncture therapy, CTCA = chorea and tremor control area, EA = electroacupuncture, LMSA = leg motor and sensor area, MA = motor area, n.r. = not reported, scalp = scalp acupuncture, UPDRS = undefined PD rating scale.

Table 2

Quality assessment of included studies.

Refs.	PEDro scale items												Cochrane risk of bias					
	A	B	C	D	E	F	G	H	I	J	K	Total	L	M	N	O	P	Q
Xu et al[18]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Wang et al[19]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Chen et al[39]	1	1	0	1	0	0	0	1	1	1	1	7	L	L	U	U	L	L
Wang et al[40]	1	1	0	1	0	0	0	1	1	1	1	7	L	L	U	U	L	L
Zhou and Zheng[20]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	L
Huang et al[21]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Jiang et al[22]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	L
Yang et al[23]	1	1	0	1	0	0	0	1	1	1	1	7	L	L	U	U	L	U
Yang et al[24]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Wang et al[25]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Sun[26]	1	0	0	1	0	0	0	1	1	1	0	5	U	U	U	U	U	U
Gu et al[27]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Yang and Chen[28]	1	0	0	1	0	0	0	1	1	1	0	5	U	U	U	U	U	L
Zhang et al[29]	1	0	0	1	0	0	0	1	1	1	0	5	U	U	U	U	L	U
Zhang et al[30]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Chen et al[31]	1	1	0	1	0	0	0	1	1	1	1	7	L	L	U	U	L	L
Fu et al[32]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Zhuang and Wang[33]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Liu et al[34]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Han et al[35]	1	0	0	1	0	0	0	1	1	1	0	5	U	U	U	U	L	U
Chang et al[36]	1	0	0	1	0	0	0	1	1	1	1	6	U	U	U	U	L	U
Chen et al[37]	1	1	0	1	0	0	0	1	1	1	0	6	L	L	U	U	L	L
Ren et al[38]	1	0	0	1	0	0	0	1	1	1	1	6	H	H	U	U	L	U

PEDro scale items (each satisfied item except the first item contributes 1 point to the total PEDro score): A = eligibility criteria, B = randomization, C = allocation concealment, D = similar at baseline, E = blinded subjects, F = blinded therapist, G = blinded assessors, H = <15% drop outs, I = ITT analysis, J = between-group comparison, K = point and variability measures, 1 = item positive, 0 = item negative or unknown. Cochrane risk of bias: L = random sequence generation (selection bias), M = allocation concealment (selection bias), N = blinding of patients and personnel (performance bias), O = blinding of outcome assessment (detection bias), P = incomplete outcome data (attention bias), selective reporting (reporting bias), Q = other bias, low risk of bias (L), high risk of bias (H), uncertain risk of bias (U).

Two studies that used a Webster scale to compare the effects of acupuncture versus conventional treatment alone observed a significant effect of acupuncture on PD symptoms (weighted mean difference, 3.08; 95% CIs, 2.81–3.35; $P < 0.001$; $I^2 = 0\%$; n = 260; Fig. 3(2)). In four studies that used a Webster scale to the effects of acupuncture plus conventional treatment versus conventional treatment alone, the combined treatment showed a significant effect on PD symptoms (weighted mean difference, 3.78; 95% CIs, 2.17–5.40; $P < 0.001$; $I^2 = 93\%$; n = 208; Fig. 3(3)).

3.6. Effects of acupuncture according to total efficacy

The pooled meta-analysis of the data related to the total efficacy (Fig. 4), 2 studies used total efficacy to compare the effects of acupuncture versus conventional treatment alone and showed a significant effect of acupuncture on PD symptoms (weighted risk ratio, 1.71; 95% CIs, 0.99–2.96; $P = 0.06$; $I^2 = 0\%$; n = 260; Fig. 4(1)). In 14 studies that used total efficacy to compare the effects of acupuncture plus conventional treatment versus conventional treatment alone, the combined treatment had a significant effect on PD symptoms (weighted risk ratio, 1.35; 95% CIs, 1.25–1.46; $P < 0.001$; $I^2 = 73\%$; n = 911; Fig. 4(2)).

4. Discussion

Our systematic review and meta-analysis suggested evidence for the effectiveness of acupuncture in the treatment of PD. Acupuncture was more effective in relieving PD symptoms than no treatment or conventional treatment alone. In addition, acupuncture plus conventional treatment had a significant effect compared to conventional treatment alone according to the UPDRS, Webster scale, and effectiveness rates.

All of the studies included in the present study were conducted in 2 Asian countries, the Republic of Korea and China. One pilot RCT in our initial sample was conducted in the West, but it was excluded because it reported insufficient outcome data. Acupuncture is today used to relieve PD symptoms in many clinics in the West as well, but there has been little research on its effectiveness. Further studies on this topic should be carried out in both the East and the West in the future.

Previous reviews carried out quality assessment only with ROB, and the number and quality of trials are too low to draw any firm conclusions on the effectiveness of acupuncture of PD.[12,13] Our study carried out quality assessment using the ROB and the Physiotherapy Evidence Database (PEDro) scale rating. A study with a PEDro scale rating of 6 points or more is considered to be a high-quality study. Our study included 25 trials with an average score of 6 on the PEDro scale, thus we can draw firm conclusions regarding the effectiveness of acupuncture of PD.

Most of the included RCTs stated that the rationale for acupuncture point selection was drawn from Traditional Chinese Medicine (TCM) theory. None of the trials included in this research used a single acupuncture point; all used various points in combination. For the RCTs that reported the variances for the number of acupuncture points, meta-analysis of the data revealed no significant between-group differences for either UPDRS total score ($P = 0.55$) or total efficacy ($P = 0.33$). It is therefore likely that a study testing a combination of 2 acupuncture points would report the same efficacy as studies evaluating more points. Points LR3, GB34, and GV20, in particular, were found to be the main acupuncture points used to treat PD in clinical trials. Some preclinical randomized trials clarify the mechanism in the substantia nigra pars compacta (SNpc) for the efficacy of

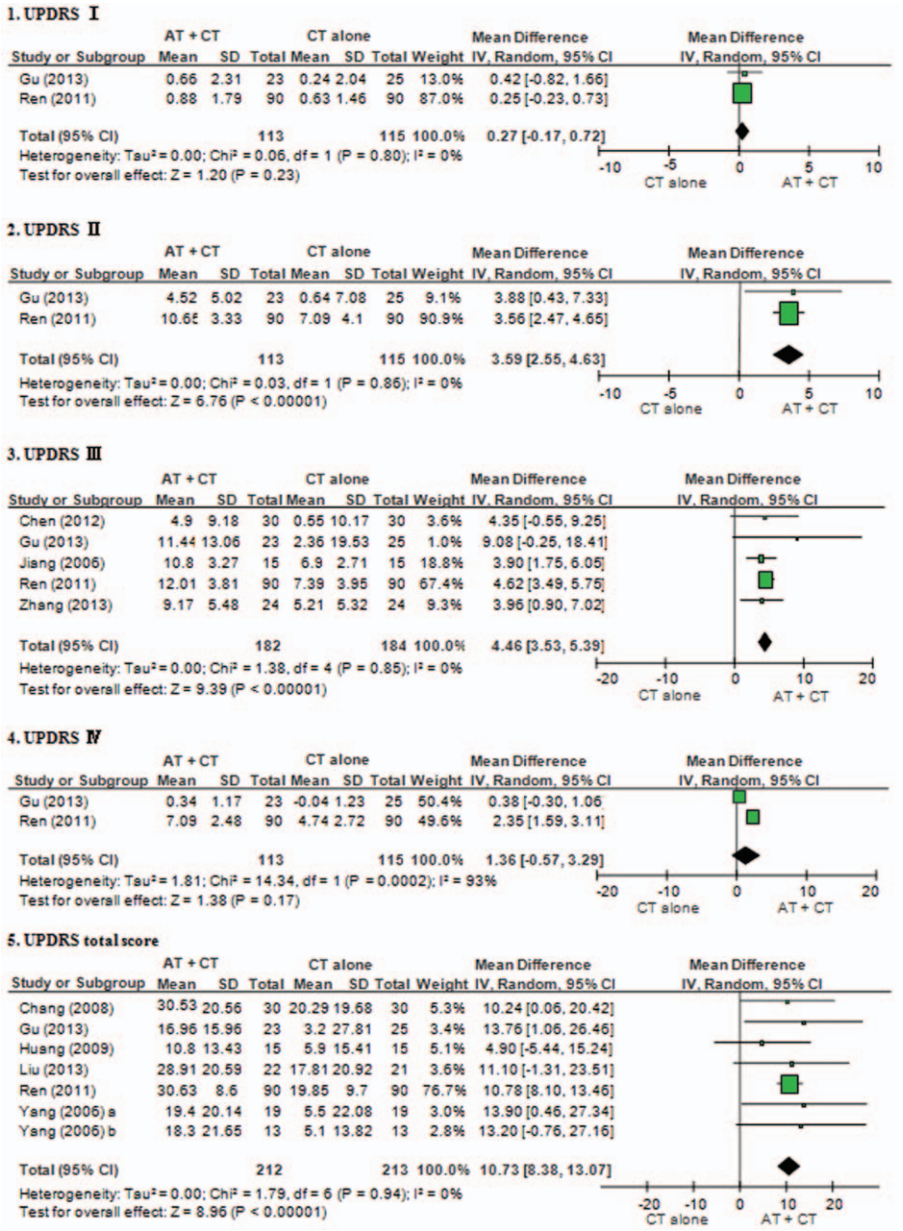

Figure 2. Effects of acupuncture according to UPDRS.

acupuncture points LR3, GB34, and GV20 in PD, such as preventing the cell death of SNpc.[41,42] According to this evidence, we recommend acupuncture points LR3, GB34, and GV20 of the WHO standard acupuncture points as the basic acupuncture points for clinical treatment settings.[43] Their use may result in higher quality clinical trials and treatment.

The included trials showed favorable results for acupuncture plus conventional treatment compared with conventional treatment alone using only UPDRS II, UPDRS III, and the UPDRS total score. The present study has publication bias as an outcome measure of the UPDRS. UPDRS I, II, and IV were used in 2 trials, UPDRS III in 5 trials as the outcome measure of the effects of acupuncture on PD. Overall, the results of UPDRS III for the outcome measure have been mainly presented instead all of the results of UPDRS I through V. Future studies must present all data measured by UPDRS as supplementary data regardless of the results of the outcome measure for the reduction of publication bias. Future trials that assess the effectiveness of acupuncture for PD must overcome publication bias.

Levodopa is the primary treatment for PD, but its long-term use can increase the potential for complications. If a patient's PD symptoms do not interfere with daily life or negatively affect his or her job during the early phase of PD, treatment with levodopa or other antiparkinsonism drugs does not need to start early.[44] In our study, we studied alternative treatments that can be used in the early phase of PD or before the use of levodopa.

According to the meta-analysis of herbal medicine performed by Wang et al,[45] combined herbal medicine and conventional treatments have significantly better effects than conventional treatments on UPDRS I to IV and the total score. The studies that used total efficacy to compare the effects of combined TCM and conventional treatment versus conventional treatment alone found that combined treatment had a significant effect on PD symptoms, and the studies that used total efficacy to compare the

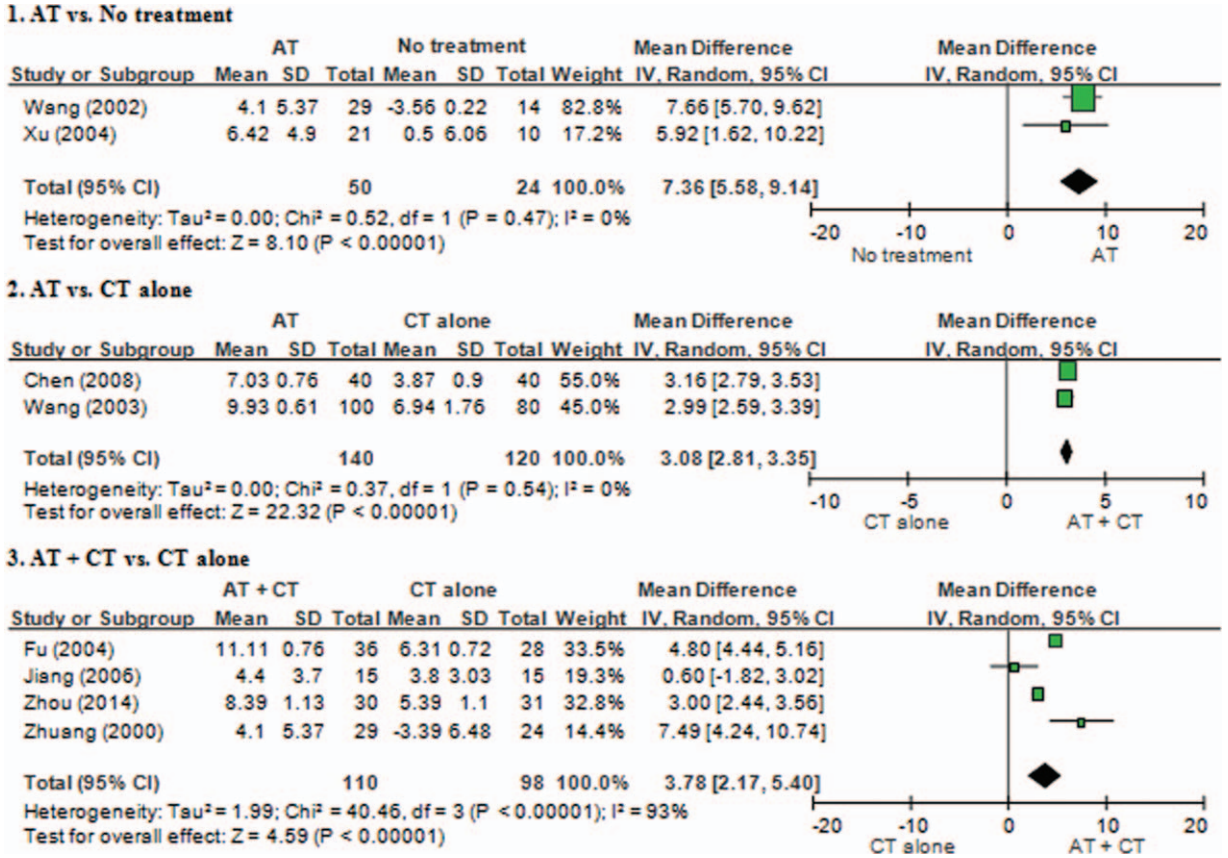

Figure 3. Effects of acupuncture according to Webster scales.

effects of TCM versus placebo found that TCM had a significant effect on PD symptoms. Two studies used total efficacy to compare the effects of acupuncture versus conventional treatment alone showed a significant effect of acupuncture on PD symptoms, but the studies are too small to allow any firm conclusions to be drawn.[46] Furthermore, a study to compare the effects of herbal medicine plus acupuncture versus conventional treatment alone on PD symptoms would help in clinical treatment.[47] In fact, clinicians have proposed treatment with acupuncture without prescribing conventional medicines for the treatment of PD. Therefore, patients in an early stage of PD before the use of levodopa may be better served by treatment with acupuncture and herbal medicine rather than with conventional medicine.

Although this meta-analysis has revealed many positive conclusions, it also has some limitations. Most importantly, some of the studies had methodological shortcomings such as an inadequate level of blinding. Although it is difficult to blind the acupuncture therapist to the patient, attempts should have been made to blind the patients and outcome assessors to minimize performance bias. There has been much discussion about the use of placebo in acupuncture research. Our study included 2 trials with placebo comparisons, but it is difficult to regard them as a real sham controls because the needle was inserted into the skin near the GB34 and LR3 acupuncture points.[16,17] Recently, phantom acupuncture has been reported as a sham control and was characterized by an acupuncture needling intervention induced solely by visual display. Phantom acupuncture can be a viable sham control for acupuncture because it completely excludes the somatosensory component of real needling while maintaining the credibility of the acupuncture context in many subjects.[48] If carried out in this method, a clinical trial with sham control will be more appropriate. In the present study, there was 0% heterogeneity in the RCTs assessing acupuncture efficacy by UPDRS I to III (Fig. 2(1–3)), UPDRS total score (Fig. 2(5)), acupuncture versus no treatment (Fig. 3(1)), and acupuncture versus conventional treatment alone by the Webster scale rating (Fig. 3(2)). Those reporting outcomes in terms of acupuncture plus conventional treatment versus conventional treatment alone by the Webster scale rating (Fig. 3(3)), in contrast, had 93% heterogeneity, and those doing so in terms of acupuncture plus conventional treatment versus conventional treatment by total effectiveness (Fig. 4(2)) had 73% heterogeneity. The source of this methodological heterogeneity may be a lack of blinding among the patients and outcome assessors involved.

Based on our findings, we recommend the use of acupuncture plus conventional treatment for patients with PD. It is also recommended that treatment efficacy be assessed with UPDRS III, which is the most effective scale in evaluating improvements in motor function. Furthermore, we recommend that future studies in this area use validated outcome measures in conjunction with subjective reports of symptom improvement and ensure the blinding of both patients and outcome assessors to obtain high-quality data.[49]

5. Conclusions

We performed a systematic review and meta-analysis to evaluate the effects of acupuncture in the relief of PD symptoms. We found

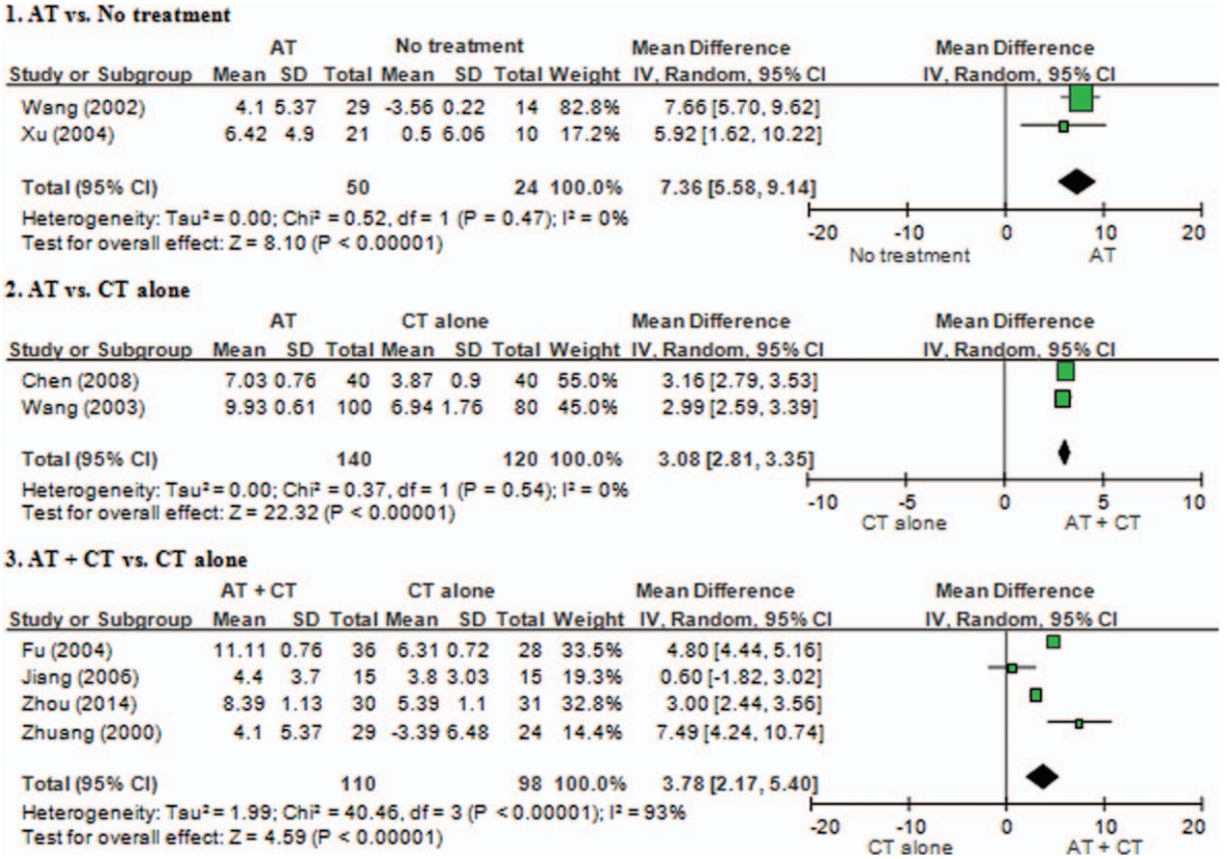

Figure 4. Effects of acupuncture according to total efficacy.

that acupuncture has significant positive effects in the relief of PD symptoms. Acupuncture can be used for patients with PD in combination with conventional treatment.

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