Efficacy of acupuncture in improving the quality of life of patient's with moderate or severe acne vulgaris: protocol for a randomized controlled trial

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Abstract

Background Acne vulgaris (AV) is a common chronic dermatologic disease that tends to impair the quality of life of patients. None of the previous clinical trials of acupuncture therapy for AV used the quality of life as a primary outcome or employed a sham acupuncture control arm. Methods/design Participants with AV will be randomly assigned to acupuncture or sham acupuncture groups (1:1 allocation). All participants will receive 4-week treatment comprising of a total of 12 sessions (3 sessions per week). The primary outcome will be change from baseline in the Skindex-16 scale total score at treatment completion. The secondary outcomes will be Skindex-16 subscale scores, the Dermatology Life Quality Index scale total score, the total lesion count and inflammatory lesion count, itch and pain assessment using the visual analogue scale score, patient expectations of acupuncture, patient satisfaction with treatment, and the blinding of the effect of sham acupuncture. Follow-up evaluation will be performed at weeks 16 and 28. All outcome analyses will be performed in the intention-to-treat population. Discussion This is the first randomized controlled trial which will compare the effect of acupuncture versus sham acupuncture in improving the quality of life of patients with moderate or severe acne vulgaris (AV). The limitation of the design of this trial is that the sample size of a single center trial, which may lead to potential overestimation of the effect of acupuncture. Meanwhile, due to the characteristics of acupuncture, the acupuncturists will not be blinded and the use of non-acupoints and minimal acupuncture without any manipulation, which may introduce an element of bias and cause some biological effect.

Background

Acne vulgaris (AV) is a common chronic dermatologic disease involving the pilosebaceous units [1, 2]. The symptoms of AV include skin lesions such as comedones, erythematous papules, pustules, nodules, deep pustules, and scarring. The lesions typically affect the face, chest and back [1, 3]. An estimated 79–95% of the adolescent population is affected by AV. In Western populations, 40–54% of individuals affected by AV are older than 25 years [4]. As lesions of AV predominantly occur on face, the disease may induce psychosocial symptoms such as anxiety and lowered self-esteem [5, 6]. Consequently, AV may lead to a decline in the quality of life of the afflicted individual [5–8].

The American Society of Dermatology recommends topical benzoyl peroxide or combination of erythromycin, clindamycin, topical retinoids, or systemic antibiotic therapy as the first-line treatment for mild to severe AV [1–3]. However, these treatments may cause side effects such as drying, peeling, erythema, and skin irritation. In addition, long-term treatment may induce drug resistance and is associated with relatively high recurrence rate [9].

Owing to the side effects of conventional drugs, there is an increasing interest in the use of natural and safer treatment options; these include complementary and alternative treatment remedies, such as herbal medicine and acupuncture [9, 10]. Several trials have indicated that acupuncture may alleviate the skin

lesions and improve the quality of life of patients with AV [11–15]; however, these trials were of low quality and the level of evidence was low. In our pilot trial (unpublished) conducted from April 2017 to March 2018, 42 patients with moderate or severe AV were randomized into acupuncture group (n = 21) and sham acupuncture (n = 21) groups. After 4-week treatment, the reduction in the lesions of skin was −6.62 ± 15.42 and −15.10 ± 20.13 after treatment for the acupuncture and the sham acupuncture groups, respectively. And we found no significant between-group difference with respect to the the lesions of skin (P = 0.137), which contradicts the results of previous trials [11–14]. However, After 4 weeks, the reduction in the the Skindex−16 scale total score was −12.50 ± 19.09 (32.39 ± 21.36 at baseline and 19.89 ± 15.40 after treatment) and 0.40 ± 21.12 (30.03 ± 20.78 at baseline and 30.43 ± 19.39 after treatment) after treatment for the acupuncture and the sham acupuncture groups, respectively. There was a significant between-group difference with respect to the Skindex−16 scale total score (P = 0.044), which suggests that acupuncture may afford symptom relief and improve the quality of life of patients with moderate or severe AV.

Therefore, the primary objective of the present study was to evaluate the effect of acupuncture on the quality of life of patients with moderate or severe AV. The secondary objective was to evaluate the safety and efficacy of acupuncture in improving the symptoms of AV.

Methods/design

Study design

The proposed study is a prospective, randomized, sham acupuncture controlled trial with two parallel arms using a 1:1 allocation ratio. The trial will be conducted at the Guang' anmen Hospital, China Academy of Chinese Medical Sciences. The study protocol conforms to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[16] and the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [17]. Participants will be recruited between Augest 2019 to March 2020 at the Guang' anmen Hospital, China Academy of Chinese Medical Sciences. Participation will be solicited through advertisement using posters, Wechat social media application, hospital websites, and networks. A dermatologist will be responsible for diagnosis. The randomized scheme has been prepared by the National Clinical Drug testing Institute at the Guang' anmen Hospital. Block randomization using the closed envelope method will be used. Participants will be randomly assigned by the SAS software to receive acupuncture or sham acupuncture in a 1:1 ratio. The numbers of randomization and the group allocation will be sealed in an impermeable envelope, and the numbers based on the order of inclusion will be marked on the cover of the envelope. Randomization envelopes and their distribution will be handled by a researcher who is not involved in the treatment or evaluation. Additionally, all participants will undergo a baseline assessment (−1 week to 0 week) prior to randomization. The participants, effect evaluator, and data manager will be blinded to group allocation. However, because of the characteristics of acupuncture, acupuncturists will not be blinded in this trial. A schematic illustration of the study design is shown in Figure 1.

Ethical approval

This clinical trial will adhere to the principles of the Declaration of Helsinki of World medical conference. This trial has been approved by the Ethics Committee of the Guang'anmen Hospital (2018−137-KY−01) (See Additional file 1).

Participants

96 participants with AV will be recruited in the trial.

Inclusion criteria

1. Individuals aged 18−48 years who qualify the diagnostic criteria for AV[18, 19];
2. Global acne grading system (GAGS) score [20] between 19 and 38.

Exclusion criteria

Participants who qualify any of the following criteria will be excluded:

1. Individuals with polymerization acne, explosive acne, drug acne, premenstrual acne, cosmetic acne, occupational acne, or any other subtypes of acne;
2. Individuals with other severe diseases that may affect the acne, such as polycystic ovary syndrome, thyroid disease, or atypical congenital adrenal hyperplasia;
3. Individuals with other skin diseases that may influence the evaluation of AV, such as rosacea, folliculitis, or other skin diseases;
4. Individuals who have received antibiotics, retinoic acid, steroids, or anti-inflammatory drugs in the preceding month;
5. Individuals with severe heart, liver, kidney, hematopoietic system or autoimmune disorders, severe systemic malnutrition;
6. Pregnant and lactating women or those planning to conceive within 12 months;
7. Individuals who have acupuncture experience in the past 3 months.

Intervention

All participants will receive treatment for 4 weeks with 3 sessions per week (ideally every other day). Therefore, all participants will undergo a total of 12 sessions. Acupuncturists (academic background: above undergraduate degree) with over 1 year clinical experience at the Guang'anmen Hospital will be responsible for treatment. Two acupuncturists (respectively) will administer treatment in the two groups. Efforts will be made to avoid communication among the participants during the trial period.

Acupuncture group

The locations of acupoints is described as per 'the Nomenclature and Location of Acupuncture Points (National Standard of People's Republic of China, 2006 [GB/T 12346–2006]) [21]. The selections of acupoints will be decided with reference to the 'Guidelines for AV treatment in China' (revised version 2014) [22]. Participants in the acupuncture group will receive acupuncture at Dazhui (CV14), bilateral Quchi (LI11), bilateral Hegu (LI4), bilateral Zusanli (ST36), and bilateral Neiting (ST44) with disposable acupuncture needles (0.30×40 mm, Huatuo Brand, Suzhou Medical Appliance, China). After routine sterile measures, CV14 will be inserted to a depth of 30–40 mm at an angle of 15°–30° in an inferomedial direction; bilateral LI11, bilateral LI4, bilateral ST36, and bilateral ST44 will be vertically inserted to a depth of 25–30 mm for 3 times (once every 10 minutes) with slight lifting, thrusting, and twisting manipulations to produce a sensation of de-qi. Each session of acupuncture will last for 30 minutes.

Sham acupuncture group

Participants in the sham acupuncture group will receive sham acupuncture at sham CV14 (10 mm to CV14), LI11 (10 mm to LI11), LI4 (10 mm to LI4), ST36 (25 mm to ST36) and ST44 (10 mm to ST44) with disposable acupuncture needles (0.30×25 mm, Huatuo Brand, Suzhou Medical Appliance, China). Sham CV14, LI11, LI4, ST36, ST44 will be vertically inserted to a depth of 1–2 mm without any manipulation and de-qi. The treatment sessions will last for 30 minutes.

Participants will not be allowed use of other treatments for AV throughout the trial. Detailed information pertaining to use of other treatments will be recorded in the case report form.

Outcome measures

The primary outcome will be the change from baseline in the Skindex–16 scale total score at the end of 4-week treatment. The Skindex–16 scale is used to measure the effects of skin disease on the quality of life of patients. The scale includes a total of 16 items categorized into three domains: the symptoms of participants with AV, the emotions of participants with AV, and function of participants with AV [23, 24]. The Skindex–16 scale score ranges from 0 (best) to 100 (worst); the minimal clinically important difference (MCID) is 10 [23, 24].

Secondary outcomes will be included:

1. The change from baseline in the Skindex–16 scale total score at weeks 16 and 28;
2. The change from baseline in the Skindex–16 subscale (the symptoms of participants with AV, the emotions of participants with AV, and functioning of participants with AV) scores at weeks 4, 16, and 28;
3. The change from baseline in the Dermatology Life Quality Index (DLQI) [25] scale total score at weeks 16 and 28. DLQI scale is a tool for assessment of health-related quality of life of patients with skin diseases; it has a total of 10 items. The range of DLQI ranges from 0 (best) to 100 (worst); the MCID [26] is 10.

4. The change from baseline in the total lesion (inflammatory and non-inflammatory lesions) counts (TLC) at at weeks 4, weeks 16 and 28;

5. The change from baseline in the inflammatory lesions counts (ILC) at weeks 4, 16 and 28. The inflammatory lesions include the inflammatory papules, pustules, and cysts; the non-inflammatory lesions include the black and white head comedones. The lesions are assessed on the forehead, cheeks, nose, and chin. The inflammatory and non-inflammatory lesions are counted from the face pictures obtained using a digital camera.

6. The change from baseline in the itch assessment with visual analogue scale (IVAS) [27] total score at weeks 4, 16 and 28;

7. The change from baseline in the pain assessment with visual analogue scale (PVAS) [27] total score at weeks 4, 16 and 28;

8. The participants' expectations of acupuncture will be assessed at baseline using the following 2 questions: "Do you think acupuncture will be effective for treating the illness?" and "Do you think acupuncture will be effective for relieving the related symptoms of AV?" The response options will be "Yes," "No," or "Unclear.".

9. The participants' self-satisfaction of acupuncture treatment will be measured at weeks 4, 16 and 28.

The details of the evaluation of outcomes are shown in Table 1.

Safety evaluation and blinding assessment

Adverse events (AE) including AEs related to acupuncture (broken needle, local hematoma, infection, abscess, and others), AEs related to post- acupuncture (nausea, vomiting, palpitations, dizziness, headache, insomnia, or any other symptoms after acupuncture treatment), and AEs unrelated to treatment. For safety assessment, details of all AEs will be recorded in the case report form by a research assistant.

To assess the blinding effect of sham acupuncture, participants will answer the following questions within 5 minutes after any treatment session during period of week 4 treatment: "Do you think you have received traditional acupuncture?" The response options will be "Yes," "No," or "Unclear.".

Sample size and statistical analysis

The sample size of this trial was calculated based on the primary outcome, which is the change from baseline in the Skindex−16 scale score at the end of week 4. In our unpublished pilot trial, the mean (± standard deviation) reduction in the Skindex−16 scale score after 4-week treatment was −12.50 ± 19.09 and 0.40 ± 21.12 after treatment for the acupuncture and the sham acupuncture groups, respectively. Assuming an alpha risk of 5% and a beta risk of 20%, a sample size of 96 (48 participants in each group) was calculated considering a 20% dropout rate.

The data will be analyzed using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) according to intention-to-treat principle. Normally distributed continuous variables will be reported as mean±standard deviation and 95% confidence intervals; non-normally distributed continuous variables will be reported as median (interquartile range). Categorical variables will be presented as frequency (%). For data pertaining to drop-outs, multiple imputation will be used for statistical analysis. Between-group differences with respect to normally distributed continuous variables will be assessed using the *t*-test or Chi-squared test; those with respect to non-normally distributed continuous variables will be assessed using the non-parametric Wilcoxon statistics. Chi-squared test will be used for categorical variables. All P values will be two-tailed; $P \leq 0.05$ will be considered indicative of statistical significance.

Quality control

All researchers will undergo a training course before the beginning of this trial. Due measures will be implemented to ensure the traceability and confidentiality of the case report form, informed consent form, and other original data. Double input method will be used for data entry. All AEs will be recorded in detail, properly handled, and tracked. All trial-related procedures and data management will be supervised.

Discussion

Several RCTs suggest that acupuncture may be effective for patients with AV. However, the results of these RCTs are controversial due to lower quality of their design and the possible placebo effects of acupuncture [11−15]. In this trial, we aim to evaluate the therapeutic effect of acupuncture on the quality of life of patients with moderate or severe AV compared with sham acupuncture; in addition, we seek to partially exclude the possible placebo effects of acupuncture.

Generally speaking, there is no ideal placebo acupuncture control; the sham control with use of a non-insertion-type needle on non-acupoints is the best possible choice to reduce its possible biological effects as much as possible [24, 25]. However, the non-insertion-type needle leaves no marks or wounds of acupuncture on the skin; moreover, the acupoints chosen in this trial were mostly located in the chest, abdomen, and the forearm. Therefore, it will be easy for the participants to perceive this sham acupucnture which will compromise the blinding. Therefore, we opted for non-acupoints and minimal acupuncture without any manipulation as the sham acupuncture in this trial. Besides, the non-acupoints are in proximity to the classical acupoints, which will increase the feasibility of blinding.

The Skindex−16 scale and the DLQI scale are two brief, skin-related, quality-of-life scales with satisfactory reliability and validity; these will be used to evaluate the efficacy of acupuncture in improving the quality of life of patients with AV [26, 27]. The Skindex−16 scale is a skin-related measure with three domains related to patients with AV (symptoms, emotions, and functioning of patients with AV). We also use TLC, ITC, IVAS, and PVAS as secondary outcomes to assess the lesion counts and main symptoms (itch or pain) related to AV. These would provide a comprehensive evaluation of the overall effectiveness of acupuncture.

Finally, some potential limitations of our study should be acknowledged. This will be a single center study with a relatively small sample size; therefore, the results may not apply to other countries or settings. Moreover, it may lead to overestimation of the effect of acupuncture. The use of non-acupoints and minimal acupuncture without any manipulation may cause some biological effect leading to false-negative results [24, 25]. Above all, the expectant results of our trial will answer whether acupuncture is effective in improving the quality of life of patients with AV in some extent.

Trial status: No recruitment at the present (The protocol version is August 2019, the trial will recruitment at August 2019, and will be completed by December 2020).

Abbreviations

AV = Acne vulgaris, SPIRIT = Standard Protocol Items: Recommendations for Interventional Trials, STRICTA = Standards for Reporting Interventions in Clinical Trials of Acupuncture, GAGS = global acne grading syste, MCID = minimal clinically important difference, DLQI = Dermatology Life Quality Index, TLC = total lesions counts, ITC = inflammatory lesions counts, IVAS = Itch Assessment with Visual Analogue Scale, PVAS = Pain Assessment with Visual Analogue Scale, AE = Adverse events.

Declarations

References

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Table 1

Table 1. The time-points for assessment of outcomes

Measure outcomes	Enrollment and allocation Baseline	Treatment Week 1	Week 2	Week 3	Week 4	Follow-up Week 16	Week 28
Skindex-16 total score	×				×	×	×
Skindex-16 subscales score	×				×	×	×
DLQI total score	×				×	×	×
TLC	×				×	×	×
ILC	×				×	×	×
IVAS score	×				×	×	×
PVAS score	×				×	×	×
Blinding assessment					×		
Expectation	×						
Safety assessment	×	×	×	×	×	×	×

DLQI, Dermatology Life Quality Index scale; TLC, total lesion count; ILC, inflammatory lesion count; IVAS, itch assessment with visual analogue scale; PVAS, pain assessment with visual analogue scale

Figures
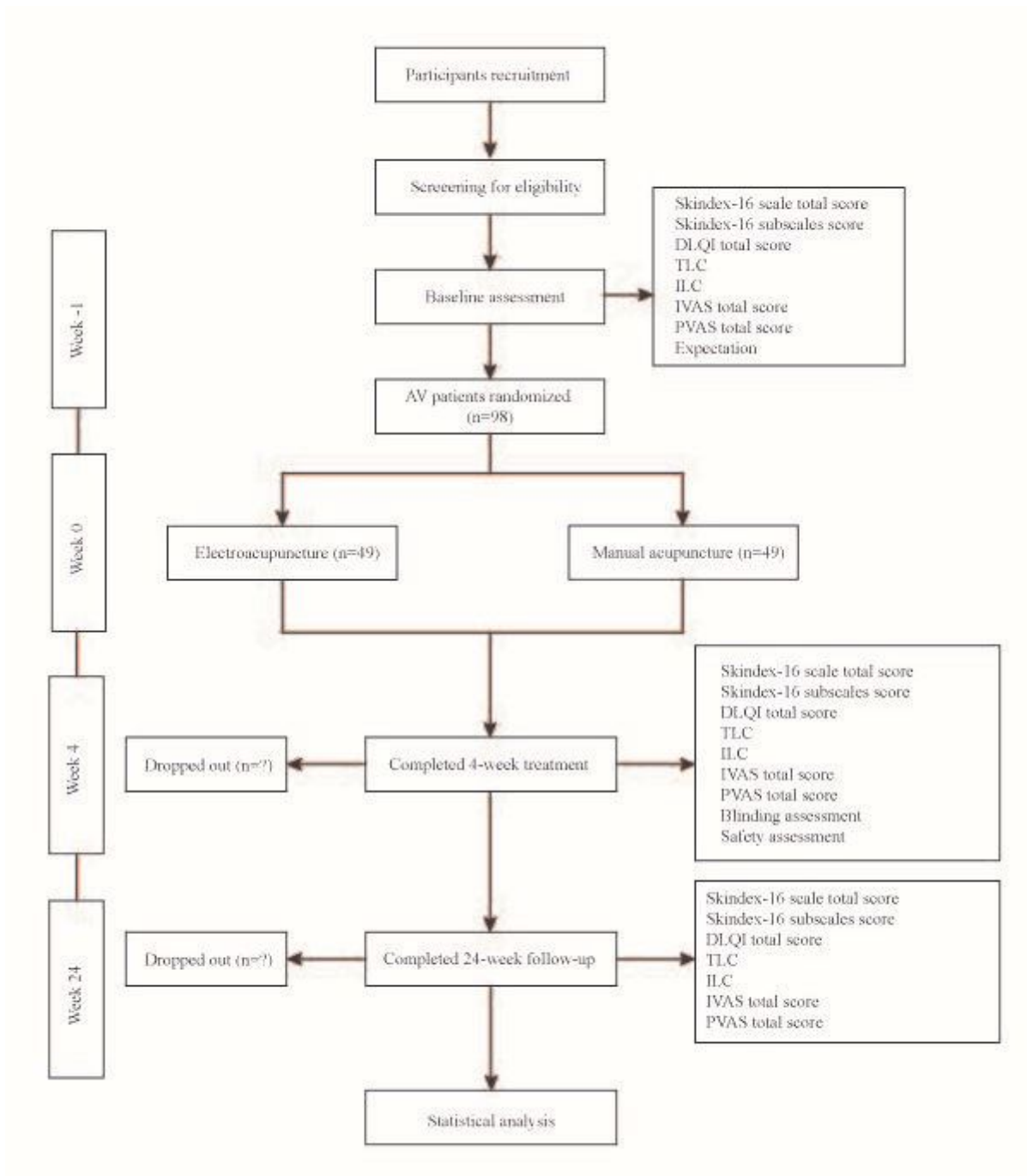
Figure 1

Trial flow diagram

Supplementary Files

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