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REVIEW

The efficacy of acupoint stimulation for the management of therapy-related adverse events in patients with breast cancer: a systematic review

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Abstract The aim of the present study was to scrutinize the evidence on the use of acupoint stimulation for managing therapy-related adverse events in breast cancer. A comprehensive search was conducted on eight English and Chinese databases to identify clinical trials designed to examine the efficacy of acupressure, acupuncture, or acupoint stimulation (APS) for the management of adverse events due to treatments of breast cancer. Methodological quality of the trials was assessed using a modified Jadad scale. Using pre-determined keywords, 843 possibly relevant titles were identified. Eventually 26 papers, 18 in English and eight in Chinese, satisfied the inclusion criteria and entered the quality assessment stage. The 26 articles were published between 1999 and 2008. They assessed the application of acupoint stimulation on six disparate conditions related to anticancer therapies including vasomotor syndrome, chemotherapy-induced nausea and vomiting, lymphedema, post-operation pain, aromatase inhibitors-related joint pain and leukopenia. Modalities of acupoint stimulation used included traditional acupuncture, acupressure, electroacupuncture, and the use of magnetic device on acupuncture points. Overall, 23 trials (88%) reported positive outcomes on at least one of the conditions examined. However, only nine trials (35%) were of high quality; they had a modified Jadad score of 3 or above. Three high quality trials revealed that acupoint stimulation on P6 (NeiGuang) was beneficial to chemotherapy-induced nausea and vomiting. For other adverse events, the quality of many of the trials identified was poor; no conclusive remarks can be made. Very few minor adverse events were observed, and only in five trials. APS, in particular acupressure on the P6 acupoint, appears beneficial in the management of chemotherapy-induced nausea and vomiting, especially in the acute phase. More well-designed trials using rigorous methodology are required to evaluate the effectiveness of acupoint stimulation interventions on managing other distress symptoms.

Keywords Acupuncture · Evidence-based Chinese medicine · Breast cancer · Adverse event · Critical appraisal

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Introduction

The prevalence of breast cancer is increasing [1–3]. More than 50% of breast cancer patients experience a

number of adverse events (AEs) such as vasomotor syndrome (with prevalence up to 80%) [4–6], chemotherapy-induced emesis (75%) [7], post-mastectomy oedema (approximately 30–60%) [8, 9], and arthralgia (over 40%) [10]. Apart from general discomfort reducing the patients' quality of life [11], these unpleasant symptoms often lead to an increased use of health care resources. AEs are also the main reason for non-adherence to oncologic treatment [12]. Both pharmacologic and non-pharmacologic interventions have been used to alleviate the AEs [13–17]. However, pharmacotherapy agents for resolving distress may produce adverse effects such as dry mouth, somnolence, drowsiness, skin rash, heart palpitations, peripheral oedema, and gastrointestinal symptoms and hence have low patient acceptance [18]. Two systematic reviews have investigated the management of AEs using Chinese medicinal herbs (CMHs) [16] and exercise interventions [15]. The conclusion was that it is difficult to make definitive therapeutic recommendations.

Acupuncture is a popular non-pharmacological therapy used for treating a variety of conditions such as low back pain [19] and allergic rhinitis [20]. It was suggested that neurochemicals released after needling or pressuring acupoints may contribute to the therapeutic effect of acupuncture [21]. Methods to stimulate acupoints include manual needling, needling combined with electric stimulation (electroacupuncture), wrist band, stimulation, magnet stimulation, lasers or heat with burning herbs (moxibustion), applying pressure to the acupoint (acupressure), as well as treating the whole body by using acupoints in the ears only (auricular acupuncture) [22]. In this review, we used the term "acupoint stimulation" (APS) to represent all these modalities.

The effectiveness of APS on the relief of symptom distress during and after cancer treatments is well documented [23, 24]. The growing interest in the use of APS modalities has also led to several studies investigating its efficacy on therapy-related AEs among oncologic patients, including hot flashes, fatigue, xerostomia [25], leucopenia [26], and emesis [23, 24, 27, 28]. However, the efficacy of acupuncture modalities on the management of breast cancer therapies-related AEs remains uncertain [28, 29]; no systematic review has been conducted to summarize the results. Previous reviews have only examined a single AE and on nonspecific groups [30, 31]. We therefore initiated this comprehensive review to scrutinize the evidence of using APS—the stimulation of acupuncture points by any modality—on managing adverse events related to anticancer therapies in patients with breast cancer.

Methods

The conduct and presentation of this systematic review adhered to the guidelines of the Quality of Reporting of Meta-analyses (QUOROM).

Search and screening strategy

Relevant articles were acquired by searching the following five English databases: PubMed, Cochrane library, EMBASE, the Cumulative Index to Nursing and Allied Health, and PsycINFO; and three Chinese databases: CNKI, CEPS, and WanFang. All databases were retrieved from their inceptions until October 2008. Manual searching was also carried out to find trials from the references cited in the articles identified. Key terms used in the search included medical terms of "breast cancer" (e.g., breast neoplasm, breast carcinoma, breast tumour), combined separately with at least one of the following words related to acupuncture modalities: "acupuncture", "acupressure", "auricular acupuncture", "ear acupuncture", "acupuncture points", "electroacupuncture", "acupoints", "transcutaneous electric nerve stimulation", and "Moxibustion".

Two independent reviewers undertook the selection of publications from the databases: in the initial stage, they screened the titles and abstracts of all the publications retrieved to determine eligibility. Then, the full text of seemingly relevant articles was read by the same two reviewers, again independently, for final inclusion in the methodological assessment. Disagreements over selection and inclusion were resolved by discussion with a third and more experienced reviewer.

Inclusion criteria

A study was considered eligible if it satisfied all the following criteria: (1) Study design: clinical trials including randomized controlled trials (RCTs), controlled clinical trials (CCTs), or single-group studies; (2) Participants: adults who were diagnosed with breast cancer at any stage and undergoing treatments such as surgery, radiotherapy, chemotherapy, hormonal therapy, or palliative treatment for metastatic breast cancer, and experiencing treatment-induced adverse events; (3) Intervention: stimulation of acupuncture points by any modality; (4) Outcome measures: at least one clinically related outcome variable such as symptom scores; as well as condition-specific outcomes or generic health status outcomes.

Exclusion criteria

Animal studies, case reports and anecdotal evidence, qualitative studies or descriptive surveys, and reports that

were available only in abstract form were excluded. The trials that included diagnosis other than breast cancer were also excluded unless separate data were available for the breast cancer subgroup.

Methodological quality assessment

All eligible trials identified were evaluated by two independent reviewers using a modified Jadad scale. The scale assesses three major aspects of RCT: (1) randomization procedure (1 point is given if patients were randomized into the group allocation; 1 bonus point if the randomization procedure is appropriate), (2) dropout and withdrawal (1 point is given for a clear description of dropouts and withdrawals) and blinding (2 points) [32]. Blinding acupuncturist is not practical in RCT design. Nevertheless, blinding patients and outcome assessors were considered critical in manual therapy trials [33]. Thus, we have adapted a modified version of the Jadad scale [30]. That is, 1 point was given for blinding of patient, and an additional 1 point was given if the outcome assessor was blinded. Therefore, each article could score 0 (lowest quality) to 5 (highest quality). Studies were classified as high quality if they attained a score of 3 or more [32].

Despite the relative ease of use of the Jadad scale, inter-rater reliability of this scale has been shown to be poor. To assess inter-rater reliability, we calculated the percentage agreement between the two independent reviewers on quality assessment. The percentage of agreement was 93.2%, and all disparities were resolved after, again, discussion with a third and more experienced reviewer.

Data extraction

The information of each trial was extracted and entered into a worksheet specially designed for this purpose. Data recorded included the following: (1) Descriptive information including first author, study location, year, language, and name of the journal; (2) Population parameters including samples size and demographic characteristics; (3) Methodologies including study design, assignment and blinding procedures, attritions, and follow-up duration; (4) Intervention parameters including type and pattern of acupuncture therapy, treatment duration, and acupoint(s) used; (5) Outcomes including measuring instrument(s) used, and main results.

Statistical analysis

The software program Number Cruncher Statistical Systems (NCSS 2004) was employed to calculate the effect size and the corresponding 95% confidence interval (CI).

Results

Overall results (all treatment modalities)

A total of 843 titles were found from the databases and reference lists. After deleting repetitious and irrelevant studies by examining the titles and abstracts, 51 possible relevant studies remained. After reading the full text of these 51 studies and applying the selection criteria, 26 articles [29, 34–58] were found eligible for methodological quality assessment. Figure 1 presents the selection process.

Of the 26 studies, 18 [29, 34–38, 41–48, 51, 52, 54, 58] were RCTs and 8 [39, 40, 49, 50, 53, 55–57] were CCTs but not RCTs; 18 [29, 34–44, 49–51, 53–55] were written in English and 8 [45–48, 52, 56–58] in Chinese. All of them were published in referred journals; none of them were theses, dissertations, or conference proceedings. Basic characteristics of the studies are summarized in Table 1.

The studies were published between 1999 and 2008 and were conducted in several counties, but mainly in the United States and China. The age of patients ranged from 28 to 76 years. Five studies reported the body mass index (BMI) of the participants, ranging from 23.1 to 28.8; but BMI was not used as an outcome variable.

The 26 trials used different types of APS, including nine trials (34.6%) of conventional acupuncture therapy [34, 35, 39, 40, 49, 51, 53–55], six trials (27.1%) of electroacupuncture [36, 37, 44, 50, 52, 58], five by drug injection in acupoints [45, 47, 48, 56, 57], three by self-acupressure [41, 43, 46], and three studies in acupoints stimulation by specific devices including wristband [29, 42] and acumagnet [38]. More than 40% of the trials (11/26; 42.3%)

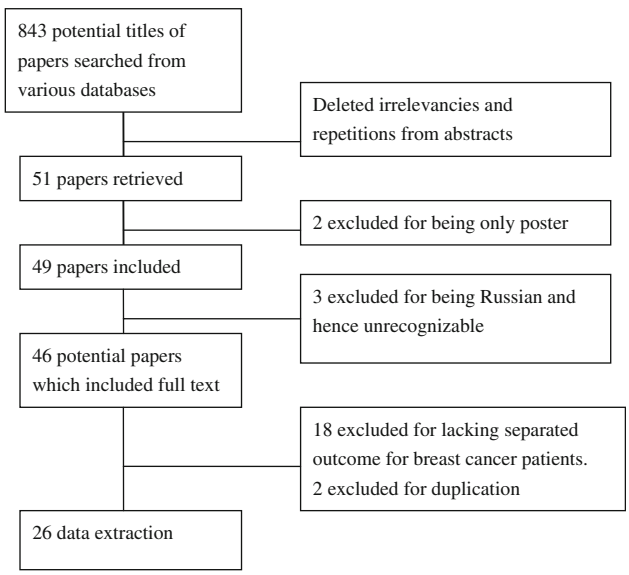

Fig. 1 A schema for illustrating the process of study selection

Table 1 Summary of demographic information of the included studies ($n = 26$)

Characteristics	Conditions					
	Vasomotor symptom	Chemotherapy-induced nausea and vomiting	Post-operation pain	Leukopenia	Other conditions	Total
Number of trials (%)	7 (26.9)	11 (42.3)	3 (11.5)	2 (7.7)	3 (11.6)	26
Study design						
RCT	5	9	2	0	2	18
CCT	0	0	1	1	0	2
Single group	2	2	0	1	1	6
Modified Jadad score						
≥3	4	4	1	0	0	9
<3	3	7	2	2	3	17
Total number of trial participants	281	776	165	211	115	1548
APS modality						
Conventional acupuncture	4	1	2	0	2	9
Electroacupuncture	2	2	1	0	1	6
Self-acupressure	0	3	0	0	0	3
Acupoint injection	0	3	0	2	0	5
Acuband	0	2	0	0	0	2
Magnet	1	0	0	0	0	1
Country (study conducted in)						
US	2	4	1	0	2	9
China	0	4	1	2	1	8
UK	2	1	0	0	0	3
Sweden	1	1	0	0	0	2
Other	2	1	1	0	0	4

APS acupoint stimulation; *RCT* randomized controlled trial; *CCT* controlled clinical trial

examined chemotherapy-induced nausea vomiting (CINV). The remaining trials examined vasomotor syndrome (VMS, 7/26; 26.9%), post-operational pain (3/26; 11.5%), radiotherapy or chemotherapy-induced leukopenia (2/26; 7.7%), AI-induced arthralgia (1/26; 3.8%), and breast cancer-related lymphoedema (1/26; 3.8%). However, information on participants' education level, background of the acupuncturists, period of symptom distress before management, and reliability of measurement tools were revealed in too few studies to allow any meaningful summary.

Quality assessment

The range of the modified Jadad methodological quality score ranged from 0 to 5. Two studies scored 5 [34, 44], one scored 4 [35], and six scored 3 points [29, 36, 37, 41, 42, 51]. Most studies (65.4%) scored 2 or less than 2 points, including three 0-point trials [53, 56, 57], nine 1-point trials [39, 40, 45, 46, 48–50, 52, 55] and five 2-point trials [38, 43, 47, 54, 58].

Effect on vasomotor syndrome (VMS)

As shown in Table 2, seven trials ($N = 281$) explored the effect of acupuncture on vasomotor syndrome [34–40], including five RCTs and two single-group pre-post comparisons. Daily flush frequency was the main outcome measure. All the studies used self-administrated questionnaires to measure this effect. Three trials also used the Kupperman Index (KI) to score climacteric symptoms [35–37]. All studies except one [36] used six or more acupoints. SP6 was the most commonly used acupoint, which was used in four studies [34, 38–40]. Four RCTs, included three high quality trials [34, 36, 37], did not find any significant difference in the primary outcome measure between the intervention and the control group [34, 36–38]. Using data from three of the four studies [34, 37, 38], the effect size (expressed as standardized difference) was calculated to be 0.39 (95% CI −1.26 to 2.02; $P = 0.428$). For the other three trials [35, 39, 40] demonstrating an association between APS intervention and lower frequency of daily hot flush, two of them were single-group studies.

Table 2 Summary of studies included for treating vasomotor symptom (VMS) in patients with breast cancer

Reference	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/dropout)	Acupoints	Length of treatment (wks)/follow-up	Key outcome measurement	Adverse event	Between-group difference	Within-group difference
[35]	RCT (subject blinding)/4	AT 30 min, twice weekly for first 5 weeks, then once a week for 5 weeks (30/NR)	Placebo: Sham AT on non-acupoints (29/NR)	LIV3, GB20, LU7, KI3, SP6, REN4, P7, LIV8	10/12	(1)Daily flash frequency, (2)KI score	N/R	(1)$P = 0.009$ during treatment; $P < 0.001$ in following (2)$P = 0.004$ during treatment; $P = 0.001$ in following	(1) N/R (2) AT group, $P < 0.001$; Sham group: NS
[36]	RCT/3	EA 30 min, twice weekly for the first 2 weeks, then once a week for 10 weeks (27/8)	Hormone therapy (18/7)	N/R	12/24 mos	Daily flash frequency, KI score	N/R	N/R	$P < 0.01$ in both groups
[34]	RCT (double blinding, cross-over)/ 5	AT twice weekly for 4 weeks (42/9)	Placebo: Sham AT on non-acupoints (30/2)	DU14, GB20, BL13, PC7, H6, K7, ST36, SP6, Ear shen men, Ear sympathetic point	4/6 mos	Daily flash frequency,	Very minor bleeding	Not significant (NS) ($P = 0.3$)	N/R
[37]	RCT/3	EA 2 Hz, 30 min, twice weekly for the first 2 weeks, then once a week for 10 weeks (19/ 2)	Relaxation programme (19/5)	BL23, BL32, HT7, SP6, SP9, LR3, PC6, GV20	12/6 mos	(1)Daily flash intensity, (2)KI score (3)Mood Scale	N/R	NS (1)$P = 0.48$ (2)$P = 0.2$ (3)$P = 0.55$	$P < 0.01$ on all parameter in both group
[38]	RCT (cross-over)/2	Magnetic device (15/4)	Placebo: Sham device, (15/4)	6 points/N/R	3 days/N/A	(1)Daily flash severity (2)Bother rating (3)Quality of life	Itching, redness	NS (1)$P = 0.21$ (2)$P = 0.02$ (3)$P = 0.13$	N/R
[39]	Single group/ 1	AT weekly for 3 months then monthly (15/NR)	NA	KI6, SP6, BL23, CV4, GB35, H5	12/6 mos	Greene menopause index: (1) Anxiety, (2) Depression (3) Somatic symptom (4) Vasomotor symptom	None	N/A	Anxiety, somatic and vasomotor symptom were improved ($P < 0.001$) lasting 6 months

Table 2 continued

Reference	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/dropout)	Acupoints	Length of treatment (wks)/follow-up	Key outcome measurement	Adverse event	Between-group difference	Within-group difference
[40]	Single group/ 1	AT 20–30 min twice a weekly for 7 weeks (22/NR)	NA	BL62, LR14, KI3, HT7, TE6, SP6, LI11, ST36, GV20, LI4	Up to 7/3–5	Flash frequency	None	N/A	88% experienced effective improve ($P < 0.001$)

CINV chemotherapy-induced nausea vomit, *BCRL* breast cancer-related lymphedema, *CILP* chemotherapy-induced leukopenia, *RILP* Radiotherapy-induced leukopenia, *RCT* randomized control trial, *EA* electroacupuncture, *AT* manual acupuncture therapy, *AC* digital acupressure, *N/R* not reported, *ROM* range of motion, *KI* Kupperman's Index (climacteric symptoms), *RINVR* Rhodes Index of Nausea, Vomiting and Retching, *SCL*: symptom checklist, *NCI* National Cancer Institute *N/A* non-applicable, *POD* post-operation day

Effect on chemotherapy-induced nausea vomiting

Eleven studies [29, 41–50] ($n = 761$) investigated the antiemetic effect of APS on distress symptoms induced by chemotherapy (Table 3). The acupoints P6 and ST36 were used in these studies. Participants received intervention over a treatment period of 5 days to 3 weeks; two of the studies stated the follow-up period [44, 49]. Of these 11 studies, ten (90.9%), including three high quality studies [41, 42, 44], reported that APS could significantly improve emesis caused by breast cancer therapy.

Effect on post-mastectomy pain

Three trials used APS to manage post-mastectomy pain [51–53] (Table 4). The results were inconsistent. Acupoint L14 was used in all the three trials. Two studies demonstrated significant effect favouring the APS group [52, 53], but one high quality RCT [51] found no significant difference between the intervention group and the control group.

Effect on joint symptoms

Of the 26 trials included, only one study [54] explored the effect of acupuncture therapy on aromatase inhibitors-related joint pain and functional ability (Table 5); and positive results were obtained.

Effect on breast cancer-related lymphoedema

One study [55] demonstrated that traditional acupuncture was effective in managing post-mastectomy oedema using a single-group design.

Effect on leukopenia

Two trials [56, 57] conducted in China found that dexamethasone injected at the ST36 intra-acupoint was effective in preventing bone marrow suppression-related leukopenia in breast cancer patients undergoing chemotherapy [56] or radiotherapy [57] (Table 5).

Adverse events

Of the 26 trials, 17 (65.4%) did not comment on adverse events. Four trials reported no adverse events occurred [39, 40, 42, 54]; and five trials reported some minor adverse events [34, 38, 44, 49, 50]. Acu-magnets device adhesive or electrocurrent stimulation generated a few side-effects including skin irritation [38] and shock sensation [44]. Although pain or minor bleeding related to

Table 3 Summary of studies included for treating chemotherapy-induced nausea and vomiting in patients with breast cancer

Reference	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/dropout)	Acupoints	Length of treatment (wks)/ follow-up	Key outcome measurement	Adverse event	Between-group difference	Within-group difference
[41]	RCT 3 arms (evaluator blinding)/3	Self-acupressure at P6, 6′ in the morning and 3′ each during the rest of the day in therapy period (53/6)	Placebo: acupressure at acupoint S13 (53/4) Control: usual care (54/3)	P6	Around 2/ N/A	(1)Acute intensity of nausea vomiting rating (RINVR) (2)Delayed emesis	N/R	(1)NS (2)$P = 0.002$ vs. Placebo; $P < 0.0001$ vs. control	N/R
[42]	RCT/3	Wear wristband acupressure device (19/ NR)	Usual care (17/2 groups total drop 18)	P6	5 days/N/A	Experience and intensity of emesis (RIN)	None	$P < 0.05$	N/R
[29]	RCT 3 arms/3,	Wear EA band for 5 days (32/NR)	Placebo: Sham acupoint (31/NR) Control: usual care (33/NR)	P6	5 days/N/A	Daily emesis episodes number, severity level	N/R	NS	N/R
[43]	RCT/2	Self-acupressure 3 min on each acupoint frequently for 21 days (9/NR)	Usual care (8/total drop:1)	P6, ST36	Around 3/ N/A	(1) Nausea experience (RINVR score 0–12) (2) Nausea intensity (0–10)	N/R	(1)$P < 0.01$ (2)$P < 0.04$	N/R
[44]	RCT 3 arms (double blinding)/5,	EA 2–10 Hz, 20 min daily for 5 days (37/total drop 7)	Placebo: Sham acupoint and no electronic current (33/NR) Control: usual care (34/NR)	P6, ST36	5 days/ 9 days	Total emesis episodes number	Shock sensation & tingling	5 days: $P < 0.001$ 9 days: NS	N/A
[45]	RCT (cross-over)/1	AT injected dexa (60/NR)	Intravenous injected dexa (60/NR)	ST36	Once/ 3 days	Antiemetic rating (0–3)	N/R	1st day: NS, 2nd day: $P = 0.017$ 3rd day: $P = 0.01$	N/R
[46]	RCT/1	Self-AC + mental support (30/NR)	Mental support (30/ NR)	P6, ST36	10 days/N/ A	Antiemetic rating (0–4)	N/R	$P < 0.05$	N/R
[47]	RCT/2	AT injected drug (50/NR)	Usual care Intramuscular injected (50/NR)	ST36	N/R	(1) Nausea rating (0–4) (2) Vomiting rating (0–4)	N/R	(1)$P < 0.05$ (2)$P < 0.05$	N/R
[48]	RCT/1	AT injected drug in ST36 (42/NR)	AT injected in LI4, P6(48)	ST36, P6, LI4	N/R	Antiemetic rating (0–3)	N/R	$P < 0.05$	N/R
[49]	Single group/1	AT 10 min bilateral, 10 times during 3 weeks (breast ca $n = 5$/NR)	N/A	P6	3/2	11 points nausea score	Pain	N/A	$P < 0.05$ in last $P < 0.01$ in 1st follow-up

Table 3 continued

Reference	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/dropout)	Acupoints	Length of treatment (wks)/ follow-up	Key outcome measurement	Adverse event	Between-group difference	Within-group difference
[50]	Single group/1	EA 10 Hz, 10 min before C/T then 20 min within C/T daily (27/NR)	N/A	P6, ST36	C/T period/ N/A	Grating intensity (NCI scale)	Shiver, headache, pain	N/A	96.3% of cases
		significantly reduced CINV grade after EA ($P < 0.001$)							

CINV chemotherapy-induced nausea vomit, *BCRL* breast cancer-related lymphedema, *CILP* chemotherapy-induced leukopenia, *RILP* Radiotherapy-induced leukopenia, *RCT* randomized control trial, *EA* electroacupuncture, *AT* manual acupuncture therapy, *AC* digital acupressure, *N/R* not reported, *ROM* range of motion, *KI* Kupperman's Index (climacteric symptoms) *RINVR* Rhodes Index of Nausea, Vomiting and Retching, *SCL* symptom checklist, *NCI* National Cancer Iinstitute, *N/A* non-applicable, *POD* post-operation day

APS was reported in some studies [38, 49, 50], there were no serious effects that required medical management.

Discussion

Breast cancer victims suffer a variety of therapy-related adverse events [4–11]; there is an urgent need to address their physical distresses [15, 20–26]. Our review has attempted to summarize comprehensively the effect of APS to resolve treatment-induced adverse events on patients with breast cancer. Conventional manual acupuncture and electroacupuncture were the most commonly used APS modalities observed in this review; they have been used for all AEs except leukopenia. Other popular modalities include acupressure (11.5%), wearing acubands (7.7%), acupuncture with injection (19.3%), and using magnetic device (3.8%).

The most common adverse events treated by APS included chemotherapy-induced nausea vomiting (11 studies), vasomotor syndrome (7 studies), and post-operational pain (3 studies). Of the 26 studies included in the critical appraisal, although 23 (88%) reported positive outcomes, only 9 studies (35%) were of high quality. Among the nine high quality studies, three studies found APS effective in reducing acute emesis [41, 42, 44]. Although P6 was the acupoint chosen, the interventions and procedures used were dissimilar in these three trials. Besides, three high quality trials [34, 36, 37] did not find any benefit of APS on VMS. These studies carried out traditional acupuncture or electroacupuncture to compare with a control group.

There were three trials using APS to resolve short-term, post-mastectomy pain. The only high quality RCT [51], which used acupuncture and massage on the first and second days following surgery, reported that APS had no significant effects when compared with usual management. However, the sample size was small ($n = 25$); lack of power was a major limitation.

Although the evidence appeared to suggest that APS is effective in managing other distress symptom such as joint pain related to adjuvant aromatase inhibitors [54], post-mastectomy oedema [55], and leukopenia [56, 57], the results should be interpreted cautiously. The evidence was still not strong enough when the methodological quality was taken into considerations. For example, one cross-over trial [54] explored the effect of acupuncture for patients experiencing joint pain related to adjuvant aromatase inhibitors (AIs) chemotherapy. Although the results showed that acupuncture could reduce AI-related joint symptoms and improve functional ability, no significant changes were observed for the two secondary outcome

Table 4 Summary of studies included for treating post-operation pain in patients with breast cancer

Reference	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/dropout)	Acupoints	Length of treat (wks)/follow-up	Key outcome measurement	Adverse event	Between-group difference
[51]	RCT/3	AT & massage 20 min daily for 2 days ($n = 93$, breast ca $n = 18$, 20%)	Usual care ($n = 45$, breast ca $n = 7$, 16%)	LI4, SP6, auricular points	POD1, POD2/N/A	Pain numeric rating scale	N/R	$P = 0.14$ (NS)
[52]	RCT/1	HANS + usual (30/NR)	Usual care (30)/NR	LI4, P6	30 min once/6, 12, 24, 48 and 72 h post-operation	(1) Overall post-operation pain VAS (2) Sedation score (3) Number of analgesia applied	N/R	(1)$P < 0.05$ (2)$P > 0.05$ (3)$P < 0.05$
[53]	Non-RCT/0	AT unclear (48/NR)	Observation (32/ NR)	GB6, SJ6, PC2, PC3, LE14, MP19, DI14, BL17, LU2, RE6, RE17	3 days/N/A	(1) Pain during arm movement (2) Abduction angle range in tolerable pain	N/R	(1)$P < 0.01$ (2)$P < 0.001$

CINV chemotherapy-induced nausea vomit, *BCRL* breast cancer-related lymphedema, *CILP* chemotherapy-induced leukopenia, *RILP* Radiotherapy-induced leukopenia, *RCT* randomized control trial, *EA* electroacupuncture, *AT* manual acupuncture therapy, *AC* digital acupressure, *N/R* not reported, *ROM* range of motion, *KI* Kupperman's Index (climacteric symptoms) *RINVR* Rhodes Index of Nausea, Vomiting and Retching, *SCL* symptom checklist, *NCI* National Cancer Institute, *N/A* non-applicable, *POD* post-operation day

Table 5 Summary of studies included for treating the other problems in patients with breast cancer

Reference	Clinical problem	Study design/ modified Jadad score	Experimental regimen (sample size/dropout)	Control group regimen (sample size/ dropout)	Acupoints	Length of treat (weeks)/ follow-up	Key outcome measurement	Adverse event	Between-group difference	Within-group difference
[54]	Arthralgias	RCT (cross-over)/2	AT 30 min twice a weekly for 6 weeks (21/2)	Observation (21/2)	TB5, GB41, GB34, LI4, ST41, KD3. LI15, SJ14, SI10, SJ4, LI5, SI5, SI3, LI3, Du3, Du8, UB23, GB30, GB39, SP9, SP10, ST34	6/6 weeks	(1) Pain (BPI-SF) (2)QOL (FACT-G) (3)Inflam. biomarker (IL-1β, TNF-α)	None	N/A	Significant improvement in joint pain ($P = 0.008$), non on QOL and inflammation control by AT
[55]	BCRL	Single group/ 1	AT 30 min, once a week for 24 weeks (29/NR)	N/A	CV2, CV3, CV12, LI15, TE14, LU5, TE5, LI4, ST36, ST6, SP9, SJ5, SJ14, REN2, REN3, REN12	24/N/A	(1) Range of motion (2) Sensation (VAS), (3) Cirtometry difference (4) Degree (0–3 score)	N/R	N/A	Significant difference on ROM of shoulder, sensation and LE degree ($P < 0.05$)
[56]	CILP	Non-RCT/0	AT injected drug (Dexa) (102/NR)	Usual care with GCS-F (102/NR)	ST36	7 days/N/A	Serum WBC account	N/R	N/R	Leukopenia was improved in two-group, intervention group is cheaper
[57]	RILP	Single group/ 0	AT injected drug (Dexa) (7/ NR)	N/A	ST36	3-5 days/ N/A	Serum WBC account	N/R	N/R	WBC increased in mathematics
[58]	Adverse event of treatment	RCT/2	EA 30 min daily for 62 days (24/NR)	Usual care (24/NR)	ST36, BL23, BL18, BL17	62 days	Multiple dimensions	N/R	GI, immune reaction ($P < 0.05$)	N/A

CINV chemotherapy-induced nausea vomit, *BCRL* breast cancer-related lymphedema, *CILP* chemotherapy-induced leukopenia, *RILP* Radiotherapy-induced leukopenia, *RCT* randomized control trial, *EA* electroacupuncture, *AT* manual acupuncture therapy, *AC* digital acupressure, *N/R* not reported, *ROM* range of motion, *KI* Kupperman's Index (climacteric symptoms) *RINVR* Rhodes Index of Nausea, Vomiting and Retching, *SCL* symptom checklist, *NCI* National Cancer Institute, *N/A* non-applicable, *POD* post-operation day

measures, i.e., the inflammatory biomarkers TNF-α and IL-1β.

Breast cancer-related lymphoedema (BCRL) occurs as a common consequence of surgery and/or radiotherapy to axillary lymph nodes [8, 9, 59]. It is associated with a range of psychological and physical distress [60]. Limb oedema could be a problem for patients receiving traditional management such as physical therapy [14]. One study [55] included in this review demonstrated that traditional acupuncture was effective in the management of BCRL. Needles were placed on 11 acupoints to enhance body circulation and to reduce the sense of heaviness. Participants had significant improvements in a range of movements of shoulder flexion and abduction on the affected limb. Moreover, there appeared to be amelioration in the sense of heaviness and tightening after 24 weeks of APS. Nevertheless, the other parameter commonly used to assess lymphoedema, namely arm circumference, was not significant ($P = 0.057$). The small sample size, lack of a control group, and lack of long-term observation in the study increased doubts about the conclusions.

Several studies demonstrated that acupuncture could modulate the representation of anti-inflammatory indicators [61] and increase the serum granulocyte colony-stimulating factor (G-CSF), white blood count (WBC) [62], and adrenocorticotrophic hormone (ACTH) [63]. In our review, two trials [56, 57] injected a drug at the ST36 intra-acupoint and proved useful on bone marrow suppression. Although 207 breast cancer patients received this modality of APS to increase the level of immune on white blood cell, the methodological quality of these two studies was poor (i.e., 0-point on the modified Jadad score for both trials—one was a non-RCT [56] and the other was a single-group study [57]). The evidence was therefore not considered strong enough.

In comparison with other therapeutic methods, two RCTs compared electroacupuncture therapy, respectively, with hormone therapy [36], and relaxation programme [37] on vasomotor symptom management. Neither of them found any positive effects for the treatments.

Overall, only 9 of 26 studies (35%) obtained a modified Jadad score of 3 or above. Only two RCTs blinded both patients and outcome assessors [34, 44]. Trials with inadequate levels of evidence increase the possibility of overestimating the effect of intervention [64, 65], thus limiting the validity of the results. Hence, we suggest that the evidence was still not strong enough to conclude that by and large APS is useful for the management of the conditions studied. On the other hand, reporting of adverse events is a matter of concern for treatment effectiveness. While 65.4% of the 26 trials did not mention adverse events, a survey [63] revealed that up to 11.4% of adverse events can be caused by acupuncture therapy. It is therefore important for researchers to interpret the results even more cautiously.

For trials on acupuncture, there are issues with the optimal placebo group. To improve the quality of future RCTs on APS, we suggest that researchers might consider using sham APS placement as a potential control. Sham acupuncture can include either administering on false points or using non-penetrating fake needles.

Limitations of the review

There is a potential that some published studies had been missing from the literature search. We started the study by searching comprehensively and did not confine to English and Chinese. In fact, we found three abstracts published in Russian [66–68]; but we had difficulties translating them and locating the full test. Moreover, because of the inclusion criteria, two poster abstracts [69, 70] included in the other review article [30] had been excluded in this review. In addition, the focus of this review limits the conclusions to be applicable only to women with breast cancer.

Conclusions

The findings from three high quality studies comparing APS with control groups indicated that it is beneficial in the management of chemotherapy-induced nausea and vomiting, especially in the acute phase, even by noninvasive pattern. Health care professionals could consider using APS, in particular acupressure on the P6 acupoint, as an option for the management of CINV. The cost-effectiveness and cost-benefit of the intervention are worth further investigations. However, for other adverse events, the quality of many of the trials identified was poor; the evidence for the effectiveness of acupuncture therapies on managing other adverse events therefore was insufficient. Further well-designed trials using more rigorous methodologies are required to provide stronger justifications that APS is effective in managing other distress symptoms.

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