Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Effectiveness of lower extremity electrical stimulation therapy in patients with COVID-19 (Phase II)

H-47781- EFFECTIVENESS OF LOWER EXTREMITY ELECTRICAL STIMULATION THERAPY IN THE TREATMENT OF LOWER EXTREMITY CRITICAL ILLNESS MYOPATHY AND NEUROPATHY IN PATIENTS WITH SEVERE COVID-19

Concise and Focused Presentation

You are being asked to participate in a voluntary research study. The purpose of this study is to see if lower extremity electrical stimulation will benefit a long stay in the hospital. In this study we will place a low risk device to measure the strength of the legs and give electrical stimulation to help reduce pain and add blood circulation and muscle movement. No research procedures will take place before signing the consent form. Your participation in this study will be voluntary. There is minimal risks and you may benefit from this study by not losing strength, mass, and reducing pain in your legs. You do not have to participate in this study and can continue to receive your normal care.

Prolonged hospital stay can cause side effects such as muscle loss, weakness and pain on the legs, specially in patients with COVID-19. Electrical stimulation has shown to improve blood circulation, decrease pain, and prevent muscle loss in patients with leg diseases. We propose the daily use of electrical stimulation for 4 weeks to address the side effects on the legs caused by prolonged hospital stay in patients with COVID-19. During the first visit, the research team will test the status of the leg muscles with a simple tool which records muscle activity while performing electrical stimulation. Low risk device pads will be attached to your calf muscles during the stimulation. Then, you will be provided your own electrical stimulation device and device pads during the complete study period, and it will not be re-used or recycled for other patients' use. We will ask you to return to the clinic once a week for leg assessment. You may be assigned an active device or a placebo device. After 4 weeks, the research team will test the status of the legs again, in order to examine the efficacy of daily use of electrical stimulation for patients with previous hospitalization due to COVID-19. After the 4 weeks, if you originally received a placebo device, the research team may give you the option to receive an active device for an additional 4 weeks.

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study.

Patients with COVID-19 admitted to the hospital could be at risk of losing their muscle strength from being unable to move for a long period of time during their stay, developing pain can cause weakness to the legs. Due to hospital-acquired weakness, Physical therapy (PT) programs are often required to prevent or recover. However, PT has some limitations due to the fact that patients are unable to perform tasks (e.g., the patient is not awake or has severe mobility limitations), or come to the facility for performance. To address this issue, we suggest the daily use of electrical stimulation (EE) therapy provided to the legs, as an alternative therapy to maintain muscle activity. We think that implementation of EE will improve myopathy among COVID-19 patients by preventing muscle leg loss and weakness.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Purpose

The purpose of this pilot study is to examine effectiveness of daily use of electrical stimulation therapy to recover from side effects on the legs caused by prolonged hospital stay in patients with COVID-19.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC).

Phase II Procedures:

We will recruit 20 subjects with that were previously admitted to the hospital due to COVID-19 infection, this will be performed by a critical care and pulmonary specialist at the BCM COVID-19 Clinic. You will begin the study after being diagnosed with neuromyopathy due to prolonged hospitalization for COVID-19.

Since electrical stimulation may offer an alternative treatment to reduce pain and improve blood flow, it could also have positive effects to improve mobility and balance by reducing the loss of sensation in your legs, which has also been shown to be a side effect of prolonged hospital stay.

The protocol will consist of 4 weeks of lower-extremity electrical stimulation. It will consist of home-based therapy, meaning you will take the device home and attend the clinic once a week for screening and assessment of therapy.

The protocol will be performed as stated in the following description:

This study will consist of up to 7 visits total and possible follow up phone calls. You will be compensated $50 per in-person visit (up to $350), with free parking.

During the first visit, the research staff will provide you with the Tennant Biomodulator PRO®. Research staff will provide you with up to one hour of stimulation using this device. During this visit, research staff may also perform the following assessments:

1) Questionnaires (pain, weakness, sleep, quality of life, frailty, depression, life and space, beck anxiety scale, Katz-daily living, fatigue)
2) Musculoskeletal assessments (non-invasive surface electromyography, vibration perception threshold, ankle strength test, leg circumference measurement)
3) Vascular assessments (non-invasive near infra-red spectroscopy)

Four optional assessments are listed below that coordinators may ask for you to complete. These can occur during the scheduled study visits should you agree. They may take up to 45 additional minutes to complete:

1. Gait and Balance Test: You will wear 5 sensors (for example, accelerometer) named LEGSys (one on lower back, 2 on each upper thigh and 2 on each shin) attached with elastic straps to test balance and record walking pattern. Research staff will ensure that the elastic straps are not too tight in order to avoid poor circulation during the visit. You may also be asked to walk on the ground on a 20 meter walkway, or on a treadmill at a preferred walking speed and a fast speed to observe your walking patterns.

2. Upper Extremity Frailty Tests: The research team will measure your arms' movements using a sensor attached at your wrists and elbow with an elastic band. There will be 3 different types of Upper Extremity Tests and you will do at least one with each arm. Flexion-extension: While being at a comfortable position, you will be asked to flex and extend your arm for 20 seconds at a fast speed. You will repeat this task while counting backwards.

3. Physical Activity Monitoring-You will be given a wearable device (PAMSys) or smart watch, that will be measuring several parameters including number of steps taken, duration of sitting, standing, walking and lying, time taken and number of transitions from sit to stand, and walking speed for 48 hours.

4. Oxygen Level Assessment: Oxygen saturation will be measured using a pulse oximeter.

Please initial below to indicate your decision regarding the optional study assessments during any study visit:

_____ I AGREE to participate in any or all of the optional study assessments listed above during any study visit.

_____ I DO NOT AGREE to participate in any of the optional study assessments listed above during any study visit.

Both extremities will have all measurements and electrical stimulation therapy at baseline and during the study period.

Once the initial visit (baseline visit, week 0) is over, you will take the Tennant Biomodulator® home and will be instructed to turn it on for one hour every day for four weeks. It is possible that the device you receive is active or inactive, this is selected at random. You will come back weekly for follow up visits. During the next 3 weekly visits (Visit 1, Visit 2, Visit 3), research staff may perform the same assessments listed above but will only provide five minutes of stimulation.

During Visit 4 (4 weeks after the initial visit), the research staff will once again provide you with one hour of stimulation and repeat all the initial assessments listed above.

Also at Visit 4 (4 weeks after initial visit), you will return the device to the research staff. If you were part of the control group (with the inactive device), the research team may notify you and ask if you are willing

to participate in an additional 4 weeks with an active device. Should you agree, you will be given an active device and would be required to have an additional follow-up visit (Visit 5) 4 weeks after Visit 4, with possible phone calls in between. If you had already completed Visit 4, you will be asked to return for Visit 5 to receive the active device and have repeated assessments. You would then come back for your final follow-up visit (Visit 6) 4 weeks after Visit 5. During these visits all study assessments will be repeated. You will return the device to the research staff at the end of those additional visits.

Phone calls between study visits will occur at an as-needed basis. You may contact study staff or study staff may contact you to review any logistics such as: address any questions/concerns, discuss feedback, schedule a weekly in-person visit, etc. You will not be compensated for study-related phone calls.

Please initial below to indicate your decision regarding the additional 4-weeks of study participation should you be a part of the control group at first:

_____ I AGREE to be contacted about an additional 4 weeks of study participation (which may involve up to 2 additional visits) should I have been initially assigned to the control group.

_____ I DO NOT AGREE to be contacted about an additional 4 weeks of study participation (which may involve up to 2 additional visits) should I have been initially assigned to the control group.

The duration of any study visit could be from 1-2.5 hours. If you need to stop the study visit at any time, you are permitted to do so.

Major adverse events (documented via electronic health record) will be tracked for planning of future studies.

The supervision of this study will be by pulmonary care specialists, and the location will be at the Baylor College of Medicine McNair Campus.

The researchers will take digital photographs /videos of both of your legs throughout the study. This is done using a special digital camera for visual images and blood flow detection. This method is non invasive and does not cause any harm to you. **We will blur your face out in the photographs/videos. While we do all our efforts to mask your face in some cases (for example journal policy) this may not be practical. We will only use videos and photos of you for scientific presentations or scientific publications.

Initial your decision below.
____I agree to have my photographs/videotape presented in scientific presentation or scientific publication
____I do NOT agree to have my photographs/videotape presented in scientific presentation or scientific publication
If you are eligible, the research personnel would like to contact you in the future for participation in other

research studies. You are not required to participate in these studies and your medical care or involvement with the current research study will in no way be affected if you choose not to participate . You may ask us to stop contacting you at any time.

_____I agree to be contacted for future research studies

_____I do not agree to be contacted for future research studies.

Please provide below your Emergency contact information:

Contact name:_____

Relationship: _____

Phone number:_____

Please note that the research staff may contact you for any study related questions or concerns during your participation of the study.

If you are a student or employee, note that your participation will NOT affect your academic position or employment. You may also refuse to participate without any penalty.

Clinically Relevant Research Results

The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information

Your identifiable private information collected as part of this research, even if the identifiers are removed, will not be used or distributed for future research studies.

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Specific information concerning alcohol abuse
- Specific information concerning drug abuse
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Billing or financial records
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, and Baylor St. Luke's Medical Center (BSLMC).

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) maintain in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC).

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, and Baylor St. Luke's Medical Center (BSLMC) may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Bijan Najafi, PhD

7200 Cambridge Street, Room B01.529

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts

This study brings no more than minimal risk to subjects as it only involves a non-invasive device. There are some risks associated with lack of comfort from Electrical Stimulation, skin allergy to the Electrical Stimulation sticky patches that are used for delivering Electrical Stimulation therapy, risk associated with electrical mal-function of Electrical Stimulation, and other unknown risks. All Electrical Stimulation devices will be checked before any use to minimize the risk associated with electrical malfunction. All Electrical Stimulation devices are FDA approved for the purpose of pain reduction. The device has provided pain relief in previous studies and their participation may help researchers identify the impact of a disorder on mobility performance as well as the changes of mobility during an intervention. This device is an investigational device. The study device and technology are non-invasive, non-toxic and non-ionizing. The potential risks are minimal. However, like any battery powered systems, there is a minimum risk of sensor malfunctioning.

The risk to you regarding the optional assessments of gait and frailty is considered to be minimal because all that is required is a simple walking or balance test in a controlled environment with a researcher. This research routine will not place you at higher risk than normal activities of daily living, and no more risk of harm or discomfort is associated with these tests than the discomfort normally incurred while performing normal muscle stretching. You will be allowed rest time between trials as needed.

The PAMSys device for the assessment of frailty is completely non--invasive, safe, non-toxic and non--ionizing. The potential risks to you are minimal. However, like any battery powered systems, there is a minimum risk of sensor malfunctioning. In addition, the study devices are not waterproof, and although they use a low powered battery (similar to a cellphone battery), in order to avoid any risk of shock the monitor should not be submerged or saturated with fluids during operations or cleaning.* Please avoid showering with the device. It does not emit any radiation to the human body, and does not offer any significant risk to you.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits
The benefits of participating in this study may be: There is a potential benefit or prevention or improvement in this study, the device has been proven to reduce pain, activate muscle mass, and increase blood flow. However, the proposed treatment may assist in preventing or improving hospital-acquired Weakness because of prolonged hospital stay. In addition, the participation in this study may help the investigators to better understand how COVID-19 may impact Myopathy and Neuropathy caused by prolonged hospital-stay. Therefore, the research team will investigate how this therapy helps COVID-19 patients to recover from prolonged hospital-stay .. However, you may receive no benefit from participating.

Alternatives
You may choose to not participate in this study.

Investigator Withdrawal of Subject from a Study

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you are not being provided the Electrical Stimulation therapy, or if you have a serious reaction to Electrical Stimulation therapy) or because the entire study is stopped. The sponsor, investigator, Food and Drug Administration, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments
You will not be asked to pay any costs related to this research.

You will be given a debit card called "ClinCard" at the first day of your visit. This study will consist of up to 7 visits total and possible follow-up phone calls. The patient will be compensated $50 per visit (up to $350), with free parking. Only Phase II participants will be compensated.

Subject's Rights
Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, BIJAN NAJAFI, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related

to the research, you may speak with a member of the study staff: BIJAN NAJAFI at 713 7987536 during the day and MARIA NOUN at 713-798-7538 after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date