Acupuncture with or without combined auricular acupuncture for insomnia: a randomised, waitlist-controlled trial

Ka-Fai Chung,[1] Wing-Fai Yeung,[2] Branda Yee-Man Yu,[2] Feona Chung-Yin Leung,[1] Shi-Ping Zhang,[3] Zhang-Jin Zhang,[4] Roger Man-Kin Ng,[5] Gar-Chung Yiu[6]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/acupmed-2017-011371).

[1]Department of Psychiatry, University of Hong Kong, Pok Fu Lam, Hong Kong
[2]School of Nursing, Hong Kong Polytechnic University, Hung Hom, Hong Kong
[3]School of Chinese Medicine, Hong Kong Baptist University, Kowloon Tong, Hong Kong
[4]School of Chinese Medicine, University of Hong Kong, Pok Fu Lam, Hong Kong
[5]Department of Psychiatry, Kowloon Hospital, Ma Tau Wai, Hong Kong
[6]Department of Psychiatry, United Christian Hospital, Kwun Tong, Hong Kong

Correspondence to
Ka-Fai Chung, Department of Psychiatry, University of Hong Kong, Pokfulam, Hong Kong SAR, China; kfchung@hku.hk

Accepted 22 August 2017
Published Online First 11 December 2017

To cite: Chung K-F, Yeung W-F, Yu BY-M, *et al*. *Acupunct Med* 2018;**36**:2–13.

ABSTRACT

Background Few high-quality, large-scale, controlled trials comparing the effectiveness and safety of acupuncture, auricular acupuncture and combined acupuncture treatment for insomnia are available.

Objective To carry out a randomised, assessor-blinded, waitlist-controlled trial to test the superiority of combination treatment.

Methods After in-person and polysomnography screening, 224 subjects (mean age 53.4 years; 75.4% female) with DSM-5 insomnia disorder, who were free from major psychiatric disorders and with sleep-diary-derived sleep efficiency averaged over 1 week of <85%, were randomised to acupuncture alone, acupuncture plus auricular acupuncture (combination treatment), or a waitlist in a 3:3:1 ratio. Standardised acupuncture and combination treatment were provided three times weekly for 3 weeks. The primary outcome was sleep-diary-derived sleep efficiency. Secondary outcomes included wrist actigraphy and self-reported scales on insomnia, anxiety and depression, fatigue, sleepiness and functioning. Assessments were conducted at baseline, 1 week, 4 weeks and 13 weeks after treatment. Participants on the waitlist were re-randomised to receive acupuncture or combination treatment after the second post-baseline assessment.

Results There was no significant difference between acupuncture and combination treatment in the primary outcome and most secondary outcomes at all time points. However, both treatments were better than waitlist in reducing insomnia, anxiety/depressive symptoms and fatigue, and improving function. Within-group improvements were maintained at 13 weeks after treatment. Of 260 adverse events, 243 were mild (93.5%). Discontinuation due to adverse events was 2.1% and 3.1% for acupuncture and combination treatment, respectively.

Conclusions Limited by short-term treatment and follow-up, the attempt to augment acupuncture by auricular acupuncture was not supported. Acupuncture and combination treatment were safe and had mild hypnotic effects, which lasted for at least 13 weeks.

Trial registration number NCT01891097; Results.

INTRODUCTION

Insomnia is the most common sleep complaint, with approximately 10–20% of the general population having insomnia symptoms that are accompanied by distress and daytime impairment.[1] Although effective pharmacological treatments are available, their use is limited by concerns about long-term efficacy and the potential for abuse, dependence and adverse effects.[2] Psycho-behavioural therapies have empirical evidence for insomnia, but they remain underused because of their time-intensive nature and the need for active participation.[3] In view of the limitations of the available treatments, complementary and alternative medicine (CAM) therapies are often sought for insomnia.

Acupuncture and auricular acupuncture are among the most popular and safe procedures of the CAM therapies. According to the National Health Interview Survey in 2012, 1.7% of the US population are current acupuncture users, compared with 1.1% in 2002.[4] A survey in 2012 showed that 1.7% of Hong Kong adults or 0.1 million people reported using acupuncture specifically for sleep in the past year.[5] Our previous studies have shown that acupuncture has hypnotic effects and is more effective than placebo acupuncture for primary or comorbid insomnia.[6–8] Auricular acupuncture, a specific form of acupuncture, is also effective for treating insomnia.[9] Other studies have shown that acupuncture can modulate autonomic tone and central activation by its direct effects on peripheral nerves and muscles,[10] while auricular acupuncture can increase vagal activity and

improve sympathovagal imbalance.[11] The mechanisms of action of acupuncture and auricular acupuncture are distinct. Stimulation at acupuncture points traditionally used for the treatment of insomnia, such as PC6 (*Neiguan*) and *Sishencong*, activates the spinal and trigeminal sensory systems. In contrast, needling of auricular points, such as *Shenmen* and *Heart*, stimulates several cranial sensory nerves, including the trigeminal, facial, glossopharyngeal and vagus nerves.[12] A combination of acupuncture and auricular acupuncture may be more effective than acupuncture or auricular acupuncture alone[13 14]; however, high methodological quality studies on the combination treatment are not available.[15]

Borneol is a commonly used Chinese herbal substance that has many therapeutic properties, including soothing irritation of the skin and antimicrobial actions when dissolved and applied locally.[16] Thin borneol crystals have been used for auricular point stimulation in the treatment of insomnia.[17] We chose borneol crystals rather than the more commonly used magnetic pellet or *Semen Vaccariae* because of their physical and chemical effects and because they have a lower risk of causing inflammation and infection when placed in situ for a long period. Previous reports[18] have suggested that borneol is absorbed through the skin and has a sedative effect through direct contact with the nerve ending of the skin[19] and possibly by the olfactory pathway.[20] In this study, we aim to optimise acupuncture by a combination of traditional needle acupuncture and auricular acupuncture using borneol crystal. We hypothesised that acupuncture combined with auricular acupuncture would be more effective than acupuncture alone in the treatment of insomnia.

METHODS

Study design

This was a randomised, assessor-blinded, parallel-group trial with a 3:3:1 ratio to acupuncture, combination treatment and waitlist. Outcome assessments were at baseline, 1 week, 4 weeks and 13 weeks after treatment. Participants in the waitlist group were re-randomised to receive acupuncture or combination treatment after the second post-baseline assessment. We followed the CONSORT (Consolidated Standards of Reporting Trials and STRICTA (Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture) recommendations in designing and reporting this controlled trial of acupuncture.[21 22] The trial was first registered at ClinicalTrials.gov (#NCT01891097) on 20 June 2013, with no subsequent changes in protocol.

Participants

Participants were recruited through the mass media and in three regional psychiatric clinics in Hong Kong from June 2013 to May 2015, when recruitment was completed. The inclusion criteria were: (1) ethnic Chinese; (2) aged ≥18 years; (3) fulfilling criteria A to E of the DSM-5 diagnosis of insomnia disorder[23] and (4) sleep onset latency or wakening after sleep onset >30 min for at least three nights a week and average sleep efficiency (SE) <85% based on a 1-week sleep diary at baseline.

Major exclusion criteria were: (1) any current major psychiatric disorder according to the DSM-5 criteria based on a structured clinical interview; (2) a 17-item Hamilton Depression Rating Scale ($HDRS_{17}$) score >18; (3) a significant risk of suicide based on a $HDRS_{17}$ suicide item score ≥3; (4) any unstable physical illnesses; (5) any acupuncture or auricular acupuncture during the previous 12 months, which might have had residual hypnotic effects; (6) receipt of psychotropic medications with dosage changes in the past 4 weeks or (7) any sleep disorders, including sleep phase disorders, parasomnia, obstructive sleep apnoea (apnoea–hypopnoea index ≥10) or periodic limb movement disorder (periodic limb movement disorder index ≥15) detected during screening or by in-laboratory overnight polysomnography. Psychotropic medications, herbal remedies and over-the-counter medications intended for insomnia could be continued, but dose escalation was not allowed. Introduction of any new insomnia treatment during the study period was also not allowed. However, reduction of hypnotics use due to symptom improvement was allowed. Individual psychotherapy could be continued if it was ongoing before the study. Treatments were provided free of charge. A HK$200 (US$26) travel allowance was paid to the participants after they completed all the study procedures.

Study procedures

All procedures were reviewed and approved by the local institutional review board. Subjects showing an interest in participation were initially assessed via telephone. After having given written consent, subjects participated in a comprehensive face-to-face interview by a research assistant and face-to-face or telephone interview by an experienced psychiatrist. Laboratory-based overnight polysomnography (Alice 4 Diagnostics System, Respironics, Atlanta, Georgia, USA) was arranged to rule out specific sleep disorders. Randomisation was conducted by an independent administrator using a computer-generated list of numbers with a block size of 14. Allocation codes were kept in sequentially numbered opaque envelopes and were known only to the acupuncturists. To minimise an expectancy effect, subjects were told that "You will be randomised to one of the three groups: acupuncture for 3 weeks followed by observation for 3 weeks; acupuncture plus auricular acupuncture for 3 weeks and observation for 3 weeks; or observation for 6 weeks then acupuncture or acupuncture plus auricular acupuncture for 3 weeks.'

Intervention

Subjects were treated three times a week for three consecutive weeks. Treatments were performed in a quiet room by acupuncturists who were registered Chinese medicine practitioners with at least 3 years of experience in providing acupuncture. In most circumstances, the same acupuncturist was responsible for the whole course of treatment. To ensure the acupuncturists' treatment quality, the first five acupuncture and combination treatment sessions were supervised by experienced acupuncturists (SZ or ZZ). The three times a week treatment schedule, which we used in our previous studies,[6–8] but not daily or less frequently, was a balance between preventing inconvenience and enhancing effectiveness. The 3-week duration of treatment was chosen to examine the short-term effect of acupuncture. The subjects had to receive a minimum of four treatments in two consecutive weeks; otherwise, they were advised to end their participation due to insufficient treatment exposure.

Combined acupuncture and auricular acupuncture

Needles were inserted bilaterally into subjects at *Sishencong*, *Anmian*, PC6, HT7 (*Shenmen*) and SP6 (*Sanyinjiao*) and ear *Shenmen*, and unilaterally at *Yintang* and GV20 (*Baihui*) (supplementary figure 1). The acupuncture points on the head, hands and legs were stimulated using 0.25×25 mm stainless steel needles, whereas those on the ears were penetrated using 0.20×25 mm stainless steel needles (Suzhou Shenlong Medical Apparatus, Tai Chi, China). The depth of insertion was between 2 mm and 25 mm, depending on the acupuncture points; *de qi* was achieved if possible. Surgical tapes or hair pins were used to secure the needles. An electric stimulator (ITO ES160, Japan) was connected to the needles at all acupuncture points and delivered a 0–16 mA, 0.4 ms, square-wave, brief-pulse stimulus of 4 Hz frequency. The electrical dosage was adjusted according to subjects' tolerance. The needles were left for 30 min and then removed. Only *Shenmen* on the ear was chosen to be punctured because it is a commonly used acupuncture point and the response evoked from puncturing this point is similar to the autonomic response evocable from puncturing other auricular points.[24] Borneol crystals were then placed at ear *Shenmen, Heart, Kidney, Liver, Spleen, Occiput* and *Subcortex* and secured using adhesive plaster. To avoid skin irritation, the left and right side were used alternately. Subjects were asked to press the borneol crystals lightly for 5 min in the morning, afternoon and evening every day and remove them after 48 hours. Subjects were reminded to remove the borneol crystals if they experienced severe itchiness. Subjects were considered non-adherent to auricular acupuncture if it was applied less than 4 days per week. The acupuncture point selection for acupuncture and auricular acupuncture was based on expert opinion, systematic reviews[9 25] and our previous placebo-controlled studies.[6–8] Evidence from randomised, sham-controlled studies of the point specificity for insomnia was not available.

Acupuncture

Subjects received acupuncture in the same way as in the combination group.

Waiting-list control

Subjects were assessed at baseline, fourth and seventh weeks; afterwards, they were re-randomised to receive combination treatment or acupuncture in a 1:1 ratio.

Measures

The primary outcome was sleep-diary-derived SE, calculated as total sleep time (TST) divided by time in bed expressed as a percentage averaged over 1 week. Secondary outcomes included wrist actigraphy, Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression Scale (HADS), Multidimensional Fatigue Inventory (MFI), Epworth Sleepiness Scale (ESS) and Sheehan Disability Scale (SDS). Sleep diary, ISI and PSQI are standard self-report measures of insomnia.[26] The HADS, MFI, ESS and SDS were used to assess anxiety and depressive symptoms, fatigue, daytime sleepiness and functional impairment. Actigraphy is a valid and objective measure of sleep–wakefulness over an extended period.[27] In this study, actigraphs (Actiwatch-2; Respironics Inc; Murrysville, Pennsylvania, USA) were worn 24 hours a day on the non-dominant wrist for 1 week before each study visit. Epoch length was set at 1 min. Data were analysed with Actiware software (version 5, Respironics Inc).

The Credibility of Treatment Rating Scale, a four-item visual analogue scale, was used to assess participants' confidence about treatment at baseline, after the second and ninth acupuncture session and at 1 week after treatment. A higher score suggested greater confidence. Local and systemic adverse events related to acupuncture were assessed by the acupuncturists after the third, sixth and ninth treatment using a 20-item scale.[28] All questionnaires used in this study are in Chinese language and have been shown to be valid and reliable.[29–33] Outcome assessors were blind to participants' intervention allocation.

Data analysis

We used the SPSS version 21.0 (IBM Corp) for statistical analyses. An intention-to-treat approach was used. All randomised subjects were included in the analysis, whether or not they received treatment. We first analysed whether there was any significant difference in primary outcome between combination treatment and acupuncture alone by independent t test, using the last observation carried forward method to impute missing data., Other analyses included the effects of intervention over time using mixed-effects group by time interaction

for continuous outcomes and the χ^2 or Fisher exact test for dichotomous outcomes. Statistical significance of the results was assessed based on both raw p values (<0.05) and Bonferroni-adjusted p values for multiple between-group comparisons (<0.05/3=0.017). The treatment impact was quantified by standardised effect size, which is the difference in means divided by the pooled SD.

Our sample size calculation was based on sleep-diary-derived SE, the primary outcome. A 5% and 10% difference in sleep-diary-derived SE between acupuncture and combination treatment and acupuncture/combination treatment and waitlist were planned. The expected differences were based on clinical impression of significant improvement. With an estimated 25% dropout, a sample size of 96, 96 and 32 in acupuncture, combination treatment and waitlist groups, respectively, would have a power of 80% to detect a significant difference at an α level of 0.05.

RESULTS

A total of 841 potential subjects were assessed for eligibility, of whom 413 were screened in person and 224 were randomised (figure 1). The mean age was 53.4 years; 75.4% were female and 70.5% were married or cohabiting (table 1). About 62.9% had insomnia as the only diagnosis, while 29.0% had past major depressive episodes and 8.0% had other psychiatric disorders. Roughly 29.5% had concomitant medical conditions

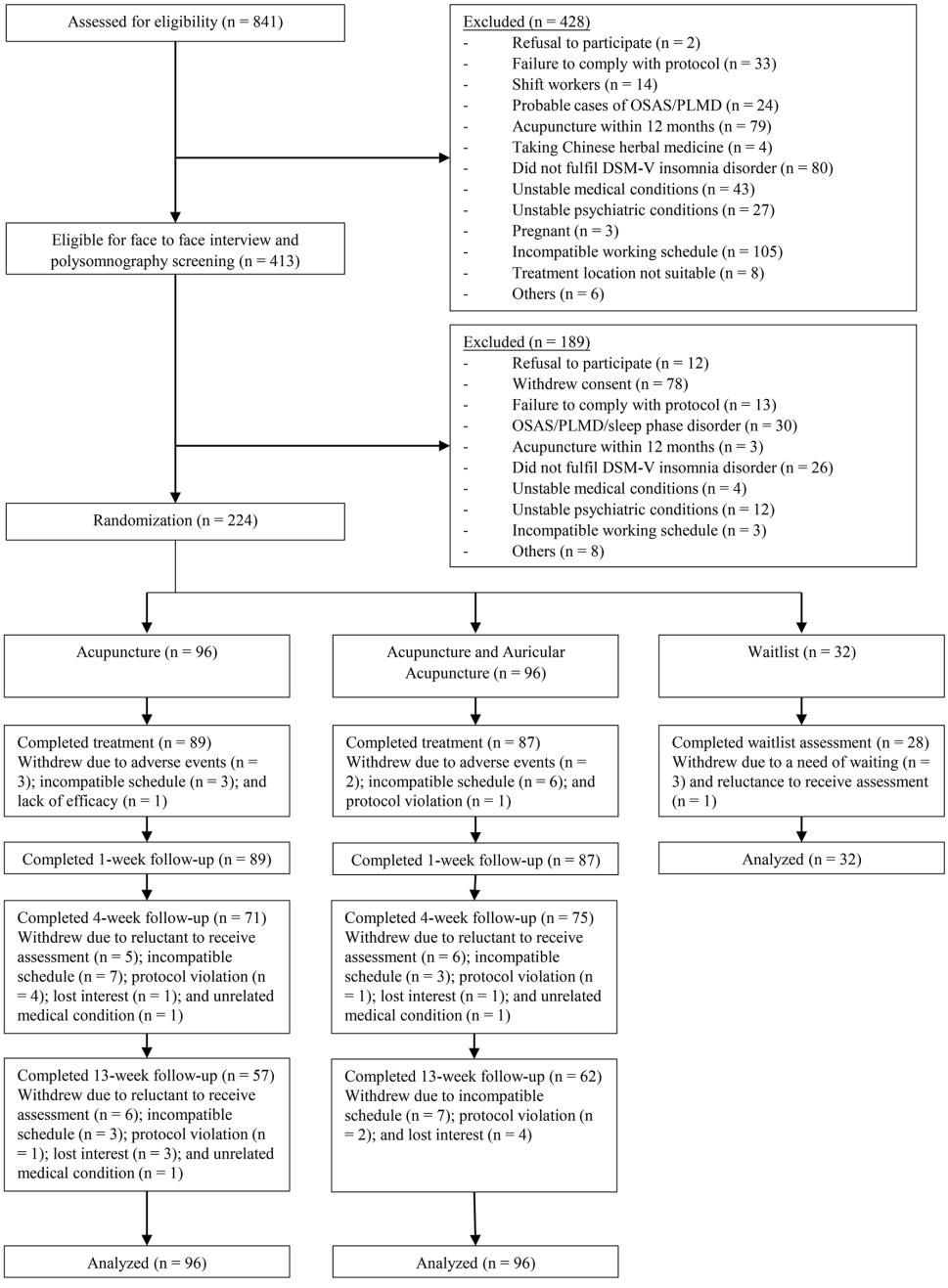

Figure 1 Study flowchart. DSM-V, Diagnostic and Statistical Manual of Mental Disorders, fifth edition; OSAS, obstructive sleep apnoea syndrome; PLMD, periodic limb movement disorder.

Table 1 Demographic and clinical characteristics of the participants

Variables*	Combined (n=96)	Acupuncture (n=96)	Waitlist (n=32)	Total (n=224)
Age, years	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, years	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 semiskilled 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/houseworker	36 (37.5)	45 (46.9)	9 (28.1)	90 (40.2)
Insomnia duration, years	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)
OTC 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)
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)
GAD/panic disorder/PTSD	10 (10.4)	5 (5.2)	1 (3.1)	16 (7.1)
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)
SSRI	10 (10.4)	8 (8.3)	2 (6.3)	20 (8.9)
SNRI	2 (2.1)	0 (0)	0 (0)	2 (0.9)
TCA	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/day	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	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/day	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)
ISI total score	18.7±4.9	20.3±4.1	19.9±4.4	19.5±4.5
PSQI total score	12.7±2.8	13.7±3.0	14.5±2.7	13.4±3.0
$HDRS_{17}$ total score	6.3±3.0	6.3±2.7	6.3±2.8	6.3±2.8

*Data are presented as mean ±SD or number (%).
†Others included health and dietary products, massage and hypnosis.
‡Participants were receiving regular medications for the illnesses.
§Significant group difference (p=0.04, $\chi 2$ test).
GAD, generalised anxiety disorder; $HDRS_{17}$, 17-item Hamilton Depression Rating Scale; ISI, Insomnia Severity Index; OTC, over-the-counter; PSQI, Pittsburgh Sleep Quality Index; PTSD, post-traumatic stress disorder; SNRI serotonin and noradrenalin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

that required regular drug treatment. About 36.2% were taking hypnotics nightly, while 18.3% were taking non-benzodiazepine hypnotics alone. The average daily dose of hypnotics was 6.4 mg diazepam equivalent. The mean ISI and PSQI scores were 19.5 and 13.4, respectively, at baseline, indicating moderate insomnia severity. The mean $HDRS_{17}$ score was 6.3, suggesting that most participants did not have any depressive symptoms. The only significant difference between the three groups was the presence of concomitant medical conditions, of which the waitlist group had a higher proportion than the combination and acupuncture groups (table 1). Sixteen of the 192 participants allocated to the acupuncture groups (8.3%) could not complete all treatments. The reasons for non-completion were incompatible schedule (n=9), adverse events (n=5), protocol violation due to an increase in hypnotic dosage and lack of effectiveness (n=1). Two of the 32 waitlist participants (6.3%) did not complete all assessments (figure 1). There was no significant difference in the attrition rate between the acupuncture groups at all time points ($p>0.05$, χ^2 test).

Effectiveness

Sleep diary and actigraphy measures

Sleep diary and actigraph measures across the study time points are shown in table 2.

An independent t test showed that there was no significant difference between combination treatment and acupuncture in sleep-diary-derived SE, the primary outcome, across study time-points (combination vs acupuncture for SE in mean±SD at 1 week after treatment: 64.5±14.7% vs 64.2±16.5%; 4 weeks after treatment: 65.0±15.4% vs 63.9±17.2%; 13 week after treatment: 66.1±15.5% vs 64.3±16.7%, all $p>0.05$). In addition, there was no significant group-by-time interaction in all sleep diary and actigraphy measures. The within-group effect size of acupuncture for sleep-diary-derived SE and TST was 0.45 at 1 week after treatment; for combination treatment, it was 0.26 and 0.23, respectively. At 4 weeks and 13 weeks after treatment, the effect size was either similar or slightly increased in magnitude, compared with 1 week after treatment.

Sleep questionnaires

ISI, PSQI and HADS scores across study time points are shown in table 3.

Significant group-by-time interactions in ISI and PSQI were found; however, there was no significant difference between acupuncture and combination treatment. Compared with waitlist, acupuncture and combination treatment had a lower ISI score at 1 week and 4 weeks after treatment. The within-group effect size of acupuncture on ISI and PSQI at 1 week after treatment was 1.0 and 0.62, respectively; for combination treatment, the respective effect size was 0.84 and 0.53.

Anxiety, depression, fatigue, sleepiness and functional measures

SDS, ESS and MFI scores across study time points are shown in table 4.

The only significant difference between acupuncture and combination treatment was greater reduction in fatigue score in the acupuncture group at 1 week after treatment, which remained significant after Bonferroni adjustment (table 4). Compared with waitlist, acupuncture and combination treatment were significantly more effective in reducing anxiety and depressive symptoms and fatigue and improving functioning.

Treatment credibility

There was no significant difference in the Credibility of Treatment Rating Scale scores between acupuncture and combination treatment at baseline, after the second and ninth acupuncture treatment and at 1 week after treatment (mixed-effects models, all $p>0.05$, data not presented).

Adverse events

The discontinuation rate due to adverse events was 2.1% and 3.1% for acupuncture and combination treatment, respectively. The most common adverse event was needle site bruising (26.6%), followed by headache and other painful symptoms (21.4%) and needle site pain (17.7%). The incidence of any adverse event was 62.0%. Of the 260 adverse events, 243 were mild (93.5%), 14 were moderate (5.4%) and three were severe (1.2%). There was no significant difference in the incidence of adverse events between acupuncture and combination treatment ($p=0.10$, χ^2 test).

Outcomes of waitlist participants

Twenty-six participants were re-randomised to acupuncture (n=13) and combination treatment (n=13). There was no significant difference in almost all outcomes (supplementary tables 1-3), except a lower PSQI score in the combination group than in the acupuncture group at 13 weeks after treatment (supplementary table 2). The within-group effect sizes for sleep-diary variables were small to medium; for sleep questionnaires, they were medium to large.

DISCUSSION

This is one of the largest randomised controlled trials on the effectiveness and safety of acupuncture for insomnia. Our attempt to augment acupuncture by auricular acupuncture for the treatment of insomnia was not supported; perhaps limited by the short periods of intervention and follow-up. There was no significant difference between combination treatment and acupuncture in the primary and almost all secondary outcomes at all time points. Both treatments were found to be safe, acceptable to patients and associated with improvements in insomnia, anxiety and depressive symptoms and daytime functioning up to at least 13 weeks after treatment;

Table 2 Sleep diary and actigraph measures across study time points

Variables	Waitlist (n=32) Mean±SE*	Within-group effect size	Acupuncture (n=96) Mean±SE*	Within-group effect size	Combined (n=96) Mean±SE*	Within-group effect size	Acupuncture versus waitlist p Value†	Combined versus waitlist p Value†	Acupuncture versus combined p Value†
Sleep diary SE									
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 diary TST									
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	0.04
4 Weeks after treatment	306.6±14.5	−0.12	322.4±8.5	−0.46	312.6±8.4	−0.25	0.04‡	0.36	0.08
13 Weeks after treatment	–		321.0±9.0	−0.43	325.4±8.7	−0.41	–	–	0.82
Actigraphy SE									
Baseline	78.3±1.7		78.5±1.0		77.5±1.0				
1 Week after treatment	79.1±1.9	−0.07	80.1±1.0	−0.15	78.3±1.0	−0.08	0.69	0.96	0.54
4 Weeks after treatment	76.4±1.8	0.19	80.0±1.2	−0.13	79.4±1.1	−0.18	0.18	0.13	0.80
13 Weeks after treatment	–		79.7±1.3	−0.10	77.8±1.2	−0.03	–	–	0.59
Actigraphy TST									
Baseline	388.9±11.9		401.7±6.9		378.6±6.9				
1 Week after treatment	381.4±13.3	0.11	393.1±7.4	0.12	375.9±7.2	0.04	0.89	0.69	0.52
4 Weeks after treatment	370.1±13.2	0.27	393.0±8.6	0.11	383.1±8.0	−0.06	0.52	0.14	0.26
13 Weeks after treatment	–		393.0±9.5	0.11	374.9±8.8	0.05	–	–	0.72

*Estimated mean and SE from linear mixed-effects model adjusted for last assessment time, which are different from the last observation carried forward method.
†p Value for group by time interaction using linear mixed-effects models.
‡Non-significant on Bonferroni adjustment.
SE, sleep efficiency; TST, total sleep time.

Table 3 Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI) and Hospital Anxiety and Depression Scale (HADS) scores across study time points

Variables	Waitlist (n=32) Mean±SE*	Within-group effect size	Acupuncture (n=96) Mean±SE*	Within-group effect size	Combined (n=96) Mean±SE*	Within-group effect size	Acupuncture versus waitlist p Value†	Combined versus waitlist p Value†	Acupuncture versus combined p Value†
ISI									
Baseline	19.9±0.9		20.3±0.5		18.4±0.5				
1 Week after treatment	18.8±0.9	0.22	15.4±0.5	1.00	14.3±0.5	0.84	<0.001‡	0.001‡	0.25
4 Weeks after treatment	19.3±0.9	0.11	15.7±0.6	0.89	14.7±0.5	0.74	<0.001‡	0.001‡	0.30
13 Weeks after treatment	–		15.8±0.6	0.83	14.4±0.6	0.77	–	–	0.62
PSQI									
Baseline	14.4±0.6		13.6±0.3		12.6±0.3				
1 Week after treatment	13.6±0.6	0.24	11.5±0.4	0.62	10.8±0.4	0.53	0.03	0.11	0.49
4 Weeks after treatment	13.8±0.6	0.18	11.4±0.4	0.63	10.9±0.4	0.46	0.02	0.12	0.25
13 Weeks after treatment	–		11.5±0.4	0.57	10.7±0.4	0.51	–	–	0.66
HADS-Anxiety									
Baseline	8.0±0.7		7.7±0.4		7.1±0.4				
1 Week after treatment	8.5±0.8	–0.12	7.0±0.4	0.16	6.0±0.4	0.26	0.04	0.01‡	0.28
4 Weeks after treatment	8.4±0.8	–0.09	6.8±0.5	0.21	6.1±0.5	0.23	0.01‡	0.02	0.84
13 Weeks after treatment	–		7.0±0.5	0.16	6.1±0.5	0.22	–	–	0.57
HADS-Depression									
Baseline	7.6±0.7		6.9±0.4		6.1±0.4				
1 Week after treatment	8.1±0.8	–0.10	6.2±0.4	0.16	5.1±0.4	0.24	0.05	0.01‡	0.33
4 Weeks after treatment	8.5±0.8	–0.19	6.5±0.5	0.08	5.5±0.5	0.16	0.05	0.008‡	0.48
13 Weeks after treatment	–		6.5±0.5	0.08	5.4±0.5	0.18	–	–	0.42

*Estimated mean and SE from linear mixed-effects model adjusted for last assessment time.
†p Value for group by time interaction using linear mixed-effects models.
‡Remain significant on Bonferroni adjustment (p<0.05/3=0.017).

Table 4 Sheehan Disability Scale (SDS), Epworth Sleepiness Scale (ESS) and Multidimensional Fatigue Inventory (MFI) scores across study time points

Variables	Waitlist (n=32) Mean±SE*	Within-group effect size	Acupuncture (n=96) Mean±SE*	Within-group effect size	Combined (n=96) Mean±SE*	Within-group effect size	Acupuncture versus waitlist p Value†	Combined versus waitlist p Value†	Acupuncture versus combined p Value†
SDS									
Baseline	12.5±1.5		10.8±0.7		10.4±0.7				
1 Week after treatment	12.1±1.5	0.27	9.7±0.7	1.57	8.1±0.6	3.53	0.61	0.20	0.19
4 Weeks after treatment	15.4±1.6	−1.87	9.3±0.8	2.00	8.8±0.7	2.29	0.007‡	0.005‡	0.92
13 Weeks after treatment	–		9.6±0.9	1.49	8.8±0.8	2.13	–	–	0.72
ESS									
Baseline	9.4±1.0		8.8±0.6		9.8±0.6				
1 Week after treatment	10.0±1.0	−0.11	8.0±0.6	0.15	8.4±0.6	0.26	0.12	0.02	0.33
4 Weeks after treatment	8.5±1.0	0.16	7.8±0.6	0.18	9.1±0.6	0.12	0.88	0.81	0.65
13 Weeks after treatment	–		7.9±0.7	0.16	9.0±0.6	0.14	–	–	0.87
MFI									
Baseline	67.2±2.1		64.2±1.2		60.6±1.2				
1 Week after treatment	70.5±2.2	−0.28	61.2±1.2	0.25	60.9±1.2	−0.02	0.002‡	0.13	0.006‡
4 Weeks after treatment	69.2±2.2	−0.16	61.9±1.3	0.19	60.8±1.3	−0.01	0.04	0.29	0.10
13 Weeks after treatment	–		63.5±1.4	0.06	61.0±1.3	−0.03	–	–	0.48

*Estimated mean and SE from linear mixed-effects model adjusted for last assessment time.
†P-value for group by time interaction using linear mixed-effects models.
‡Remain significant on Bonferroni adjustment ($p<0.05/3=0.017$).

however, a lack of waitlist control from 4 weeks to 13 weeks after treatment limited the conclusion that the improvements were entirely due to interventions. Subjects in the waitlist group were re-randomised and they showed significant improvements after treatment. Our overall findings suggest that there is limited justification for adding auricular acupuncture to the acupuncture treatment for insomnia.

We found that the mean effect size of acupuncture for sleep-diary-derived TST and SE was 0.45 at 1 week after treatment; for combination treatment, it was 0.23 and 0.26, respectively. Compared with pharmacological and psycho-behavioural therapies, which were shown to have a mean effect size of 0.84 and 0.79 for sleep-diary variables, respectively,[34] acupuncture seems to be less effective. Few randomised controlled trials have been carried out in non-Western populations on pharmacological and psycho-behavioural therapies for insomnia. Watanabe *et al* in Japan found that four sessions of individualised behavioural therapy was more effective for treating residual insomnia associated with major depression than treatment as usual.[35] The effect size based on ISI was 1.0, but sleep-diary variables were not assessed. Another study of self-help cognitive-behavioural therapy for insomnia found that the mean effect size for sleep-diary variables was 0.36.[36] Further studies are needed to clarify the comparative effectiveness of acupuncture and pharmacological and psycho-behavioural therapies in non-Western populations. Our previous study suggested that a positive response to acupuncture in the treatment of insomnia was difficult to predict,[37] but an integrative Chinese–Western diagnostic approach might improve the prediction of treatment response.[38] Further replication studies are needed to understand the use of acupuncture for the treatment of insomnia.

We found that the effect size of acupuncture on ISI and PSQI was higher than that on sleep-diary variables. It is possible that the strong non-specific therapeutic component of acupuncture[39] has a greater impact on insomnia rating scales, which have several items on distress and functional impairment. Compared with the waitlist, we found that acupuncture produced significant improvements in anxiety and depressive symptoms, fatigue and daytime functioning. The overall results are in line with the observation that acupuncture possesses a mild hypnotic effect.

Both acupuncture and combination treatment were acceptable to the participants. The completion rate was 91.7%. The treatments were well-tolerated, as only 2.6% of the participants terminated acupuncture or combination treatment owing to adverse events. The incidence of adverse events was 62.0%, which was much higher than the 7–11% in previous studies (reviewed by Chung *et al*[40]). The use of a standardised adverse event scale in this study might have primed the participants to report discomforts that they initially thought were part of acupuncture treatment and were inappropriate to report as complaints.[40] We found that the adverse events were mostly mild.

Our study has both strengths and some methodological limitations. Our sample size was sufficient to demonstrate a meaningful difference between acupuncture and combination treatment. The dropout rate was 8.9% and 22.3% at 1 week and 4 weeks after treatment, respectively, which was lower than the 25% dropout rate assumption in sample size calculation. Another strength was that we recruited our sample from the community and psychiatric clinics; hence the results were likely to be generalisable. Lastly, we used a well-documented screening process to recruit participants who had moderate severity of insomnia that might require intervention. One of the limitations was that participants were not blind to the treatment allocation. However, there was no difference in creditability rating in participants allocated to acupuncture or combination treatment. Those on the waitlist were eventually provided with treatment without any condition for insomnia severity; hence, the likelihood of over-rating in the waitlist group was low. Another limitation was that we used a standardised acupuncture protocol instead of an individualised treatment, which is more commonly used in a 'real-world' setting. Although the acupuncture procedure in the acupuncture and combination groups was performed by the same acupuncturist, we did not know whether *de qi* was attained similarly in both groups. Finally, our 3-week acupuncture treatment was relatively short and the follow-up of 13 weeks after treatment could reflect only short-term outcomes.

CONCLUSIONS

The attempt to augment acupuncture by auricular acupuncture for the treatment of insomnia was not supported. Although acupuncture had a moderate to large effect size on insomnia rating scales, the improvement in sleep-diary variables was mild. However, acupuncture was considered to be acceptable and well-tolerated and improvement was seen up to at least 13 weeks. Our findings suggest that acupuncture may be considered as an alternative treatment for people who do not accept, or have insufficient response to, pharmacological and psycho-behavioural therapies for insomnia. Further studies are needed to clarify the comparative effectiveness of acupuncture and conventional therapies for insomnia.

Contributors K-FC and W-FY designed the study and drafted the manuscript. W-FY, BY-MY and FC-YL were responsible for data collection and analysis. K-FC and W-FY interpreted the results. Z-JZ, RM-KN and G-CY reviewed the manuscript. All authors declare that they made substantial contributions to the study, including drafting or revising the work; read and approved the final version of the manuscript accepted for publication, and agreed to be accountable for all aspects of

the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding Health and Health Services Research Fund (HHSRF #10111301), Food and Health Bureau, Hong Kong SAR.

Competing interests None.

Patient consent Obtained.

Ethics approval Institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Chung KF, Yeung WF, Ho FY, *et al*. Cross-cultural and comparative epidemiology of insomnia: the Diagnostic and Statistical Manual (DSM), International Classification of Diseases (ICD) and International Classification of Sleep Disorders (ICSD). *Sleep Med* 2015;16:477–82.
2 Schutte-Rodin S, Broch L, Buysse D, *et al*. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008;4:487–504.
3 Krystal AD. The changing perspective on chronic insomnia management. *J Clin Psychiatry* 2004;65(Suppl 8):20–5.
4 Cui J, Wang S, Ren J, *et al*. Use of acupuncture in the USA: changes over a decade (2002-2012). *Acupunct Med* 2017;35:200–7.
5 Yeung WF, Chung KF, Yung KP, *et al*. The use of conventional and complementary therapies for insomnia among Hong Kong Chinese: a telephone survey. *Complement Ther Med* 2014;22:894–902.
6 Chung KF, Yeung WF, Yu YM, *et al*. Acupuncture for residual insomnia associated with major depressive disorder: a placebo- and sham-controlled, subject- and assessor-blind, randomized trial. *J Clin Psychiatry* 2015;76:e752–60.
7 Yeung WF, Chung KF, Tso KC, *et al*. Electroacupuncture for residual insomnia associated with major depressive disorder: a randomized controlled trial. *Sleep* 2011;34:807–15.
8 Yeung WF, Chung KF, Zhang SP, *et al*. Electroacupuncture for primary insomnia: a randomized controlled trial. *Sleep* 2009;32:1039–47.
9 Yeung WF, Chung KF, Poon MM, *et al*. Acupressure, reflexology, and auricular acupressure for insomnia: a systematic review of randomized controlled trials. *Sleep Med* 2012;13:971–84.
10 Huang W, Kutner N, Bliwise DL. Autonomic activation in insomnia: the case for acupuncture. *J Clin Sleep Med* 2011;7:95–102.
11 Zhou J, Li S, Wang Y, *et al*. Effects and mechanisms of auricular electroacupuncture on gastric hypersensitivity in a rodent model of functional dyspepsia. *PLoS One* 2017;12:e0174568.
12 Gao XY, Li YH, Liu K, *et al*. Acupuncture-like stimulation at auricular point Heart evokes cardiovascular inhibition via activating the cardiac-related neurons in the nucleus tractus solitarius. *Brain Res* 2011;1397:19–27.
13 Dm F, Ke R. Acupuncturing at Shenmen point combined with stimulated auricular points for insomnia: clinical research on 60 cases. *J Clin Acup Moxibust* 2014;30:22–4. in Chinese.
14 Bk L. Study on clinical effect of acupuncture combined with ear point tapping in treatment of anhypnia. *Chin Foreign Med* 2016;2:158–9. in Chinese.
15 Yeung WF, Chung KF, Poon MM, *et al*. Prescription of Chinese herbal medicine and selection of acupoints in pattern-based traditional Chinese medicine treatment for insomnia: a systematic review. *Evid Based Complement Alternat Med* 2012;2012:1–16.
16 Mai LM, Lin CY, Chen CY, *et al*. Synergistic effect of bismuth subgallate and borneol, the major components of Sulbogin, on the healing of skin wound. *Biomaterials* 2003;24:3005–12.
17 Wu X. Three hundred cases of borneol auricular pressure treatment for insomnia. *Shanghai J Acup Moxibust* 1991;1:24–5.
18 Wang S, Zhang D, Hu J, *et al*. A clinical and mechanistic study of topical borneol-induced analgesia. *EMBO Mol Med* 2017;9:802–15.
19 Ohtsubo S, Fujita T, Matsushita A, *et al*. Inhibition of the compound action potentials of frog sciatic nerves by aroma oil compounds having various chemical structures. *Pharmacol Res Perspect* 2015;3:e00127.
20 Kunihiro K, Myoda T, Tajima N, *et al*. Volatile components of the essential oil of artemisia montana and their sedative effects. *J Oleo Sci* 2017;66:843–9.
21 Boutron I, Moher D, Altman DG, *et al*. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Ann Intern Med* 2008;148:295–309.
22 MacPherson H, Altman DG, Hammerschlag R, *et al*. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. *Acupunct Med* 2010;28:83–93.
23 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*. 5th ed. Arlington: American Psychiatric Publishing, 2013.
24 Gao XY, Zhang SP, Zhu B, *et al*. Investigation of specificity of auricular acupuncture points in regulation of autonomic function in anesthetized rats. *Auton Neurosci* 2008;138:50–6.
25 Yeung WF, Chung KF, Leung YK, *et al*. Traditional needle acupuncture treatment for insomnia: a systematic review of randomized controlled trials. *Sleep Med* 2009;10:694–704.
26 Buysse DJ, Ancoli-Israel S, Edinger JD, *et al*. Recommendations for a standard research assessment of insomnia. *Sleep* 2006;29:1155–73.
27 Lichstein KL, Stone KC, Donaldson J, *et al*. Actigraphy validation with insomnia. *Sleep* 2006;29:232–9.
28 Chung KF, Yeung WF, Yu YM, *et al*. Adverse events related to acupuncture: development and testing of a rating scale. *Clin J Pain* 2015;31:922–8.
29 Chung KF, Kan KK, Yeung WF. Assessing insomnia in adolescents: comparison of Insomnia Severity Index, Athens Insomnia Scale and Sleep Quality Index. *Sleep Med* 2011;12:463–70.
30 Chung KF, Tang MK. Subjective sleep disturbance and its correlates in middle-aged Hong Kong Chinese women. *Maturitas* 2006;53:396–404.
31 Chung KF, Yu BY, Yung KP, *et al*. Assessment of fatigue using the multidimensional fatigue inventory in patients with major depressive disorder. *Compr Psychiatry* 2014;55:1671–8.
32 Leung CM, Wing YK, Kwong PK, *et al*. Validation of the Chinese-Cantonese version of the hospital anxiety and depression scale and comparison with the Hamilton Rating Scale of Depression. *Acta Psychiatr Scand* 1999;100:456–61.

33 Chung KF. Use of the Epworth Sleepiness Scale in Chinese patients with obstructive sleep apnea and normal hospital employees. *J Psychosom Res* 2000;49:367–72.
34 Smith MT, Perlis ML, Park A, *et al*. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry* 2002;159:5–11.
35 Watanabe N, Furukawa TA, Shimodera S, *et al*. Brief behavioral therapy for refractory insomnia in residual depression: an assessor-blind, randomized controlled trial. *J Clin Psychiatry* 2011;72:1651–8.
36 Ho FY, Chung KF, Yeung WF, *et al*. Weekly brief phone support in self-help cognitive behavioral therapy for insomnia disorder: relevance to adherence and efficacy. *Behav Res Ther* 2014;63:147–56.
37 Yeung WF, Chung KF, Yu YB, *et al*. What predicts a positive response to acupuncture? A secondary analysis of three randomised controlled trials of insomnia. *Acupunct Med* 2017;35:24–9.
38 Chung KF, Yeung WF, Leung CY, *et al*. An integrative Chinese-Western diagnostic approach to predict a positive response to acupuncture. *Acupunct Med* 2017;35:306–8.
39 Yeung WF, Chung KF, Yu BY, *et al*. Response to placebo acupuncture in insomnia: a secondary analysis of three randomized controlled trials. *Sleep Med* 2015;16:1372–6.
40 Chung KF, Yeung WF, Kwok CW, *et al*. Risk factors associated with adverse events of acupuncture: a prospective study. *Acupunct Med* 2014;32:455–62.