



Research Article

# Research Protocol for a Pilot Study. The Effect of ST (36) and Ren12 in the Control of Hyperglycemia in Diabetic Patients

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## Abstract

This pilot study seeks to demonstrate the hypoglycemic effect in diabetic patients with the use of the *Zusanli* (ST36) and *Zhongwan* (CV12) acupuncture points stimulated with Electro-Acupuncture (EA) with a continuous wave and frequency of 10Hz.

Diabetes mellitus is considered a public health problem. It is defined as a multifactorial metabolic disorder characterized by hyperglycemia.

The sample will be divided into two groups with 10 patients in each. The first group will be fasting patients and the second group with postprandial glucose. Plasma glucose dipstick tests will be done before and after treatment.

These acupuncture points stimulated with EA have shown their hypoglycemic effect in animal models. One of the main mechanisms by which this effect is supported is the regulation of the hypothalamic-pituitary-adrenal axis, regulating the secretion of adrenal cortical hormone.

**Keywords:** Diabetes; Electroacupuncture; Hyperglucemy

## Introduction

Diabetic Mellitus is considered public health problems [1]. It is defined as a metabolic disorder of multifactorial origin that is characterized by chronic hyperglycemia associated with alterations

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in the metabolism of carbohydrates, proteins and fats, which are produced by defects in insulin secretion or its action. Insulin is a protein (hormone) synthesized in the beta cells of the pancreas in response to various stimuli such as glucose, sulfonylureas and arginine, however, glucose is the main determinant [2].

The number of people with diabetes increased from 108 million in 1980 to 422 million in 2014 [3]. Also, in the worldwide statistics it can be identified that the population of the countries with middle and low income are more affected with this disease [4].

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia and blurred vision [5].

Traditional Chinese Medicine (TCM) from its oldest texts makes mention of diabetes disease. The term given to diabetes mellitus is “Xiao Ke” which can be translated as thirst and emaciation. At present, this term is no longer used; currently diabetes is referred to as “Tangniao” which literally means sweet urine [6]. This is due to the glycosuria that is usually seen in diabetic patients.

Acupuncture treatment that is part of TCM can be considered a treatment for diabetes. Acupuncture treatment has been shown to have a specific beneficial effect with notable advantages in the treatment of diabetes mellitus. Furthermore, numerous studies have shown that the use of Electroacupuncture (EA) can effectively lower plasma glucose and improve insulin sensitivity [7].

EA is a treatment method in which low frequencies of electricity are applied, transmitted through acupuncture needles previously inserted into acupuncture points [8]. EA treatment is part of the modern stimulation of acupuncture. In addition, it is a continuous and painless stimulation method for the patient.

EA has been shown to have favorable effects on lowering plasma glucose levels by promoting insulin production and improving insulin sensitivity by increasing the production of  $\beta$ -endorphin [9,10]. It has been used by stimulating the points of *Zusanli* (ST36) and *Zhongwan* (CV12) to address different symptoms of diabetes mellitus. *Zhongwan* (CV12) hypoglycemic effect has been demonstrated in rats. This mechanism is through the release of  $\beta$ -endorphins from the adrenal gland [8]. The *Zusanli* (ST36) is widely known and studied within acupuncture and electroacupuncture due to its effects on the increase of  $\beta$ -endorphin [11-13].

Previously, we found that a bilaterally applied specific EA frequency in *Zusanli* (ST36) induced a significant reduction in plasma glucose. The mechanism by which plasma glucose levels are reduced is believed to involve the promotion of  $\beta$ -endorphin secretion, which stimulates insulin secretion [14,15].

A human study also showed that acupuncture improved insulin sensitivity in patients with type 2 diabetes mellitus, as a result of the reduction in endogenous insulin concentration and the preservation of pancreatic  $\beta$ -cell function [16].

The use of the *Yishu* point (EXB3), which is located below 8th spinous process of thoracic vertebrae, where there is part of T8 that innervates the pancreas, 1.5cun lateral to the posterior midline has also been documented. It has hypoglycemic effects when stimulated with EA and, in addition, provides protection to the islets of Langerhans. This is supported by the innervations course of the T8 spinal nerve. The regulation of the hypothalamic-pituitary-adrenal axis is also attributed to this point, decreasing the levels of cortical adrenal hormone [7,17].

When *Zusanli* (ST36) is stimulated bilaterally with EA with a frequency of 15Hz, it has the effect of improving the cholinergic activity of the nerve and also, increasing the activity of the enzyme nitric oxide synthetase and thus improving the activity of insulin [18]. Furthermore, it induces a positive regulation in the signaling of the IRS-1 and AKT-2 proteins [9,19].

In a study carried out on rats, it was shown that the hypoglycemic effect of the *Zhongwan* (CV12) and *Zusanli* (ST36) stimulated at 10Hz has a greater efficacy than if they are stimulated at 100Hz. The effect was carried out with continuous stimulation for 30 minutes [8].

## Hypothesis

Based on the literature reviewed and with the effects that have been found in animal models, we hypothesize that stimulation with AD in *Zusanli* (ST36) and *Zhongwan* (CV12), choosing points at random as anchors, may have a short-term effect by reducing glucose. Plasma of treated patients. It is expected that at the end of the 30 minutes that the treatment lasts, plasma glucose levels will fall.

It is expected that by reducing plasma glucose levels the patient will improve their quality of life by reducing the symptoms of hyperglycemia.

## Objectives

Raise and confirm that acupuncture in combination with EA may have beneficial effects by lowering plasma glucose levels in patients with type 2 diabetes so that it can be used with greater support in the treatment of such patients.

### General objective

Raise and confirm that acupuncture in combination with EA may have beneficial effects by lowering plasma glucose levels in patients with type 2 diabetes so that it can be used with greater support in the treatment of such patients.

### Specific objectives

To demonstrate the efficacy of EA as a hypoglycemic agent in diabetic patients through the mechanisms studied in animal models.

Create a synergy between the *Zusanli* (ST36) and *Zhongwan* (CV12) points since both are mentioned in the literature as points with a strong influence in promoting hypoglycemia.

To demonstrate the safety and the effect on hyperglycemia in patients with type 2 diabetes mellitus with electroacupuncture treatment at the *Zusanli* (ST36) and *Zhongwan* (CV12) points.

Motivate the population to adopt the use of EA as a complementary therapy for the treatment of type 2 diabetes mellitus.

## Methods / Design

### Study design

This study will be carried out as a pilot study. Both authors will be in charge of the entire study, including study design, conduct, coordination, data analysis and reporting of results.

Patients who meet the inclusion criteria will be recruited and subsequently invited to participate in this study. Each patient will be randomly assigned a number so that they can be randomized into two groups. This ratio will be 1:1 using the numbers previously assigned. One group will be treated fasting and the other group with postprandial glucose. All patients will be treated with the same principle of treatment. A plasma glucose test will be taken with a dipstick and a brand glucometer *accu-Check Active* (Figure 1). Subsequently, the treatment will be placed on the *Zusanli* (ST36) and *Zhongwan* (CV12) points with an anchor point respectively for each point. The puncture will be carried out perpendicularly forming a 90° angle between the needle and the skin. The depth of all needles is 25mm. The needles to be used will be 30mm x 0.20mm acupuncture filiform needles. In addition, they will be stimulated through EA with the WQ-6F electro stimulation machine (Figure 2) with a continuous wave and a frequency of 10Hz for 30 uninterrupted minutes at maximum tolerance of the patient. Red alligators (positive) will go on *Zhongwan* (CV12) and *Zusanli* (ST36). The black (negative) alligators will go on the anchor points.



**Figure 1:** Description of the glucometer. The Accu-Check Active meter features no coding technology. The meter can only be used with Accu-Check Active test strips. Send alerts in case of damaged strips or if the blood dose was low, with the opportunity to redose within the next 10 seconds.



**Figure 2:** Description of the electro stimulator. The WQ-6F Electronic Acupuncture scope has a load of no more than 250 and an electrical load of 40 mA (10 V). The pulse frequency can range from 0 to 200 Hz and the pulse width can be adjusted from 0.2 to 0.8 ms. The power supply is direct current (4.5 V) inserting 3 size D batteries. It has 7 outputs divided into 2 sections. In section A there are 4 outputs and in section B there are 3 outputs.

At the end of the stimulation time, a glucose reading will be taken again and the results will be emptied into a table formulated in the Microsoft Excel program in order to perform an analysis of the glucose readings before and after the treatment and in this way, determine changes in plasma glucose in patients.

This study will be carried out on a single occasion to assess whether favorable results are obtained.

## Ethical Principles

This research protocol follows the decrees proposed by the Declaration of Helsinki of the WMA. All patients will be informed about the treatment to which they will be submitted in this research protocol. In addition, each patient will sign a letter of consent in which they express their agreement to carry out said treatment. The data provided by the patient such as the identification card will be protected and the only thing that will be published will be the results before and after the treatment.

## Sample size

As our study is designed in a pilot way and seeks to evaluate the effect of *Zusanli* (ST36) and *Zhongwan* (CV12) with electroacupuncture and its effect as a hypoglycemic agent, it is estimated to have a sample of 20 patients, who will be divided into two groups: group A, which will be 10 fasting patients and group B, which will be formed by 10 patients without fasting.

## Recruitment of patients

Patients will be recruited from the Acupuncture Medical Clinic, affiliated with the College of Acupuncture. Our study will be promoted through the dissemination of posters. Each of those interested in participating will be contacted to give them details about the treatment procedure, the effects that are being sought based on scientific documentation and the possible adverse effects of the treatment. Those interested who wish to be part of the sample will be contacted and summoned at the facilities of the Acupuncture Medical Clinic to carry out the treatment.

## Informed consent

Our informed consent adheres to the Official Mexican Standard for clinical records NOM-004-SSA3-2012 where the patient is informed of the treatment with acupuncture and electroacupuncture with which he will be treated. It also includes the possible adverse effects that the patient may suffer from the treatment. In addition, it is reported that the results of said treatment will be included in our results to carry out said study.

## Inclusion criteria

- Patients with a history of hyperglycemia
- Previously diagnosed with Type 2 Diabetes Mellitus
- Patients with drug treatment based on hypoglycemic agents or insulin replacement therapy

## Exclusion criteria

- Patients without a diagnosis of Diabetes Mellitus
- Patients diagnosed with Type 1 Diabetes Mellitus
- Female patients with gestational diabetes
- Pacemaker patients

- Patients with osteosynthesis in the tibia and fibula
- Patients with current acupuncture or electroacupuncture treatment

## Outcome measures

Two plasma glucose readings will be taken through test strip tests. The first sample will be prior to treatment and the second after treatment. The data will be collected and recorded by both authors.

## Analysis of Results

All the results obtained from both groups will be emptied into the Microsoft Excel program, in which will be the data of the plasma glucose readings before and after the treatment. For the analysis and comparison of both groups, the data will be included in tables showing both results and the difference in glucose between the two readings. At the end, the differences between both groups will be analyzed by means of graphs, both in the parameters of each patient and the mean between both groups.

## Discussion

Acupuncture and EA have potential benefits in efficacy and safety and therefore is expected to be a promising adjunct treatment for type 2 diabetes mellitus.

The main reason for conducting this pilot study is to verify the short-term hypoglycemic effect that EA may have. If the effect is significant, a decrease in glycosylated hemoglobin levels may be obtained.

The endocrine system and the nervous system regulate metabolic activities and mutually influence their functions<sup>7</sup>. This effect is mainly caused by the regulation in the release of adrenal cortical hormone. In addition, the application of EA has the ability to improve insulin resistance as well as increase the expression of glucose transporters in muscle and liver [20].

Combination treatment with EA and other drugs appears to be an alternative treatment to achieve better therapeutic goals that deserve future research [17]. Despite the results demonstrated in animal models, the use of EA needs further support with experimentation in animal models. And clinical research so that it can be consolidated as a useful therapy capable of being implemented with greater safety in the treatment of Type 2 Diabetes.

## Conflict of Interest

The authors have no conflict of interest

## References

1. Grimaldi A (2012) diagnóstico de diabetes. EMC - Tratado de Medicina 16: 1-6.
2. Asmat U, Abad K, Ismail K (2016) Diabetes mellitus and oxidative stress-A concise review. Saudi Pharmaceutical Journal 24: 547-553.
3. World Health Organization. Diabetes (Internet). World Health Organization, Geneva, Switzerland.
4. Moreno-Altamirano L, García-García J, Soto-Estrada G, Capraro S, Limón-Cruz D (2014) Epidemiology and social determinants of obesity and type 2 diabetes in Mexico. Revista Médica Del Hospital General De México 77: 114-123.

5. American Diabetes Association (2012) Diagnosis and Classification of Diabetes Mellitus. *American Diabetes Association* 35: 64-71.
6. Tejeiro E (2016) Traditional Chinese Medicine Differential Diagnosis of Diabetes Mellitus (from the Yellow Emperor to Modern Day Research). *Journal Of Chinese Medicine* 112: 24-31.
7. Feng Y, Fang Y, Wang Y, Hao Y (2018) Acupoint Therapy on Diabetes Mellitus and Its Common Chronic Complications: A Review of Its Mechanisms. *BioMed research international* 2018: 3128378.
8. Medeiros L, Honório A, Ximenes de Prado A, Nasser M, Leitao de Vasconcelos P, et al. (2011) Electroacupuncture stimulation using different frequencies (10 and 100 Hz) changes the energy metabolism in induced hyperglycemic rats. *Acta Cirúrgica Brasileira* 26: 47-52.
9. Lee Y, Li T, Tzeng C, Chen Y, Ho W, et al. (2011) Electroacupuncture at the Zusanli (ST-36) Acupoint Induces a Hypoglycemic Effect by Stimulating the Cholinergic Nerve in a Rat Model of Streptozotocine-Induced Insulin-Dependent Diabetes Mellitus. *Evidence-Based Complementary and Alternative Medicine* 2011: 1-6.
10. Pai H, Tzeng C, Lee Y, Chang C, Lin J, et al. (2009) Increase in Plasma Glucose Lowering Action of Rosiglitazone by Electroacupuncture at Bilateral Zusanli Acupoints (ST.36) in Rats. *Journal of Acupuncture and Meridian Studies* 2: 147-151.
11. Huang X, Huang K, Bai D, Hao Y, Wu Q, et al. (2020) Electroacupuncture improves cognitive deficits and insulin resistance in an OLETF rat model of Al/D-gal induced aging model via the PI3K/Akt signaling pathway. *Brain Research* 1740: 146834.
12. Ali U, Apryani E, Wu H, Mao X, Liu H, et al. (2020) Low frequency electroacupuncture alleviates neuropathic pain by activation of spinal microglial IL-10/ $\beta$ -endorphin pathway. *Biomedicine & Pharmacotherapy*. 125: 109898.
13. Zhang R, Lao L, Berman B (2014) Mechanisms of Acupuncture-Electroacupuncture on Persistent Pain. *Anesthesiology* 120: 482-503.
14. Tzeng CY, Lee YC, Ho TY, Chen Y, Hsu T, et al. (2015) Intracellular signalling pathways associated with the glucose-lowering effect of ST36 electroacupuncture in streptozotocin-induced diabetic rats. *Acupunct Med* 33: 395-399.
15. Pevlow PV, Baxter GD (2012) Electroacupuncture for control of blood glucose in diabetes: literature review. *J Acupunct Meridian Stud* 5: 1-10.
16. Liu M, Chen J, Ren Q, Zhu W, Yan D, et al. (2019) Acupuncture and related techniques for type 2 diabetes mellitus. *Medicina (Baltimore)* 98: 1-6.
17. Gao S, Li R, Tian HH, Pei ES, Cao BY, et al. (2014) Effects of electroacupuncture at “Yishu” (EX-B 3) on the relative hormones of HPA axis in rats with type-2 diabetes mellitus. *Zhongguo Zhen Jiu* 34: 1099-1105.
18. Lin RT, Tzeng CY, Lee YC, Chen YI, Hsu TH, et al. (2014) Acupoint-specific, frequency-dependent, and improved insulin sensitivity hypoglycemic effect of electroacupuncture applied to drug-combined therapy studied by a randomized control clinical trial. *Evid Based Complement Alternat Med* 2014: 371475.
19. Lee YC, Li TM, Tzeng CY, Cheng YW, Chen YI, et al. (2011) Electroacupuncture-induced cholinergic nerve activation enhances the hypoglycemic effect of exogenous insulin in a rat model of streptozotocin-induced diabetes. *Exp Diabetes Res* 2011: 947138.
20. Tominaga A, Ishizaki N, Naruse Y, Kitakoji H, Yamamura Y (2011) Repeated application of low-frequency electroacupuncture improves high-fructose diet-induced insulin resistance in rats. *Acupunct Med* 29: 276-83.



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