Combined electroacupuncture and auricular acupuncture for primary insomnia: a randomised controlled trial of dose-response effect

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KEY MESSAGES

1. Acupuncture alone and a combination of acupuncture and auricular acupuncture were well-tolerated and better than the waiting list for the treatment of insomnia.

2. Acupuncture alone and combination treatment both produced durable effects on sleep, anxiety, and depressive symptoms, and improved daytime functioning up to at least 13 weeks after treatment.

3. Augmentation of acupuncture by auricular acupuncture to enhance efficacy was not supported.

4. Future head-to-head comparisons between Chinese medicine treatments and conventional therapies for insomnia are required.

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Introduction

Acupuncture possesses a mild hypnotic effect.[1-3] Auricular acupuncture is a form of acupuncture in which seeds, needles, or other materials are applied to the acupoints on the outer ears for a few days to 2 weeks. Acupuncture and auricular acupuncture are based on distinct Chinese medicine theories. Combination of acupuncture and auricular acupuncture may be more effective than either alone. We hypothesised that combined acupuncture and auricular acupuncture was more efficacious than acupuncture alone for treating insomnia.

Methods

This was a randomised assessor-blind parallel-group trial with a 3:3:1 ratio of combination treatment, acupuncture alone, and waiting list. Assessments were conducted at baseline, 1 week, 4 weeks, and 13 weeks after treatment. The trial was registered at ClinicalTrials.gov (NCT01891097). All procedures were approved by the local institutional review board (HKU/HA HKW IRB UW 12-340).

Participants were recruited from June 2013 to May 2015. Inclusion criteria were: (1) aged ≥18 years, (2) fulfilling the DSM-5 diagnosis of insomnia disorder, and (3) sleep onset latency or wake after sleep onset >30 minutes and sleep efficiency <85% for at least three nights based on a 1-week sleep diary at baseline.

Exclusion criteria were: (1) any current major depressive disorder, generalised anxiety or panic disorder, manic or hypomanic episode, substance use disorder, organic mental disorder, or schizophrenia or other psychotic disorder, as defined by the DSM-5 criteria; (2) a Hamilton Depression Rating Scale score of >18; (3) a suicide item score of ≥3 in the above scale; (4) any unstable psychiatric conditions or serious physical illnesses; (5) any sleep disorders including sleep phase disorders, parasomnia, obstructive sleep apnoea (apnoea-hypopnoea index of ≥10), or periodic limb movement disorder (periodic limb movement disorder index of ≥15) detected by overnight polysomnography; and (6) having received any acupuncture or auricular acupuncture during the previous 12 months.

Psychotropic medications, hypnotics, herbal remedies, and over-the-counter medications that were intended for insomnia could be continued, but dose escalation was not disallowed. Introduction of any new insomnia treatment during the study period was disallowed. Acupuncture treatment was provided free of charge. A HK$200 travel allowance was given after completion of all study procedures.

Subjects were treated three times per week for 3 consecutive weeks. Treatments were performed by a registered Chinese medicine practitioner with at least 3 years of experience in acupuncture. To ensure treatment quality, the first five sessions of each type of treatment were supervised by experienced acupuncturists. The thrice-weekly treatment schedule was selected to enhance treatment adherence, whereas the 3-week treatment duration was chosen to examine the short-term effect of acupuncture.

In the combination treatment group, subjects

were needled bilaterally at Ear Shenmen, Sishencong (EX-HN1), Anmian, Neiguan (PC6), Shenmen (HT7), and Sanyinjiao (SP6), and unilaterally at Yintang (EX-HN3) and Baihui (GV20), using the traditional style of acupuncture. The acupoints on the head, hands, and legs were treated using 0.25×25 mm needles, whereas those on the ears were treated using 0.20×25 mm needles. The depth of insertion was between 2 and 25 mm. Deqi was achieved if possible. An electric stimulator was connected to all needles and delivered a constant current of 4 Hz frequency. The needles were left for 30 minutes and then removed. Borneol crystals were placed at Ear Shenmen, Heart, Kidney, Liver, Spleen, Occiput, and Subcortex on the left and right side of the ear in alternation between sessions. Borneol crystals were used instead of magnet pellets or Semen Vaccariae because the former could produce continuous chemical stimulation in addition to mechanical stimulation. Subjects were asked to press the borneol crystals lightly for 5 minutes, three times a day, and remove them after 48 hours.

In the acupuncture group, subjects received acupuncture in the same way. In the waiting-list controls, subjects were assessed at baseline, week 4, and week 7; afterwards, they were randomised to receive combination treatment or acupuncture in a 1:1 ratio.

The primary outcome was the sleep diary–derived sleep efficiency. Secondary outcomes included other sleep diary parameters, actigraphy measures, Insomnia Severity Index, Pittsburgh Sleep Quality Index, Hospital Anxiety and Depression Scale, and Sheehan Disability Scale. In addition, two outcome measures (Multidimensional Fatigue Inventory and Epworth Sleepiness Scale) and two outcome predictors (Dysfunctional Beliefs and Attitudes about Sleep and Sleep Hygiene Practice Scale) were added. Treatment expectancy was assessed using the Credibility of Treatment Rating Scale. Adverse events were monitored after the 3rd, 6th, and 9th treatment using a structured adverse event form.[4]

We estimated the sample size based on sleep diary–derived sleep efficiency. A 5% and 10% difference in sleep efficiency between combination treatment and acupuncture and between acupuncture and waiting list were planned. With an assumption of 25% dropout, a sample size of 96, 96, and 32 for combination treatment, acupuncture, and waiting list, respectively, was needed.

The intention-to-treat approach was used. The primary analysis was mixed-effects group-by-time interaction. Missing data were handled by the mixed-effects model. Standardised effect size was computed by dividing the difference in means with the pooled standard deviation. Dichotomous outcome was assessed using the χ^2 or Fisher exact test. Statistical analyses were performed using SPSS (Windows version 21; IBM Corp, Armonk [NY], US).

Results

A total of 841 subjects were assessed for eligibility, of whom 413 were screened and 224 were randomised (Fig). The mean age of the 224 participants was 53.4 years and 75.4% were female (Table 1). About 63% had insomnia disorder as the primary psychiatric condition, whereas 29% had previous major depressive episodes. At baseline, the mean Insomnia Severity Index score was 19.5, mean Pittsburgh Sleep Quality Index score was 13.4, and mean Hamilton Depression Rating Scale score was 6.3. Of the 192 participants allocated to the two treatment groups, 16 (8.3%) could not complete all treatments. The attrition rate in the two groups was comparable.

There was no significant group-by-time interaction in sleep diary–derived sleep efficiency. However, significant interactions were found in total sleep time and sleep quality (Table 2), with acupuncture superior to combination treatment at 1 week after treatment. In addition, acupuncture was more effective than waiting list in improving total sleep time and sleep quality at 1 week and 4 weeks after treatment, but no significant difference was detected between combination treatment and waiting list. The within-group effect size of acupuncture for sleep diary–derived sleep efficiency variables ranged from 0.16 to 0.45 at 1 week after treatment (Table 2), with mean effect size of 0.32. For combination treatment, the mean effect size was 0.22.

There were significant group-by-time interactions in Insomnia Severity Index and Pittsburgh Sleep Quality Index scores but no significant difference between acupuncture and combination treatment. However, compared with waiting list, combination treatment resulted in lower Insomnia Severity Index score, whereas acupuncture produced lower scores of both Insomnia Severity Index and Pittsburgh Sleep Quality Index at 1 week and 4 weeks after treatment (data not shown).

The only significant difference between acupuncture and combination treatment was the fatigue score at 1 week after treatment, with greater reduction of fatigue after acupuncture. Compared with waiting list, acupuncture produced significantly greater reduction in anxiety, depression, and fatigue and greater improvement in family and social functioning, whereas combination treatment produced significantly greater improvements in anxiety, depression, daytime sleepiness, and occupational, family, and social functioning (data not shown). Results on outcome predictors were not analysed in this report.
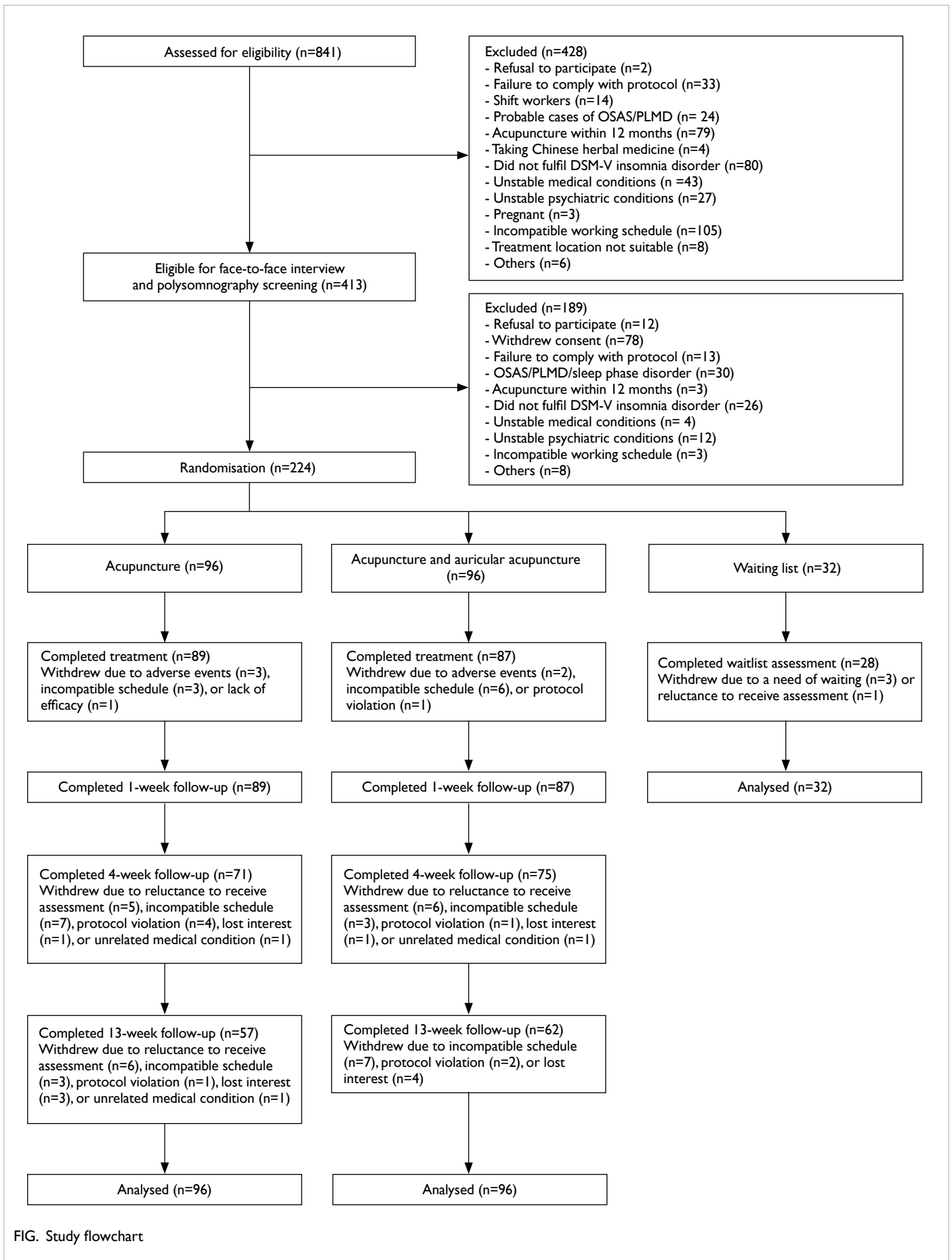
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┌─────────────────────────────────┐        ┌──────────────────────────────────────────────┐
│ Assessed for eligibility (n=841)│        │ Excluded (n=428)                               │
└─────────────────────────────────┘        │ - Refusal to participate (n=2)                 │
                                            │ - Failure to comply with protocol (n=33)       │
                                            │ - Shift workers (n=14)                          │
                                            │ - Probable cases of OSAS/PLMD (n= 24)          │
                                            │ - Acupuncture within 12 months (n=79)          │
                                            │ - Taking Chinese herbal medicine (n=4)         │
                                            │ - Did not fulfil DSM-V insomnia disorder (n=80)│
                                            │ - Unstable medical conditions (n =43)          │
                                            │ - Unstable psychiatric conditions (n=27)       │
                                            │ - Pregnant (n=3)                                │
                                            │ - Incompatible working schedule (n=105)        │
                                            │ - Treatment location not suitable (n=8)        │
                                            │ - Others (n=6)                                  │
                                            └──────────────────────────────────────────────┘

┌─────────────────────────────────┐        ┌──────────────────────────────────────────────┐
│ Eligible for face-to-face       │        │ Excluded (n=189)                               │
│ interview and polysomnography   │        │ - Refusal to participate (n=12)                │
│ screening (n=413)               │        │ - Withdrew consent (n=78)                       │
└─────────────────────────────────┘        │ - Failure to comply with protocol (n=13)       │
                                            │ - OSAS/PLMD/sleep phase disorder (n=30)        │
                                            │ - Acupuncture within 12 months (n=3)           │
                                            │ - Did not fulfil DSM-V insomnia disorder (n=26)│
                                            │ - Unstable medical conditions (n= 4)           │
                                            │ - Unstable psychiatric conditions (n=12)       │
                                            │ - Incompatible working schedule (n=3)          │
                                            │ - Others (n=8)                                  │
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│ Randomisation (n=224)           │
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Acupuncture (n=96)	Acupuncture and auricular acupuncture (n=96)	Waiting list (n=32)
Completed treatment (n=89) Withdrew due to adverse events (n=3), incompatible schedule (n=3), or lack of efficacy (n=1)	Completed treatment (n=87) Withdrew due to adverse events (n=2), incompatible schedule (n=6), or protocol violation (n=1)	Completed waitlist assessment (n=28) Withdrew due to a need of waiting (n=3) or reluctance to receive assessment (n=1)
Completed 1-week follow-up (n=89)	Completed 1-week follow-up (n=87)	Analysed (n=32)
Completed 4-week follow-up (n=71) Withdrew due to reluctance to receive assessment (n=5), incompatible schedule (n=7), protocol violation (n=4), lost interest (n=1), or unrelated medical condition (n=1)	Completed 4-week follow-up (n=75) Withdrew due to reluctance to receive assessment (n=6), incompatible schedule (n=3), protocol violation (n=1), lost interest (n=1), or unrelated medical condition (n=1)	
Completed 13-week follow-up (n=57) Withdrew due to reluctance to receive assessment (n=6), incompatible schedule (n=3), protocol violation (n=1), lost interest (n=3), or unrelated medical condition (n=1)	Completed 13-week follow-up (n=62) Withdrew due to incompatible schedule (n=7), protocol violation (n=2), or lost interest (n=4)	
Analysed (n=96)	Analysed (n=96)	

FIG. Study flowchart

TABLE 1. Demographic and clinical characteristics of the participants*

Variables	Combination (n=96)	Acupuncture alone (n=96)	Waiting list (n=32)	Total (n=224)
Age, y	53.7±9.5	53.1±9.5	53.7±10.7	53.4±9.6
Female	70 (72.9)	78 (81.3)	21 (65.6)	169 (75.4)
Education attainment, y	10.7±3.9	11.0±3.8	12.1±3.7	11.0±3.8
Marital status				
Never married	12 (12.5)	10 (10.4)	4 (12.5)	26 (11.6)
Married/cohabiting	70 (72.9)	69 (71.9)	19 (59.4)	158 (70.5)
Divorced/widowed	14 (14.6)	17 (17.7)	9 (28.1)	40 (17.9)
Occupation				
Professional and associate professional	13 (13.5)	7 (7.3)	7 (21.9)	27 (12.1)
Skilled and semi-skilled worker	21 (21.9)	21 (21.9)	4 (12.5)	46 (20.5)
Unskilled worker	10 (10.4)	3 (3.1)	2 (6.3)	15 (6.7)
Retired	16 (16.7)	20 (20.8)	10 (31.3)	46 (20.5)
Unemployed/housework	36 (37.5)	45 (46.9)	9 (28.1)	90 (40.2)
Insomnia duration, y	12.0±9.9	13.5±11.2	11.3±10.5	12.5±10.6
Previous treatment for insomnia	83 (86.5)	95 (99.0)	31 (96.9)	209 (93.3)
Western medication	60 (62.5)	68 (70.8)	26 (81.3)	154 (68.8)
Psychological treatment	12 (12.5)	11 (11.5)	5 (15.6)	28 (12.5)
Over-the-counter drug	46 (47.9)	58 (60.4)	19 (59.4)	123 (54.9)
Chinese herbal medicine	7 (7.3)	11 (11.5)	6 (18.8)	24 (10.7)
Acupuncture	21 (21.9)	23 (24.0)	10 (31.3)	54 (24.1)
Others	25 (26.0)	36 (37.5)	11 (34.4)	72 (32.1)
Primary psychiatric diagnosis				
Insomnia disorder	60 (62.5)	60 (62.5)	21 (65.6)	141 (62.9)
Major depressive disorder	25 (26.0)	30 (31.3)	10 (31.3)	65 (29.0)
Generalised anxiety disorder / panic disorder / post-traumatic stress disorder	10 (10.4)	5 (5.2)	1 (3.1)	14 (6.3)
Bipolar disorder	1 (1.0)	1 (1.0)	0 (0)	2 (0.9)
Current psychotropic medications other than hypnotics	29 (30.2)	26 (27.1)	8 (25.0)	63 (28.1)
Selective serotonin reuptake inhibitor	10 (10.4)	8 (8.3)	2 (6.3)	20 (8.9)
Serotonin and noradrenalin reuptake inhibitors	2 (2.1)	0 (0)	0 (0)	2 (0.9)
Tricyclic antidepressant	3 (3.1)	4 (4.2)	1 (3.1)	8 (3.6)
Others	5 (5.2)	6 (6.3)	2 (6.3)	13 (5.8)
Combination	9 (9.4)	8 (8.3)	3 (9.4)	20 (8.9)
Equivalent dose of antidepressants in fluoxetine, mg/d	19.2±15.5	20.9±20.3	19.5±12.1	19.9±17.0
Current hypnotics	32 (33.3)	31 (32.3)	18 (56.3)	81 (36.2)
Benzodiazepines	7 (7.3)	1 (1.0)	3 (9.4)	11 (4.9)
Non-benzodiazepine hypnotics	14 (14.6)	16 (16.7)	11 (34.4)	41 (18.3)
Combination	4 (4.2)	12 (12.5)	2 (6.3)	18 (8.0)
Antihistamine or melatonin	7 (7.3)	2 (2.1)	2 (6.3)	11 (4.9)
Equivalent dose of hypnotics in diazepam, mg/d	6.0±8.6	6.6±8.5	6.6±8.5	6.4±7.7
Chronic medical illnesses†	29 (30.2)	22 (22.9)	15 (46.9)	66 (29.5)
Insomnia Severity Index score	18.7±4.9	20.3±4.1	19.9±4.4	19.5±4.5
Pittsburgh Sleep Quality Index score	12.7±2.8	13.7±3.0	14.5±2.7	13.4±3.0
Hamilton Depression Rating Scale score	6.3±3.0	6.3±2.7	6.3±2.8	6.3±2.8

* Data are presented as mean±standard deviation or No. (%) of participants.
† Significant group difference (P=0.04, Chi-squared test)

TABLE 2. Sleep diary–derived variables across study time points in linear mixed-effects models

Variables	Waiting list (n=32)	Within-group effect size	Acupuncture alone (n=96)	Within-group effect size	Combination (n=96)	Within-group effect size	Acupuncture vs waiting list	Combination vs waiting list	Acupuncture vs combination
	Mean±SE*		Mean±SE*		Mean±SE*		P value†	P value†	P value†
Sleep efficiency									
Baseline	60.8±2.6		57.8±1.5		60.8±1.5				
1 week after treatment	64.6±2.8	-0.25	64.6±1.5	-0.45	64.7±1.5	-0.26	0.21	0.96	0.07
4 weeks after treatment	63.3±2.8	-0.17	64.9±1.6	-0.46	65.7±1.6	-0.31	0.08	0.42	0.20
13 weeks after treatment	-		65.4±1.7	-0.48	66.8±1.7	-0.38	-	-	0.39
Sleep onset latency									
Baseline	64.7±8.3		77.1±4.8		61.2±4.8				
1 week after treatment	61.9±8.8	0.06	67.6±4.9	0.20	49.0±4.9	0.26	0.41	0.20	0.61
4 weeks after treatment	57.1±8.8	0.16	61.5±5.2	0.32	50.4±5.1	0.22	0.28	0.73	0.41
13 weeks after treatment	-		61.7±5.4	0.31	48.7±5.3	0.25	-	-	0.65
Wake after sleep onset									
Baseline	70.5±8.3		65.1±4.8		65.8±4.8				
1 week after treatment	53.8±8.9	0.34	57.4±4.9	0.16	59.2±4.9	0.14	0.37	0.27	0.85
4 weeks after treatment	64.1±9.0	0.13	51.0±5.3	0.29	50.0±5.2	0.32	0.43	0.20	0.85
13 weeks after treatment	-		47.8±5.7	0.34	51.9±5.5	0.28	-	-	0.64
Total sleep time									
Baseline	297.1±13.7		285.4±7.9		292.4±7.9				
1 week after treatment	313.5±14.3	-0.21	320.2±8.0	-0.45	310.3±8.0	-0.23	0.14	0.89	0.042
4 weeks after treatment	306.6±14.5	-0.12	322.4±8.5	-0.46	312.6±8.4	-0.25	0.035	0.36	0.08
13 weeks after treatment	-		321.0±9.0	-0.43	325.4±8.7	-0.41	-	-	0.82
Sleep quality									
Baseline	2.2±0.1		2.0±0.1		2.2±0.1				
1 week after treatment	2.2±0.1	-0.04	2.4±0.1	-0.69	2.4±0.1	-0.36	0.001	0.09	0.017
4 weeks after treatment	2.2±0.1	0.01	2.3±0.1	-0.54	2.4±0.1	-0.34	0.004	0.08	0.19
13 weeks after treatment	-		2.4±0.1	-0.63	2.5±0.1	-0.54	-	-	0.48

* Adjusted for the last assessment
† For group by time interaction

Sleep onset latency was reduced to a greater extent at 4 weeks after treatment in acupuncture than waiting list (P=0.048). No significant group-by-time interaction was found in other actigraphy-derived measures (data not shown).

There was no significant difference in treatment credibility between the three groups at baseline and 1 week after treatment (data not shown).

Discontinuation rate due to adverse events was 2.1% and 3.1% for acupuncture and combination treatment, respectively (Fig). The most common adverse event was needle site bruise (26.6%), followed by headache and other painful symptoms (21.4). The incidence of adverse events was comparable between acupuncture and combination treatment (P=0.22, Mann-Whitney *U* test).

Discussion

Augmenting acupuncture by auricular acupuncture for treatment of insomnia was not supported. In fact, acupuncture was marginally better than combination treatment for prolonging sleep diary–derived total sleep time, improving sleep quality, and reducing fatigue at 1 week after treatment. Nonetheless, the two groups were comparable in terms of sleep diary–derived sleep efficiency and other secondary outcomes. Hence, acupuncture and combination treatment were largely similar in efficacy for the treatment of insomnia. Both treatments were well-tolerated (based on the low discontinuation rate) and resulted in durable effects on sleep, anxiety, and depressive symptoms and daytime functioning up to at least 13 weeks after treatment.

Acupuncture with or without auricular acupuncture had a mild hypnotic effect, with a mean effect size of 0.22 to 0.32 for sleep diary measures at 1 week after treatment. Our previous studies reported a mean effect size of 0.48 for primary insomnia[1] and

0.12 for residual insomnia associated with major depression at 1 week after treatment.[2,3]

Compared with pharmacological and psycho-behavioural therapies that have a mean effect size of 0.84 and 0.79, respectively, acupuncture seems to be less effective in terms of sleep diary–derived variables.[5] However, there are limited randomised controlled trials comparing Chinese medicine treatments with pharmacological and psycho-behavioural therapies for insomnia.

There are several limitations in our study. Participants were not blind to their treatment allocation. Those on the waiting list were told that they would be eventually treated, and thus the likelihood of symptom over-reporting was low. In addition, participants allocated to different groups had similar expectation toward acupuncture; hence, the influence of treatment expectancy on outcome was minimal. A standard acupuncture protocol was used; therefore, the effectiveness of acupuncture might be lower.

Conclusion

Augmentation of acupuncture by auricular acupuncture to enhance efficacy in treatment of insomnia was not supported. Future head-to-head comparisons between Chinese medicine treatments and conventional therapies for insomnia are required.

Acknowledgements

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