The Effectiveness of Fixed Dose Combination of Alpha Lipoic Acid and Vitamin B Preparation for Treatment of Diabetic Polyneuropathy in Type 2 diabetes mellitus patients : A randomized placebo-controlled trial.

DATE: 31ST MARCH 2024

RESEARCH INFORMATION

***Research Title*:**

The Effectiveness of Fixed Dose Combination of Alpha Lipoic Acid and Vitamin B Preparation for Treatment of Diabetic Polyneuropathy in Type 2 diabetes mellitus patients : A randomized placebo-controlled trial.

Researcher's Name: **Dr. Che Nur Ain Che Abdullah (MPM : 67428)**
Dr Noraini Mohamad (MPM: 42668)
Associate Professor Dr. Nani Draman (MPM: 35488)
Dr. Zainab Mat Yudin@Badrin (MPM: 40301)
Associate Prof. Dr. Wan Muhamad Amir Bin Wan Ahmad
Dr. Ritzzaleena Rosli Binti Mohd Rosli (MPM: 58719)

INTRODUCTION

You are invited to take part voluntarily in a research. This research is about the effectiveness of a fixed-dose combination of Alpha Lipoic Acid and Vitamin B preparations for the treatment of diabetic polyneuropathy in type 2 diabetes mellitus patients. Diabetic polyneuropathy is a common complication among diabetic patients which causes the patient to experience numbness, prolonged pain especially on the legs. If not treated, it will affect the quality of life due to chronic pain on the feet, the risk of foot ulcers and amputations. Furthermore, the effects of this pain often bring to sleep disorders, anxiety and depression and a lower quality of life (QoL) in diabetic patients. This study is an intervention study that will involve 2 groups, namely the intervention group and the control group.

It is important that you read and understand this research information before agreeing to participate in this study. You will receive a copy of this form to keep for your records if you agree to participate.

Your participation in this study is expected to take 50-60 minutes per visit. A total of 76 people is expected to participate in this study.

PURPOSE OF THE STUDY

The purpose of this study is to determine the effectiveness of a fixed dose combination of alpha lipoic acid and vitamin B preparations in comparison with placebo for treatment of diabetic polyneuropathy (DPN) in type 2 diabetes mellitus patients attending Hospital Universiti Sains Malaysia patients.

PARTICIPANTS CRITERIA

The research team members will discuss your eligibility to participate in this study. It is important that you are completely truthful with the staff.

This study will be included

- Aged 18 years and over.
- Diagnosed with type 2 diabetes mellitus based on WHO diagnostic criteria for diabetes.

- Diagnose with diabetic polyneuropathy by Neurological Symptom Score (NSS) and Neuropathy Disability Score (NDS).

This study will not be included

- Those with a documented mental impairment which impacted on their ability to answer questions independently.
- Patients with peripheral vascular disease (non-palpable foot pulses, intermittent claudication).
- Patients with an amputated foot or leg.
- Aspartate aminotransferase or alanine aminotransferase levels >3 times normal levels
- Patients with renal impairment - CKD stage IV and V.
- Patients using drugs with possible influence on the study results (antidepressants, anticonvulsants, opiates, neuroleptics, antioxidants, and particularly methylcobalamin, pyridoxine and other B complex preparations).
- Pregnancy, lactation, or childbearing age without safe contraception.
- History of allergy with vitamin B complex preparations (i.e. Vitamin B12, B6 and B1) and alpha lipoic acid.

STUDY PROCEDURES

If you meet the eligibility criteria as listed above, you will be informed about this study. If you agree to participate, you will be asked to read and sign this consent form.

Once you agree to participate in this study, the socio-demographic data of the participants will be taken by the researcher. For this study, interviews will be conducted by trained researchers. Data or information about the diabetes will be filled in by researchers such as how long you have had diabetes as well as the medications was taken. In addition, the researcher will also ask about the signs or severity of polyneuropathy diabetic. A physical examination including measurement of height, weight and blood pressure will be performed. You also need to answer a questionnaire on Diabetes Quality of Life. Researchers will always be there nearby to clarify and answer any questions if you encounter any problems.

You will be divided into two groups, which are either the intervention group or a control group. This division is done by randomization through computer generated blocks. Your medications will be adjusted accordingly.

You need to fast for first blood taken at the start of the study. 6 ml of venous blood will be taken for measurement of HbA1c, fasting blood glucose, kidney function test, liver function test and lipid profile. The same blood collection will be done at follow-up treatment at 12 weeks.

Control Group

If you are selected in the control group, you will be given a placebo medicine that contains Croscamellose Sodium, Microcrystalline Cellulose, Silicon Dioxide, Magnesium stearate. You need to take 2 pills once a day after breakfast. You are asked to come for a follow-up visit during the week 6th and for blood collection at the 12th week visit. Placebo drugs will not make a difference to fasting blood sugar test results and other blood results such as blood test results for kidney and liver.

Intervention Group

If you are selected in the intervention group, you will receive a combination of fixed doses of alpha acids lipoic and vitamin B. It contains Alpha lipoic acid 300mg, Vitamin B12 (methylcobalamin) 500mcg, Vitamin B6 (pyridoxine) 8mg, Vitamin B1 (thiamine) 39mg. You need to take 2 pills once a day after breakfast morning. You are asked to come for a follow-up visit at week -6 and for a blood draw at the visit 12th week.

You can contact the researcher at any time if you face any problem.

You are required to take the medicines that have been given for diabetes and other medicine periodically as recommended by the attending physician.

RISKS

There is no risk to you. You may experience some nausea at the beginning of the intake of medicine. However, previous studies show that most patients do not experience any side effects of this medicine and can take it without any problem.

Please inform the study staff if you encounter any problems or have any important information that may change your consent to continue participating in this study.

Participants in this study will be covered by insurance. If something happens that is not desired like disability or death as a result related to this study, compensation for participants or participants' families will be given.

PARTICIPATION IN THE STUDY

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at anytime, without any penalty or loss of benefits to which you are otherwise entitled. Your participation may also be stopped by the research team without your consent if, in any form, you have violated the study eligibility criteria. The research team member will discussed with you if the matter arises.

However, this study does not involve making a new commercial product. Therefore, study participants will not accept honorariums for the purpose of producing a commercial product. The honorarium is only given for the purpose of this study only.

Study participants will not be contacted to inform about the results of this study. However, during the period of this study, at each follow-up treatment, drug side effects and problems encountered can be discussed with the researcher.

Participants were not allowed to see treatment reports in hospital records because they were confidential. However, participants have the right to know the disease they are suffering from and the dosage of the medicine accepted.

After the study has taken place, participants may have the right to know whether they received the drug (intervention group) or control drug only (control group).

The researchers in this study are researchers and do not provide treatment for the disease faced. Further treatment for related diseases will be carried out by the attending physician.

This study is industry-sponsored research by BREGO Life Sciences Sdn Bhd.

POSSIBLE BENEFITS [Benefit to Individual, Community, University]

The results of this study are expected to help to determine the effectiveness of a combination of fixed doses of alpha acids, lipoic acid, and B vitamins versus a placebo for the treatment of diabetic polyneuropathy in patients with type 2 diabetes mellitus. It will help in treating diabetic polyneuropathy patients by giving more effective options to medical experts and patients to choose the best treatment in treating diabetic polyneuropathy subsequently can improve the quality of life.

Study participants will be given an honorarium of RM50 at each follow-up treatment.

QUESTIONS

If you have any question about this study or your rights, please contact;

1. **Dr Noraini Mohamad**
   School of Dental Sciences, Health Campus,
   Universiti Sains Malaysia,
   16150 Kubang Kerian, Kelantan, Malaysia
   Contact No: 09-7675894 or 013-9855968
   Email: mnoraini@usm.my

2. **Dr Che Nur Ain Che Abdullah**
   School of Health Sciences, Health Campus,
   Universiti Sains Malaysia,
   16150 Kubang Kerian, Kelantan, Malaysia
   Contact No:019-9216023
   Email: chenurain@student.usm.my

If you have any questions regarding the Ethical Approval or any issue / problem related to this study, please contact;

Mr. Mohd Bazlan Hafidz Mukrim
Secretary of Human Research Ethics Committee USM
Division of Research & Innovation (R&I)
USM Health Campus
Tel. No. : 09-767 2354 / 09-767 2362
Email : bazlan@usm.my

CONFIDENTIALITY

Your information will be kept confidential by the researchers and will not be made publicly available unless disclosure is required by law.

Data obtained from this study that does not identify you individually will be published for knowledge purposes.

Your original records may be reviewed by the researcher, the Ethical Review Board for this study, and regulatory authorities for the purpose of verifying the study procedures and/or data. Your

information may be held and processed on a computer. Only research team members are authorized to access your information.

By signing this consent form, you authorize the record review, information storage and data process described above.

Research questions, data in SPSS will be saved for analysis purposes to obtain research results. Data destruction will be done after the results of the study have been found. The blood taken will used for analysis and excess blood will be destroyed.

SIGNATURES

To be entered into the study, you or a legal representative must sign and data the signature page **[ATTACHMENT S or ATTACHMENT G (for genetic sample only) or ATTACHMENT P]**

Subject Information and Consent Form
(Signature Page)

Research Title: **The Effectiveness of Fixed Dose Combination of Alpha Lipoic Acid and Vitamin B Preparation for Treatment of Diabetic Polyneuropathy in Type 2 diabetes mellitus patients : A randomized placebo-controlled trial.**

Researcher's Name: **Dr. Che Nur Ain Che Abdullah (MPM : 67428)**
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Dr. Zainab Mat Yudin@Badrin (MPM: 40301)
Associate Prof. Dr. Wan Muhamad Amir Bin Wan Ahmad
Dr. Ritzzaleena Rosli Binti Mohd Rosli (MPM: 58719)

To become a part this study, you or your legal representative must sign this page. By signing this page, I am confirming the following:

- I have read all of the information in this Patient Information and Consent Form **including any information regarding the risk in this study** and I have had time to think about it.
- All of my questions have been answered to my satisfaction.
- I voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested.
- I may freely choose to stop being a part of this study at anytime.
- I have received a copy of this Participant Information and Consent Form to keep for myself.

_____

Participant Name

_____

Participant I.C No

_____ _____

Signature of Participant or Legal Representative **Date** (dd/MM/yy)

_____

Name of Individual
Conducting Consent Discussion

Signature of Individual Conducting Consent Discussion	**Date** (dd/MM/yy)
Name & Signature of Witness	**Date** (dd/MM/yy)

Note: i) All participants who are involved in this study will be covered by insurance.

ATTACHMENT P

Participant's Material Publication Consent Form
Signature Page

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To become a part this study, you or your legal representative must sign this page.

By signing this page, I am confirming the following:

- I understood that my name will not appear on the materials published and there have been efforts to make sure that the privacy of my name is kept confidential although the confidentiality is not completely guaranteed due to unexpected circumstances.
- I have read the materials or general description of what the material contains and reviewed all photographs and figures in which I am included that could be published.
- I have been offered the opportunity to read the manuscript and to see all materials in which I am included but have waived my right to do so.
- All the published materials will be shared among the medical practitioners, scientists and journalist worldwide.
- The materials will also be used in local publications, book publications and accessed by many local and international doctors worldwide.
- I hereby agree and allow the materials to be used in other publications required by other publishers with these conditions:
- The materials will not be used as advertisement purposes nor as packaging materials.
- The materials will not be used out of contex – i.e.: Sample pictures will not be used in an article which is unrelated subject to the picture.

Participant Name

Participant I.C No. **Participant's Signature** **Date** (dd/MM/yy)

Name and Signature of Individual Conducting Consent Discussion **Date** (dd/MM/yy)

Note: i) All participants who are involved in this study will be covered by insurance.