THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 20, Number 3, 2014, pp. 147–161

DOI: 10.1089/acm.2013.0238

Review Article

Sham Control Methods Used in Ear-Acupuncture/ Ear-Acupressure Randomized Controlled Trials: A Systematic Review

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Abstract

Ear-acupuncture/ear-acupressure (EAP) has been used for a range of health conditions with numerous randomized controlled trials (RCTs) investigating its efficacy and safety. However, the design of sham interventions in these RCTs varied significantly. This study systematically reviewed RCTs on EAP for all clinical conditions involving a number of sham EAPs as a control intervention. The review is guided by the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 and investigated the types and differences of sham EAP interventions. Four electronic English databases (The Cochrane Library, PubMed, Embase, CINAHL®) and two Chinese databases (CQVIP, CNKI) were searched in December 2012 and 55 published RCTs comparing real and sham EAP for any clinical condition were included. Characteristics of participants, real and sham interventions, and outcomes were extracted. Four types of sham methods were identified. Among the 55 RCTs, 25 studies involved treatment on nonspecific ear acupoints as the sham method; seven studies used nonacupoints on the ear; nine studies selected placebo needles or placebo ear-acupressure on the same ear acupoints for the real treatment; 10 studies employed pseudo-intervention; and five studies combined two of the above methods to be the sham control. Other factors of treatment such as number of points, treatment duration, and frequency also varied greatly. Risk of bias assessment suggests that 32 RCTs were "high risk" in terms of participants blinding, and 45 RCTs were "high risk" in terms of personnel blinding. Meta-analysis was not conducted due to the high clinical heterogeneity across included studies. No relationship was found between the sham designs and efficacy outcomes, or between the sham types and dropout rate. No solid conclusion of which design is the most appropriate sham control of EAP could be drawn in this review.

Introduction

Randomized controlled trials (RCTs) are generally considered the criterion standard experiment to provide evidence for an intervention's efficacy and safety.[1] When researchers aim to differentiate the specific treatment effect from the nonspecific effect of a therapy, a placebo control is appropriate.[2,3] In drug trials, the placebo control usually is inert and designed to be identical to the active intervention, thus reducing the risk of unblinding the participants to their group allocation. However, if the intervention to be tested is a physical procedure, the design of the control methods becomes more complex. "Sham" is the term used to refer to a faked operative intervention used in the same manner as a placebo to enable blinding and reduce bias.

The methodological difficulties in designing appropriate sham controls for manual or physical therapies such as acupuncture have attracted considerable research but remained challenging.[4] A recent meta-analysis on individual data of 17,922 randomized patients from 23 high-quality RCTs concluded that the total effects of acupuncture consist of specific effects associated with needle insertion according to acupuncture theory, nonspecific physiologic effects of needling, and nonspecific psychological (placebo) effects related to the patient's belief that the treatment is effective.[5] In order to determine the specific effects of the intervention by controlling for any placebo effect (nonspecific effects), it is important that the control group experience the same placebo effect as the intervention group. Therefore, it is essential that participants be blinded and remain blind to their group allocation.[6]

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Sham acupuncture methods can be broadly categorized into five approaches[2]: (1) superficial needling of the same points used in the treatment arm; (2) needling of irrelevant acupuncture points; (3) needling nonacupoints; (4) placebo needles; and (5) pseudo-interventions (interventions that are not "true" acupuncture; e.g., use of switched-off laser acupuncture devices). Among them, the stimulating of "non-acupoints" method was the most commonly used design and has been used in many acupuncture RCTs.[7,8] However, the review by Dincer et al. (2003) did not find any link between the type of sham acupuncture method used and the reported clinical trial results.[2]

Ear-acupuncture/ear-acupressure (EAP), which applies stimulation to ear acupoints, is a subtype of acupuncture. Similar to the RCTs on acupuncture or other physical interventions, sham control methods have been used in EAP studies. According to the latest version of National Standards of China on Nomenclature and Location of Auricular Points,[9] there are 93 specific acupoints located on the ear. Clinically, the ear acupoints are commonly stimulated by needling, seed/pellet pressing, electrostimulation, or laser stimulation to achieve therapeutic effects.[10] In clinical research, sham EAP methods have been varied. These include nonspecific points, nonacupoints, and other sham methods used in body acupuncture but, unlike body acupuncture, it is difficult to locate any nonacupoints or apply superficial needling on the ear to be the sham design, due to the small size of the ear and the large number of identified acupoints. However, which design is the most appropriate sham EAP remains unclear. Therefore, we conducted this systematic review to investigate the sham control procedures utilized in EAP RCTs, and to explore whether the type of sham control used is related to efficacy results and dropout rates in the RCTs.

Methods

This review was conducted following the methods specified in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.[11]

Search strategy

Four electronic English databases (The Cochrane Library, PubMed, Embase, CINAHL®) and two Chinese databases (CQVIP, CNKI) were searched from their respective inceptions to December 2012. Search terms were in two blocks: (1) ear acupuncture, auricular acupuncture, ear acupressure, and related terms; and (2) RCT, clinical trial, and related terms. Full lists of search terms are available on request. The two groups of terms were combined and the results were downloaded to an Endnote library.

Study selection

Upon the completion of the searches of the electronic databases, two independent reviewers (CZ and AY) screened all study titles and abstracts. Full-text articles were retrieved where necessary to confirm eligibility. Any disagreement between the reviewers was resolved by a third-party researcher (AZ).

RCTs were included if they were published in English or Chinese, and used any type of ear-acupuncture or ear-acupressure (such as needle insertion into ear points, electrical stimulation on ear points, laser stimulation on ear points, seeds, stainless steel pellets, or magnetic pellets attached on ear points) as the intervention, and any type of sham/placebo ear-acupuncture or ear-acupressure control as comparator, even if the term "sham/placebo" is not mentioned in the article. RCTs comparing EAP with other treatments were excluded. Co-intervention was permitted as long as the same co-intervention was involved in all arms of the RCT. If a study consists of more than two arms, only the real EAP and the sham EAP arms are included in this review.

Data extraction

Data were extracted by two reviews (CZ and AY) independently using a predefined Excel form. Extracted data included trial setting, year, country, condition treated, characteristics of participants, real and sham interventions, outcome measures, duration, efficacy results, and dropouts.

Classification of EAP stimulation

First, all RCTs were categorized into four types of EAP intervention according to the real treatment stimulation: ear-acupuncture with needles, ear-acupressure with pellets or seeds, electro-ear-acupuncture, and laser-ear-stimulation. Then, RCTs in each category were categorized in line with the method of sham intervention and the condition being treated.

Descriptive analysis of included studies

Once studies had been clustered according to the real treatment type, sham method, and the condition, the details of the real and sham interventions were then examined, including the number and location of ear acupoints, and number and duration of treatment sessions. The results for the primary outcome measures were summarized as: T > C (real treatment group was significantly superior to sham control group) and ND (no differences between real and sham groups) (Table 1). For the RCTs that claimed "T > C" but did not conduct between-group statistical analysis, if original data were available, effect size analysis, (risk ratio or mean difference with 95% confidence interval), was conducted to determine the between-group differences. If original data were not available, the study was listed as ""T > C"?" (Table 1).

Categorizing the sham types

Sham methods were categorized into four types as in a previous review on acupuncture sham designs[2] but excluding superficial needling technique, which is not possible in EAP:

I. Same treatment on ear acupoints that are not theoretically effective for the condition
II. Same treatment on nonacupoints on the ear
III. Placebo needles or adhesive patches without pellet/seed on the same ear acupoints as experimental group
IV. Pseudo-interventions (e.g., switched-off laser acupuncture devices, electro- acupuncture devices with minimum emission, Vaccaria seeds without pressing) on the same ear acupoints as experimental group (Table 2).

Table 1. Characteristics of 55 Randomized Controlled Trials Included in This Review

Ear-acupuncture sham control RCTs

Sham control type	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Duration (minutes) of each treatment session/no. of treatment sessions/ total treatment period*	*Credibility of blinding of participants*	*Primary outcome measures*	*Results*
Type I	Anxiety	Wang, 2001	59/NS US	32/27	3/3	NS	Unilateral	30/1/30 min	NS	STAI score	T>C
		Wang, 2004	67/0 US	34/33	3/3	NS	Unilateral	30–80/1/30–80 min	NS	Mother's STAI score	T>C
		Michalek-Sauberer, 2012	121/0 Austria	61/60	3/3	NS	Unilateral	20/1/20 min	Tested	STAI score	T>C
	Pain	Wang, 2009a	159/7 US	58/54	3/3	NS	Unilateral	1 wk[a]/1/1 wk	NS	30% Pain reduction rate	T>C
		Allais, 2011	94/5 Italy	43/46	1/1	Using pain-pressure test, no sensation	Bilateral	NS/NS/NS	NS	Pain VAS	T>C
	Drug dependence	Avants, 2000	55/25 US	13/17	4/4	NS	Bilateral	40/40/8 wks	NS	Urine drug-negative cases	T>C
		Berman, 2004	158/82 Sweden	32/44	5/5	NS	Bilateral	40/14/4 wks	NS	Urine drug-positive rate	ND
		Bullock, 1999	236/NS US	NS	5/5	Confirmed by galvanometric response	Bilateral	45/28/4 wks	NS	Urine drug-positive rate	ND
		Killeen, 2002	30/0 US	15/15	5/5	NS	NS	40/1/40 min	NS	Cocaine craving score	ND
		Lipton, 1994	192/42 US	73/77	4/4	NS	NS	45/10/1 month	NS	Urine drug-positive rate	ND
		Margolin, 2002	425/232 US	100/93	4/3	NS	Bilateral	40/40/14 d	NS	Urine drug-positive rate	ND
		Washburn, 1993	100/80 US	16/4	4/4	NS	Bilateral	20–45/5/21 d	NS	Self-reported drug use	T>C
	Smoking cessation	Wu, 2007	131/13 Taiwan	59/59	4/4	NS	NS	1 wk[a]/8/8 wks	NS	Smoking cessation rate	ND
	Alcohol dependence	Bullock, 2002	503/150 US	132/133	4/4	Confirmed by galvanometric response	NS	40/18/3 wks	NS	Breathe test, Alcohol Dependence Scale, Alcohol Severity Index	ND
		Sapir-Weise, 1999	72/36 Sweden	21/15	3/3	NS	Bilateral	45/20/10 wks	NS	Successful drinking pattern	ND
	Overweight	Shen, 2009	14/1 Taiwan	6/7	4/4	NS	Unilateral	1 wk[a]/4/4 wks	NS	Body weight	"T>C"?
	Insomnia	Sjoling, 2008	28/0 Sweden	14/14	5/5	NS	Bilateral	45/15/6 wks	NS	Karolinska Sleep Diary	T>C
Type II	Pain	Alimi, 2003	90/11 France	29/30	3/3	Using an electrical probe	NS	NS/2/60 d	NS	Pain VAS	T>C
		Usichenko, 2005	61/7 Germany	28/23	5/5	NS	NS	3 d[a]/1/3 d	Tested	Pain medication use	T>C
		Usichenko, 2007	120/15 Germany	29/25	4/4	NS	NS	1 d[a]/1/1 d	NS	Pain medication use	T>C
		Wetzel, 2011	120/4 Germany	57/59	3/3	NS	Unilateral	1 d [a]/1/1 d	Tested	Analgesic medication use	T>C
	Anxiety in drug withdrawal	Black, 2011	140/91 Canada	15/19	4/4	NS	Bilateral	45/3/2 wks	NS	STAI score	ND
Type III	Pain	Wang, 2012	60/0 China	31/29	4/4	NS	Bilateral	3 d[a]/1/3 d	NS	Pain medication use	T>C
	Obesity	Hsu, 2009	60/15 Taiwan	23/22	5/5	NS	Unilateral	NS/12/6 wks	NS	Body weight, BMI, WC and HC	ND
Type I+III	Anxiety	Karst, 2007	38/0 Germany	19/19	3/2	NS	NS	Surgery period/1/ surgery period	NS	STAI scores, Anxiety VAS	ND
Type I+IV	Pain	Simmons, 1993	40/0 US	10/10	5/5	NS	Unilateral	15/1/15 min	NS	Pain threshold	T>C

Ear-acupressure sham control RCTs

Sham control method	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Each pressing session (min), no. of pressing sessions each d*	*Total treatment period*	*Credibility of blinding of participants*	*Primary outcome measures*	*Results*
Type I	Anxiety and pain	Barker, 2006	38/0 Austria	18/20	3/1	NS	Bilateral	Ambulance transport/1/ Ambulance transport		NS	Anxiety VAS and Pain VAS	T>C
	Anxiety	Kober, 2003	36/0 Austria	17/19	1/1	NS	Bilateral	Ambulance transport/1/ Ambulance transport		NS	Anxiety VAS	T>C
		Mora, 2007	100/0 Italy	50/50	1/1	NS	Bilateral	Ambulance transport/1/ Ambulance transport		NS	Anxiety VAS	T>C
	Insomnia	Pi, 2002	300/47 China	132/121	5/3	NS	Bilateral	3/3	8 wks	NS	PSQI score	T>C reconfirmed

(*continued*)

TABLE 1. (CONTINUED)

Ear-acupressure sham control RCTs

Sham control method	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Each pressing session (min), no. of pressing sessions each d*	*Total treatment period*	*Credibility of blinding of participants*	*Primary outcome measures*	*Results*
	Nausea and vomiting	Yeh, 2012	20/0 Taiwan	10/10	5/4	Using an electrical detector	NS	3/3	7 d	NS	Morrow Assessment of Nausea and Emetics	ND
	COPD	Cao, 2012	30/0 China	15/15	5/5	NS	NS	NS/3	20 d	NS	Lung function (FEV_1, FEV_1/FVC)	T>C reconfirmed
	Allergic rhinitis	Xue, 2011	63/8 Australia	31/32	5/5	NS	Bilateral	1–2/3	8 wks	Tested	Symptom score and quality of life score	T>C
Type II	Drug dependence	Tian, 2006	17/4 US	5/4	5/2	NS	Bilateral	1–2/when craving	6 wks	Tested	SCL-20 Depression Scale	"T>C"?
	Insomnia	Ye, 2011	64/0 China	32/32	7/7	NS	Unilateral	3–5/5	NS	NS	PSQI score<7 rate	T>C
Type III	Primary dysmenorrhea	Wang, 2009	74/3 Taiwan	36/35	3/3	NS	NS	15/3	20 d	NS	Menstrual Distress Questionnaire	T>C
	Pain	Chang, 2012	62/0 Taiwan	31/31	2/2	NS	NS	3/3	3 d	NS	Pain score, medication use	T>C
	Anxiety	Li, 2011	62/0 China	31/31	7/7; 3/3	Using an electrical detector	Bilateral	3–5/3–5	30 d	NS	Anxiety score	T>C
		Kao, 2012	50/6 Taiwan	25/19	4/4	NS	Bilateral	No pressing	8 wks	NS	Medication use	T>C reconfirmed
	Drug dependence	Wei, 2011	60/0 China	30/30	6/6	Using an electrical detector	Bilateral	5/3	30 d	NS	Symptom score Chinese version	T>C
Type III	Obesity	Hsieh, 2010	100/16 Taiwan	27/28	4/4	NS	Bilateral	5/3	6 wks	NS	Kupperman scale, hormone test	T>C
	Menstrual disorders	Jin, 2011	276/21 China	126/129	4/4	NS	Bilateral	5/3	6 wks	NS	Kupperman scale, hormone test	T>C
Type I+III	Obesity	Abdi, 2012	204/35 Iran	86/83	**6/4**	NS	Bilateral	20 s/before eating	6 wks	NS	Body weight, BMI	T>C reconfirmed

Electro-ear-acupuncture RCTs

Sham control method	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Duration of each treatment session/ no. of treatment sessions/ total treatment period*	*Credibility of blinding*	*Primary outcome measures*	*Results*
Type I	Nausea and vomiting	Li, 2012	240/0 China	80/80	1/1	NS	NS	Surgery period/1/ surgery period	NS	Percentage of patients who had nausea and vomiting	T>C
Type IV	Pain	Michalek-Sauberer, 2007	113/39 Austria	48/26	3/3	Using a point-finding device	Unilateral	48 h/1/48 h	NS	Medication use	ND
		Sator-Katzenschlager, 2004	61/6 Austria	31/30	3/3	Using an electrical detector	Unilateral	48 h/6/6 wks	NS	Reduction of pain intensity	T>C
		Sator-K Katzenschlager, 2003	23/2 Austria	11/10,	4/4	Using an electrical detector	Unilateral	48 h/6/6 wks	NS	Reduction of pain intensity	T>C
		Sator-K Katzenschlager, 2006	94/1 Austria	32/32	3/3	Using an electrical detector	Unilateral	Surgery period/1/ surgery period	NS	Pain VAS	T>C
		Holzer, 2011	40/0 Austria	20/20	3/3	NS	Unilateral	72 h/1/72 h	NS	Overall pain score	ND
	Nausea and vomiting	Li, 2012	240/0 China	80/80	1/1	NS	NS	Surgery period/1/ surgery period	NS	Nausea rate	T>C

(*continued*)

TABLE 1. (CONTINUED)

Electro-ear-acupuncture RCTs

Sham control method	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Duration of each treatment session/ no. of treatment sessions/ total treatment period*	*Credibility of blinding*	*Primary outcome measures*	*Results*
Type II+IV	Smoking cessation	Waite, 1998	78/0 US	40/38	1/1	Using an electrical detector	Bilateral	1 needling session+ pellets/pellets remained as long as being helpful	NS	Smoking cessation rate	ND
	Smoking cessation	White, 1998	76/24 Germany	27/25	1/1	NS	Bilateral	20 min/3/7 d	NS	Withdrawal symptom score	ND

Laser-ear-stimulation RCTs

Sham control method	*Condition*	*Author, year*	*Total sample size and dropout (N/n), county*	*Analyzed sample size (T/C)*	*No. of ear points (T/C)*	*How to locate the ear points*	*Unilateral or bilateral*	*Duration of each treatment session/ no. of treatment sessions/ total treatment period*	*Credibility of blinding*	*Primary outcome measures*	*Results*
Type IV	Pain	Mazzetto, 2007	48/NS Brazil	24/24	1/1	NS	Bilateral	NS/8/4 wks	NS	Pain VAS	"T>C"?
	Alcohol withdrawal	Trumpler, 2003	49/1 Switzerland	17/16	2–10 (median 8)	Using an electrical detector	NS	30–45 min/1 per d until withdrawal	NS	Duration of withdrawal	ND
	Smoking cessation	Cai, 2000	268/60 Singapore	101/107	4/4	NS	Unilateral	4 min/12/4 wks	NS	Smoking cessation rate	ND
	Balance control	Bergamaschi, 2011	25/0 Italy	9/16	NS	Using an electrical detector	NS	15 min/1/15 min	NS	Balance test	ND

[a]Needles remained in ear-acupuncture treatment.

Results: T>C: Between-group difference reported by the study (treatment group significantly more effective than control group); "T>C"?: Within-group difference reported by the study and no data provided for further analysis; T>C reconfirmed: Within-group difference reported by the study and between-group difference was reconfirmed in this review.

T, treatment group; C, control group; COPD, chronic obstructive pulmonary disease; NS, not stated; ND, no differences between treatment and control groups; VAS, Visual Analogue Scale; BMI, body–mass index; WC, waist circumference; STAI, State-Trait Anxiety Inventory; FEV_1, forced expiratory volume in 1 s; HC, hip circumference; FVC, forced vital capacity; PSQI, Pittsburgh Sleep Quality Index; SCL-20, The 20-item Symptom Checklist Depression Scale; RCTs, randomized controlled trials.

Table 2. Sham Methods Used in the 55 Randomized Controlled Trials

Type of sham methods		*Points used for sham compare with real interventions*	*Stimulation of sham methods compare with real interventions*	*No. of RCTs*	*References*
Type I	Same treatment on ear acupoints that are not theoretically effective for the condition (nonspecific ear acupoints)	Different points	Same stimulation	25	12–14, 17, 20–23, 27–29, 32, 36, 37, 43–46, 48, 51, 57, 59, 60, 64, 66
Type II	Same treatment on nonacupoints on the ear	Different points	Same stimulation	7	19, 38, 40, 41, 50, 63, 65
Type III	Placebo needles or adhesive patches without pellet/seed on the same ear acupoints	Same points	Less or no stimulation	9	25, 42, 52, 54–56, 58, 61, 62
Type IV	Pseudo-interventions (e.g., switched off laser acupuncture devices, electro-acupuncture devices with minimum emission, Vaccaria seeds without pressing) on the same ear acupoints	Same points	Less or no stimulation	10	24, 30, 31, 33–35, 39, 49, 53, 57
Type I+ Type III	Placebo pellets (adhesive patches without pellet/seed) on nonspecific ear acupoints	Different points	Less or no stimulation	2	26, 47
Type I+ Type IV	No electrical stimulation on nonspecific ear acupoints	Different points	Less or no stimulation	1	15
Type II+ Type IV	Electro-acupuncture on nonacupoints on the ear, with pseudostimulation	Different points	Less or no stimulation	2	16, 18

One RCT employed two types of sham methods (Type I and Type IV) in two control arms (Li, 2011 study).

Risk of bias assessment

The methodological quality of each included RCT was assessed by two reviewers (CZ and AY) using the Cochrane Collaboration's tool for assessing risk of bias in the Cochrane Review Manager (RevMan) 5.1.[11] Risk of bias for blinding was judged separately for participants and personnel, since blinding is the primary issue as regards the type of control method. Therefore, bias was assessed in seven categories: random sequence generation, allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessors, incomplete outcome data, and selective reporting. The main issue for this review as regards "incomplete outcome data" was the effect of dropouts. The judgments were entered into RevMan and a graph was generated.

Efficacy

Variations of clinical conditions, treatment methods, and outcome measures were expected in this review, and thus it is not appropriate to pool the efficacy data for meta-analysis. Therefore, the efficacy results of included RCTs were summarized within the categories of sham types and clinical conditions and are presented in Table 3.

Statistical analysis

Chi-square analysis was conducted to discover whether the sham designs are associated with dropout rate or efficacy results of RCTs.

Results

A total of 92 potentially relevant articles were identified, and 55 studies involving 5,844 participants were included in the review. The study selection process is shown in Figure 1.

Description of included studies

Of 55 RCTs, seven studies were published between 1990 and 1999,[12–18] 28 were between 2000 and 2009,[19–46] and 20 were published after 2010.[47–66] Clinical conditions treated included pain (15 studies),[15,19,30,31,33–35,40,41,43,48,52,53,61,63] anxiety (10 studies),[21,26,28,32,44,45,50,56,58,59] substance abuse (alcohol, drug, or smoking) (16 studies),[12–14,16–18,20,22–24,27,29,38,39,46,62] obesity/overweight (four studies),[25,36,47,54] insomnia (three studies),[37,60,65] nausea and vomiting (two studies),[57,66] chronic obstructive pulmonary disease (one study),[51] allergic rhinitis (one study),[64] primary dysmenorrhea (one study),[42] menstrual disorders (one study),[55] and balance control (one study).[49] Among the 55 RCTs, one study employed two sham control arms[57]; all other RCTs included one sham control arm with or without other control arms such as usual care or conventional medication treatment (Table 1).

Twenty-six (26) studies[12–15,17,19,20,22,23,25–27,29,36,37,40,41,43–46,48,50,59,61,63] utilized ear-acupuncture; 17 studies[21,28,32,38,42,47,51,52,54–56,58,60,62,64–66] used ear-acupressure; eight studies used electro-ear-acupuncture,[16,18,31,33–35,53,57] and four[24,30,39,49] employed laser-ear-stimulation as the intervention. Except for three studies that lacked information on the number of acupoints,[39,49,54] seven studies chose more points for the real intervention than for the sham intervention,[21,26,29,38,47,60,66] and the others used equal numbers of acupoints for real and sham interventions. The number of acupoints used ranged from one point[16,28,30,32,48,57] to seven points.[65] To locate the acupoints, 14 studies employed a point-detecting device,[12,16,19,23,31,33–35,39,48,49,58,62,66] while others did not provide any information. With regard to the treatment sessions and duration, one study did not report any details[48]; among the others, the total number of countable treatment sessions ranged from one session[15,16,21,26–28,32,40,43–45,48,49,53,57,59,63] to 168 sessions.[60,64] Total duration of treatment varied from 15 minutes[49] to 8 weeks.[12,54,60,64] For the RCTs with multiple treatment sessions, the frequency of ear-acupuncture or electro/laser ear-acupuncture was from one session within 30 days[19] to one session each day,[29] while the ear-acupressure pellets/seeds were pressed three to five times a day[42,51,52,55,58,60,62,64,66] or as needed.[38,47,67] *De qi* sensation was mentioned in two RCTs.[55,58] The characteristics of the included studies are summarized in Table 1.

Sham types

Among the 55 RCTs, 25 studies used Type I sham;[12–14,17,20–23,27–29,32,36,37,43–46,48,51,57,59,60,64,66] seven studies were with Type II,[19,38,40,41,50,63,65] nine studies used Type III,[25,42,52,54–56,58,61,62] and 10 studies employed Type IV sham for the control group[24,30,31,33–35,39,49,53,57] (Table 2).

For the 25 RCTs that selected nonspecific points (Type I) for sham control, eight studies used points located on the helix or ear lobe,[20,22,27,29,37,57,59,64] three trials used points at the tip of the concha,[28,32,45] five studies located nonspecific ear points within 5 mm from the real treatment points,[12–14,17,23] and one study chose back of the ear to locate sham points.[51] The other eight trials did not provide the principles for selecting the nonspecific ear points.[21,36,43,44,46,48,60,66] Seven trials used nonacupoints on the ear (Type II) as the sham control points[19,38,40,41,50,63,65]; however, only one of them used an electrical probe to confirm that the sham areas were not acupoints.[19] Type III sham design was applied in nine studies; two of them employed placebo needles (needles with blunt tips)[25,61] and seven studies[42,52,54–56,58,62] taped adhesive patches (without pellets/seeds) on the same ear points as were used in the real groups. In addition, one RCT with two sham control arms used two types of methods (Type I and Type IV), respectively.[57]

Furthermore, some studies used a combination of two types of sham: Type I + III in two studies,[26,47] Type I + IV in one study,[15] and Type II + IV[16,18] in two studies (Table 2).

Risk of bias assessment

Risk of bias assessment results are summarized in Figure 2.

Sixty percent (60%) of studies ($n = 33$) were judged as low risk for randomization and 29% ($n = 16$) were low risk for allocation concealment. For blinding, 22 RCTs[13,14,17,22,24,25,27,28,30,32,36,37,40,41,44–46,48,49,51,63,64] were classified "low risk" of participant blinding by providing a sham treatment using the same number of points, same level of stimulation and same treatment duration, although only three of them[40,63,64] proved it successful by conducting a credibility of blinding test. Thirty-two (32) studies were judged "high risk" because fewer points or less intensity of stimulation was applied to the sham group.[12,15,16,18–21,23,26,29,31,33–35,38,39,42,43,47,50,52–62,66] One study was "unclear" due to lack of information.[65] Forty-five (45) RCTs[12–23,25–27,29,31,36–38,40–48,50–52,54–66] were assessed as "high risk" for practitioner blinding because the one practitioner who delivered both

Table 3. Summary of Efficacy Results of Randomized Controlled Trials

Conditions	*No. of RCTs with different sham methods and efficacy results*						
	Sham type I	*Sham type II*	*Sham type III*	*Sham type IV*	*Sham type I+III*	*Sham type I+IV*	*Sham type II+IV*
Anxiety 10 RCTs	T>C: 6 RCTs	ND: 1 RCT	T>C: 1 RCT; T>C reconfirmed: 1 RCT		ND: 1 RCT		
Pain 15 RCTs	T>C: 2 RCTs	T>C: 4 RCTs	T>C: 2 RCTs	T>C: 3 RCTs; "T>C"?: 1 RCT; ND: 2 RCTs		T>C: 1 RCT	
Substance abuse (Alcohol, drug, smoking) 16 RCTs	T>C: 2 RCTs; ND: 8 RCTs	"T>C"?: 1 RCT	T>C: 1 RCT	ND: 2 RCTs			ND: 2 RCTs
Obesity 4 RCTs	"T>C"?: 1 RCT		T>C reconfirmed: 1 RCT; ND: 1 RCT		T>C: 1 RCT		
Insomnia 3 RCTs	T>C: 1 RCTs; T>C reconfirmed: 1 RCT	T>C: 1 RCT					
Other conditions 7 RCTs	T>C: 1 RCTs; ND: 2 RCTs T>C reconfirmed: 1 RCT		T>C: 2 RCTs	T>C: 1 RCT; ND: 1 RCT			

One RCT employed two types of sham methods (Type I and Type IV) in two control arms (Li, 2011 study).

Results: T>C: Between-group difference reported by the study (treatment group significantly more effective than control group); "T>C"?: Within-group difference reported by the study and no data provided for further analysis; T>C reconfirmed: Within-group difference reported by the study and between-group difference was reconfirmed in this review.

T, treatment group; C, control group; ND, no differences between treatment and control groups.

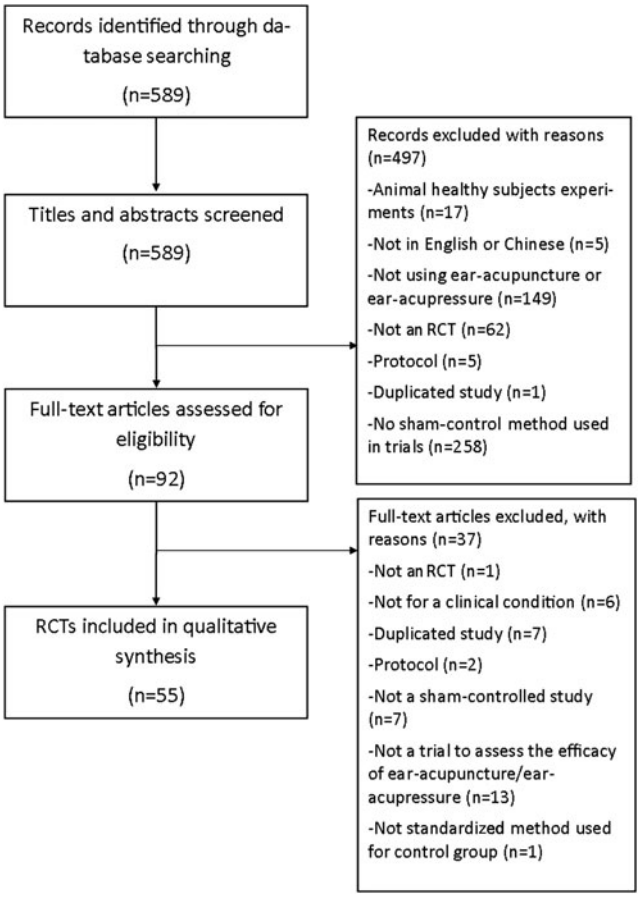

FIG. 1. Flowchart of study selection process. RCT, randomized controlled trial.

real and sham treatments must be aware of group allocation. Eight studies[28,30,32–35,39,53] employed different practitioners for the real and sham groups, so those studies were assessed as "low risk." The other two studies were "unclear" due to lack of information.[24,49] Regarding the blinding of outcome assessors, two studies[38,65] were assessed as "high risk" because the person who delivered treatments was also the outcome assessor; 26 RCTs[12–15,18,21,23,24,26,28,29,32,35,39–41,43,44,48,50,52,53,56,59,63,64] employed independent blinded persons to assess outcomes, hence they were assessed as "low risk." The other 27 studies were "unclear" because no such information was provided. Twenty (20) RCTs[12–14,16,17,20,22–25,29,31,38,40,45,47,48,54,56,60] were assessed as "high risk" for incomplete data because these studies did not include subjects who dropped out in post-treatment data analysis and the high dropout rate is likely to cause attrition bias. Seventeen (17) studies were "low risk" due to no dropout or few dropouts.[16,19,21,27,28,32,34–36,39,42,46,50,52,59,63,66] Others were "unclear" due to not providing information on this aspect. Selective reporting was judged as low risk in all studies since all outcome measures specified in the methods sections of the journal articles were also reported in the results.

Credibility of blinding

Among the 55 RCTs, five studies reported successful participant blinding by conducting a credibility of blinding test.[38,40,59,63,64] No study conducted this test on outcome assessors.

Trial efficacy results

Twenty-nine (29) trials reported that the real EAP groups had a significant superiority over the sham control groups.[15,17,19,21,28,32–35,37,40–45,48,52,54,55,57–59,61–65] Nineteen (19) studies found that there were no significant differences between the real and sham groups.[12–14,16,18,22–27,29,31,39,46,49,50,53,66] The remaining seven studies did not conduct between-group statistical analysis, four of which were confirmed as T>C by extracting published data and performing effect-size analysis. These are stated as "T>C, reconfirmed,"[47,51,56,60] and another three studies without original data were stated as ""T>C"?".[30,36,38] No studies found the sham group to be superior. The efficacies of the included RCTs are presented in Table 1, and summarized in Table 3.

Dropout rate

Thirty-two (32) studies reported dropouts,[8,13,14,17–20,22–25,29,31,33–36,38–43,46–48,50,54–56,60,63] three studies did not provide information about participants' completion/dropouts,[22,30,45] and others had no dropout. When analyzing the dropout rate of real or sham EAP groups, 10 studies[8,12,13,26,30,34,43,45,49,54] without sufficient data of this aspect were excluded. As a result, the total dropout rate among 45 included studies was 21.25%, with 20.69% in the real and 20.52% in the sham EAP groups ($X^2=0.020$, $df=1$, $p=0.888$) (Table 4). The reasons for

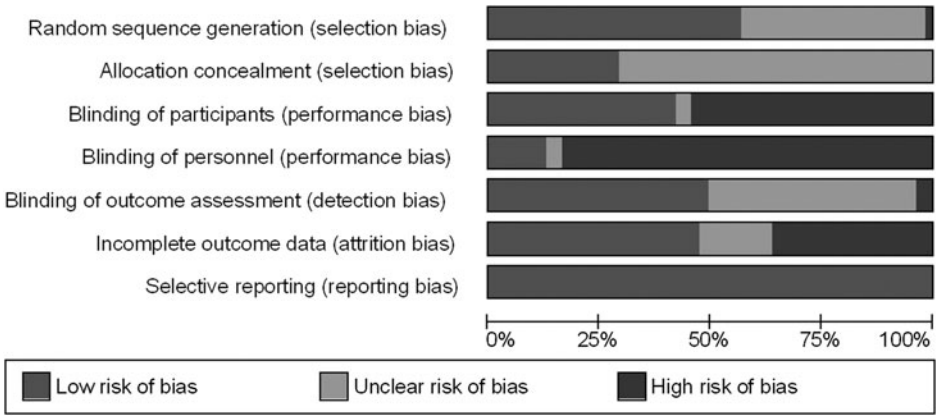

FIG. 2. Graph detailing risk of bias assessment.

Table 4. Summary of Dropout Rate Based on Sufficient Data

Dropout rate in studies by sham type							
Sham types		Type I (20 RCTs), (*n*/*N*)%	Type II (7 RCTs), (*n*/*N*)%	Type III (8 RCTs), (*n*/*N*)%	Type IV (7 RCTs), (*n*/*N*)%	Other combinations (4 RCTs), (*n*/*N*)%	All 45 RCTs, (*n*/*N*)%
Dropout number/ sample size, and dropout rate	Real EAP groups	(315/1139) 27.65%	(45/264) 17.05%	(22/355) 6.20%	(57/384) 14.84%	(27/190) 14.21%	(466/2252) 20.69%
	Sham EAP groups	(288/1105) 26.06%	(57/271) 21.03%	(23/349) 6.59%	(49/355) 13.80%	(32/188) 17.02%	(449/2188) 20.52%
	Total	(775/2784) 27.83%	(105/612) 17.16%	(45/704) 6.39%	(106/871) 12.17%	(59/378) 15.61%	(1090/5129) 21.25%
Between real/sham group analysis		$X^2=0.724$, $df=1$, $p=0.395$	$X^2=1.428$, $df=1$, $p=0.232$	$X^2=0.045$, $df=1$, $p=0.831$	$X^2=0.327$, $df=1$ $p=0.567$	$X^2=0.567$, $df=1$ $p=0.452$	$X^2=0.020$, $df=1$, $p=0.888$
Dropout rate in studies by condition treated							
Conditions		Pain (12 RCTs), (*n*/*N*)%	Anxiety (7 RCTs), (*n*/*N*)%	Substance abuse (15 RCTs), (*n*/*N*)%	Insomnia (3 RCTs), (*n*/*N*)%	Obese/overweight (3 RCTs), (*n*/*N*)%	Other conditions (5 RCTs), (*n*/*N*)%
Dropout number/ sample size, and dropout rate	Real EAP groups	(47/458) 10.26%	(2/238) 0.84%	(362/941) 38.47%	(18/196) 9.18%	(24/139) 17.26%	(13/280) 4.64%
	Sham EAP groups	(37/416) 8.89%	(4/236) 1.69%	(351/921) 38.11%	(19/196) 9.69%	(27/139) 19.42%	(11/280) 3.92%
	Total	(87/961) 9.05%	(6/474) 1.27%	(885/2384) 37.12%	(37/392) 9.43%	(51/278) 18.35%	(24/640) 3.75%
Between real/ sham group analysis		$X^2=0.469$, $df=1$, $p=0.493$	$X^2=0.692$, $df=1$, $p=0.405$	$X^2=0.025$, $df=1$, $p=0.873$	$X^2=0.030$, $df=1$, $p=0.863$	$X^2=0.216$, $df=1$, $p=0.642$	$X^2=0.174$, $df=1$, $p=0.676$

One RCT employed two types of sham methods (Type I and Type IV) in two control arms (Li, 2011 study).
EAP, ear-acupuncture/ear-acupressure; *n*, number of dropouts; *N*, number of randomized participants.

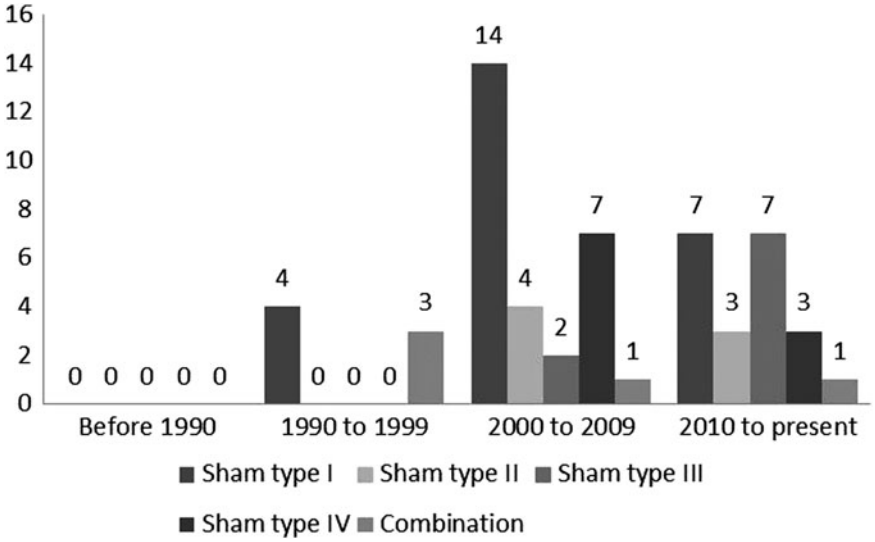

FIG. 3. Number of published randomized controlled trials of ear-acupuncture/ear-acupressure by sham type used and year of publication. Sham type I: Same treatment on ear acupoints that are not theoretically effective for the condition (nonspecific ear acupoints); Sham type II: Same treatment on nonacupoints on the ear; Sham type III: Placebo needles or adhesive patches without pellet/seed on the same ear acupoints; Sham type IV: Pseudo-interventions (e.g., switched-off laser acupuncture devices, electroacupuncture devices with minimum emission, Vaccaria seeds without pressing) on the same ear acupoints. Combination: combination of more than one sham type.

dropouts reported by the RCTs included loss of contact, participants being unsatisfied with the treatment effect or who suffered from adverse events. No RCT reported dropouts due to the belief of being allocated to the sham group. The total dropout rates across sham types varied from 6.59% (sham type III RCTs) to 27.83% (sham type I RCTs), there was no significant difference between real and sham EAP groups for any sham type (Table 4). When the 45 studies were grouped according to the conditions, the lowest dropout rate was in anxiety RCTs (1.27%) and the highest dropout rate was in substance-abuse RCTs (37.12%), but there was no difference between real and sham groups for any condition (Table 4).

Relations between sham types and other factors

All included RCTs were published after 1990, and the number of published studies increased from seven in the decade 1990–1999 to 28 in the decade 2000–2009, with 20 being published between 2010 and 2012. Sham Type I and II appeared between 1990 and 1999, while the other three types appeared in or after 2000 (Fig. 3).

Figure 4 indicates that Sham type I was commonly used in ear-acupressure and ear-acupuncture trials, while Sham type IV was commonly used in electro/laser ear-acupuncture trials and Sham type III was most common in ear-acupressure. Figure 5 shows that Sham type I dominates the substance abuse and anxiety studies while Sham type IV is most common in studies of pain.

No relationship was found between Sham types I–IV and trial outcomes, but it was still possible that differences in methods between real and sham groups had an effect, so comparisons between trials that used equal or unequal number of acupoints, same or different intensity of stimulation, and same or different acupoints were investigated. None of these factors were found to significantly affect efficacy outcomes (Table 5).

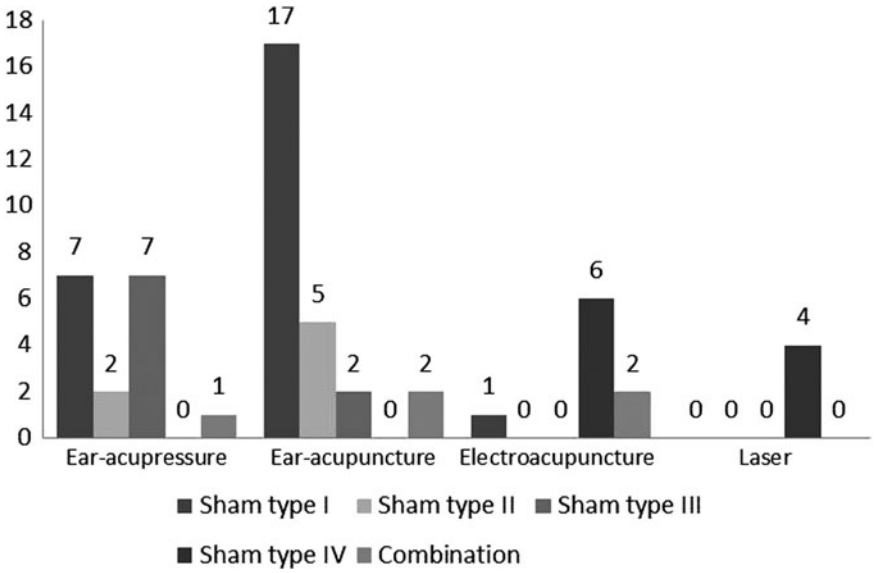

FIG. 4. Number of published randomized controlled trials of ear-acupuncture/ear-acupressure (EAP) by sham type used and EAP method. Sham type I: Same treatment on ear acupoints that are not theoretically effective for the condition (nonspecific ear acupoints); Sham type II: Same treatment on nonacupoints on the ear; Sham type III: Placebo needles or adhesive patches without pellet/seed on the same ear acupoints; Sham type IV: Pseudo-interventions (e.g., switched-off laser acupuncture devices, electroacupuncture devices with minimum emission, Vaccaria seeds without pressing) on the same ear acupoints. Combination: combination of more than one sham type.

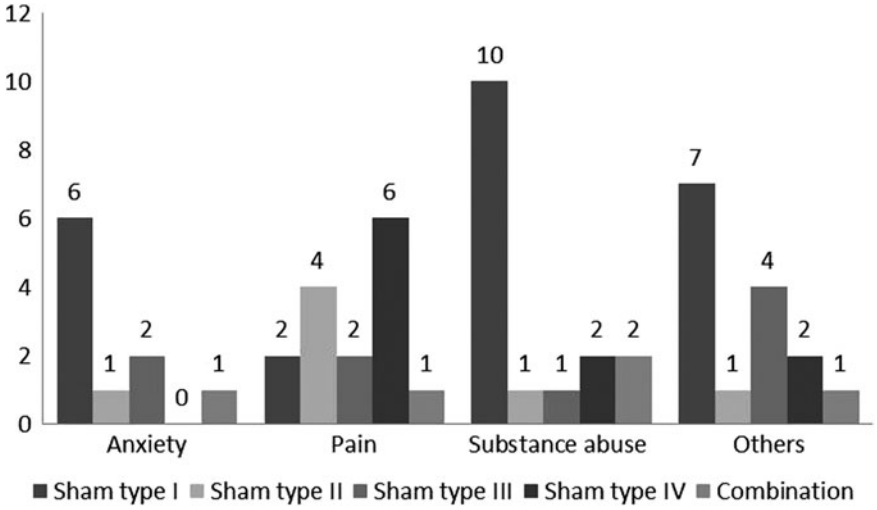

FIG. 5. Number of published randomized controlled trials of ear-acupuncture/ear-acupressure by sham type used and type of condition treated. Sham type I: Same treatment on ear acupoints that are not theoretically effective for the condition (nonspecific ear acupoints); Sham type II: Same treatment on nonacupoints on the ear; Sham type III: Placebo needles or adhesive patches without pellet/seed on the same ear acupoints; Sham type IV: Pseudo-interventions (e.g., switched-off laser acupuncture devices, electroacupuncture devices with minimum emission, Vaccaria seeds without pressing) on the same ear acupoints. Combination: combination of more than one sham type.

Discussion

This article is a comprehensive systematic review of the sham control methods used in EAP clinical trials between 1990 and 2012 and the relationship between sham-type, blinding, dropout rate, condition treated, and outcomes. In order to capture all RCTs using any type of sham or placebo control, we did not limit the search terms with the words of "sham" or "placebo." As a result, a few studies[14,20,29] that could not be captured by searching "sham" or "placebo" are also included in this review.

Among all studies, Sham Type I (nonspecific ear acupoint) was the most frequently used method followed by Type IV methods (pseudo-interventions). A similar result was found in a review of sham controls for body acupuncture.[2] However, the earlier review was published 10 years ago, so the situation may have changed for body acupuncture trials.

The risk of bias assessment raised concerns about the methodological quality of the trials, particularly in respect to blinding. A recent study concluded that in trials with subjective outcomes, the effect estimates were exaggerated when there was inadequate or unclear allocation concealment, or lack of blinding.[68] In this review, only five of the 55 RCTs reported an assessment of participant blinding. Based on the descriptions of sham control methods, Type I and Type II sham methods (which apply the same stimulation to nonspecific or nonacupoints) can avoid the possibility of unblinding participants due to their different treatment experiences. The other two sham methods employ less stimulation compared to the real intervention, or even no stimulation for sham; therefore, it is not feasible to blind participants except when inactive laser therapy is the comparator. This needs particular attention when researchers are planning RCTs of EAP and associated sham interventions. It

Table 5. Relations Between Design of Real/Sham Treatments and Efficacy Results

Design of real/sham EAP treatments		*Efficacy results*		
		T>C and T>C reconfirmed	*ND and "T>C"?*	
Equal/unequal number of acupoints for real/sham treatments	No. of RCTs using equal number of acupoints	29	16	$X^2=1.193$, $df=1$, $p=0.275$
	No. of RCTs using unequal number of acupoints	3	4	
Equal/unequal intensity of stimulation for real/sham treatments	No. of RCTs using equal intensity of stimulation	20	12	$X^2=0.100$, $df=1$, $p=0.752$
	No. of RCTs using unequal intensity of stimulation	14	10	
Same/different acupoints for real/sham treatments	No. of RCTs using same acupoints	12	7	$X^2=0.072$, $df=1$, $p=0.788$
	No. of RCTs using different acupoints	22	15	

One RCT employed two types of sham methods (Type I and Type IV) in two control arms (Li 2011 study) and was counted as two studies in this analysis.

Results: T>C: Between-group difference reported by the study (treatment group significantly more effective than control group); "T>C"?: Within-group difference reported by the study and no data provided for further analysis; T>C reconfirmed: Within-group difference reported by the study and between-group difference was reconfirmed in this review.

is worth noting that almost half of the RCTs blinded outcome assessors by employing independent researchers.

There was considerable variation in dropout rates, but there was no statistical difference between the real and sham EAP groups in total or within any of the sham types. Also, no RCT reported dropouts due to participants being aware of group allocation. This suggests that the sham design used in the EAP RCTs does not affect the dropout rate. When the clinical condition treated was considered, high dropout rates (greater than 20%) occurred in RCTs on substance abuse (38.94%) and obesity/overweight (22.89%) (Table 4). Since a greater than 50% dropout rate from the entire trial occurred in four studies of substance abuse (i.e., 80%,[17] 54.6%,[29] 51.9%,[22] and 50%[14]) as well as in a study of anxiety in drug withdrawal (65%),[50] this tended to inflate the dropout rate in this group. For each of the main types of conditions, there was no significant difference in the dropout rates between the real and sham groups (Table 4). Due to the great variety of trial characteristics, design, and conditions treated, it was not feasible to further investigate any effects of sham type plus condition on dropout rate. Nevertheless, since the substance abuse trials tended to employ Sham type I, it appears unlikely that the dropout rates were elevated by participants believing they were in the sham group.

The results of RCTs should include the number of dropouts with reasons as required by the Consolidated Standards of Reporting Trials (CONSORT) statement,[69] and the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) guidelines.[70] When reasons are properly reported, the data become available for further analysis to determine the likely causes of dropouts.

No relationship was found between efficacy outcomes and EAP design in terms of sham type, or any differences between real and sham groups in the number of acupoints used, the level of stimulation of the acupoints, or whether the same or different acupoints were used. The above statistical analysis results suggested that the choice of EAP sham methods does not influence the efficacy outcomes or attrition in EAP RCTs.

However, there was considerable variation across trials in treatment methods, clinical conditions, and outcome measures. Consequently, the data used in the analyses were grouped into broad categories to enable statistical comparisons between groups of studies. This approach could not capture smaller differences between studies, particularly with regard to efficacy, which was measured using a variety of outcome measures. Also, it was not possible, on the basis of the available data, to determine whether any of the sham methods produced a physiological effect or whether any could be considered a true "placebo." Hence, these findings need to be interpreted with caution due to the limitations of the review.

Conclusions

This review included 55 sham-controlled RCTs of EAP and found that the nonspecific ear-acupoints type of sham control (Sham type I) was the most frequently used of four EAP sham types. This method first appeared in the 1990s and continues in use. Sham type I and Sham type II (non-acupoints) were considered the methods most likely to achieve blinding of participants. No relationship was found between the sham type used and the efficacy outcomes or dropout rates in these studies.

Acknowledgment

This article was part of the PhD project of the first author, who was supported by an RMIT University PhD scholarship and partially funded by National Health and Medical Research Council research grant (No. 55421), Australia.

Disclosure Statement

All authors are researchers of the School of Health Science, RMIT University. The authors declare no competing financial interests exist.

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