Study Protocol Clinical Trial

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The efficacy of niacin supplementation in type 2 diabetes patients

Study protocol of a randomized controlled trial

Xiaoying Yan, MM, Shunyu Wang, MM*

Abstract

Background: Dyslipidemia is a main risk factor of cardiovascular disease in the diabetic patients. Niacin was found acutely to decrease the plasma concentration of free fatty acids by inhibiting their mobilization from adipose tissue. This present study is a double blinded, randomized, and prospective trial to determine the effect of niacin during dyslipidemia in type 2 diabetic patients.

Methods: This randomized controlled, double-blinded, single center trial is carried out according to the principles of Declaration of Helsinki. This present study was approved in institutional review committee of the Second Affiliated Hospital of Dalian Medical University. All the patients received the informed consent. Diabetic patients were randomized (1:1) to receive 3-month treatment with extended-release niacin or matching placebo. The major outcome of our present study was the change in the level of HbA1c from the baseline to week 12. Secondary outcome measures contained the levels of fasting blood glucose, the concentrations of serum transaminase, the other laboratory variables, and self-reported adverse events. The $P < .05$ was regarded as statistically significant.

Results: We assumed that adding the niacin to the medication in patients with type 2 diabetes would reduce dyslipidemia and achieve target lipid levels.

Trial registration: This study protocol was registered in Research Registry (researchregistry5925).

Abbreviations: HDL = high density lipoprotein, LDL = low density lipoprotein.

Keywords: dyslipidemia, niacin, randomized controlled trial, study protocol, type 2 diabetic patients

1. Introduction

Dyslipidemia is a main risk factor of cardiovascular disease in the diabetic patients. Diabetic dyslipidemia is characterized by an increased low density lipoprotein (LDL) -cholesterol particles concentration, low concentration of high density lipoprotein (HDL) -cholesterol, and a high concentration of plasma triglyceride.[1–5] The changes in lipid related to the diabetes are due to an increase in flux of free fatty acids secondary to the insulin resistance.[6]

Niacin was found acutely to decrease the plasma concentration of free fatty acids by inhibiting their mobilization from adipose tissue.[7–9] The term "niacin" is generally defined as the nicotinic acid, but can also be more broadly defined as "nicotinic acid, nicotinamide, as well as the derivatives with the nicotinamide biological activity". Whether conversion to the nicotinic acid or other compounds involving nicotinamide, nicotinic acid or their releasable parts can be considered "niacin" depends primarily on the interpretation of evidence for uptake and the metabolic rates, and the biological effects of the compound, and/or release of chemical components that generate the biological effects similar to those of major forms of the niacin.[10–16] Extended release nicotinic acid is an effective lipid-modifying agents at a dose sufficient to generate the pharmacological activities and has a wide range of effects, containing the effects aimed at reducing the risks related to high LDL cholesterol, low HDL cholesterol, high triglyceridemia and high lipoprotein. Niacin offers novel opportunities for the patients to reach target levels of lipid.[17–22]

This present study is a double blinded, randomized, and prospective trial to determine the effect of niacin during dyslipidemia in type 2 diabetic patients. We assumed that adding the niacin to the medication in patients with type 2 diabetes would reduce dyslipidemia and achieve target lipid levels.

2. Material and method

2.1. Study design

This randomized controlled, double-blinded, single center trial is carried out according to the principles of Declaration of Helsinki.

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The authors have no conflicts of interest to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the present study.

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This present study was approved in institutional review committee of the Second Affiliated Hospital of Dalian Medical University (DL0094130). All the patients received the informed consent. It was also registered at the Research Registry (researchregistry5925).

2.2. Eligibility criteria

Inclusion criteria included:

1. type 2 diabetic patients;
2. aged between 30 and 65 years old;
3. the statin therapy with stable-dose for six weeks or more;
4. serum low-density lipoprotein-cholesterol $\leq$2.5 mmol/L and endothelial dysfunction.

Exclusion criteria included: Patients with poor control of diabetes mellitus (HbA1c .9.0%), renal disease, peptic ulcer disease, liver disease, and parents with the history of diabetic coma or ketoacidosis, hyperuricemia, and gout.

2.3. Randomization and blinding

The number of envelopes in each research group was equal and they were produced via a research assistant through utilizing a computer-based random number generator who did not participate in any follow-up studies or contact with other

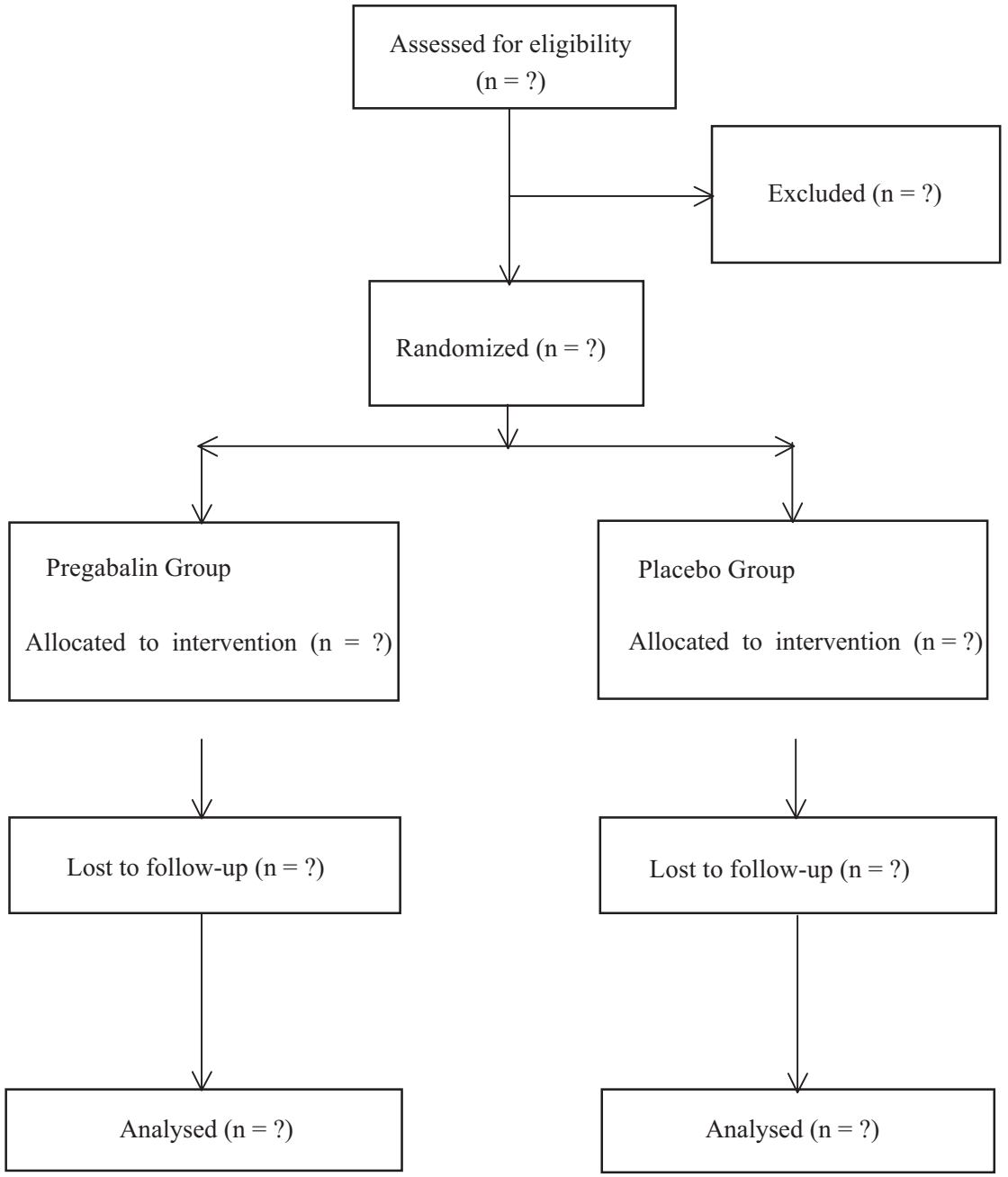

Figure 1. Flow diagram of the study.

members of study team throughout the whole study period. He prepared 80 identical, sealed bound, opaque, sequentially numbered envelopes; forty envelopes containing the instructions for group A mixing solution and other forty envelopes for the group B. These envelopes were placed in file with the principal investigator (Fig. 1).

2.4. Intervention and control groups

Diabetic patients were then randomized (1:1) to receive 3-month treatment with extended-release niacin or matching placebo. In randomized trials, the dose of niacin or its placebo was enhanced to 750 mg twice a day, then to 1000 mg, afterwards, increases to 1500 mg twice a day at intervals of six weeks, or until achieving the maximum tolerated dose. In order to prevent flushing, the subjects who did not take aspirin started taking aspirin 100 mg/day at least three weeks before the measurements of baseline vascular. During follow-up period, the levels of fasting glucose were monitored every six weeks. If the level of fasting blood glucose was greater than 10.5 mmol/L, the level of HbA1c needed to be measured, and if it was greater than 10.0%, we should reduce the dose of niacin (or its placebo). There was no change in the medication of diabetic patients during the treatment period.

2.5. Outcome measures

The major outcome of our present study was the change in the level of HbA1c from the baseline to week 12. Secondary outcome measures contained the levels of fasting blood glucose, the concentrations of serum transaminase, the other laboratory variables, and self-reported adverse events. The other laboratory variables involved the apolipoprotein, lipoprotein, and plasma lipid, uric acid, glucose, as well as the insulin concentrations. The serum levels of uric acid, glucose and the serum transaminase concentrations or the plasma were determined in local clinical laboratory via a standard automatic analyzer.

2.6. Statistical analysis

Statistical analysis was conducted through utilizing the Statistical Package for Social Sciences (SPSS for Windows, release 12.0; SPSS Inc, Chicago, IL). The statistical analysis was carried out by independent experts who did not participate in the research program. The values of mean (range) and median were presented. Non-paired t test was utilized for the numerical data of normal distribution. Non-parametric simulation was utilized where appropriate. The comparison of categorical variables was performed by χ^2 test. The $P < .05$ was regarded as statistically significant.

3. Discussion

Despite progress in prevention and treatment of the cardiovascular diseases, incidence rate and mortality rate of diabetic patients are still strikingly high, second only to the cardiovascular diseases. Nicotinic acid (also know as niacin), is an indispensable B-complex vitamin. At the pharmacological dose, it is an effective drug to reduce plasma triglyceride and increase HDL-cholesterol, and has moderate activities on the LDL-cholesterol. Niacin has been proven to reverse the coronary atherosclerosis and decrease the coronary mortality rate. Niacin possesses complex actions mechanisms, which has not been completely elucidated. This present study is a double blinded, randomized, and prospective trial to determine the effect of niacin during dyslipidemia in type 2 diabetic patients. We assumed that adding the niacin to the medication in patients with type 2 diabetes would reduce dyslipidemia and achieve target lipid levels.

Author contributions

Conceptualization: Shunyu Wang.
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Formal analysis: Xiaoying Yan, Shunyu Wang.
Funding acquisition: Shunyu Wang.
Investigation: Xiaoying Yan.
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Project administration: Shunyu Wang.
Resources: Shunyu Wang.
Software: Xiaoying Yan.
Supervision: Shunyu Wang.
Validation: Xiaoying Yan.
Writing – original draft: Xiaoying Yan.
Writing – review & editing: Shunyu Wang.

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