The Efficacy And Safety of Traditional Chinese Medicine (TCM) To The Patient With Dizziness In Emergency Department — A Randomized Controlled Trial

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Study protocol

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Abstract

• **Background**: A new way of heat treatment with far-infrared and / or acupuncture on acupoints is studied to treat the stubborn dizziness of patients.

• **Methods**: A single-blinded 4-arms parallel randomized controlled trial is designed: arm of acupuncture, arm of far-infrared, arm of acupuncture plus far-infrared, arm of placebo with no far-infrared. There are four acupoints on left limbs and four acupoints on right limbs correspondingly, named as Neiguan (PC6), Hegu (LI4), Zusanli (ST36), and Taichong (LR3). The intervention time is 20 minutes for each. After treatment, visual analogue scale of dizziness, dizziness handicap intervention questionnaire and heart rate variability are used to measure and evaluate the results.

• **Discussion**: This is a prior study in use of far-infrared and / or acupuncture on acupoints for the treatment of stubborn dizziness. It promotes the basis to further acupoints treatment according to the concept of traditional Chinese medicine.

• **Trial registration**: It was registered in ClinicalTrials.gov with number NCT04415307 on date June 1, 2020.

Introduction

Background and rationale {6a}

Dizziness is a common symptom of emergency visit (1–3). Although the majority is peripheral type and not serious (4, 5), but a small portion is central type and life-threatening (6, 7). In judging that there is no danger, it is extremely important to handle the patient's discomfort as soon as possible. Traditionally, oral and injectable drugs are given, sometimes in addition with canalith repositioning procedure, and the symptom of dizziness will usually be terminated (8). But in practice, after the above treatment, parts of the patients will still suffer to stubborn dizziness, and in turn prolonged the emergency staying time or even resulted in hospitalization. Acupuncture at related acupoints has been proven to shorten the symptom of stubborn dizziness (9). Moxibustion to dizziness treatment has been recorded in traditional Chinese medicine classics and has been in clinical practice for many years (10). However, moxibustion at acupuncture points will produce a strong odour and is not suitable for indoor use. Also, wormwood is dangerous during smoldering. The use of far-infrared (FIR) to apply heat energy on acupoints in traditional Chinese medicine (TCM) has not been reported so far.

Objectives {7}

The research specific objectives are the FIR and / or acupuncture on acupoints treatment of stubborn dizziness.

Trial design {8}

To explore the therapeutic effect of FIR and / or acupuncture on acupoints for stubborn dizziness, a single-blinded 4-arms parallel randomized controlled trial (RCT) is designed: arm of acupuncture, arm of current-carrying (CC) FIR, arm of acupuncture plus CC FIR, arm of placebo with no CC FIR. The framework is in equivalence. If there is stubborn dizziness in patient after conventional treatment, the above interventions are applied for 20 minutes in each group. There are four acupoints on left limbs and four acupoints on right limbs correspondingly, named as Neiguan (PC6), Hegu (LI4), Zusanli (ST36), and Taichong (LR3). After treatment, visual analogue scale (VAS) of dizziness, dizziness handicap intervention (DHI) questionnaire and heart rate variability (HRV) are used to measure and evaluate the results. General laboratory examination is recorded. The study will conduct from July of 2020 to June of 2011.

Methods: Participants, Interventions And Outcomes

Study setting {9}

The population is obtained from the acute observation unit (AOU) of emergency department (ED) in an academic medical center in Taiwan (Republic of China).

Eligibility criteria {10}

Inclusion criteria

a. Patients between 20 and 80 years old who are able to cooperate with the entire treatment, testing and questionnaire.

b. Patients with non-central type dizziness and no unstable condition after inspected by emergency physicians.

c. Patients who have signed a clinical trial consent.

Exclusion criteria

a. Patients who cannot accept the research content.

b. Patients who cannot complete the test.

c. Patients who are unwilling to cooperate with acupuncture, FIR and other treatments.

d. Patients with abnormal blood clotting profile.

e. Patients with wounds or allergy at the skin treatment site.

f. Patients with unstable vital signs.

g. Patients with major trauma.

Who will take informed consent? {26a}

Principal investigator or the authorised assistance will act the role to obtain informed consent after detailed description and full explanation of the study to the potential trial participants or authorised surrogates.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

This item is not applicable.

Interventions

Explanation for the choice of comparators {6b}

Acupuncture, acupuncture plus CC FIR, and no CC FIR are chose as the comparators to contrast the effect of CC FIR.

Intervention description {11a}

The acupoints of four arms are the same but the disposals are in difference. Arm of acupuncture is performed with single-use, sterile, disposable, size 0.25 mm x 40 mm, silver-handled needles with guide-tubes which are inserted at correct acupoints and manually stimulated until the “De Qi” sensation is elicited. Arm of CC FIR is performed with CC FIR device (including current stability controller) (LinkWin Technology Company, Taiwan) covered on corresponding acupoints. Arm of acupuncture plus CC FIR is performed with needles inserted first on the corresponding acupoints and in turn with CC FIR device covered at the same sites. Arm of placebo is performed with covering no CC FIR device on corresponding acupoints.

Criteria for discontinuing or modifying allocated interventions {11b}

Unwilling of patients for performance or toxic symptoms/signs appearance will discontinue the interventions for a given trial participant.

Strategies to improve adherence to interventions {11c}

Well explanation and fluency of procedure will improve adherence to intervention protocols.

Relevant concomitant care permitted or prohibited during the trial {11d}

During the trial, gentle constant temperature of CC FIR is permitted, but bleeding over the acupoints is prohibited.

Provisions for post-trial care {30}

This item is not applicable.

Outcomes {12}

Primary outcome

a. VAS expresses the degree of symptom improvement visually. Because the method is fast, friendly, easy to learn and no constrain by different words or language, it plays as an effective evaluation tool.

b. DHI is a questionnaire for dizziness, including functional, emotional and physical aspects. There are totally 25 daily questions related to dizziness answered in 3 items (yes/sometimes/no) with a corresponding 3 points score (4/2/0).

c. HRV is a body test for Autonomic Nervous Dysfunction. It reflects physiological, hormonal, and emotional balance within our body system. In other words, it measures the activity balance of the sympathetic and parasympathetic nervous system. It is measured by ANSWatch wrist monitor (Taiwan Scientific Corporation, Taipei, Taiwan; Taiwan Department of Health medical device product registration number 001525). It contains multiple piezo-electrical sensors, which can directly measure the blood pressure waveforms on the radial artery, which are high frequency (HF), low frequency (LF), very low frequency (VLF), sympatho-parasympathetic balance index (LF/HF), total power, root mean square of successive differences (RMSSD), and the proportion of NN50 divided by total number of NNs (PNN50). This method is simple and non-invasive.

Secondary outcome

a. The change of blood pressure, white blood cell counts and red blood cell counts before and after intervention are evaluated.

b. The duration of the patients stay in the emergency room and observation room are calculated.

Participant timeline {13}

The patients recruited are single-blindly allocated into four parallel arms with acupuncture, CC FIR, acupuncture plus CC FIR, and no CC FIR according to the random number table made beforehand in one year timeline simultaneously according to Fig. 1.

Sample size {14}

Totally 136 patients are needed whom are divided into four arms with 34 patients each individually. The number of total participants is estimated via the software of G-power in setting with significance level 0.05, power 0.8 and effective size 0.5, grouping clinically into four arms including acupuncture, CC FIR, acupuncture plus CC FIR and no CC FIR in the design.

Recruitment {15}

The participant enrolment is achieving by the detailed inspection and well explanation to all the patients with stubborn dizziness in the AOU of ED in one year duration.

Assignment of interventions: allocation

Sequence generation {16a}

The allocation sequence is random and computer-generated using Microsoft Excel software. Four arms are in the same weighting during randomization.

Concealment mechanism {16b}

The allocation sequence of participant is assigned by a clinical research coordinator (CRC) into one arm via a predetermined randomized table over bedside to the intervention performer.

Implementation {16c}

The allocation sequence is generated by principle investigator. The participants will be enrolled by emergency physicians and assigned by CRC to interventions according to the predetermined allocation sequence.

Assignment of interventions: Blinding

Who will be blinded {17a}

The trial participants will be blinded to the allocation sequence because no information of the predetermined randomized table will be disclosed to them.

Procedure for unblinding if needed {17b}

This item is not applicable.

Data collection and management

Plans for assessment and collection of outcomes {18a}

The assessment of the study mainly determined with VAS of dizziness, DHI questionnaire and HRV. The baseline data is collected before intervention and the result is got after intervention. The time interval before and after intervention is 20 minutes.

Plans to promote participant retention and complete follow-up {18b}

Well explanation and fluency of procedure will improve adherence to interventions.

Data management {19}

Data entry, coding, security and storage are performed by the authorized assistant. And the process is double checked by the principal investigator.

Confidentiality {27}

Personal information of the participants will be collected before, during and after the trial by the study team which will be protect confidentiality under the guidance of Institutional Review Board. The information shared and maintained by the study team is depersonalized.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

This item is not applicable.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Paired t-test is used as the statistical method to analyse the collected data of the trial. The significant difference in the results of pre-test and post-test for primary and secondary outcomes are analysed to the four arms. Computer analysis is performed under Microsoft Excel software.

Interim analyses {21b}

Principal investigator will access the interim results. If there are conditions against the

acupuncture or coagulopathy, the trial will be terminated.

Methods for additional analyses (e.g. subgroup analyses) {20b}

This item is not applicable.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

The randomization of study is predetermined. Clinically, some participants may not fulfil the condition of the assigned arm and non-adherence. The cases will be treated as missing data and replaced statistically by multiple imputation.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

This item is not applicable.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

This item is not applicable.

Composition of the data monitoring committee, its role and reporting structure {21a}

This item is not applicable.

Adverse event reporting and harms {22}

Overheat of the FIR device and bleeding over acupoints are monitored and reported to Institution Review Board, in turn with reconsideration to conduct of the trial.

Frequency and plans for auditing trial conduct {23}

This item is not applicable.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Any protocol amendments will be reported to Institutional Review Board Committee of Changhua Christian Hospital in Taiwan.

Dissemination plans {31a}

The trial results are presented in posters or oral reports at seminars and published to journals.

Discussion

Dizziness is a common symptom encountered daily (1–3). Most patients are without life- threatening condition except intolerable symptoms (4, 5). In addition to drug treatment and canalith repositioning maneuver (8), a new way to use non-invasive simple techniques, methods or equipment that can quickly resolve the problem is a gospel for patients.

The treatment of dizziness over acupoints by acupuncture has been reported effectively years before (9). The way of implementation in TCM is mainly acupuncture, moxibustion (10), massage with acupressure by pressing and rubbing. Massage is simple and easy, but the effect is limited. Acupuncture and moxibustion are better especially in “qi” regulation and blood flow fluency, but they require qualified Chinese medicine practitioner for operation.

Lesion of dizziness is recognized from brain or ear in conventional medicine. In TCM, dizziness is caused by the flow disturbance of visceral “qi” and blood. To improve the symptom of dizziness, conventional medicine focuses on the organic treatment of lesions inside the brain and the ears that is time-consuming; TCM focuses on the functional treatment of flow fluency inside visceral “qi” and blood that is rapid-responding.

In TCM, besides acupuncture (9), non-invasive moxibustion (10) is also used on acupoints for treatment. To get rid of the strong odour and the dangerous condition of smoldering, FIR device is used instead of moxibustion. The device can be applied to patients in many places other than hospital or clinic. Moreover, no special practitioner is needed.

The effect of acupuncture treatment on acupoints to dizziness has been proven (9). The short-term goal of the design is to study the rapid therapeutic effect using FIR device instead of acupuncture or moxibustion on specific acupoints. The long-term goal is to apply FIR device on other relevant acupoints for rapid and easy treatment of more diseases or symptoms.

Trial Status

The trial was registered at ClinicalTrials.gov with number NCT04415307 on June 1, 2020. Participant had been recruited since December 1, 2020. The approximate date of recruitment will be completed on April 21, 2022.

Abbreviations

1.	FIR	far-infrared
2.	TCM	traditional Chinese medicine
3.	RCT	randomized controlled trial
4.	CC	current-carrying
5.	VAS	visual analogue scale
6.	DHI	dizziness handicap intervention
7.	HRV	heart rate variability
8.	AOU	acute observation unit
9.	ED	emergency department
10.	HF	high frequency
11.	LF	low frequency
12.	VLF	very low frequency
13.	RMSSD	root mean square of successive differences
14.	PNN50	proportion of NN50 divided by total number of NNs
15.	CRC	clinical research coordinator

Declarations

Acknowledgements

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Authors' contributions {31b}

CC is the principle investigator in charge the study, conceiving idea and guiding the schedule. LL acts as the supervisor to make sure the study following the research method. TL contributes to study design. CC offers the information of TCM with solution of problem encountered.

Funding {4}

The funding is subsidized by the Research Department of Changhua Christian Hospital in Taiwan. The original funding document is shown as attachment 1. The funding source acts no direct role to the study.

Availability of data and materials {29}

The final trial dataset will be accessed by the authors of the trial.

Ethics approval and consent to participate {24}

The trial is approved by Institutional Review Board Committee of Changhua Christian Hospital in Taiwan. The Clinical Trials Approval Certificate is shown as attachment 2. Written informed consent to participate will be obtained from all participants.

Consent for publication {32}

This item is not applicable.

Competing interests {28}

The authors declare that they have no competing interests.

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Figures

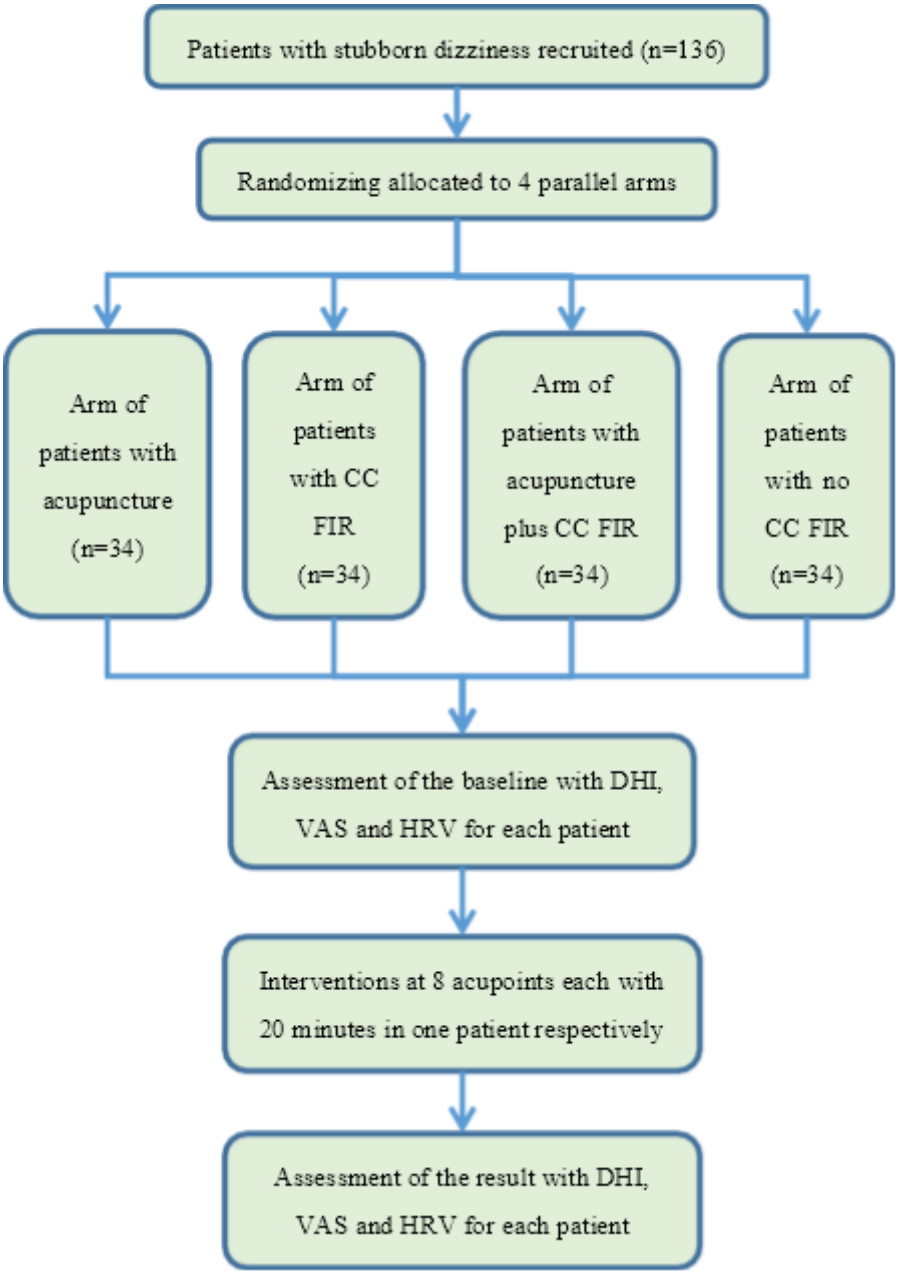

Figure 1

Flow chart of the study procedure