MEXICAN SOCIAL SECURITY INSTITUTE
EDUCATION, RESEARCH AND HEALTH POLICY UNIT
HEALTH RESEARCH COORDINATION
HIGH SPECIALTY MEDICAL UNIT (UMAE) "DR. BERNARDO SEPÚLVEDA"
CENTRO MÉDICO NACIONAL SIGLO XXI, IMSS, CDMX.
MEDICAL RESEARCH UNIT IN BIOCHEMISTRY.
DEPARTMENT OF NEUROLOGY AND NEUROPHYSIOLOGY.
FAMILY MEDICINE UNITS NUMBER 20, 41 AND 44, IMSS, CDMX.
SPECIALTY OF HUMAN ACUPUNCTURE OF THE ENMH OF THE IPN

Official Title of the study:

"Evaluation of the effect of electroacupuncture on the sensory symptoms of Symmetrical Distal Polyneuropathy of Diabetic origin and its correlation with changes in Nerve Conduction Velocity."

MEXICAN SOCIAL SECURITY INSTITUTE AND EDUCATION, RESEARCH AND HEALTH POLICY UNIT STUDY VERIFICATION ID:
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PROTOCOL SUMMARY

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1.- TITLE.

"EVALUATION OF THE EFFECT OF ELECTROACUPUNCTURE ON THE SENSORY SYMPTOMS OF SYMMETRICAL DISTAL POLYNEUROPATHY OF DIABETIC ORIGIN AND ITS CORRELATION WITH CHANGES IN NERVE CONDUCTION VELOCITY"

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3.- SUMMARY OF THE PROTOCOL.

"EVALUATION OF THE EFFECT OF ELECTROACUPUNCTURE ON THE SENSORY SYMPTOMS OF SYMMETRICAL DISTAL POLYNEUROPATHY OF DIABETIC ORIGIN AND ITS CORRELATION WITH CHANGES IN NERVE CONDUCTION VELOCITY".

Neuropathic Pain is one of the most complex painful syndromes due to its pathophysiology and diagnosis, which presents various symptoms and signs that fluctuate over time, varying in number and intensity, affecting social activity, work and quality of life.

Diabetes Mellitus (DM) is considered as a set of diseases associated with alterations in glucose metabolism, the most common being Type 2 Diabetes (T2D). In Mexico, T2D is the main cause of Neuropathy, with Symmetric Distal Polyneuropathy (PNDS) being the most common of the Neuropathies of diabetic origin. Its diagnosis is usually late because its screening based on signs and symptoms is confusing and even the patient can be asymptomatic for years, it has been reported that up to 12% of patients with PNDS do not report symptoms, and that 39% of patients do not receive any treatment.

The National Health and Nutrition Survey (ENSANUT) 2016, reported that 41.2% of adults diagnosed with DM reported the presence of burning, pain or loss of sensation in the soles of the feet, 20.4% can not walk more than 6 minutes without feeling fatigue, and that 46.4% do not take any preventive measures to delay or avoid complications. On the other hand, it has been described that the presence of Diabetic Neuropathy (ND) represents a deficit in the quality of life of subjects suffering from it, which can be evaluated with validated tools such as SF36, in addition, it has been correlated with a high morbidity with complications, mortality and risk of amputation in subjects with DM.

The importance of diagnosis lies in screening, with the most commonly used instruments being the Michigan Neuropathy Screening Instrument (MNSI) and the Michigan Diabetic Neuropathy score (MDNS), which include semiologist and clinical evaluation. On the other hand, the evaluation of sensory and motor Nerve Conduction Velocity (NVC) by means of electrophysiological techniques has been considered as the gold standard for diagnosis and the most used instrument to measure the Pain Scale is the Numerical Rating Scale (NRS).

The treatment of ND is usually based on glycemic control, however, the presence of the intensity of symptoms and pain is associated with a little pharmacological attachment and therapeutic failure. The most commonly used drugs in the symptomatology are antidepressants and anticonvulsants, however, their success has been unsatisfactory due to their variability in efficacy and presence of side effects that create in the patient little pharmacological attachment.

Electroacupuncture is a variant of Traditional Chinese Medicine (TCM) which has reported an analgesic effect, where a small electric current is applied and passed between pairs of acupuncture needles of various shapes, mainly using electrostimulation equipment. There are few Controlled Clinical Trials (CCTs) with the use of Electroacupuncture for the control of ND, however, the analyses are inconclusive and there is some tendency towards successful results. Therefore, the WHO has suggested since 2014, to perform CCTs adhering to the CONSORT guidelines to have studies with verifiable clinical evidence.

In 2018 Shin et al., have reported the only ECC based on the CONSORT guidelines, concluding electroacupuncture can be recommended as an effective non-pharmacological treatment to relieve the pain of ND. However, they suggest conducting more studies to verify the results obtained.

This ECC will be the first of its kind to be developed in Mexico and aims to evaluate the effect of electroacupuncture on quality of life, on the relief of sensory symptoms of PNDS of diabetic origin and on changes in sensory and motor NCV.

GENERAL OBJECTIVE

- To assess the effect of electroacupuncture on quality of life, relief of sensory symptoms and its correlation on changes in NCV in people with T2D and diagnosis of PNDS.

SPECIFIC OBJECTIVES

- To compare changes in the MNSI, MDNS, NRS and SF36 instruments at the beginning and end of the intervention between the two groups.
- Correlate the changes evaluated by the MNSI, MDNS, NRS and SF36 instruments with the NCV outcomes of both groups at the beginning and end of the intervention.
- To compare NCV in patients with T2D and PNDS with and without electroacupuncture therapy at baseline and its changes at the end of the intervention.
- Correlate Sham with NCV changes at the beginning and end of the intervention.
- To compare changes in anthropometric, blood pressure and biochemical parameters at the beginning and end of the intervention in both groups.
- To correlate anthropometric, blood pressure and baseline biochemical parameters in patients with T2D and PNDS with NCV in groups with and without electroacupuncture intervention.
- To correlate anthropometric, blood pressure and biochemical parameters in patients with T2D and PNDS with NCV at the end of the intervention in the groups with and without electroacupuncture.
- To compare changes in NCV in both groups three months after the intervention was concluded.
- To correlate the changes evaluated by the MNSI, MDNS, NRS and SF36 instruments with NCV in both groups evaluated three months after the intervention was concluded.
- To correlate anthropometric, blood pressure and biochemical parameters in patients with T2D and PNDS with NCV three months after completion of the intervention in the groups with and without electroacupuncture.

MATERIAL AND METHODS:

It is a CCS, multicenter, simple random assignment, longitudinal, experimental, prospective, analytical and comparative. The protocol has a duration of 14 months, (2020 – 2021), which includes the stages of screening, intervention, analysis of results and generation of deliverable products (thesis work, manuscripts etc).

The total sample contemplated in the study is **262 subjects** entitled to the IMSS recruited from UMF 20, 41 and 44 in Mexico City. Subjects must meet the study's inclusion criteria.

The study is divided into **five phases**, which in general terms are described below:

Phase 1. The **preparation of the fieldwork and training** for the study, which will last **one month**.

Phase 2 Recruitment of patients, will have a **duration of 2 months**, which includes the **screening and randomization of groups**, that is, they will be explained the importance of the study, in case of acceptance they must sign a CCI and a clinical history will be applied, the MNSI, MDNS, NRS and SF36 questionnaires, if the patient is a candidate they will be given an appointment for clinical evaluation that consists of determination of anthropometry, blood pressure, biochemical parameters and the analysis of sensory and motor NVC by electrophysiological techniques.
Once the patient is accepted, the study groups will be **simply randomized**, that is, two groups will be formed (cases: control), one with electroacupuncture treatment (**N = 131**) and another with Sham treatment also called placebo (**N = 131**), giving a **total of 262 subjects**, the Random Number Generator program of the STATS® program will be used for **randomization**.

Phase 3. Intervention of the subjects under study. It will **last for 2 months**. The interventions will be carried out by an acupuncturist with experience in electroacupuncture, who will also apply the Sham therapy. The Sham intervention will be represented by the use of auriculotherapy (no puncture, no electrostimulation), using steel microspheres and millet seeds which will be adhered with Micropore only in the outer ear. The Sham, in addition, has the characteristic that it will not be placed in the same place as the electroacupuntural points selected for treatment. Several systematized studies and meta-analyses have reported that Sham therapy has no clinical evidence suggestive of changes or activity in the treatment of ND therefore it will be considered as placebo. Note: Both groups will have access to a conventional treatment in the corresponding UMF, which will be based in accordance with the clinical practice guidelines NOM-015-SSA2-2010, for the prevention, treatment and control of diabetes mellitus.

In the intervention, 16 electroacupuncture or Sham sessions of 20 minutes each will be carried out, therefore, two sessions per week will be implemented in a period of 2 months. At the end of the 16 sessions, the evaluation of the MNSI, MDNS, NRS and SF36 instruments, the anthropometric parameters (weight, height, BMI, blood pressure), biochemical (glucose, urea, creatinine, uric acid, triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol, and HbA1c%) and the study of sensory and motor VCN by electrophysiological techniques will be carried out.

For the intervention of the present ECC we will consider as ***the patient's primary clinical endpoint*** the existence of greater symptoms in the intensity of the pain of the ND, determined by a clinical evaluation and the instruments MNSI, MDNS, NRS and SF36, or that the patient decides to withdraw from the study. While the ***primary clinical endpoint of the intervention*** will be determined by the fact that there is a loss of 30% of the total sample during the course of the intervention.

Phase 4. **Evaluation of the success of the intervention over time.** It will last **3 months**, that is, the anthropometric and biochemical parameters, the MNSI, MDNS, NRS and SF36 instruments will be evaluated, and the NCV study three months after the intervention has been completed.

Phase 5. Analysis of results and generation of deliverable products, which includes thesis papers and manuscripts. It will last for **six months.**
It should be considered that at the end of the intervention and after three months of follow-up, the changes in the evaluation of the MNSI, MDNS, NRS, SF36 instruments will be analyzed, and in the study of sensory and motor NCV by electrophysiological techniques, in addition, a multivariate analysis adjusted for confounding variables as anthropometric parameters will be carried out, blood pressure and biochemicals.

In both groups, the baseline evaluation vs evaluation at the end of the intervention will be correlated and compared. Subsequently, the final evaluation vs evaluation will be correlated and compared over the time three months after the intervention.

The **blind** person will be carried out in the statistical analysis, that is; the statistician who will analyze and interpret the results will not know what intervention has been performed in each of the groups.
Two specialty final thesis works and at least two manuscripts are considered in this work as deliverable products.