Acupoint Catgut Embedding Combined with Time-restricted Feeding for the Treatment of Simple Obesity: A Randomized Controlled Trial

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Abstract: Obesity is known as being closely related to a variety of diseases and harm to health. Obesity has become a worldwide major public health, affecting adults, adolescents, and children of both genders. In recent years, acupoint catgut embedding(ACE) with other therapies for the treatment of obesity has attracted attention, studies have shown combination therapies have more significant effect. Meantime, time-restricted feeding(TRF), as a new research hot-spot, has been confirmed to improve metabolism and control obesity by regulating human rhythm. But there have been not clear trials of those two combinations. This study aims to explore the clinical effects of acupoint catgut embedding combine with time-restricted feeding in the treatment of simple obesity people. This study is a parallel-design, randomized, and controlled clinical study. A total of 162 participants will be randomly assigned to three different groups in a 1:1:1 ratio. Participants in the ACE group will receive ACE treatment, and participants in the ACE + TRF group will have time-restricted eating on base of the ACE treatment, with a daily eating time of 8am-6pm. The control group received no treatment during the experiment. All participants will receive treatment for 12 weeks, and are followed for another 12 weeks. The primary outcome is the participants' weight and body mass index(BMI). Secondary indicators are participants' waist circumference, hip circumference, waist-hip ratio (WHR), body fat percentage (BFR), blood lipids, blood sugar, and uric acid. Trial efficacy will be assessed by measurement results.

1. Introduction

Simple obesity refers to disorders caused by over-accumulated or distorted fat in the body which is characterized by non-endocrine and metabolic factors. Obesity occurs at all age periods, especially the prevalence in children. A data prediction in 2016 declare that the global overweight rate of children aged 5~17 will increase from 13.9% in 2010 to 15.8% in 2025 [1]. Meantime, simple obesity could induce a variety of diseases, such as hypertension, diabetes, gout and cardiovascular diseases

[2,3]. Some studies suggest that obesity, especially abdominal obesity can clearly increase the risk of diabetes [4]. Obesity has also been linked to induce cancers, including breast and rectal cancer [2,5]. A survey in 2002 showed that Obesity is associated with increases in annual health-care costs of 36% and medication costs of 77% compared with being of average weight [6], it seems that obesity and its complications impose a heavy burden on economic and social development and become a serious health problem.

Therapeutic methods in modern medicine for anti-obesity such as lifestyle modification (specifically dietary modification and regular exercise), surgery or drugs. However, there still exists many shortcomings. For example, controlling diet calorie may cause nutrient absorption problems and the long-term effect of weight losing will drop sharply [7]. Exercise treatment recommend obesity people participating in at least 150 minutes of moderate-intensity or 75 minutes of vigorous intensity aerobic exercise weekly, and resistance muscle strengthening training to lose weight [8], apparently, it is hard for them to persist. At the same time, the surgical treatment operation is complicated and expensive. On the other hand, drugs seem to be questionable in the aspect of their side-effect, such as serious suicidal tendency and the high risk of cerebrovascular diseases [9,10]. Such side effects are underestimated.

ACE (Figure 1), as the extension and development of acupuncture, has been used for many years to treat obesity. ACE have a definite therapeutic effect in the treatment of simple obesity, which is closely associated with the decline of serum insulin, glucose and TNF-alpha levels, and the decrease of insulin resistance [11]. Previous research revealed that the weight and body mass index (BMI) of obese patients could be significantly decreased after ACE therapy [12].

Figure 1: Acupoint catgut embedding (ACE)

Nowadays, as a new diet method for losing weight, time-restricted feeding(TRF) has attained great attention, as shown in Figure 2. It refers to that feeding time is restricted to certain hours of the day, generally 8-12 h, and it does not limit the number of calories. In contrast to other dietary intervention modalities, TRF emphasizes eating at a specific time [13]. Animal experiments have confirmed that TRF can reduce body weight, improve blood sugar control, reduce insulin levels, lower blood pressure, prevent hyperlipidemia, and reduce liver fat in rodents fed the same calorie food conditions

[14,15]. Mechanistic studies have shown that time-restricted eating can promote white fat browning, reduce obesity and improve metabolic disorders by remodeling the intestinal flora [16,17]. Clinical studies have shown that time-restricted eating can reduce weight, body fat and waist circumference in overweight and obese people, and even under high-fat diets, it has a significant effect; Time-restricted eating in normal-weight individuals can also reduce or maintain weight, reduce body fat, and improve the ratio of fat to nonfat mass [18].

Figure 2: Time-restricted feeding (TRF)

Hence, this study is designed as a RCT to assess the effectiveness of ACE combine with TRF for treatment of obesity.

2. Ethical approval

The study protocol was approved by the Ethics Committee of The Affiliated Traditional Chinese Medicine Hospital of Southwest Medical University (permission number: KY2022048-FS01). The study will be conducted in accordance with the 1975 Declaration of Helsinki. Trained operators will provide skilled treatment. Both verbal and written information describing the potential risks and benefits of the clinical study will tell participants. Written informed consent will be obtained from all participants before enrollment. Any modifications to the protocol will be reported and approved by the ethics committee and will be communicated to the trial registry, investigators and data monitoring researchers.

3. Study design

This is a parallel-design, randomized trial that uses the blind method separately to implement measures for operator, efficacy evaluator, and statistical analyst to achieve. This trial is conducted at The Affiliated Traditional Chinese Medicine Hospital of Southwest Medical University (Luzhou, Sichuan, China). Ninety eligible participants will be randomly assigned to a controlled treatment group(group A), ACE group(group B) or ACE + TRF group(group C) in a 1:1:1 ratio. The total experiment period will be about 6 mouths, including 3-mouths'treatment and 3-mouths' following period. Participants received 6 sessions of ACE or ACE + TRF treatment in the first 3 months, ACE is operated every two weeks, 3 times' treatments are a course of treatment. During the treatment and follow-up periods, participants will be not allowed to take any anti-obesity measures such as drugs. Efficacy evaluators need to record participants' body index indicators such as weight, BMI, waistline, hipline, waist-hip ratio, abdominal circumference(AC), and biochemical indicators such as fasting blood glucose, blood lipids, and uric acid after every treatment course.

4. Recruitment

Patients are recruited by reviewing and screening at The Affiliated Traditional Chinese Medicine Hospital of Southwest Medical University, and through media advertisement.

5. Participants

5.1. Inclusion criteria

(1) Patients with the body mass index (BMI) of ≥ 24 kg/m2, or the waist circumference of ≥ 90 cm for male, ≥ 80 cm for female (measured when breathing slightly in a calm breathing state) will be included;

(2) Patients aged between 45 and 65 years old (including 45 and 65 years old) will be included;

(3) Patients without major diseases of the heart, liver, kidney and other organs will be included;

(4) Patients without mental illness will be included;

(5) Patients without obvious cognitive impairment will be included;

(6) Patients who voluntary participation in this trial and signed the informed consent will be included.

5.2. Exclusion criteria

(1) Patients who are pregnant, breastfeeding or plan to become pregnant will be excluded;

(2) Patients who can not cooperate with the completion of the research process will be excluded;

(3) Patients who take other weight loss products at the same time will be excluded;

(4) Patients who have other serious diseases of the circulatory system, hematopoietic system, digestive system, endocrine system will be excluded;

(5) Patients with a lower pain threshold or participated in clinical trials of other drugs will be excluded.

5.3. Randomization and allocation concealment

Randomization will be performed via a computerized random number allocation method operated by a statistician who doesn't take part in this trial. After 162 participants are recruited, they will be allocated into 3 groups by 1:1:1 ratio. 1-162 are distributed for representing 3 groups by computer in advance. Then we will prepare 162 invisible envelopes where store these numbers. Every participant gets a envelop randomly in the order of patient enrollment, and the operator assistant opens the envelope, and then assign the participant into the group A, B, C.

5.4. Blinding

Because of the particularity of ACE treatment, it is difficult for practitioners to be blinded. Therefore, operators are not allowed to take part in the data-collecting and assessment procedure. Participants in different groups will receive treatment in different therapeutic rooms. Blind evaluation of participants will be conducted at the end of the observation period. The outcome assessors, data collectors, and statisticians will be blinded to group allocations during the study.

5.5. Sample

According to the relevant studies, the effective rate of the combination treatment in this study is about 90%; The effectiveness rate of the ACE group was 85%, which was estimated according to the

estimation formula of the sample size of the two-sample rate comparison completely randomly designed in "Statistics and Software Application of Traditional Chinese Medicine" published by China Traditional Chinese Medicine Press. The formula is as follows:n=[2(μα+μβ)2·p(1-P)]/(P2-P1)2. Let α=0. 05, β=0. 1, p=(p1+p2)/2, p1=85%, p2=90%, we calculate that n=54. The number of samples required for each group is set to be 54 cases.

5.6. Interventions

After baseline measurements, patients satisfying the inclusion criteria will be randomly divided into the groups, as shown below:

(1) Group A: The control group. This group will not receive any treatment during the experiment.

(2) Group B: The ACE group. This group will receive ACE treatment, the points will be selected as: Tianshu. Daheng. Qihai. Guanyuan. Shuidao. Zusanli. Shuifen. Zhongwan. Daimai. The subjects will be receive 2 periods of treatment.

(3) Group C: The ACE +TRF group. The ACE intervention in this group will be the same as that for the group B. Furthermore, this group will be demanded to control the mealtime at 8:00 to 18:00.

The ACE intervention is compliant with the Standards for Reporting Interventions in Clinical Trials of Acupuncture (S The control group TRICTA) guidelines. The intervention process is shown in Table 1.

Table 1: The intervention process

Time point(weeks)	0	2	4	6	8	10	12	24
Eligibility	×							
Informed consent	×							
Allocation	×							
Treatment		×	×	×	×	×	×	
Index assessment	×	×	×	×	×	×	×	×
Follow-ups		×	×	×	×	×	×	×

6. Outcome measures

6.1. Primary outcome measure

The clinical outcomes will be used to assess patients' obesity levels. All measurements will be undertaken at baseline and every treatment period and three months after the completion of treatment. The primary outcome is the variation of BMI and weight from baseline to the end. The BMI is calculated as follows: BMI = weight(kg)/ (height(m))^2. According to the Fifth National Academic Conference on Obesity Research in 1997, our criteria for judging the final efficacy are: Clinical recovery: clinical symptoms disappear, weight nears to normal or overweight range, weight loss >80%, or BMI closes to 26-27kg/m² Markedly effective: Most clinical symptoms disappear, weight decreases by 30%-70% or BMI decreases by ≥4kg/m² Effective: clinical symptoms are significantly improved, body weight is reduced by 25%-30% or BMI is reduced by 2-4kg/m² Invalid: There is no significant improvement in clinical symptoms, the weight loss does not reach <25% or the BMI decreases <2kg/m² The secondary outcomes will include waist circumference (WC), hip circumference (HC), waist:hip ratio (WHR), body fat percentage (BFP). WC will be measured by a stretch-resistant tape at the midpoint between the top of the iliac crest and the lower margin of the least palpable rib. In addition, HC will be measured around the widest portion of the buttocks using a tape parallel to the floor. WHR = waist circumference (cm) / hip circumference (cm). Body fat percentage is measured by a professional measuring instrument (Inbody). The other outcome

parameters include blood sugar, blood fat, blood uric acid.

6.2. Statistical analysis

All data will be collected by excel. The independent t test and chi-square tests will be used to assess and compare the baseline patient characteristics between the treatment and the control groups. Repeated measure analysis of variance and the generalized estimating equation will be used to evaluate changes in the weight, BMI, waistline, hipline, WHR and BFP, blood sugar, blood fat, blood uric acid between the treatment and the control groups. The difference in efficacy between groups was tested using Chi-square test. Statistical significance will be considered at a P-value of $< .05$. All statistical analyses will be performed with the SPSS for Windows, version 26 (Statistics 26, SPSS).

6.3. Safety

During the treatment, adverse events such as redness, swelling, fever or allergy, infection, fat liquefaction, nerve damage, and non-absorption of collagen threads were recorded, and the treatment method, prognosis, etc. will be recorded in the CRF table, and the safety evaluation was finally completed.

7. Strengths and limitations of this study

(1) This trial used a randomized controlled study to determine whether acupoint catgut embedding combine with time-restricted feeding is effective in the treatment of simple obesity;

(2) In this experiment, three groups were set up, control group, ACE group, ACE + TRF group, and the three groups could be compared in every two groups to form multiple comparison;

(3) However, the selection of acupuncture points in this test may be too single, and all the test-subjects will select the same acupuncture points,which means lacking specificity.

8. Discussion

Obesity is an important public health issue of global concerning [19]. Finding an effective and sustained way to lose weight has become a highlight at the moment. The mechanism of obesity is mainly believed to be that adipose tissue regulates the body's energy metabolism by secreting adipokines (leptin, adiponectin, resistin, etc.), or be induced by systemic inflammation caused by secreting some pro-inflammatory factors (tumor necrosis factor, interleukin 6, etc.) [18]. Traditional Chinese Medicine has its own unique advantages in the treatment of obesity. For example, Traditional Chinese medicine can regulate energy metabolism by reducing intestinal mucosal inflammatory response, thereby restoring the normal physiological function of the intestinal mucosal barrier. But there still exists some systemic and comprehensive shortcomings in current research [20]. Previous research has shown that acupoint massage can reduce the weight, blood lipid and body fat ratio of patients who suffer from simple obesity with hypertension[21]. Acupuncture can intervene in obesity by regulating glucose and lipid metabolism, intervening in the expression of inflammatory factors and leptin receptor genes to influence hypothalamus to suppresses appetite [22.23]. As a modern product of acupuncture, acupoint thread has a more powerful stimulation than acupuncture, and experiments have proved that acupoint thread is more effective in treating obesity [24], so it is also widely used in weight management. Comprehensive treatment is the advantage of TCM treatment, and it has been found that the overall effectiveness of acupuncture combined with Chinese traditional medicine, or ACE combined with moxibustion are better than the single treatment in reducing weight, BMI and lowering biochemical indicators such as cholesterol and triglycerides [25,26]. It is generally

accepted that the time of taking food also affects weight regulation and metabolism. TRF is one of the most widely studied eating modes, which refers to eating freely for a defined period of time (generally 8 hours) throughout the day, while maintaining hungry at the other time. Animal studies have shown that TRF can regulate metabolism by maintaining the circadian rhythm, thereby fighting obesity [27]. Clinical trials have found that TRF has benefits for a variety of healthy conditions can preventively improve blood lipids, blood sugar, insulin resistance, and reduce cardiovascular risk in obese patients [28]. However, most of these studies are short-term, and the long-term effectiveness and safety for losing weight remains unclear. This trial innovatively combined the two weight loss methods of acupoint thread insertion and TRF with traditional Chinese and Western medicine, not only recorded the changes in indicators during the trial, but also measured the relevant indicators again 3 months after the end of the trial to clarify whether they had long-term effectiveness, and the difference in efficacy between the two methods of comprehensive treatment and single thread burial treatment. We hope to provide a long-term treatment of simple obesity.

Acknowledgements

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