

Application of autologous peripheral blood-derived stem cell/progenitor cell (CD34+) + stem cells and hyperbaric oxygen therapy for patients with severe limb ischemia

Submission date 18/09/2017	Recruitment status Stopped	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 03/10/2017	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 22/05/2023	Condition category Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Peripheral arterial occlusive disease (PAOD) is a narrowing of the arteries other than those that supply the heart or the brain, most commonly affecting the legs. It affects up to 15% of adults over the age of 55. Without appropriate and aggressive treatment, the one-year mortality (death) rate of PAOD has been reported to be as high as 25%. Patients with PAOD may develop critical limb ischemia (CLI) at the late stage of the disease (reduced blood flow) and lose their limb. Current treatment of PAOD consists of lifestyle changes, medication, or surgery. Treatment failure can lead to limb loss and a high economic/family burden for care following amputation. In fact, about 30% of patients cannot be treated with any of abovementioned methods and the only option is amputation, especially in diabetic patients. Currently, although surgery has been used for the treatment of CLI with an acceptable success rate, the overall clinical outcomes remain dismal. Therefore, there is still an unmet need for treatment of PAOD at present. The aim of this study is to find out whether a combination of stem cells and hyperbaric oxygen (HBO) treatment may be a treatment option for patients with limb ischemia. The combined treatment may promote blood vessel growth (angiogenesis) and prevent disease progression and amputation.

Who can participate?

Patients aged 20-80 with severe limb ischemia

What does the study involve?

Participants are randomly allocated to either the control group or the experimental group. The control group is treated with standard antiplatelet drugs plus HBO treatment. The experimental group is treated with HBO treatment combined with a transfusion of their own stem cells. HBO treatment involves breathing pure oxygen at high pressure for 100 minutes once daily for ten days.

What are the possible benefits and risks of participating?

The stem cell treatment may help to save the affected limb. The risks of stem cell infusion are irregular heart rhythm, heart attack, heart failure, brain ischemia, bleeding, anemia, worsening kidney function, electrolyte imbalance and malignancy. However, the reported rate of these side effects is less than 1%. The possible side effects from HBO treatment are serous otitis media (glue ear; 2%), tympanic rupture (eardrum rupture; <1%), nasal congestion, temporary reversible blurred vision, cataract and seizure.

Where is the study run from?

Kaohsiung Chang Gung Memorial Hospital (Taiwan)

When is the study starting and how long is it expected to run for?

December 2016 to May 2023

Who is funding the study?

Ministry of Science and Technology (Taiwan)

Who is the main contact?

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Contact information

Type(s)

Public

Contact name

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Additional identifiers

Study information

Scientific Title

Combination autologous peripheral blood-derived stem cell/progenitor cell (CD34+) + stem cells and hyperbaric oxygen therapy for the treatment of severe limb ischemia: investigate the safety and efficacy

Study objectives

The combination autologous peripheral blood-derived stem cell/progenitor cell (CD34+) + stem cells and hyperbaric oxygen therapy for severe limb ischemia may be a therapeutic option for patients with limb ischemia.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Chang Gung Memorial Hospital, 08/02/2017, ref: 201601217A0

Primary study design

Interventional

Study design

Prospective single-center interventional trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Severe limb ischemia

Interventions

Patients will be randomized in a 1:1 ratio. The randomization procedure is stratified by the research department and the permuted block design within strata is utilized. The study treatment is randomly assigned according to the randomization list held by a biostatistician and using sealed envelopes provided to the core laboratory. The envelopes will be opened only when the next study subject is enrolled. Concealment is realized in a way that only team members of the research department will have access to the randomization code. All members have signed an agreement that the randomization code will be kept confidential.

Control group: standard antiplatelet plus HBO therapy (n=20)

Experimental group: HBO therapy combined with intraarterial transfusion of autologous peripheral blood-derived stem cell/progenitor cell (CD34+) stem cells: 1×10^7 - 3×10^7 cells

Hyperbaric oxygen (HBO) therapy will be arranged at the time of admission with a dose of 2.5 Bar for 100 minutes, frequency once daily and duration ten days.

Intervention Type

Mixed

Primary outcome(s)

Limb salvage, defined as alive without amputation within 12 months

Key secondary outcome(s)

1. Relief of rest pain was measured using Canadian cardiovascular society grading of angina pectoris (CCS) score at 1 week, 1 month, 3, 6, 9 and 12 months after hospitalization or enrollment
2. Ankle brachial index (ABI) was measured by duplex echography at 1, 3, 6 and 12 months after hospitalization or enrollment
3. New collateral vessel formation measured by magnetic resonance angiography (MRA) at 6 and 12 months
4. The amount of O₂ diffused from capillaries through the epidermis of diseased foot, measured using transcutaneous oximetry (TcPO₂) at 6 and 12 months
5. Walking distance and cardiopulmonary function measured using six-minute walk test (if

possible), and quality of life measured using Short Form-36 (SF-36) at 1, 3, 6 and 12 months after hospitalization or enrollment

Safety endpoint: adverse events and severe adverse events (death or hospitalization) of study patients measured using case report form at clinical visit every three months or as necessary

Completion date

31/05/2023

Reason abandoned (if study stopped)

A total of 5 patients were selected in the phase I trial, 1 patient was failed in the screen stage, and others were enrolled. Due to not testing the TcPO₂ measurement, 4 patients were unable to be treated and followed up, and this trial period will expire on 31/05/2023. Therefore, the clinical trial will be terminated.

Eligibility

Key inclusion criteria

Age between 20-80 with severe limb ischemia due to diffuse atherosclerosis. Inclusion criteria for the study were all of the following:

1. Ischemic peripheral vascular disease with rest pain defined as pain that occurs at night and at rest. Clinical evaluation by Fontaine classification (Fontaine stage III: rest pain, stage IV: ulcer and/or necrosis)
2. Ankle-brachial index (ABI)<0.7
3. A non-surgical candidate for revascularization, for example, diffuse multi-segment disease, inability to locate a suitable vein for grafting, or extensive infra-popliteal disease not amenable to a vascular graft
4. The image analysis includes the MRA or angiocardiology by diagnostic intravascular catheter (depended on clinical results). The above results show that obstruction more than 75% stenosis will considerate into this test
5. Use of contraception
6. The trialists accept the laboratory data within 3 months since initial screening
7. TcPO₂<45mmHg

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

1. Age <20 y/o or >80 y/o
2. Pregnant or feeding women
3. Adventitious agents (HIV, syphilis, hepatitis B virus, hepatitis C virus, will be excluded. If the

examination result is positive, Centers of Disease Control will be notified by law)

4. Infective disease

5. Myocardial infarction within 3 months, heart failure, or functional class IV

6. Malignant or hematologic disease, or severe disease with life span less than one year

7. End stage renal disease or eGFR less than 30 ml/min

8. Patients after treatment improved in the case using bypass surgery or stenting ischemic cardiac catheterization

9. Receiving other clinical trials monitor

10. Patients can't receive therapy or examination in this study

11. Blood sugar and blood pressure control poorly (SBP>160 mmHg, AC F/S>200mg/dL and PC F/S>300mg/dL)

12. Not suitable for cardiac catheterization

13. Contraindications to G-CSF or HBO

14. Patient is unconscious

15. Untreated active infection

16. Those who undergo major surgery within one month

17. Patients with stroke or unstable angina within 3 months

18. Unsuitable candidates after initial evaluation

19. Those of unsuitable for HBO therapy, e.g., active pulmonary tuberculosis, spontaneous pneumothorax etc

20. TcOP2 \geq 46mmHg

Date of first enrolment

01/10/2017

Date of final enrolment

31/03/2020

Locations

Countries of recruitment

Taiwan

Study participating centre

Kaohsiung Chang Gung Memorial Hospital

No.123, Ta Pei Road, Niao Sung District

Kaohsiung

Taiwan

83301

Sponsor information

Organisation

Ministry of Science and Technology (Taiwan)

ROR

<https://ror.org/02kv4zf79>

Funder(s)

Funder type

Government

Funder Name

Ministry of Science and Technology, Taiwan

Alternative Name(s)

Ministry of Science and Technology, R.O.C. (Taiwan), Ministry of Science and Technology of Taiwan, MOST

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Taiwan

Results and Publications

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date