Effect of Liraglutide combined with Jinlida granules on glycolipid metabolism and islet function of type 2 diabetes mellitus

Xianjuan Wang, Kun He, Jing Li, Ying Liu, Zhaokang Peng, Lijuan Zhao, Shumin Ji

Department of Endocrinology, Xingtai Third Hospital, Xingtai City, Hebei Province, 054000, China

Abstract

To investigate whether Liraglutide combined with Jinlida granules affects glycolipid metabolism and islet function in the treatment of type 2 diabetes mellitus (T2DM), a control group and an observation group were established with 90 T2DM patients. The control group was given Jinlida treatment and the observation group was given liraglutide combined treatment for 12 weeks. The clinical efficacy, glycolipid metabolism, bone metabolism, islet function, and endothelial function. The curative effect of the observation group was better than that of the control group. After treatment, FBG, 2hPG, HbAlc, TC, TG, and LDL-C in the observation group were lower and HDL-C was higher than those in the control group (P<0.05). After treatment, the observation group showed higher bone mineral density, osteocalcin, FINS, and HOMA-β and lower HOMA-IR than the control group (P<0.05). After treatment, endothelin-1 level in the observation group was lower than that in the control group, and the NO level was higher (P<0.05). No significant difference was found in the incidence of adverse reactions between the two groups (P>0.05). Liraglutide combined with Jinlida in T2DM can improve glucose, lipid, and bone metabolism, promote the recovery of islet function, and enhance vascular endothelial function.

Keywords: Combination therapy, Islet function, Jinlida, Lipid metabolism, Liraglutide, Type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus (T2DM) is the most common type of diabetes that usually occurs in adulthood and often as a result of a wrong lifestyle. Obesity, abdominal fat, lack of exercise and family history of diabetes are risk factors for this disease. Urinary frequency, feeling of extreme hunger and thirst, weakness and fatigue, dry skin and unwanted weight loss are the main symptoms of this disease [1, 2].

T2DM is a serious disease in which the insulin produced by the pancreas does not work properly or the pancreas is not able to produce enough insulin. As a result, the level of blood sugar (glucose) becomes higher than the standard state. The body cells of a person with T2DM are not able to absorb sugar from food. Failure to treat this disease, which is also called adult diabetes, causes problems and diseases such as heart disease, kidney disease, and stroke. The best way to control the disease is through lifestyle changes, medication or insulin, and regular periodic checkups [1-3].

T2DM is mainly caused by insulin resistance and is accompanied by insufficient insulin secretion. High glucose and high lipid toxicity in patients will aggravate insulin resistance and inhibit insulin secretion by islet beta cells, resulting in insufficient insulin secretion [1]. In the past, T2DM was primarily treated with metformin with poor clinical efficacy [2]. Jinlida granule is a proprietary Chinese medicine that can regulate blood lipids, glucose, and triglycerides in the body, thus alleviating T2DM and reducing blood glucose and insulin levels in diabetic patients to a certain extent. However, the clinical efficacy of monotherapy is not satisfactory [3, 4]. Liraglutide is a glucagon-like peptide-1 receptor agonist, which can control blood glucose, reduce body weight, and improve islet function. It has been reported in the past that Liraglutide has a high therapeutic effect on T2DM [5]. Based on this, this study was to explore the effects of liraglutide combined with Jinlida in T2DM on glycolipid metabolism and islet function.

2. Materials and methods

2.1. Clinical data

90 patients with T2DM from October 2021 to February 2023 were selected. A control group and an observation group were established by the random number table method. In the control group, there were 26 males and 19 females, aged from 41 to 78 years with an average age of (59.67±5.31) years. The course of disease ranged from 6 months to 9 years, with an average of (2.58 ± 0.56) years. BMI ranges from 18.5 to 28.3 kg/m², with an average of (23.01 ± 1.26) kg/m². The observation group included 24
males and 21 females, with an average age of (58.53±5.68) years, ranging from 40 to 75 years. The course of disease ranged from 5 months to 9 years, with an average of (2.54±0.59) years. BMI ranges from 18.1-27.9 kg/m², with an average of (22.98±1.42) kg/m². The above data indicated no significant difference between the two groups (P>0.05).

2.2. Inclusion criteria
Inclusion criteria included: The relevant diagnostic criteria for T2DM were met [6]; All patients signed the consent form; Patients with no previous treatment history of li raglutide or Jinlida.

2.3. Exclusion criteria
Exclusion criteria included: Type 1 diabetes mellitus; Patients with diabetic nephropathy; Patients with heart, liver, and kidney dysfunction; Patients with ketoacidosis; Patients with other diseases that affect glucose metabolism, such as pituitary growth hormone tumor and hypercortisolism; Patients who have recently taken drugs that affect blood glucose.

2.4. Methods
The control group was treated with Jinlida granules (Z20050845, specification: 9 g/packet; Yiling Pharmaceutical, Shijiazhuang, China) and taken with boiling water, 9 g/time, 3 times/day. The observation group was given subcutaneous injections of Liraglutide injection (J20160037, specification: 3mL:18mg; Novo NordiskA/S) combined treatment, 1.2 mg/time, once/day. Both groups were treated continuously for 12 weeks.

2.5. Outcome measures
(1) Clinical efficacy [7] was measured after 12 weeks. Obviously efficacy: FPG < 7.0 mmol/L or reduced by >30%; effective: FPG < 8.5 mmol/L or reduced by 10-29%; ineffective: FPG showed no significant change or decreased by less than 10%.

(2) Glycolipid metabolism index: Before treatment and 12 weeks after treatment, 3 ml fasting venous blood was collected to measure fasting blood glucose and 2 h postprandial blood glucose by OneTouch Ultra (Johnson, Shanghai, China), HbAlc was determined by high-performance liquid chromatography using variant II analyzer (BioRad), and insulin was determined by radioimmunoassay. All kits were purchased from Diagnostic Systems Laboratories. TC, TG and LDL-C, and HDL-C were detected by an automatic biochemical analyzer (Hitachi, Japan).

(3) Islet function indicators: Fasting insulin (FINS) before treatment and 12 weeks after treatment were detected by radioimmunoimmunoassay, and HOMA-IR and HOMA-β were evaluated by homeostasis model assessment.

(4) Bone metabolism indices: Bone mineral density (BMD) of lumbar vertebra L-4 was measured with GE DEXA dual-energy X-ray bone densitometer. Serum osteocalcin (BGP) levels were measured by radioimmunoassay.

(5) Vascular endothelial function: Serum endothelin (ET) level was detected by enzyme-linked immunosorbent assay and NO level by nitric acid reduction colorimetry.

2.6. Statistical analysis
Data were processed by SPSS22.0 software. Enumeration data were expressed as percentages and compared by χ² test. Measurement data were expressed as (±s) after the normality test and compared by t-test. P<0.05 meant that the difference was statistically significant.

3. Results
3.1. Clinical efficacy
Table 1 shows that the therapeutic efficacy of the observation group was better than that of the control group (P<0.05).

3.2. Glucose metabolism indices
Glucose metabolism indices showed no significant difference in the two groups before treatment (P>0.05). After treatment, observation group had reduced FBG, 2hPG, and HbAlc versus control group (P<0.05, Figure 1).

3.3. Lipid metabolism indices
Lipid metabolism indices indicated no significant difference between the two groups before treatment (P>0.05). After treatment, observation group showed reduced TC, TG and LDL-C and enhanced HDL-C versus control group (P<0.05, Figure 2).

3.4. Islet function indices
Pre-treatment islet function indices showed no significant difference between the two groups (P>0.05). After treatment, higher FINS and HOMA-β and lower HOMA-IR were measured in observation group rather than control group (P<0.05, Figure 3).

3.5. Bone metabolic indices
No significant difference could be seen in pre-treatment bone metabolic indices between the two groups (P>0.05). Observation group expressed higher BMD value and BGP level than control group (P<0.05, Figure 4).
Liraglutide combined with Jinlida granules in T2DM patients mainly relying on multi-flavor Chinese medicine with multi-target and multi-link effects to improve insulin resistance and thus reduce blood glucose [10]. However, according to relevant reports, single-drug therapy is not effective [11]. Liraglutide can well control blood glucose, reduce patients' weight, and improve islet function [12]. This study found that lilaglutide combined with Jinlida achieved a better therapeutic effect, lowered FBG, 2hPG, HbAlc, TC, TG, and LDL-C and elevated FINS, HOMA-β, and HDL-C, indicating that lilaglutide combined with Jinlida can improve the body glucose and lipid metabolism. The reason is that liraglutide can promote the secretion of insulin, improve the sensitivity of body tissue cells to insulin, inhibit the apoptosis of islet beta cells, and restore the function of islet beta cells. In addition, liraglutide has a long half-life when injected subcutaneously, which can prolong its action time, make patients feel full for a certain period, and continuously control blood glucose levels [13, 14]. In addition, this study showed that liraglutide combi-

3.6. Endothelial function indices
Before treatment, there was no significant difference in endothelial function indices between the two groups (P>0.05). After treatment, ET-1 level in the observation group was lower and NO level was higher than that in the control group (P<0.05, Figure 5).

3.7. Incidence of adverse reactions
There was no statistical significance in the incidence of adverse reactions between the two groups (P>0.05, Table 2).

4. Discussion
T2DM has shown increasing incidence. High glucose and high lipid toxicity in T2DM patients will aggravate insulin resistance and inhibit insulin secretion [8, 9]. Jin-

Table 2. Comparison of the incidence of adverse reactions between the two groups (e.g., %)

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Nausea and vomiting</th>
<th>Hypoglycemia</th>
<th>Rash</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>45</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2.22</td>
</tr>
<tr>
<td>Control group</td>
<td>45</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>6.67</td>
</tr>
</tbody>
</table>

χ²: 1.047

P: 0.306
Liraglutide combined with Jinlida granules in T2DM

Data available
Data is available from the corresponding author on request.

Authors' contributions
XW and KH the initiator of the study conducted the main experimental part, described the results, and wrote the article. JL and SJ performed the statistical calculations and participated in drafting the manuscript. YL, ZP and LZ participated in collecting the research material. SJ supervised the work.

References

ned with Jinlida elevated BMD value and BGP level, thus improving bone metabolism in the body, which is mainly related to the improvement of bone density by liraglutide regulating intestinal calcium and phosphorus metabolism [15].

In the condition of long-term hyperglycemia, the body of T2DM patients gradually presents inflammatory responses, and most diabetic patients also have dyslipidemia, which destroys vascular endothelial function of patients [16]. However, vascular endothelial function impairment is the basic pathological change of various complications in T2DM patients, which will lead to atherosclerosis and thrombosis [17]. NO and ET-1 are a pair of antagonistic vasoactive substances synthesized by vascular endothelial cells and can maintain vascular homeostasis. Hyperglycemia can decrease NO synthesis and activity, weaken the vasodilatory effect, and thus aggravate the disturbance of blood microcirculation. Due to long-term hyperglycemia in diabetic patients, blood viscosity increases, lipid metabolism disorders, and insufficient perfusion of blood microcirculation lead to tissue ischemia and hypoxia, induce vascular endothelial injury, and increase the synthesis and release of ET-1 [4, 18]. In addition to the hypoglycemic effect, liraglutide has the function of protecting vascular endothelia and improving neuromuscular microcirculation [19]. Liraglutide can inhibit vascular adhesion molecules and plasminogen activators in the body, reduce high reactive oxygen species, and then reduce the damage to vascular endothelial cells, thereby improving vascular endothelial function and protecting vascular function in patients. This study indicated that liraglutide combined with Jinlida could improve vascular endothelial function in T2DM patients by reducing ET-1 and elevating NO. This is mainly because liraglutide can protect the blood glucose regulation function of the remaining islet cells, improve the insulin resistance of diabetic patients, reduce or relieve the toxic effect caused by hyperglycemia, thus relieving the oxidative stress reaction in the body, maintaining the normal function of vascular endothelium, promoting NO expression, inhibiting endothelial cell apoptosis and inducing proliferation, thereby reducing vascular endothelial damage and maintaining a stable endothelial environment [20-26]. In addition, this study found that T2DM patients receiving liraglutide treatment based on Jinlida would not increase the incidence of adverse reactions, suggesting that combination therapy is relatively safe.

In summary, Liraglutide combined with Jinlida in T2DM can improve the body's glucose and lipid metabolism and bone metabolism, promote the recovery of islet function, and improve vascular endothelial function.

Acknowledgments
Not applicable.

Ethics approval and consent to participate
This study was approved by the ethical committees of Xingtai Third Hospital. Written inform consent was obtained from all patients.

Funding Statements
Not applicable.

Conflicts of Interest
The authors declare no conflicts of interest.
Liraglutide combined with Jinlida granules in T2DM


