Ear Acupressure for Perennial Allergic Rhinitis: A Multicenter Randomized Controlled Trial

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Ear acupressure for perennial allergic rhinitis: A multicenter randomized controlled trial

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ABSTRACT

Background: *Perennial allergic rhinitis (PAR) has a high and increasing prevalence worldwide. Ear acupressure (EAP) is a noninvasive semi–self-administered form of acupuncture. Previous studies indicated that EAP could be effective and safe for AR symptom management. However, there was insufficient evidence to confirm this. This study investigated whether EAP, a noninvasive clinical alternative to acupuncture, is effective and safe for PAR.*

Methods: *This is an international, multicenter, randomized, single-blind, sham-controlled trial. The trial was conducted at two centers: Royal Melbourne Institute of Technology University (Melbourne, Australia) Clinical Trial Clinic and Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, China. PAR participants were randomized to receive real or sham EAP treatment once a week for 8 weeks and then were followed-up for 12 weeks. Participants were instructed to administer EAP stimulation three times daily. Symptom severity and quality of life (QoL) were evaluated. Adverse events (AEs) were also monitored. Intention-to-treat analysis on change of symptom scores and QoL was applied.*

Results: *Two hundred forty-five participants were randomly assigned to real (n = 124) and sham EAP (n = 121) groups. Twenty-five participants discontinued during treatment and 15 participants dropped out during follow-up. At the end of treatment and follow-up periods, changes of global QoL score were significantly greater in the real EAP group compared with the sham group. At the end of follow-up, scores for total nasal symptom, runny nose, and eye symptoms in the real EAP group had a greater reduction compared with the sham group. Overall, both real and sham EAP were well tolerated. Two severe AEs were reported but were not considered related to the EAP procedures.*

Conclusion: *In conclusion, EAP showed short-term and extended benefit for improving PAR symptoms and QoL for PAR patients.*

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Allergic rhinitis (AR) has a high and increasing prevalence worldwide.[1,2] AR prevalence is reported at around 20% in Europe, 14% in the United States, 9% in the Asia–Pacific area, and 15% in Australia.[3–5] Traditionally, AR is classified into "seasonal" AR and "perennial" AR (PAR) based on the occurrence of symptoms. PAR denotes sensitivity to allergens that may be present throughout the year.[6] Although PAR is not a life-threatening disease, it has a significant impact on patients' quality of life (QoL) and leads to a substantial health and economic burden.[2,7–10] In addition, PAR is considered a risk factor for asthma, sinusitis, and other comorbidities.[2,6]

The current management of PAR includes pharmacotherapy and allergen-specific immunotherapy. Acupuncture has a long history of treating AR and recent randomized controlled trials (RCTs) have shown its benefits in AR management.[11,12] Ear acupressure (EAP) is a noninvasive semi–self-administered form of acupuncture. Previous studies indicated that EAP could be effective and safe for AR.[13] However, there was insufficient evidence to confirm this.[13] Therefore, we conducted this international, multicenter, single-blinded, RCT to determine the efficacy and safety of EAP for PAR treatment.

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METHODS

Setting and Ethical Consideration

This RCT was conducted at two centers: the Royal Melbourne Institute of Technology University (Melbourne, Australia) Clinical Trial Clinic and Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, China. The trial protocol was approved by the Human Research Ethics Committees at both centers, registered with the Australian New Zealand Clinical Trial Registry (ACTRN12608000149369) and filed with the Australian Therapeutic Goods Administration before the commencement of the trial. C.S. Zhang and J. Xia contributed equally to this work.

Participants

Participants were recruited from the general population in Australia through media advertisement and from the Outpatient Department in China. The inclusion criteria were aged 18–70 years, history of at least 2 years of typical PAR symptoms, and positive allergy test to any of the common PAR allergens. The exclusion criteria were current systemic corticosteroid therapy; other active respiratory disease such as asthma, structural defects of the upper respiratory tract, wearing a hearing aid, having used EAP for respiratory diseases within the last 6 months, history of contact allergy to adhesive tape, history of being positive for human immunodeficiency virus, hepatitis B or C, and current pregnancy. Written informed consent was obtained from potentially eligible participants before an initial assessment that included allergy tests of common PAR allergens and a physician-confirmed diagnosis.

Randomization and Blinding

Randomization numbers (in blocks of eight) were generated by an independent statistician using a computer system and were sealed in individual opaque envelopes. The randomization was stratified based on the baseline total nasal symptom score. This study was designed as a participant-blinded trial, *i.e.*, only the acupuncturist who delivered the EAP treatments knew participants' group allocation. The participants and personnel involved in recruitment, assessment, data entry, and data analysis were blinded.

Treatment

Participants attended the trial clinic once a week over 8 weeks to receive EAP treatments. Each treatment session took 10–15 minutes. Acupuncturists who delivered the EAP treatments all had a 5-year degree level training and over 10 year of' clinical experience in acupuncture. During the first visit, the acupuncturists provided detailed information concerning the EAP technique to participants, sterilized the ear skin surface with a commercial 70% isopropyl alcoholic skin cleansing swab, located the acupoints with a detecting probe, attached five stainless steel pellets (1.2 mm in diameter; PELSST S/Steel Tan; Acuneeds Co., Camberwell, Victoria, Australia; Fig. 1) to the real or sham acupoints on the left ear, and then instructed participants on the method of maintaining adhesion of the pellets. Participants were required to gently press the pellets three times a day (morning, midday, and evening) to promote the acupoint stimulation. Each pellets were pressed for ~10 seconds or until the ear became red or slightly sore. During the subsequent visits, the acupuncturists removed the previous treatment pellets and repeated the same procedure on the other ear alternately on a weekly base. There was no skin penetration involved in EAP treatments.

Five ear acupoints were used for real EAP; these include shenmen (TF_4), internal nose (TG_4), lung (CO_{14}), wind stream ($SF_{1,2i}$), and adrenal gland (TG_{2p}). They were selected based on clinical trials,[13] Chinese medicine theory,[12] and consultation with experts. Five sham EAP acupoints are helix 2 (HX_{10}), shoulder ($SF_{4,5}$), clavicle (SF_6), OCCIPUT (AT_3), and tooth (LO_1). In practice, these acupoints are not used to treat allergy or any nasal symptoms.[15] The locations of the acupoints are shown in Fig. 2.

Outcome Measures

The primary outcome measures were the reduction of nasal and nonnasal symptom scores. The secondary outcomes were the change of QoL score, change of relief medication usage, adverse events (AEs), and credibility of blinding. Data were collected during the run-in (2 weeks, weekly), treatment (8 weeks, weekly), and follow-up (12 weeks, every 4 weeks) periods through Case Report Forms (CRFs). The Spector 7 point (from 1 to 7) Visual Analog Scale questionnaire was used to measure symptom severity and QoL.[14] Considering the pellets may fall off during the treatment week, participants were required to record how many pellets remained attached to the ear acupoints each day in the CRFs. The weekly total number of pellets remaining was analyzed as treatment dosage data.

During the entire trial period, participants were permitted to use symptomatic relief medications and keep records in the CRFs. Relief medication usage was calculated as 1 point for each standard dose of a tablet, eye drop, or nasal spray. A question about which group the participants thought they were allocated was used at the end of the first and last treatment weeks to assess the credibility of blinding procedure.

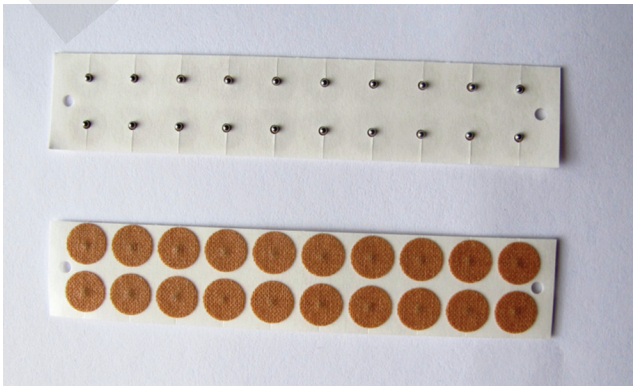

Figure 1. *Pellets used for ear acupressure (EAP) treatment.*

Statistical Analysis

The sample size was determined based on reported results of a pilot study with an effect size on total nasal symptom scores of 0.47 (2.16 ± 1.92 and 3.09 ± 2.09 for the real/sham EAP groups respectively; $p = 0.02$).[16] Aiming for 90% statistical power with a significance level of 5% (two tailed), the required sample size was 98 participants per group. Allowing for a dropout rate of up to 18%, the minimum sample size required was 116 participants in each group with 232 in total. Data were analyzed using Statistical Package for the Social Science (SPSS), Version 18.0 for Windows (SPSS, Inc., Chicago, IL). Demographic and other baseline characteristics were analyzed by χ^2-square or independent-samples *t*-test. Intention-to-treat analysis was used. PAR symptoms are largely affected by the change of seasons; therefore, the Last Observation Carried Forward method or Worst-Case Scenario method are not appropriate for this study. Instead, we used the SPSS missing data analysis (expectation–maximization) method to estimate missing data. The change from baseline to end of treatment or end of follow-up period of each symptom scale and medication usage data was assessed across the two groups using the independent-samples *t*-test and presented as a mean difference, 95% confidential interval. For all analysis, $p \leq 0.05$ was considered statistically significant. Credibility of blinding and the occurrence of AEs in the two groups were analyzed by the χ^2-test.

RESULTS

Participants and Baseline Characteristics

The trial was conducted between 2009 and 2011. In total, 245 were randomized into either real ($n = 124$) or sham EAP group ($n = 121$). During the 8-week treatment period, 14 participants in the real EAP group and 11 in the sham group discontinued; during the follow-up period, six participants in the real group and nine in the sham group lost contact and failed to return the CRFs. As a result, 220 participants completed the treatment and 205 participants completed the follow-up assessment (Fig. 3). The demographics of the included participants in the two groups were all comparable ($p > 0.05$; Table 1).

Baseline Symptom and QoL Severity

Significant differences were found at baseline for two symptom scales: runny nose score ($p = 0.03$), global QoL score ($p = 0.02$). Overall, the participants in the real EAP group had more severe PAR symptoms and poorer QoL compared with those in the sham group. These differences were not imputed since the change of symptom scores were analyzed as treatment outcome.

Treatment Effect

Change of Symptom Severity (Comparison of Change over Time between Groups). At the end of treatment period, the following scores of the real EAP group were reduced more significantly than that of the sham group: sneezing score (−0.39 [−0.77, −0.01]); at the end of follow-up, these scores in real the EAP group were reduced more significantly: runny nose score (−0.51 [−0.92, −0.11]), total nasal symptom score (−0.49 [−0.87, −0.10]), and eye symptom score (−0.36 [−0.67, −0.05]).

Change of QoL Scores (Comparison of Change over Time between Groups. At the end of treatment and end of follow-up, the global QoL score in the real EAP group achieved a greater improvement when compared with that in the sham group (0.50 [0.17, 0.83] and 0.42 [0.04, 0.80]), respectively; Table 2).

Treatment Dosage and Credibility of Blinding

There was no significant difference for the pellet dosage between two groups in any week of the treatment period or for the total pellets (Table 3). For the credibility of blinding, there was no significant difference between the two groups in their answers to the question of group allocation at the end of week 1 and at the end of week 8 (Table 4).

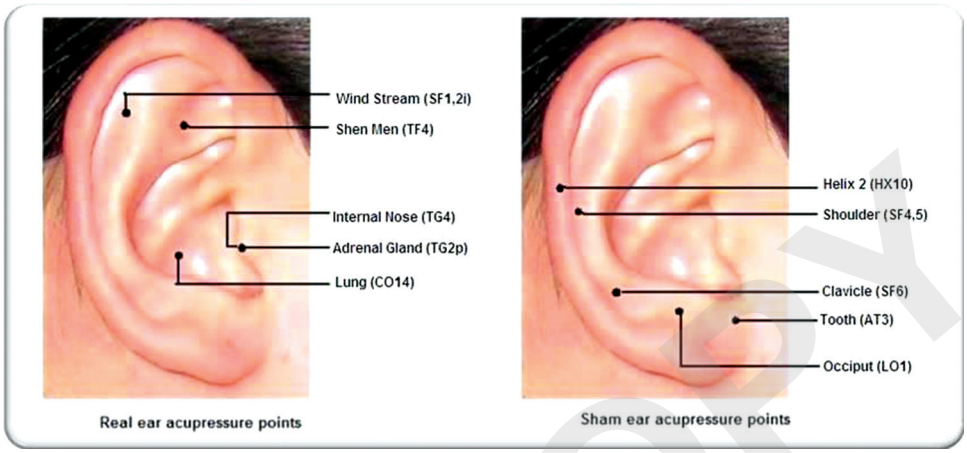

Figure 2. Real (L) and sham (R) ear acupressure (EAP) stimulation points.

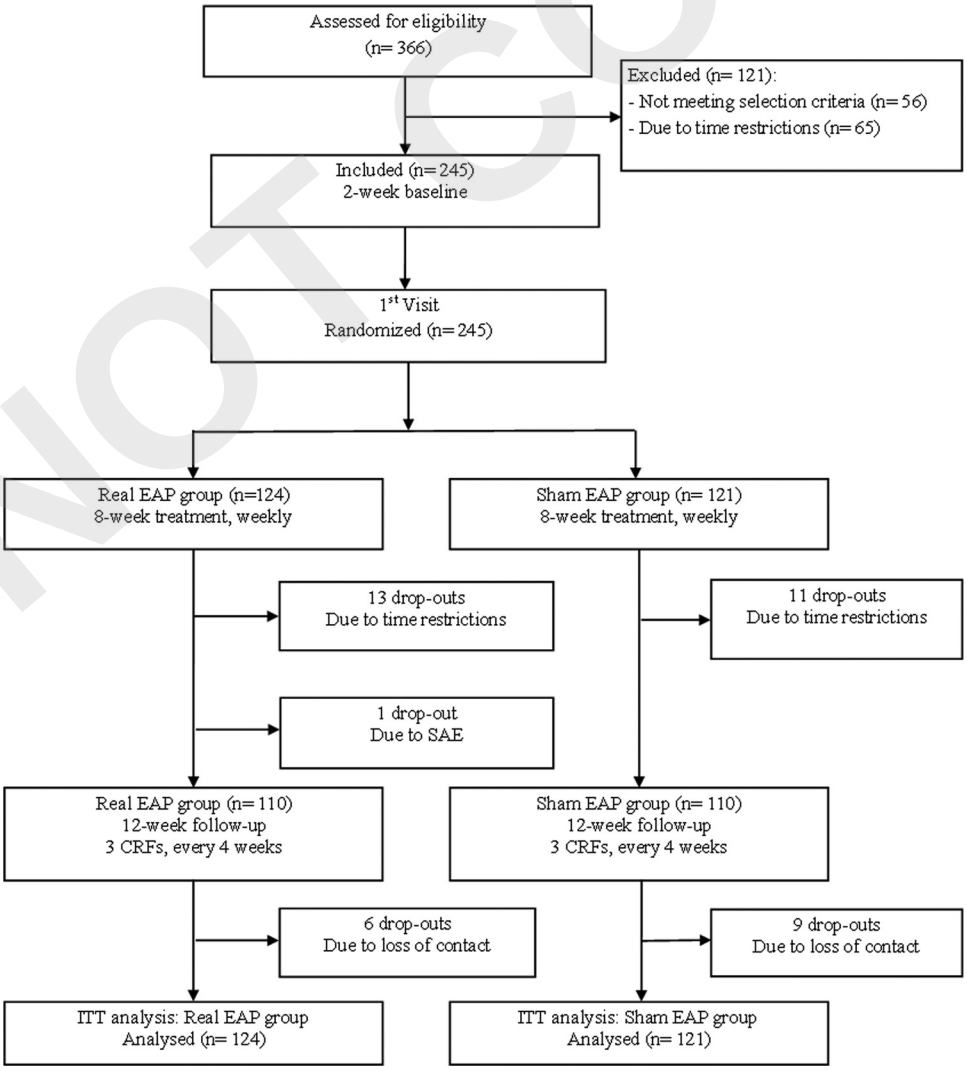

Figure 3. Flow diagram of trial procedure.

Change of Medication Usage Data

There was no difference between two groups for the change of medication usage at the end of treatment (0.09 [−0.18, 2.64]) and at the end of follow-up periods (0.11 [−1.14, 3.45]).

Adverse Events

During the treatment period, some participants reported discomfort such as sore/itchy around pellets or bothering with pellets, which are intrinsic to EAP treatment. Overall, there were eight

Table 1 **Demographic characteristics of included participants**

	Mean ± SD		Significance	
	Real EAP (n = 124)	**Sham EAP (n = 121)**		
Age (yr)	36.98 ± 11.89	38.69 ± 12.97	$t = -1.08$	$p = 0.28$
Duration of AR (yr)	14.92 ± 12.43	14.13 ± 12.94	$t = 0.49$	$p = 0.63$
Gender	No. of Participants			
Male	56	51	$\chi^2 = 0.27$	$p = 0.64$
Female	68	70		
Smoking status				
Current	12	9	$\chi^2 = 0.42$	$p = 0.81$
Former	19	18		
Never	93	94		
Family history of AR	53	40	$\chi^2 = 2.44$	$p = 0.12$

EAP = ear acupressure; AR = allergic rhinitis.

Table 2 **Summary of treatment effects**

Symptom Score	Group	Baseline (mean ± SD)	Change from Baseline to the End of Treatment (mean ± SD)	Change from Baseline to End of Follow-up (mean ± SD)	Comparison of Changes between Groups (change in real EAP − change in sham EAP; mean difference, 95% CI; p value)	
					End of Treatment	**End of Follow-up**
Total nasal symptom score	Real EAP	3.28 ± 2.22	−0.66 ± 1.51	−0.68 ± 1.50	−0.40 (−0.73, 0.05)	−0.49 (−0.87, −0.10)
	Sham EAP	3.00 ± 2.19	−0.29 ± 1.57	−0.19 ± 1.58	$p = 0.09$	$p = 0.02$
Sneezing score	Real EAP	3.13 ± 2.30	−0.49 ± 1.45	−0.40 ± 1.57	−0.39 (−0.77, −0.01)	−0.39 (−0.80, 0.02)
	Sham EAP	2.88 ± 2.09	−0.10 ± 1.56	−0.01 ± 1.67	$p = 0.04$	$p = 0.06$
Runny nose score	Real EAP	3.11 ± 2.32	−0.42 ± 1.57	−0.52 ± 1.43	−0.27 (−0.68, 0.14)	−0.51 (−0.92, −0.11)
	Sham EAP	2.76 ± 2.14*	−0.15 ± 1.67	−0.00 ± 1.78	$p = 0.12$	$p = 0.01$
Eye symptom score	Real EAP	2.10 ± 2.15	−0.23 ± 1.14	−0.30 ± 1.25	−0.18 (−0.45, 0.10)	−0.36 (−0.67, −0.05)
	Sham EAP	2.03 ± 2.10	−0.06 ± 1.03	0.07 ± 1.22	$p = 0.20$	$p = 0.02$
Global QoL score	Real EAP	4.00 ± 3.01	0.93 ± 1.32	0.76 ± 1.50	0.50 (0.17, 0.83)	0.42 (0.04, 0.80)
	Sham EAP	4.31 ± 3.07*	0.43 ± 1.30	0.34 ± 1.50	$p = 0.003$	$p = 0.03$

**Baseline difference between groups: $p < 0.05$.*
EAP = ear acupressure; QoL = quality of life.

Table 3 **Pellets dosage**

	Intervention (n = 124) Mean ± SD	Control (n = 121) Mean ± SD	Significance p Value
Total pellets dosage—8 wk	241.80 ± 66.60	247.94 ± 58.03	0.44
Weekly total pellets dosage—wk 1	32.62 ± 3.59	33.00 ± 3.53	0.40
Weekly total pellets dosage—wk 2	31.74 ± 4.92	33.4 ± 2.45	0.52
Weekly total pellets dosage—wk 3	32.68 ± 4.48	33.15 ± 3.22	0.37
Weekly total pellets dosage—wk 4	32.90 ± 4.10	32.80 ± 3.36	0.99
Weekly total pellets dosage—wk 5	33.01 ± 3.40	33.54 ± 2.67	0.20
Weekly total pellets dosage—wk 6	32.82 ± 3.53	32.81 ± 3.47	0.98
Weekly total pellets dosage—wk 7	33.22 ± 3.03	33.25 ± 3.50	0.95
Weekly total pellets dosage—wk 8	33.06 ± 3.64	33.61 ± 2.41	0.19

participants in the real group who reported 17 AEs and nine participants in the sham group who reported 20 AEs ($\chi^2 = 0.01$; $p = 0.76$).

Some EAP-related AEs such as pellets irritating skin (one and two in real/sham groups) and ear acupoint inflammation (two and one event[s] in real/sham groups) was reported during the 1st week.

Table 4 **Credibility of blinding**

	No. of Participants (intervention group)	No. of Participants (control group)	Significance
Credibility of blinding, wk 1			$\chi^2 = 1.00$ $p = 0.61$
Real	41	44	
Sham	11	7	
Not sure	69	70	
Total	121	121	
Credibility of blinding, wk 8			
Real	48	36	$\chi^2 = 2.93$ $p = 0.23$
Sham	11	15	
Not sure	49	57	
Total	108	108	

These events were effectively managed by refining the pressing techniques by the participants, without any medical assistance required. Some participants reported headache or dizziness (11 and 14 events in real/sham group) and insomnia (two events in sham group), but whether these sensations were caused by EAP treatment remains unclear. Two severe AEs occurred in China and were reported to the Human Research Ethics Committees, one from the real EAP group (benign paroxysmal positional vertigo required hospitalization) and one from the sham group (sudden deafness required medical assistance). Both events were participants' preexisting conditions and the investigation revealed that the reoccurrences were not related to EAP treatment. Both participants recovered but the participant in the real EAP dropped out.

DISCUSSION

Efficacy of EAP for PAR

The results of this multicenter trial indicated that 8-week EAP has a short-term effect on sneezing and an extended effect on eye and nose symptoms. In addition, PAR-related QoL was improved both in the short term at the end of treatment and was extended for 12 weeks after the treatment. It is important to note that because of the overall mild–moderate symptoms at baseline, the scope for improvement over the treatment period was limited (Table 2), and whether the EAP treatment is effective for mild PAR only or for severe PAR as well remains unclear.

In Australia, patients' PAR symptoms usually have a seasonal trend, which is during the pollen season (September–December); PAR symptoms tend to be more severe than that of other seasons. Considering that the entire trial lasted for 22 weeks, the follow-up period of some cohorts might fall into Melbourne's early pollen season. Therefore, the magnitude of change of symptom severity in follow-up period was limited. On the other hand, the Chinese center is located in southern China with a tropical climate; thus, there is less seasonal factor affecting the symptom severity. Therefore, seasonal difference between trial sites and pollen counts are not considered factors that may affect the study results.

There was no between-group difference in the change of PAR relief medication usage. In this study, participants were permitted to take their own PAR symptom relief medication, as long as they recorded the usage in the CRFs. This was based on ethical considerations and the likely practice in the "real world." There are a range of relief medications used by the participants in this trial and thus it is not feasible to conduct subgroup analyses based on the types of relief medication such as topical and oral antihistamine or corticosteroids. The use of standardized relief medication is strongly recommended for future researches.

Safety of EAP for PAR

This study also showed that EAP is safe for the treatment of PAR. The two severe AEs reported were not considered to be caused by EAP treatment. All other mild EAP related AEs were addressed by fine tuning of the self-administering of the pressing technique. Furthermore, there was no between-group difference in the change of PAR relief medication usage. Compared to the results of a recent study[17] on a large population (229,230 subjects) 8.6% of the acupuncture users experienced at least one AE and 2.2% reported one that required treatment, our trial showed that participants who received EAP experienced less AEs. This may be attributable to not involving skin penetration in the EAP treatment. Moreover, EAP is a semi–self-administered technique and many of the reported discomforts were alleviated when the participants became more experienced.

How Does EAP Work

The underlying mechanism of EAP is still to be elucidated, which is beyond the scope of this study. An understanding of mechanisms of acupuncture may offer insight into how EAP works for PAR. Animal experiments and clinical trials have shown anti-inflammatory effects[18,19] and immunomodulation[20] of acupuncture. It has been suggested that acupuncture may exert anti-inflammatory effects through a complex neuroendocrinoimmunologic network of actions and thus relieve AR symptoms.[21] An RCT showed that EAP and body acupuncture had similar effects on reducing cytokines (IL-4) and serum total IgE level.[22] Whether EAP shares the similar functions is still to be investigated.

Implications for Clinical Practice and Further Research

Applying stimulation on ear acupoints has been widely used in clinical practice and proved to be effective for a large group of conditions, such as pain,[23] anxiety,[24] drug dependence,[25] obesity,[26] *etc*. Compared with needling acupuncture (usually twice a week, 30–40 minutes each session), EAP requires once a week, 5–10 minutes per session, there is clear strength of the EAP techniques in terms of cost-effectiveness when compared with acupuncture. Moreover, being a semi–self-administered method, the strength and duration of acupoint stimulation are managed by participants, making the EAP treatment more flexible for obtaining symptomatic relief. However, the difference of effectiveness between EAP techniques and needling acupuncture was not investigated by this study. Additional study could take this into consideration and provide more evidence of "cost-effectiveness."

AR has a significant impact on patients' QoL associated with direct and indirect economic burden. Despite a recent large-size trial concluding that using acupuncture in addition to routine care to treat AR was cost-effective,[27] there is inadequate evidence supporting the overall cost-effectiveness of acupuncture for AR.[28] Likewise, the impact of the EAP needs further investigation. Consequently, future studies should include cost-effectiveness analysis such as the use of 36-item Short Form for quality-adjusted life year determination.

In conclusion, it is suggested that EAP is a safe and effective alternative to needling acupuncture for the clinical management of PAR.

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