Study on Effect of Different Dosages of Ligustrazine on Level of Plasminogen Activator Inhibitor-1 Activity in Type 2 Diabetes Mellitus Patients

XUE Xian-zhong (薛现中)¹, ZHANG Zhao-hua (张兆华)¹, and XING Xiao-yan (邢小燕)²

ABSTRACT

Objective: To observe the effect of different dosages of ligustrazine (LG) on the level of plasminogen activator inhibitor-1 (PAI-1) activity in patients with type 2 diabetes mellitus. Methods: Ninety cases of type 2 diabetes mellitus inpatients were selected, and randomly divided into LG small dosage group (SDG), LG large dosage group (LDG) and control group. The 120 mg LG, 400 mg LG and normal saline 250 ml were given through intravenous dripping respectively, once daily, 20 days as one treatment course. Before and after treatment, all the patients had their fasting blood taken for PAI-1 and tissue plasminogen activator (t-PA) assessment test to perform the comparative study. Results: Seventy-three out of the 90 patients completed the observation course, the PAI-1 activity of three groups after treatment all lowered compared with that before treatment, and the difference between groups was also significant (all \( P<0.01 \)). After treatment the PAI-1 level of SDG and LDG of LG were all markedly lowered (all \( P<0.01 \)), the LDG's lowering was more evident than that of SDG, and comparison between these two groups of patients showed significant difference (\( P<0.01 \)). Although in the control group there was some difference between before and after treatment, it was not so significant like the above-mentioned two groups (\( P = 0.0140 \)). No adverse reaction occurred in the 3 groups during the observation period. Conclusion: LG could safely and effectively lower type 2 diabetes mellitus patient's plasma PAI-1 activity level, and LDG of LG proved to be particularly effective.

KEY WORDS type 2 diabetes mellitus, ligustrazine, plasminogen activator inhibitor-1
In SDG-LG, there were male 13 and female 12 cases; ages 27–70 years, mean 55.16 ± 12.63 years; illness course 0 – 23 years, mean 6.16 ± 5.78 years; body mass index (BMI) 19.4 – 31.8 kg/m², mean 24.18 ± 3.00 kg/m²; and fasting blood glucose (FBG) 6.7 – 18.6 mmol/L, mean 12.41 ± 3.73 mmol/L.

In LDG-LG, there were 24 cases, male 12 and female 12; ages 33–71 years, mean 54.71 ± 11.09 years; illness course 0 – 19 years, mean 6.29 ± 4.75 years; BMI 20.8 – 31.0 kg/m², mean 24.57 ± 3.16 kg/m²; and FBG 7.6 – 17.2 mmol/L, mean 12.18 ± 3.92 mmol/L.

In the control group, there were 24 cases, male 11 and female 13; ages 30–72 years, mean 55.08 ± 12.06 years; illness course 0 – 20 years, mean 6.56 ± 5.19 years; BMI 19.6 – 30.1 kg/m², mean 24.05 ± 2.87 kg/m²; and FBG 6.8 – 20.0 mmol/L, mean 12.89 ± 4.20 mmol/L.

Before treatment, analysis of variance showed that in the ratio between male and female, age, illness course, BMI and FBG in the 3 groups, there was no significant difference, all P > 0.05. All the patients 2 weeks before entry, the observation period used no hypoglycemics such as dimethyl-biguanide, hypo-lipidemics, anti-coagulants or antiplasmin agents.

**Therapeutic Methods**

The ligustrazine used in the present observation was produced by Shandong Weifang Pharmaceutic Factory Co., Ltd, 40 mg/amp, batch No. 000802. SDG-LG: LG 120 mg was added into 0.9% normal saline 250 ml, and given through intravenous dripping, once daily; LDG-LG: LG 400 mg was added into 0.9% normal saline 250 ml, and given through intravenous dripping, once daily; the control group: 0.9% normal saline 250 ml was given through intravenous dripping, once daily. And the treatment course for every group was 20 days. All the patients went on in the observation period with their treatment of insulin, sulfaurea drugs or a-glucosidase inhibitor to control the blood glucose, and the dosage would be adjusted according to the blood glucose level alteration.

**Observation Item**

Before treatment all the patients had the following items determined; PAI-1, tissue plasminogen activator (t-PA), fibrinogen (FIB), prothrombin time (PT), fasting blood glucose and that 2 hrs after meal, blood and urine routine measurement, etc. For the determination of PAI-1 and t-PA, the reagents are produced by Shanghai Sun Bio-Engineering Co., and the enzyme labeling device is the product of Austria, type Spectra Classic.

PAI-1 determination: Blood sample 3.6 ml was collected and placed in a silica glass test tube containing 3.8% sodium citrate, mixed, centrifuged with 3000 r/min for 10 min, and then the upper layer of plasma was collected and placed in −20°C refrigerator to be preserved for use. Determination was done with enzyme linked immunosorbent assay (ELISA) or color developing substrate assay.

For FIB, fasting blood glucose and that 2 hrs after meal and blood lipid determination, turbidity method was adopted, and prothrombin time determination was done with coagulation method.

**Statistical Analysis**

Various parameters were all expressed with x ± s. The present study belongs to the protocol design for repeated determination, and therefore, a design for repeated determination should be established in managing