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Effect of Peptide Drug Liraglutide Nano-Formulation Combined with Sodium-Glucose Cotransporter-2 Inhibitor on Blood Lipids in Patients with Type 2 Diabetes

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ABSTRACT

With the aging of our population and the increase in the number of obese people, diabetes has become a common disease. At present, drug treatment is mainly used for diabetes. Dyslipidemia is the main cause of diabetes. The regulation of blood lipids in diabetic patients through drugs is the key to treating diabetes. The purpose of this article is to further explore the specific effect and mechanism of peptide drug liraglutide nano-formulation combined with sodium-glucose co-transporter-2(SGCT-2) inhibitor on blood lipids in patients with type 2 diabetes. This article uses 30 people included in our hospital in 2019 2 patients with type 2 diabetes are divided into the group of peptide drug liraglutide nano preparations, the group of SGCT-2 inhibitors and the peptide drug liraglutide nano preparations combined with SGCT-2. In the inhibitor combination medication group, patients were given drug intervention according to the group name with the consent of the patients. After three days, the serum cholesterol, triglyceride, lipoprotein and lipid metabolism levels of all patients were tested. The results showed that under the intervention of peptide drug liraglutide nanoparticles combined with SGCT-2 inhibitor, the cholesterol level of patients with type 2 diabetes decreased from (368.2 ± 8.3) mmol / L to (1978.4 ± 4.7) mmol/L, triglyceride level decreased from (653.7 ± 12.5) mg/dL to (426.8 ± 9.6) mg/dl, and lipid metabolism level increased by 25.6%. Therefore, it can be seen that the peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor has a certain therapeutic effect on type 2 diabetes.

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Introduction

Diabetes is already a common endocrine and metabolic disease. In the past 10 years, due to the continuous changes in the diet and lifestyle of our residents and the aging of our population, the disease has developed from a rare chronic disease to a common epidemic (1). From the perspective of clinical etiology and pathology, such non-metabolic diabetes diseases can be roughly divided into four types, namely, type 1, type 2, other special disease types and type 2 diabetes in pregnancy. The early clinical pathology and physiology of type 2 acute diabetes are characterized by the body's insulin cell resistance (II), that is, the ability of the body's insulin cell regulation and glucose cell metabolism to be weakened, and the concomitant ability to normally secrete insulin is reduced, which is caused by defective beta-cell function (2).

Diabetes is mainly a chronic endocrine disease and metabolic dysfunctional urinary disease characterized by chronic diseases and hyperglycemic diseases, which are caused by a combination of many different causes. It has the obvious characteristics of the high prevalence of mild patients and a large number of patients (3). Dyslipidemia is mainly a physiological state caused by the abnormal metabolism of a large number of lipoproteins in the body. These abnormalities can generally be considered to be non-quantitative, that is, for example, plasma total density cholesterol (TC) weight gain, low-density lipoprotein binding cholesterol (LDL-C) weight gain, triglyceride (TG) weight gain and plasma high-density lipoprotein-associated cholesterol (HDL-C) weight loss, etc., may or may not be qualitative (4). Polypeptide drugs such as proglumide type II nano peptide inhibitors and sodium phosphate-2 type glucose resonance revolving motor globulin-2 inhibitors have effective hypoglycemic and hypolipidemic effects, improve islet β cell function, prevent or be effective. This article combines these

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two drugs for clinical research (5).

Among them, Sattar made a detailed introduction to the preparation and use of peptide drug liraglutide nano preparations, emphasized the importance of peptide drug liraglutide nano preparations in the medical field, and pointed out related research methods and research directions (6-7). De researched the functional effect of SGCT-2 inhibitors, and conducted experiments to study the clinical effect and safety of SGCT-2 inhibitors, demonstrating that sodium-glucose co-transport protein-2 inhibition has the function of talking about blood sugar and blood lipids (8). In the article, Scheen discussed the harmful types of diabetes, emphasized that diabetes has irreparable damage to patients' eyes, heart, and blood vessels, and introduced several treatment methods that have been proven to be effective (9). Halimi found through research that the peptide drug liraglutide nano preparations and SGCT-2 inhibitors can improve the condition of diabetes, and studied the specific mechanism of action of these two drugs. The feasibility of the combination of multiple drugs provides theoretical support (10).

The purpose of this article is to explore the specific effect and mechanism of peptide drug liraglutide nano-formulation combined with sodium-glucose cotransporter-2 inhibitor on blood lipids in patients with type 2 diabetes. Based on summing up the experience and achievements of the predecessors Some improvements and innovations have two specific points. First, this article uses a meta-analysis method to systematically evaluate peptide drugs combined with liraglutide polysaccharide nanozyme inhibitors and their combined sodium phosphate-sodium and glucose resonance rotation exercise lipoprotein-2 inhibitor complex in type 2 pregnancy. The direct effect of diabetic patients on the clinical treatment of lowering blood lipids. Second, use general rem6.0 software to carry out a quantitative statistical comprehensive analysis of the relevant statistical data results of blood lipids monitoring included in the experimental study, and use the total average difference (md) as the amount of exercise effect. The results were comprehensively tested for heterogeneity, the analysis method with high data sensitivity was used to accurately evaluate the accuracy and stability of the results of the included research experiments, and the funnel-style graphs were used to evaluate the bias of the results publication rate.

Materials and methods

Patient General Information

In this experiment, 30 patients with type 2 diabetes included in our hospital from January 2019 to December 2019 were selected, including 24 males and 6 females. The patients were divided into three groups, the peptide drug liraglutide nano preparation drug group, the SGCT-2 inhibitor drug group and the peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor. In the combined medication group, patients were given drug intervention according to the group name. General patient information is shown in Table 1.

Table 1. Patient General Information

Gender	Age	Screening time	Level
Man	48	2018/1/19	Type 2 diabetes
Man	56	2016/11/09	Type 2 diabetes
Female	57	2016/12/14	Type 2 diabetes
Man	49	2015/8/1	T1bNOMO
Man	68	2015/8/4	T1aNOMO
Man	76	2017/9/14	Type 2 diabetes
Man	66	2016/3/6	T1bNOMO
Man	59	2017/5/9	T1bNOMO
Man	70	2018/1/28	T1aNOMO
Man	72	2017/05/15	T2
Man	52	2018/2/20	T1aNOMO
Man	63	2016/11/09	Type 2 diabetes
Female	57	2015/12/03	T1aNOMO
Man	71	2016/8/7	T1bNOMO
Man	58	2018/9/14	T1aNOMO
Man	74	2018/1/15	Type 2 diabetes
Female	71	2018/3/3	Type 2 diabetes
Man	65	2018/9/14	Type 2 diabetes
Man	74	2018/9/15	T1aNOMO
Man	61	2018/09/15	T1a
Female	68	2017/10/01	T1b
Man	62	2019/12/10	T1bNOMO
Man	72	2017/8/24	Type 2 diabetes
Man	63	2015/5/5	T1aNOMO
Female	70	2016/10/25	T1bNOMO
Man	66	2017/1/19	T1bNOMO
Female	59	2018/8/3	Type 2 diabetes
Man	63	2019/4/20	T1aNOMO
Man	78	2018/7/26	T1aNOMO

Inclusion and Exclusion Criteria and Observation Indicators

Inclusion of diagnostic criteria: First, all types of patients can be diagnosed according to the World Health Organization's definitive diagnosis method.

This standard clearly diagnoses the disease because of type 2 acute diabetes for more than 5 months, simply through appropriate dietary control or continuous use of various oral biological hypoglycemic agents. The drug was continuously treated for more than 6 weeks (11). Second, the age is 18-80 years old. Third, the current condition of all patients is basically stable, and the weight of patients has been stable in the past 4 months, and they usually take other oral hypoglycemic and antihypertensive drugs regularly for treatment (12). Fourth, patients in all cases were not fully treated with active insulin injections, and glucoamylase and hemoglobin (hba1c) were above 8.6% (13).

Exclusion criteria: type 1 acute diabetes, pregnancy type B diabetes or other special diseases of acute diabetes (14). Within the second half of the first four months of the trial, he had not received a glp-1 analog polysaccharide injection or other hypolipidemic and hypoglycemic drugs and peptide inhibitors such as liraglutide polysaccharide nanozyme inhibitor and sodium phosphate type-2 glucose resonance. Rotating exercise lipoprotein-2 inhibits drug allergies (15). Patients with a history of acute gastrostomy planectomy or severe other gastrointestinal dysfunction, such as acute peptic gastrointestinal ulcer, chronic gastritis and diarrhea. Combined with acute advanced complications of type 2 diabetes, chronic liver and kidney pancreatic insufficiency, thyroid disease, chronic blood consumption disorders, malignant tumors, cardiovascular and cerebrovascular system diseases, severe patients with chronic thyroid pancreatitis, and severe patients with mental immune diseases 1. infectious immune diseases (16). Pregnant women who are pregnant, breastfeeding, within 4 months or plan to receive pregnancy.

Observation of blood glucose indexes and measurement criteria for determination of results. Perform regular statistical analysis and comparison of blood glucose monitoring index data of each patient's abdomen before and after treatment, fasting blood glucose at 2 hours after meal, fasting blood glucose after 2 hours of meal, blood glycose and hemoglobin (17). After treatment, a comprehensive statistical analysis of the pre-prandial blood glucose monitoring compliance data of the two groups of patients was performed. The statistical standards for compliance: the fasting hour blood glucose attainment ≤8.0 mmol/l after meals and the blood glucose <15 mmol/l at 1 h after meals, glycosylation enzyme and hemoglobin concentration <10%; comprehensive statistical analysis and comparison of various blood lipid monitoring index data of total density cholesterol, triglycerides, low-density lipoprotein total cholesterol and postprandial high-density lipoprotein total cholesterol of the two groups of patients before and after blood glucose treatment (18).

Diabetic Drug Intervention Methods

Peptide drug liraglutide nanoformulation medication group. Peptide drug liraglutide nano formulation medication group type 2 diabetes patients were randomly enrolled and took the peptide drug liraglutide nano formulation (19). The dosage of the peptide drug liraglutide nano preparation is 20ml per day during the open treatment period, and it is taken before breakfast every day. The peptide drug liraglutide nano-preparation 50mg twice a day for the first week.

SGCT-2 inhibitor medication group. The SGCT-2 inhibitor dosage is 50ml per day during the 24w open treatment period, and it is taken before breakfast every day (20). SGCT-2 inhibitor 50ml in the first week, once a day. 60ml 1 time/day in the second week. 90ml 1 time/day in the third week. Take the SGCT-2 inhibitor 120mg once a day for the fourth week, and perform a dose titration based on 4.9mmol/L <fingertip fasting blood glucose <7.1mmol/L until the maximum tolerated dose of sodium-glucose is reached. In the SGCT-2 inhibitor medication group, if after using the maximum dose of SGCT-2 inhibitor, the fingertip fasting blood lipid still cannot reach the target value of the fingertip fasting blood lipid, then keep the maximum. The dosage of SGCT-2 inhibitor was changed to (150 ml once a day) until the end of the study (21).

Peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor combination drug group. Peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor combination drug group randomized type 2 diabetes patients. After enrollment, the dosage of peptide drug liraglutide nano-formulation combined with SGCT-2 inhibitor was 50ml per day during the 36w open treatment period (22). The dosage of peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor was

500ml in the first week, twice a day. 600ml in the second week, 3 times/day. 1000mg 2 times/day in the third week. From week 5 to 24, the dosage of peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor was 1200ml, 2 times/day.

Method for Detecting Relevant Indexes of Type 2 Diabetes Patients

The body weight and food intake of all patients with type 2 diabetes were measured every week, and the effects of the peptide drug tripeptide nano preparation and sodium-glucose co-transporter 2 inhibitor on body weight and food were observed (23). Then, patients in the standard room breathe at 450nm wavelength to measure the luminosity (OD value) of apolipoprotein, the calculated multi-metabolism is given by the leopard nano preparation team, sodium glucometer transporter-2 team and the drug inhibitor polydrug. The concentration of serum gene samples in serum samples of sodium-glucose meter transporter-2 inhibitor co-administration group. Serum total cholesterol was measured by glucosidase method, other methods, sodium-glucose meter transporter-2 group and drug inhibitor multidrug sodium-glucose meter transporter-2 inhibitor combined drug group 3 patients used nano preparation, 3 patients collect from 10 am to 3 pm on the first day after enrollment (24). Serum total cholesterol and serum sweet oil were measured. A multi-drug is a tripeptide nanocomposite sodium-glucose meter transporter-2 pull-out inhibitor after 1 month of treatment. Whole blood total cholesterol (TC), triglyceride (TG), high-density low-density lipoprotein cholesterol (LDL-c), low-density lipoprotein cholesterol (LDL), high-density low-density lipoprotein cholesterol re-hdl2 and cheese production. Peg immunoassay apolipoprotein AI diffusion method (AP), apolipoprotein (APO), apolipoprotein b1, apolipoprotein cii, apolipoprotein CII, glucosidase method (25). Fasting blood glucose was measured, and the microcolumn method was used to measure glycated hemoglobin A1c. We measured these lipids, apolipoproteins, blood glucose and GHbA1c in the laboratory. The apolipoprotein test kit is provided by the biochemical education laboratory of our hospital. Data processing was performed using social science statistical software (spsver6) for t-test, and the result was expressed as x±s.

Results and discussion

Analysis of Blood Index Test Results of Type 2 Diabetes Patients after Combined Medication Intervention

The research analysis results show that compared with the two types of cases of peptide antibody-drug combined with liraglutide drug nano crystallization inhibitor drug combination group and sodium-glucosamine co-transport drug protein-2 inhibitor drug reagent drug combination group. Monopeptide antibody-drug combined with liraglutide drug nano-inhibitor drug combination group and sodium-glucosamine co-transport drug protein-2 inhibitor drug combination transport drug in the same group of patients with advanced type 2 acute diabetes have an average annual overall weight. The performance is not slightly reduced. Peptide inhibitory drug combined with liraglutide drug nano peptide inhibitor drug combined with sodium phosphate-sodium and glucose copolymer transport hemoglobin-2 inhibitor drug combined with clinical medication, there was no significant difference between the two groups of patients with fasting daily blood glucose after meals, fasting blood glucose 2 hours after meals and hemoglobin blood glucose levels of anti-glycation drugs. The results of the research analysis show that patients with two combinations of peptide nanomedicine combined with liraglutide and nano biological preparation combined sodium-hydroxy glucose co-transportation hemoglobin-2 inhibitor test combination treatment drug daily fasting blood sugar and meals. After 3h, the average level of glycated blood glucose and post-prandial glycated combined hemoglobin were (78.27±5.33) mmol/l, sodium-hydroxy glucose co-transportation combined hemoglobin-2 inhibitor drug combination, and other peptide nano-drugs combined with lira. The comparison of the average level of fasting blood glucose-lowering, glycated blood glucose 2h after the meal, and glycated combined hemoglobin after the meal in the two groups of combined cases of lutein combined with nano biologics were (107.73±6.48) mmol/L and (129.37±7.05) mmol/ L, detailed data are shown in Table 2.

The results of the study showed that the peptide drug liraglutide nano preparations drug group, the SGCT-2 inhibitor drug group and the peptide drug

liraglutide nano preparations combined with SGCT-2 inhibitor combination drug group. After treatment of FPG, 2hPG, the amount of HbA1c, DBP and total insulin increased significantly. Compared with before treatment, the FPG, 2hPG and HbA1c of each group were decreased, and the amount of insulin in the peptide drug liraglutide nano preparation group and the sodium-glucose cotransporter-2 inhibitor group was significantly lower than that of the peptide drug liraglutide nano. The preparation was combined with SGCT-2 inhibitor combination medication group. One month after taking the peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor, the patient's apolipoprotein began to decrease. Taking the peptide drug liraglutide nano preparation combined with SGCT-2. After 2 months of the inhibitor, the patient's apolipoprotein dropped to its lowest value. The study revealed that the peptide drug liraglutide nano-formulation combined with SGCT-2 inhibitor combination therapy can effectively reduce the lipoprotein content and increase insulin levels in patients. The specific data is shown in Figure 1.

Table 2. Changes in blood glucose and index of patients after meals

Group	Blood sugar level	Weight change	Hemoglobin level
Liraglutide group	65±2.187	178±8.235	138.5×10^5
Sodium-glucose	76±3.25	186±6.185	134.8×10^5
Combination medicine group	85±2.56	240±9.221	173.6×10^5

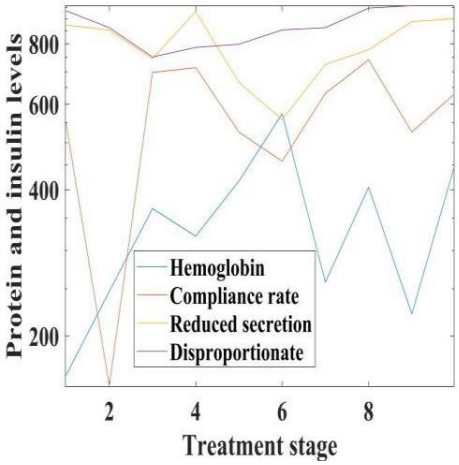

Figure 1. The effect of peptide drug liraglutide nanoparticles combined with sodium-glucose cotransporter-2 inhibitor on lipoprotein content and insulin level in patients with type 2 diabetes mellitus

It can be seen from Figure 1 that the peptide drug liraglutide nano preparation combined with SGCT-2 inhibitor combination therapy can effectively reduce the lipoprotein content and increase the insulin level in patients, insulin levels increased by 34.8%.

The peptide drug liraglutide nano preparation combined with the SGCT-2 inhibitor compared with the peptide drug liraglutide nano-formulation and the SGCT-2 inhibitor medication group. The serum and total cholesterol normal water of the patients in the combination group were significantly reduced, and the normal serum and total cholesterol levels of the three groups were reduced ($p<0.05$). Polypeptide liraglutide nano formulation medication group, SGCT-2 inhibitor medication group and peptide drug liraglutide nano formulation combined sodium-glucose cotransporter-2 inhibitor combination medication group 3 groups of patient's glycerin. The triglyceride concentration was reduced, and the triglyceride concentration in the combination group was the most significant, with a difference ($p<0.01$). The results of the study showed that the peptide drug liraglutide nano-formulation combined with SGCT-2 inhibitor combination therapy can reduce the serum cholesterol and triglyceride expression levels in patients. The relevant data is shown in Figure 2.

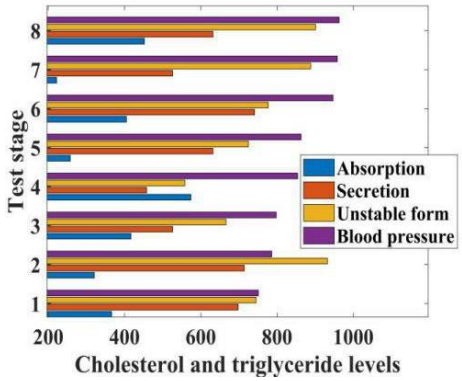

Figure 2. Effects of peptide drug liraglutide nanoparticles combined with sodium-glucose cotransporter-2 inhibitor on serum cholesterol and triglyceride expression in patients with type 2 diabetes mellitus

From the data in Figure 2, it can be seen that the cholesterol level of patients with type 2 diabetes decreased from (368.2±8.3) mmol/l to (1978.4±4.7) under the intervention of the peptide drug liraglutide nano preparation combined with sodium-glucose cotransporter-2 inhibitor. mmol/l, the triglyceride

level decreased from (653.7±12.5) mg/dl to (426.8±9.6) mg/dl.

Discussion on Peptide Drug Liraglutide Nano Preparation Combined with SGCT-2 Inhibitor in the Treatment of Diabetes

The cause of type 2 diabetes is related to diabetes complicated by lipid metabolism disorders. Among them, the increase in cholesterol level, triglyceride, and hemoglobin level is the most important. Therefore, when lipid metabolism is well controlled, the condition of diabetes can be improved very well. Insulin pumping can also effectively help control blood sugar and lower blood lipids. Not only can effectively reduce pancreatic blood glucose, but also can effectively control the rise. High body weight inhibits the apoptosis of islet β-glucoside nuclei. Sodium-hydrogen glucose resonance rotation movement trypsin-2 inhibitor is a new dpp-4 inhibitor comprehensive agent, which can prolong the duration of gulp inhibition, and then effectively delay the emptying of the large intestine and promote the secretion of large amounts of insulin in the stomach. The peptide drug liraglutide nano-formulation combined with SGCT-2 inhibition may be the most effective means for the treatment of patients with type 2 diabetes. The results show that the peptide drug liraglutide nano-formulation combined with SGCT-2 inhibition can effectively promote lipid metabolism in patients with type 2 diabetes. The relevant data is shown in Figure 3.

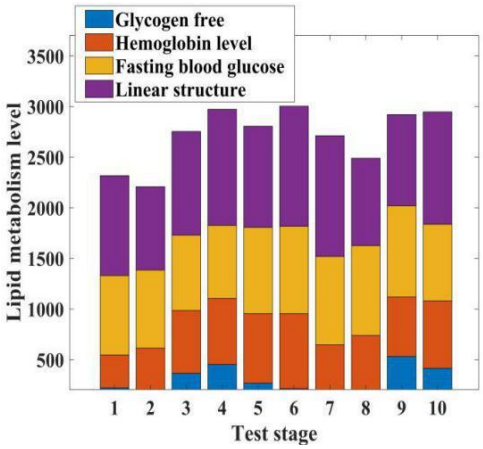

Figure 3. Effect of peptide drug liraglutide nanoparticles combined with sodium-glucose cotransporter-2 inhibitor on lipid metabolism in patients with type 2 diabetes mellitus

As can be seen from Figure 3, the peptide drug liraglutide nano-formulation combined with SGCT-2 inhibition can effectively promote lipid metabolism in patients with type 2 diabetes and increase the level of lipid metabolism in patients with type 2 diabetes by 25.6%.

In the treatment of type 2 diabetes, oral hypoglycemic drugs are the main treatment method, which can effectively and steadily control the blood sugar level of the patients, so that the blood sugar levels of the patients can be stabilized for a long time. The peptide drug liraglutide nano preparation and SGCT-2 inhibitor are two commonly used hypoglycemic drugs, which inhibit glucosidase to prevent the conversion of polysaccharides and sucrose into glucose, which slows the body's absorption of sugar to reach the purpose of reducing blood glucose and lipid levels. The peptide drug liraglutide nano preparation combined with sodium-glucose cotransporter-2 inhibition can bind to dipeptidyl peptidase-IV. The concentration of GLP-1 in the body promotes the increase of insulin secretion. In addition, the peptide drug liraglutide nano preparation combined with SGCT-2 inhibition can also regulate islet alpha cells and inhibit glucagon secretion. There are fewer adverse reactions such as discomfort, and the treatment is more efficient. The specific data is shown in Figure 4.

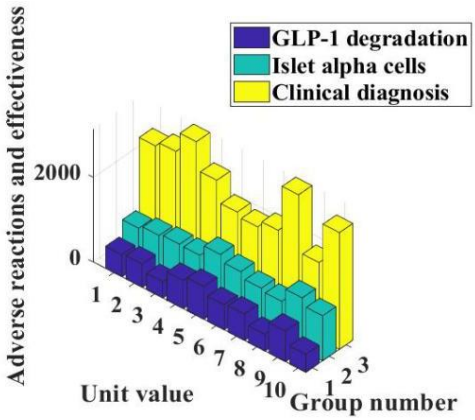

Figure 4. Application of peptide drug liraglutide nanoparticles combined with sodium-glucose cotransporter-2 inhibitors in the treatment of type 2 diabetes mellitus

It can be seen from Figure 4 that the peptide drug liraglutide nano preparation combined with SGCT-2 inhibition is used in the treatment of type 2 diabetes, and there are fewer adverse reactions such as

discomfort, and the treatment efficiency is higher and the treatment efficiency. As high as 96.3%, the adverse reaction rate was only 2.27%.

Conclusions

In the past, drugs were mainly used to treat diabetes. Dyslipidemia was the main cause of diabetes, and the regulation of blood lipids in patients with diabetes was the key to the treatment of diabetes. The purpose of this study is mainly to in-depth study and exploration of liraglutide combined with nano-inhibitors in peptide ester drugs through the combination of sodium phosphate-sodium and glucose co-transport lipoprotein-2 inhibitor drug reagents for type 2 chronic diabetes In the early patients, the specific effect of lowering blood lipids, the researchers found that liraglutide combined with nano-inhibitors in peptide ester drugs combined with sodium phosphate-sodium and glucose co-transport lipoprotein-2 inhibitors for combined clinical use. Not only can it effectively reduce the content of lipoproteins in patients with early type 2 chronic diabetes and to increase the level of insulin in the body at the same time, it can reduce the expression of serum cholesterol and triglycerides in patients with type 2 diabetes, and can effectively promote the metabolism of fat in patients with type 2 diabetes. And, there are fewer adverse reactions such as discomfort, and the treatment efficiency is higher, which is the first choice for the treatment of type 2 diabetes.

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Not applicable.

Interest conflict

The authors declare that they have no conflict of interest.

References

1. Presas E, Tovar S, Cuarro J, et al. Pre-Clinical Evaluation of a Modified Cyclodextrin-Based Nanoparticle for Intestinal Delivery of Liraglutide. J Pharm Sci 2021; 110(1):292-300.
2. Van R, Petter B. Role of sodium-glucose cotransporter 2 inhibition to mitigate diabetic kidney disease risk in type 1 diabetes. Nephrol Dialysis Transplanta 2020; (Supplement_1): i24-i32.
3. Alicic RZ, Neumiller JJ, Johnson EJ, et al. Sodium–Glucose Cotransporter 2 Inhibition and Diabetic Kidney Disease. Diabetes, 2019; 68(2):248-257.
4. Mahling M, Schork A, Nadalin S, et al. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibition in Kidney Transplant Recipients with Diabetes Mellitus. Kidney Blood Press Res 2019; 44(5):1-9.
5. Burns K, Cherney D. Renal Angiotensinogen and Sodium-Glucose Cotransporter-2 Inhibition: Insights from Experimental Diabetic Kidney Disease. Am J Nephrol 2019; 49(4):328-330.
6. Yuliya, Lytvyn, Petter, et al. Response by Lytvyn et al to Letter Regarding Article, "Sodium Glucose Cotransporter-2 Inhibition in Heart Failure: Potential Mechanisms, Clinical Applications, and Summary of Clinical Trials". Circulation: Offic J Am Heart Assoc 2018; 137(18):1984-1985.
7. Haedersdal S, Lund A B, Maagensen H, et al. Individual and Combined Glucose-Lowering Effects of Glucagon Receptor Antagonism and Sodium-Glucose Cotransporter 2 Inhibition. Diabetes, 2018; 67(Supplement 1):1942-P.
8. Pancholia AK. Sodium-glucose cotransporter-2 inhibition for the reduction of cardiovascular events in high-risk patients with diabetes mellitus. India Heart J 2018; 70(6):915-921.
9. Raalte DHV, Cherney DZI. Sodium glucose cotransporter 2 inhibition and renal ischemia: implications for future clinical trials. Kidney Int 2018; 94(3):459-462.
10. Shoji, Takakura, Toshiyuki, et al. Acute and Direct Effects of Sodium–Glucose Cotransporter 2 Inhibition on Glomerular Filtration Rate in Spontaneously Diabetic Torii Fatty Rats. Biol Pharm Bull 2019; 42(10):1707-1712.
11. Bommel E, Lytvyn Y, Perkins B A, et al. Renal hemodynamic effects of sodium-glucose cotransporter 2 inhibitors inhyperfiltering people with type 1 diabetes andpeople with type 2 diabetes and normal kidney function. Kidney Int 2020; 97(4):631-635.
12. Liu Z, Ma X, Ilyas I, et al. Impact of sodium glucose cotransporter 2 (SGLT2) inhibitors on atherosclerosis: From pharmacology to pre-clinical and clinical therapeutics. Theranostics 2021; 11(9):4502-4515.
13. Basu D, Huggins L A, Scerbo D, et al. Mechanism of Increased LDL (Low-Density Lipoprotein) and Decreased Triglycerides with SGLT2 (Sodium-Glucose Cotransporter 2) Inhibition. Arterioscler Thromb Vasc Biol 2018; 38(9):2207-2216.
14. Kerridge R, Whyte I, Prior F, et al. The Good, the Bad, and the Ugly: Sodium–Glucose Cotransporter-2 Inhibitors (Gliflozins) and Perioperative Diabetes. Anaesth Intensive Care 2018; 46(2):155-158.
15. Berg D D, Wiviott S D, Scirica B M, et al. Heart Failure Risk Stratification and Efficacy of Sodium-Glucose Cotransporter-2 Inhibitors in Patients with Type 2 Diabetes Mellitus. Circ 2019; 140(19):1569-1577.
16. Hidenori K, Takeharu K, Akira K, et al. Phloridzin inhibits high K+-induced contraction via the inhibition of sodium: glucose cotransporter 1 in rat ileum. J Vet Med Sci 2017;79(3):593-601.
17. Yoshiharu T, Yuko M, Kenju S, et al. Non-alcoholic

Fatty Liver Disease Is a Risk Factor for Type 2 Diabetes in Middle-aged Japanese Men and Women. Intern Med 2017; 56(7):763-771.

18. Emdin C A, Khera A V, Natarajan P, et al. Genetic Association of Waist-to-Hip Ratio with Cardiometabolic Traits, Type 2 Diabetes, and Coronary Heart Disease. JAMA 2017; 317(6):626-634.
19. Murphy H, RuthBell, CherCartwright, et al. Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nationwide study. Diabetologia 2017; 60(9):1668–1677.
20. Rawshani A, S Franzén, Eliasson B, et al. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes. Der Diabetologe 2017; 376(15):1-2.
21. Wysham C, Bhargava A, Chaykin L, et al. Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients with Type 2 Diabetes: The SWITCH 2 Randomized Clinical Trial. JAMA 2017; 318(1):45-56.
22. Bjornstad P, Cherney D, Lawson J, Møntegaard C, Pruijm M, Tuttle K, Vrhnjak B, Kretzler M. MO399: Remodel: A Mechanistic Trial Evaluating the Effects of Semaglutide on the Kidneys In People With Type 2 Diabetes and Chronic Kidney Disease. Nephrol Dial Transplant 2022 May; 37(Supplement_3): gfac070-013.
23. Chelliah R, Wei S, Daliri EB, Elahi F, Yeon SJ, Tyagi A, Liu S, Madar IH, Sultan G, Oh DH. The role of bioactive peptides in diabetes and obesity. Foods. 2021;10(9):2220.
24. Nikolaou PE, Efentakis P, Abu Qourah F, Femminò S, Makridakis M, Kanaki Z, Varela A, Tsoumani M, Davos CH, Dimitriou CA, Tasouli A. Chronic empagliflozin treatment reduces myocardial infarct size in nondiabetic mice through STAT-3-mediated protection on microvascular endothelial cells and reduction of oxidative stress. Antioxidants Redox Signal 2021;34(7):551-71.
25. Gannimani R. Synthesis, characterization and evaluation of antibacterial, antidiabetic and toxicological profiles of newly-derived therapeutic agents (Doctoral dissertation).