Effect of liraglutide and metformin on constitution, metabolism and micro-inflammatory state in newly diagnosed type 2 diabetic mellitus patients with obesity

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ABSTRACT

Objective: To analyze the effect of liraglutide and metformin on the constitution, metabolism and micro-inflammatory state in newly diagnosed type 2 diabetic mellitus patients with obesity. Methods: A total of 55 cases of newly diagnosed type 2 diabetic mellitus patients with obesity were included for study and divided into observation group (n=30) and control group (n=25) according to different treatment plans. Control group received metformin treatment alone, observation group received liraglutide and metformin treatment, and levels of glucolipid metabolism indicators, body mass index and fibrinolytic activity-related indicators, micro-inflammation-related signaling pathways, illness-related indicators, etc of two groups were detected after one course of treatment. Results: FPG, GHbA1c, TC, TG and LDL-C values in venous blood of observation group after treatment were lower than those of control group; waistline, hipline and waist-hip ratio of observation group decreased after treatment, TM value was lower than that of control group while t-PA value was higher than that of control group; TLR4-NF-κB signaling pathway and DAG/PKC signaling pathway downstream TLR4, p-NF-κB p65, DAG and PKC protein expression levels of observation group after treatment were significantly lower than those of control group; serum APN, Nesfatin-1 and ISI values of observation group after treatment were higher than those of control group while LP, Chemerin, RBP4 and FINS values were lower than those of control group. Conclusions: Combined therapy of liraglutide and metformin can significantly improve the constitution of newly diagnosed type 2 diabetic mellitus patients with obesity, optimize the general condition and be expected to improve treatment outcome.

1. Introduction

Newly diagnosed type 2 diabetic mellitus is mostly associated with different levels of obesity, the obese people have poor metabolic state, diabetes will further lead to glucolipid metabolic disorders, and vessel-related complications increase. The treatment of type 2 diabetes patients with obesity should be different from that of patients with type 2 diabetes alone, and at the same time of strengthening the management of the blood glucose, it should pay attention to the regulation of the body's insulin and glucagon levels[1,2]. Metformin is the most common oral drug for clinical control of blood glucose, and it can increase the hypoglycemic effect of insulin, decrease insulin dosage and reduce hypoglycemic events. Liraglutide is a kind of human glucagon-like peptide-1 (GLP-1) analogue, its curative effect is ideal in patients with poor glycemic control after the application of metformin, and at the same time, it can promote insulin cell regeneration and protect cardiovascular system[3]. At present, some scholars put forward that for type 2 diabetes patients with obesity, blood glucose control and vascular protection should be strengthened, so the effect of liraglutide and metformin on the constitution, metabolism and micro-inflammatory state in newly diagnosed type 2 diabetic mellitus patients with obesity was mainly analyzed, hereby reported as follows.

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2. Materials and methods

2.1. Case information

A total of 55 cases of newly diagnosed type 2 diabetic mellitus patients with obesity were included for study and received treatment in our hospital from April 2013 to October 2015. The treatment process and related test results of the included patients were retrospectively analyzed, and according to different treatment plans, patients were divided into observation group (n=30) and control group (n=25). Control group included 15 male cases and 10 female cases, they were 37-65 years old, the average age was (48.92±7.51) years, newly diagnosed fasting blood glucose was 7.82-11.27 mmol/L, the average was (8.39±1.28) mmol/L, BMI was 28-31 and the average was (29.17±1.05); observation group included 17 male cases and 13 female cases, they were 34-67 years old, the average age was (49.53±7.27) years, newly diagnosed fasting blood glucose was 7.65-11.53 mmol/L, the average was (8.45±1.17) mmol/L, BMI was 28-32 and the average was (29.32±1.17). Differences in gender, age, diabetic condition, body mass index and other baseline information were not statistically significant between two groups (P>0.05).

2.2. Treatment plans

All included patients received health education of diabetes-related knowledge after admission, and were given diabetes diet according to the illness severity. Control group received metformin treatment alone, specifically as follows: oral administration of metformin tablets, 1.0 g each time, twice a day and 16 weeks in a row. Hypoglycemic events should be paid attention to during the treatment, and those with hypoglycemia could decrease the dosage of metformin.

Observation group received liraglutide combined with metformin, specifically as follows: subcutaneous injection of liraglutide, 0.6 mg each time, once a day and 16 weeks in a row. The usage and dosage of metformin were the same as those of the control group.

2.3. Observation indexes

Glucolipid metabolism indexes: after 1 course of treatment, 5ml fasting peripheral venous blood was extracted from patients in the morning to detect fasting plasma glucose (FPG), glycosylated hemoglobin A1 (GHbA1c), total cholesterol (TC), triglyceride (TG) and low density lipoprotein cholesterol (LDL-C).

Body mass index and fibrinolytic activity: included patients wore light clothing and were barefoot, flexible rule was used to measure waistline and hipline, and waist-to-hip ratio was calculated; height and body mass were measured and body mass index (BMI) was calculated. Automatic analyzer was used to detect thrombomodulin (TM), plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) levels in fasting venous blood.

TLR4-NF-κB signaling pathway and DAG/PKC signaling pathway: TLR4, p-NF-κB p65, DAG and PKC protein expression.

Illness-related factor levels: adiponectin (APN), leptin (LP), chemerin, Nesfatin-1, retinol binding protein 4 (RBP4), fasting insulin (FINS) and insulin sensitivity index (ISI).

2.4. Statistical methods

Data obtained in the research was analyzed by SPSS 23.0 software, measurement data was in terms of Mean ± SD, comparison between two groups was performed by t test, and P<0.05 was set as the standard of statistical significant differences.

3. Results

3.1. Glucolipid metabolism indexes

The results showed that FPG, GHbA1c, TC, TG and LDL-C values in venous blood of observation group after treatment were lower than those of control group (P<0.05), shown in Table 1.

3.2. Body mass index and fibrinolytic activity indexes

The results showed that waistline, hipline and waist-hip ratio of observation group decreased after treatment, TM value was lower than that of control group while t-PA value was higher than that of control group (P<0.05), and differences in PAI-1 levels between two groups were without statistical significance after treatment (P>0.05), shown in Table 2.

3.3. Micro-inflammation-related signaling pathways

The results showed that TLR4-NF-κB signaling pathway and DAG/PKC signaling pathway downstream TLR4, p-NF-κB p65, DAG and PKC protein expression levels of observation group after treatment were significantly lower than those of control group (P<0.05), shown in Table 3.

3.4. Illness-related indexes

The research results showed that serum APN, Nesfatin-1 and ISI values of observation group after treatment were higher than those of control group while LP, Chemerin, RBP4 and FINS values were lower than those of control group (P<0.05), shown in Table 4.

4. Discussion

The incidence of type 2 diabetes mellitus is high in the obese, the hyperinsulinemia and hyperglycemia are more serious in diabetes patients with obesity, and meanwhile, sympathetic activity increases and the incidence of diabetic vascular complications increases. Given the special significance of obesity in diabetes progression, clinical intervention should be strengthened for newly diagnosed type 2 diabetes patients with obesity. Metformin is the first selection of obese patients with type 2 diabetes, and can effectively improve insulin sensitivity and reduce insulin resistance, thus reducing liver glucose generation and exerting hypoglycemic effect[4,5]. The liraglutide belongs to a new type of human glucagon-like peptide-1 (GLP-1) analogue, and can combine and activate GLP-1 receptors, promote pancreatic β cells to secrete insulin glucose concentration-dependently, and at the same time, reduce excessive glucagon
Comparison of micri-inflammation-related signaling pathway molecule expression between two groups.

Table 3

Comparison of serum illness-related index values between two groups after treatment.

Table 4

Comparison of body mass index and fibrinolytic activity between two groups after treatment.

Table 3

Comparison of micro-inflammation-related signaling pathway molecule expression between two groups.

Table 4

Comparison of serum illness-related index values between two groups after treatment.

secretion in glucose concentration-dependent manner. Unlike natural GLP-1, liraglutide can be used once a day, and it has a longer plasma half-life[6]. Many clinical scholars believe that for type 2 diabetes patients with obesity, metformin alone may not be able to effectively reverse the disease progression and the joint application of metformin and the liraglutide may be a more ideal solution. In the research, newly diagnosed type 2 diabetes patients with obesity were selected as research subjects, and the effect of different drug intervention on patients' constitution, metabolism, micro-inflammation, etc. was determined. Obese patients are with glucolipid metabolism difficulties, and when type 2 diabetes occurs, the ability of body to metabolize blood glucose and blood lipid further reduces, causing that the blood glucose and fat molecules accumulate in the body, obesity increases and diabetes is aggravated[7]. In the research, observation group received combined therapy of liraglutide and metformin, and the changes of glucolipid metabolism indexes in circulating blood of patients were detected after one course of treatment. Fasting plasma glucose (FPG), glycosylated hemoglobin A1 (GHbA1c), total cholesterol (TC), triglyceride (TG) and low density lipoprotein cholesterol (LDL-C) are the most common and the most representative clinical blood glucose and blood lipids indexes, FPG and GHbA1c represent the recent and about 8-week blood glucose levels respectively, and TC, TG and LDL-C levels can directly measure the blood lipid metabolism in patients[8,9]. Specific detection results showed that FPG, GHbA1c, TC, TG and LDL-C values in venous blood of observation group were lower after treatment, indicating that combined liraglutide and metformin treatment could significantly improve the body’s glucolipid metabolism ability and improve patients’ hyperglycemia and hyperlipidemia state.

The constitution of type 2 diabetes patients with obesity declines, blood is in a relatively hypercoagulable state, and the incidence of thrombotic diseases increases. At the same time of lowering blood glucose, clinical treatment can also reduce a series of complications brought by hyperglycemia. In the research, waistline, hipline, waist-hip ratio and BMI value were positively correlated with glucolipid metabolism difficulties, and the combination therapy of liraglutide and metformin could optimize patients’ constitution on the whole[10]. A study shows that there is common abnormal fibrinolytic activity in patients with type 2 diabetes, blood hypercoagulable state increases with the aggravation of diabetes, and it is an important factor that leads to high incidence of thrombosis diseases. Thrombomodulin (TM), plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) are all fibrinolytic activity-related parameters. TM is a thrombin-binding activator (t-PA) and plasminogen activator inhibitor (PAI-1) are all fibrinolytic activity-related parameters. TM is a thrombin-binding protein expressed by the endothelial cells, TM levels rise in diseases associated with endothelial cell damage, and it can be used as the marker of endothelial cell injury. t-PA and PAI-1 levels can directly represent the activity of fibrinolytic system, and when t-PA level increases and PAI-1 level is stable, the incidence of thrombosis diseases decreases in patients[11]. The research results showed that serum TM value of observation group after treatment was lower, t-PA value was higher and differences in PAI-1 levels between two groups were not significant, indicating that the fibrinolytic system status was improved, and the probability of vascular endothelial damage and thrombotic diseases reduced. Adipose tissue in type 2 diabetes patients with obesity shows the
characteristic of chronic inflammation, and the chronic inflammation plays a key role in various metabolic abnormalities of diabetes. Toll-like receptor 4/transcription factors-κB (TLR4/NF-κB) is a signaling pathway closely associated with inflammation, a study shows that obesity patients with different levels metabolic disorders can induce TLR4/NF-κB signaling pathway activation in different extent, and the expression of its downstream TLR4 and p-NF-κB p65 molecule will directly affect the patients’ systemic micro-inflammatory state[12]. DAG/PKC signal pathway activation can start the polypol pathway, oxidative stress, etc., participating in the occurrence of inflammation and microvascular lesions, PKC belongs to the family of serine/threonine protein kinase, DAG is the main material to activate PKC, and activated PKC transfers to the cell membrane, changes vascular permeability and regulates gene expression[13]. In the study, western-blot method was used to detect the protein expression levels of TLR4/NF-κB signaling pathway and DAG/PKC signaling pathway downstream molecules, and results showed that TLR4, p-NF-κB p65, DAG and PKC protein expression levels of observation group after treatment were lower, suggesting that the combined application of liraglutide and metformin also had positive significance in improving the micro-inflammatory state in type 2 diabetes patients with obesity.

The disease progress is fast in type 2 diabetes patients with obesity, and joint detection of a variety of illness-related indicators is a good way to judge the severity of disease and the progress of illness. Adiponectin (APN) decrease in patients with type 2 diabetes is independent of other factors, and it has the effect of improving insulin resistance, resisting atherosclerosis formation, and so on. Leptin (LP) is secreted by adipocyte, and can inhibit appetite and increase energy consumption[14]. There is leptin resistance in obese patients, and it is positively correlated with the degree of insulin resistance[15]. Chemerin is a new adipokine that is associated with obesity and metabolic syndrome, chemerin is produced in the early inflammation, and its level reflects the extent of body inflammation. Nesfatin-1 is a newly discovered secretory peptide, and research has found that Nesfatin-1 is closely related to obesity and type 2 diabetes. Retinol binding protein 4 (RBP4) is a new kind of adipose-derived signal, and is involved in insulin resistance and type 2 diabetes. Study has shown that RBP4 is positively correlated with various body fat parameters and the degree of insulin resistance[16]. Both fasting insulin (FINS) and insulin sensitivity index (ISI) are the objective indicators that reflect the degree of insulin resistance, FINS level is higher and the ISI value is lower in patients with type 2 diabetes. The research results showed that serum APN, Nesfatin-1 and ISI values of observation group after treatment were higher while LP, Chemerin, RBP4 and FINS values were lower, suggesting that the combination therapy of liraglutide and metformin could optimize and relieve the illness severity in type 2 diabetes patients with obesity.

To sum up, it is concluded as follows: combined therapy of liraglutide and metformin can significantly improve the constitution of newly diagnosed type 2 diabetic mellitus patients with obesity, optimize the general condition and be expected to improve treatment outcome, and is worth popularization and application in clinical practice in the future.

References