Study of Tripterygium Associated with Nicotinamide in Treating Late-onset Autoimmune Diabetes Mellitus in Adults*

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ABSTRACT Objective: To explore the effect of Tripterygium polyglycoside (TP) associated with nicotinamide on the islet cell function, immune parameters and lipoperoxide (LPO) in adult patients with late-onset autoimmune diabetes mellitus (LADA). Methods: Thirty-six cases of LADA were randomly divided into three groups: TP group (n = 12), treated with TP plus orally taken metformin; combined treatment group (n = 12), treated with TP combined with nicotinamide and metformin, and control group (n = 12) treated with metformin alone. They were followed-up for 18 months. Results: (1) Compared with the control group after 9 months of treatment, postprandial plasma glucose and LPO in combined treatment group were decreased (P < 0.05), and the postprandial C-peptide was higher (P < 0.05). At the 18th month, the value of postprandial C-peptide in the TP and combined treatment group was higher than that in the control group. The sIL-2R level of both TP and combined treatment groups were lowered (P < 0.01); (2) Islet cell antibody (ICA) positive of 5 cases in the TP group and 6 cases in the combined treatment group got converted to the negative respectively, while only one in the control group at the time (P < 0.05); (3) The level of LPO in the combined treatment group was significantly lower than that in the TP group at the 18th month of treatment (P < 0.05). Conclusion: TP combined with nicotinamide played a role in immunity regulation, decreasing the titer of islet cell antibody and sIL-2R, which also reduced the production of LPO and had a tendency to improve islet cell function in early LADA patients.

KEY WORDS late-onset autoimmune diabetes mellitus in adults, Tripterygium, nicotinamide

Late-onset autoimmune diabetes mellitus in adults (LADA) is a kind of special type of diabetes mellitus (DM), which accounts for more than 10% of DM. LADA is an autoimmune disease, there are many kinds of autoimmune antibody in the blood serum, and the oxygen free radical participates in the immune injury of β cells. The process of autoimmunity destroying islets' β cell is slow, which facilitates the implementation of early intervention treatment, hence it becomes a hot topic of clinical diabetology study in recent years. And recent study suggested that there is certain clinical efficacy in drug intervention therapy, but the study method adopts separate medication, which acts on certain link of pathogenesis procedure of LADA. And multiple pathological factors were to participate and many action links existed.

The present study tries to use China produced immuno-suppressor Tripterygium polyglycoside combined with oxygen free radical scavenger nicotinamide to study the clinical intervention treatment in the early stage of LADA (non-insulin-dependent stage) patients, to explore the clinical efficacy of combined therapy for intervention treatment in treating LADA and its relevant therapeutic mechanisms. The present study uses the approach of prospective and open clinical trial design.

METHODS

Inclusion Criteria

(1) According to the criteria made by America Diabetes Association (ADA) in 1997, the diagnosis was type 2 DM, in the stage of non-insulin dependency (fasting blood C-peptide > 0.25 nmol/L); (2) Age of...
onset was >20 years old, with no ketosis within 1 year after onset; (3) Glutamic acid decarboxylase antibody (GAD-Ab) and islet cell antibody (ICA) were all positive, and still remained positive when rechecked 3 months later; (4) The patients that accepted hypoglycemic therapy, after 1 week of washing-out period, had their fasting plasma glucose (FPG) be equal to or more than 7.0 mmol/L and equal or less than 13.9 mmol/L, and the difference between two consecutive tests of FPG had to be less than 1.67 mmol/L.

**Exclusion Criteria**

(1) Clinical diagnosis indicates that the patient is suffering from secondary DM, mitochondria gene mutation DM, DM of typical type 1 or maturity-onset type diabetes of the young (MODY); (2) Those who have heart dysfunction and apparent liver or renal dysfunction; (3) Pregnant or lactation women; (4) Those the researchers held to possibly have other illnesses that might intervene in the trial study or its evaluation as well as those who had taken drugs that might intervene in the trial study or its assessment.

**Patients Grouping**

In accordance with the above-mentioned conditions the practically enrolled patients were 36 cases, who were according to C-peptide etc., level stratified and randomly divided into 3 groups, 12 cases in each group: TP group, combined treatment group (Tripterygium polyglycoside + niacinamide) and control group. TP group: Male 6 and female 6 cases, ages 33–47 years old, mean 39.24 ± 7.62 years; illness course 1–6 years, mean 3.67 ± 2.08 years, mean body mass index (BMI) 21.05 ± 1.56 kg/m²; Combined treatment group: Male 7 and female 5 cases, ages 34–51 years old, mean 43.11 ± 8.73 years, illness course 1–6 years, mean 3.86 ± 2.69 years; Control group: Male 7 and female 5 cases, ages 33–48 years old, mean 40.30 ± 7.51 years, illness course 1–7 years, mean 4.05 ± 3.52 years, mean BMI 20.14 ± 1.60 kg/m². The 3 groups in age, sex, illness course and BMI, etc. matched one another, and therefore, they were comparable.

**Therapeutic Method**

Therapeutic regimen: The baseline hypoglycemic program for the 3 groups were the same, i.e. on the basis of dietary control and exercise therapy, metformin tablet (provided by Sino-American Squibb Pharmaceutical Co., Ltd.), was orally taken, initial dosage: 0.25 g, 3 times per day, with the dose adjusted according to blood glucose, and the maximal dosage 2.55 g per day. TP group: Tripterygium polyglycoside tablet (provided by Guangzhou Biochemical Pharmaceutical Factory), was orally taken, initial dosage: 1.5 mg/kg per day, and after administration for 6 months, it was changed to 0.5 mg/kg per day for maintenance; Combined treatment group: on the basis of medication of TP, niacinamide tablet (provided by Wuhan Tongji Mingzhi Pharmaceutical Co., Ltd.) was added, with the dosage 50 mg/kg per day orally taken; Control group: merely used was the baseline hypoglycemic regimen. The follow-up period was 18 months. The trial program was approved by the Ethics Committee, and all the patients signed the Informed Consent.

**Chief Parameters and Examination Mode**

The following parameters were observed in months 0, 9 and 18: FPG, 2 hrs of postprandial plasma glucose (PPG) and C-peptide, glutamic acid decarboxylase (GAD-Ab), islet cell antibody (ICA), soluble receptor of interleukin-2 (sIL-2R), lipid peroxide (LPO). For GAD-Ab determination applied ELISA assay (provided by German Boehringer Co., more than 50 ng/L as positive, within batch CV 4.6%); for ICA used ELISA assay (provided by USA Biomerica Co., within batch CV 3.9%); for serum C-peptide applied RIA (provided by Tianjin Depu Co., within batch CV 4.6%); for sIL-2R determination used monoclonal and multclonal double antibody sandwich assay (provided by Wuhan Boshide Bioengineering Co., Ltd., within batch CV 4.0%). WBC count, liver function and renal function, etc., were routinely checked-up every 2 months.