Research Paper

Evaluation of the Efficacies of Liraglutide and Glargine in Type 2 Diabetes Patients with Malignant Tumors Treated with Glucocorticoids

D. L. PU, J. JIANG[1], C. SONG[2], J. Z. XI[3] AND Q. WU[3]*

Endocrinology Department, The People's Hospital of Yubei District of Chongqing City, Chongqing 401120, [1]Department of Endocrinology and Nephrology, Chongqing University Cancer Hospital, School of Medicine, Chongqing University, Shapingba, Chongqing 400044, [2]Endocrinology Department, Children's Hospital of Chongqing Medical University, Yuzhong, Chongqing 400015, [3]Endocrinology Department, Dazu Hospital of Chongqing Medical University, The People's Hospital of Dazu, Chongqing 402360, China

To explore the efficacies of liraglutide and glargine in type 2 diabetes patients with malignant tumors treated with glucocorticoids. Overall, 120 patients were recruited, 60 patients were divided into the glargine group (chemotherapy with glucocorticoids and hypoglycemic therapy including glargine) and 60 patients were divided into the liraglutide group (chemotherapy with glucocorticoids and hypoglycemic therapy including liraglutide). Fasting plasma glucose, 2 h postprandial plasma glucose, glycosylated hemoglobin, body mass index, systolic blood pressure, diastolic blood pressure, C peptide, insulin resistance index, insulin secretion index, total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, Karnofsky performance status score, rehospitalization rate, average hospitalization days and adverse reactions before and after intervention were compared between the two groups. After treatment, total cholesterol, high-density lipoprotein, C peptide, systolic blood pressure, diastolic blood pressure and homeostatic model assessment of insulin resistance were not significantly different between the groups. The body mass index, fasting plasma glucose, 2 h postprandial plasma glucose, glycosylated hemoglobin test (A1c) and homeostasis model assessment of beta cell function were significantly lower in the glargine group than the liraglutide group ($p<0.05$). The hypoglycemia rate was lower in the liraglutide group than the glargine group ($p<0.05$). The Karnofsky performance status score was increased ($p<0.05$) and the rehospitalization rate and average hospitalization days ($p<0.05$) were decreased in the liraglutide group. Pearson and linear regression analyses indicated that liraglutide treatment was associated with better glucose control, a better homeostasis model assessment of beta cell function, hypoglycemia rate and Karnofsky performance status score and reduced rehospitalization rate and average hospitalization days. Liraglutide treatment significantly improved glucose control, homeostasis model assessment of beta cell function and the hypoglycemia rate and Karnofsky performance status score and reduced the rehospitalization rate and average hospitalization days of type 2 diabetes patients with malignant tumors treated with glucocorticoids.

Key words: Malignant tumor, liraglutide, glargine, glucocorticoid, type 2 diabetes mellitus

Type 2 diabetes is closely related to malignant tumors. While China becoming the country with the most cases of type 2 diabetes and malignant tumors, how to better manage blood glucose and improve the quality of life and prognosis of patients with type 2 diabetes with malignant tumors needs to be further explored[1]. In the past, the traditional hypoglycemic therapy for diabetic patients with malignant tumors was insulin, such as glargine[2], but there were challenges with insulin treatment in patients with type 2 diabetes mellitus combined with malignant tumors requiring glucocorticoid treatment, such as poor glucose control, weight gain, multiple hypoglycemic events and reduced quality of life[3]. With the wide application of various kinds of hypoglycemic drugs, such as Glucagon-Like Peptide-1 (GLP-1), in type 2 diabetes patients, liraglutide has been suggested to be effective in the treatment of type 2 diabetes patients with malignant tumors with glucocorticoid treatment[4]. However, there is a lack of comparative studies of glargine for blood glucose control in type 2 diabetes patients with malignant tumors. Therefore, the aim of this study

***Address for correspondence**
E-mail: wqn11@126.com

was to evaluate the clinical efficacies of glargine and liraglutide during glucocorticoid treatment in type 2 diabetes patients with malignant tumors.

MATERIALS AND METHODS

Subjects:

The protocol was approved by the Chongqing University Cancer Hospital, School of Medicine, Chongqing University Institutional Review Board, conformed to the standards of the Declaration of Helsinki and is registered with Chinese Clinical Trial Registry (ChiCTR2100049169). 120 patients who were diagnosed with type 2 diabetes with malignant tumors at our hospital from January 2019 to December 2020 were randomly divided into the glargine group and the liraglutide group.

Inclusion criteria:

Diagnosis of type 2 diabetes mellitus was made according to World Health Organization (WHO) or American Diabetes Association (ADA) criteria. Patients should receive glucocorticoids and chemotherapy periodically; patients should receive metformin (daily dose of 1000-2000 mg) for at least 4 w before recruitment; glycosylated hemoglobin test (A1c) (HbA1c)>7.0 %; males and females aged 18-79 y; Body Mass Index (BMI)≤45 kg/m^2; all patients participated voluntarily and signed informed consent.

Exclusion criteria:

Type 1 diabetes mellitus; severe diabetic acute and chronic complications; previous use of Dipeptidyl Peptidase-4 (DPP-4) inhibitors or GLP-1 analogs; hemoglobin history; severe hepatic and renal insufficiency; allergy to GLP-1, metformin or insulin or contraindications for use; pregnant women, lactating women and women who improperly used contraception; medullary thyroid carcinoma; patients with obvious infection; patients who had mental or neurological diseases and were unable to cooperate or unwilling to cooperate.

All the patients received chemotherapy according to their disease and glucocorticoids. In the glargine group, the blood glucose levels were managed using conventional blood glucose management and patients received glargine treatment once a day, and the patients in the liraglutide group received liraglutide treatment once a day. During the study, no patients were lost to follow-up. Blood glucose detection was performed as follows: Venous blood was collected at specific times using the glucose oxidase method. The blood glucose meter and testing paper were provided by Roche Diagnostic Products (Shanghai) Co., Ltd.

Treatment methods:

All patients were instructed to control their diet, adjust their lifestyle and make appropriate exercise plans. The patients in the liraglutide group received liraglutide treatment (trade name Novolin, China Pharmaceutical Co., Ltd., National Medicine Standard j20160037) as a subcutaneous injection once a day. The initial dose was 0.6 μg/d which can be adjusted according to the specific situation of patients and the maximum dose didn't exceed 1.8 μg/d. The patients in the glargine group received glargine treatment (trade name Lai DeShi, Sanofi Beijing Pharmaceutical Co., Ltd., Guoyao Zhunzi j20090113) as a subcutaneous injection once a day. The initial dose was 8 U/d, the dose was adjusted according to the patient's specific condition and the maximum dose did not exceed 40 U/d. The control target Fasting Plasma Glucose (FPG) level was less than or equal to 7.0 mmol/l, those of the Postprandial Plasma Glucose (PPG) and bedtime blood glucose level were less than or equal to 10.0 mmol/l and that of HbA1c was less than or equal to 7 % in both groups; the treatments continued for 6 mo.

Data collection and outcome measures:

We collected data including FPG, PPG, HbA1c, BMI, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), fasting C peptide, insulin resistance index-Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), insulin secretion index-Homeostasis Model Assessment of beta (β) Cell Function (HOMA-β), Total Cholesterol (TC), Triglyceride (TG), Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), creatinine, uric acid levels, Karnofsky Performance Status (KPS) score and adverse reactions (gastrointestinal reactions and hypoglycemia). All these data were recorded as a baseline. Follow-up took place during outpatient visits 6 mo after hospitalization. During follow-up, all the above data and the rehospitalization rate and average hospitalization days were compared between the two groups. HOMA-IR=1.5+FPG×fasting C peptide/2800; HOMA-β=0.27×fasting C peptide/(FPG-3.5). Readmission to the hospital for hyperglycemia was classified as "rehospitalization".

Statistical analyses:

The statistical software Statistical Package for the Social Sciences (SPSS) 19.0 was employed to perform statistical analyses. $p<0.05$ indicated statistical significance. The data are shown as the mean±standard deviation (x±s). Prior to the statistical analysis, the data were subjected to normal distribution analysis using

Kolmogorov-Smirnov's test. The differences between groups were tested using a t test. Relationships among each parameter were analyzed by simple correlation analyses. The correlation of variables was determined by Pearson's correlation and linear regression was used to correct the effects of the covariates and test independent factors.

RESULTS AND DISCUSSION

Baseline characteristics of the patients were discussed below. There were no significant differences in the general information, age, sex, weight, BMI, FPG, PPG, HbA1c, SBP, DBP, fasting C peptide, HOMA-IR, HOMA-β, TC, TG, LDL, HDL, creatinine, uric acid level, KPS score or treatment regimen between the two groups ($p>0.05$) (Table 1). There were no significant differences between the two groups in terms of the effects of drugs such as glucocorticoids, paclitaxel, cisplatin and Programmed Cell Death Protein 1 (PD-1)/ Programmed Death-Ligand 1 (PD-L1) targeted agents on blood glucose.

Each parameter was compared after treatment. There was no significant difference in baseline between the two groups. After treatment, there were no significant differences between the two groups in TC, HDL, C peptide, SBP, DBP, or HOMA-IR. BMI, FPG, PPG, HbA1c and HOMA-β levels were significantly lower in the glargine group than those in the liraglutide group ($p<0.05$). The hypoglycemia rate in the liraglutide group was lower than that in the glargine group ($p<0.05$). Compared with the glargine group, the liraglutide group had an increased KPS score ($p<0.05$) and their hospitalization rate and average hospitalization days were decreased in the liraglutide group ($p<0.05$) (Table 2).

Analysis of the correlations among each parameter and regression analysis is shown here. Pearson correlation analysis suggested that BMI was significantly positively correlated with FPG, PPG, TG and average hospitalization days and negatively correlated with HOMA-β and KPS score ($p<0.05$). HbA1c was significantly positively correlated with FPG, PPG and average hospitalization days and negatively correlated with KPS score ($p<0.05$). The KPS score was significantly positively correlated with HOMA-β and negatively correlated with BMI, FPG, PPG, LDL, rehospitalization rate and average hospitalization days ($p<0.05$). The rehospitalization rate was significantly positively correlated with average hospitalization days and negatively correlated with KPS score ($p<0.05$). The average hospitalization days were significantly positively correlated with BMI, FPG, PPG, HbA1c and rehospitalization rate, and negatively correlated with KPS score ($p<0.05$) (Table 3).

TABLE 1: BASELINE CHARACTERISTICS OF PATIENTS IN EACH GROUP (x±s)

Parameter	Glargine	Liraglutide	p value
Age (years)	59.27±8.15	59.25±9.59	0.99
Male/female	40/20	43/17	0.855
Duration (years)	4.45±2.35	4.47±2.44	0.958
BMI	24.52±2.65	24.93±1.54	0.303
FPG (mmol/l)	9.05±1.45	9.12±1.70	0.817
PPG (mmol/l)	16.17±4.58	16.20±3.95	0.962
C peptide	1.56±0.46	1.55±0.63	0.972
HbA1c (%)	9.03±1.95	8.99±1.03	0.891
LDL (mmol/l)	2.41± 0.71	2.53±1.06	0.455
HDL (mmol/l)	1.91±0.83	1.89±0.49	0.854
TC (mmol/l)	3.42±1.63	3.46±2.34	0.905
TG (mmol/l)	4.63±1.61	4.67±1.89	0.896
Creatinine (mmol/l)	73.47±9.83	73.42±10.28	0.981
Uric acid (μmol/l)	307.85±52.42	310.76±60.55	0.778
Diabetic retinopathy	10.17 %	12.90 %	0.642
Diabetic peripheral neuropathy	30.51 %	30.65 %	0.987
Diabetic kidney disease	18.64 %	22.58 %	0.597
Coronary heart disease	8.47 %	9.68 %	0.82

Peripheral Artery Disease (PAD)	25.42 %	27.42 %	0.806
Metformin	100 %	100 %	1
Insulin secretagogues	8.06 %	6.78 %	0.79
Acarbose	9.68 %	6.78 %	0.567
Angiotensin-Converting Enzyme Inhibitors (ACEI)/ Angiotensin Receptor Blocker (ARB)	16.13 %	13.56 %	0.694
Calcium Channel Blockers (CCB)	12.90 %	10.17 %	0.642
Diuretic	6.45 %	3.39 %	0.442
SBP (mm Hg)	130.27±13.00	130.46±13.44	0.939
DBP (mm Hg)	79.10±15.17	80.46±11.56	0.581
HOMA-IR	1.51±0.00	1.51±0.00	0.88
HOMA-β	0.08±0.03	0.08±0.04	0.98
KPS score	78.15±7.57	77.90±7.39	0.856

TABLE 2: CHANGES IN PARAMETERS AFTER EACH TREATMENT (x±s)

Parameter	Glargine	Liraglutide	p value
BMI	24.83±2.38	23.01±2.63	0.000
FPG (mmol/l)	9.05±1.45	7.87±1.71	0.000
PPG (mmol/l)	15.90±4.37	7.65±1.42	0.000
C peptide	1.50±0.44	1.95±2.47	0.154
HbA1c (%)	8.43±1.63	7.86±0.61	0.014
LDL (mmol/l)	2.18±1.29	1.76±0.64	0.028
HDL (mmol/l)	1.74±0.74	1.98±0.75	0.073
TC (mmol/l)	2.74±1.22	2.39±1.15	0.11
TG (mmol/l)	3.79±1.28	3.11±1.15	0.003
Creatinine (mmol/l)	72.06±9.34	73.39±8.68	0.421
Uric acid (μmol/l)	306.92±55.86	302.03±64.47	0.656
Metformin	100 %	100 %	1
Insulin secretagogues	24.19 %	8.47 %	0.02
Acarbose	27.42 %	15.25 %	0.105
SBP (mm Hg)	127.76±11.78	128.31±16.64	0.834
DBP (mm Hg)	79.44±14.47	79.66±9.45	0.92
HOMA-IR	1.50±0.00	1.51±0.01	0.326
HOMA-β	0.08±0.03	0.14±0.14	0.005
KPS score	35.50±14.11	41.52±13.87	0.000
Rehospitalization rate	0.23±0.42	0.08±0.28	0.033
Average hospitalization days	8.92±1.89	6.49±1.14	0.000

Note: *p<0.05, **p<0.01

TABLE 3: RELATIONSHIPS AMONG EACH PARAMETER

Parameters	BMI	FPG	PPG	HbA1c	KPS score	Rehospitalization rate	Average hospitalization days
BMI	-	0.181*	0.351**	0.048	-0.222*	0.057	0.207*
FPG	0.181*	-	0.489**	0.333**	-0.212*	0.015	0.203*
PPG	0.351**	0.489**	-	0.216*	-0.605**	0.074	0.484**
HbA1c	0.048	0.333**	0.216*	-	0.125	0.126	0.242**
LDL	0.082	-0.081	0.139	0.098	-0.231*	0.073	0.093
TG	0.220*	0.082	0.285**	0.01	-0.179	0.133	0.169
HOMA-β	-0.107	-0.197*	-0.266**	-0.088	0.213*	-0.013	-0.125
KPS score	-0.222*	-0.212*	-0.605**	-0.188*	-	-0.228*	-0.409**
Rehospitalization rate	0.057	0.015	0.074	0.126	-0.228*	-	0.322**
Average hospitalization days	0.207*	0.203*	0.484**	0.242**	-0.409**	0.322**	-

Note: *p<0.05, **p<0.01

Linear regression analysis indicated that BMI had the greatest correlation with PPG (p=0.039). FPG had the greatest correlation with PPG (p=0.000). PPG had the greatest correlation with KPS score (p=0.000) and FPG (p=0.000). HbA1c had the greatest correlation with FPG (p=0.002). KPS score had the greatest correlation with PPG (p=0.000). Rehospitalization rate had the greatest correlation with average hospitalization days (p=0.004). Average hospitalization days had the greatest correlation with PPG (p=0.000) (Table 4-Table 10).

TABLE 4: LINEAR REGRESSION ANALYSIS OF BMI

Variable quantity	B	Standard Error (SE)	β	t	p	95 % confidence interval	
Constant quantity	20.812	3.408	-	6.107	0	14.061	27.562
FPG	0.041	0.158	0.026	0.257	0.797	-0.272	0.354
PPG	0.138	0.066	0.274	2.083	0.039*	0.007	0.269
TG	0.276	0.191	0.13	1.442	0.152	-0.103	0.654
KPS score	-0.003	0.034	-0.01	-0.094	0.926	-0.071	0.065
Average hospitalization days	0.057	0.134	0.043	0.426	0.671	-0.209	0.323

Note: *p<0.05, **p<0.01

TABLE 5: LINEAR REGRESSION ANALYSIS OF FPG

Variable quantity	B	SE	β	t	p	95 % confidence interval	
Constant quantity	1.688	2.355	-	0.717	0.475	-2.978	6.353
PPG	0.169	0.034	0.529	4.897	0.000**	0.101	0.237
KPS score	0.029	0.019	0.148	1.499	0.137	-0.009	0.067
Average hospitalization days	-0.058	0.077	-0.068	-0.747	0.457	-0.211	0.095
BMI	0.014	0.052	0.023	0.274	0.785	-0.09	0.118
HbA1c	0.339	0.107	0.255	3.17	0.002**	0.127	0.551
HOMA-β	-1.144	1.293	-0.071	-0.884	0.378	-3.706	1.418

Note: *p<0.05, **p<0.01

TABLE 6: LINEAR REGRESSION ANALYSIS OF PPG

Variable quantity	B	SE	β	t	p	95 % confidence interval	
Constant quantity	11.001	5.692	-	1.933	0.056	-0.276	22.278
KPS score	-0.24	0.042	-0.392	-5.703	0.000**	-0.324	-0.157
Average hospitalization days	0.557	0.182	0.209	3.066	0.003**	0.197	0.917
BMI	0.257	0.127	0.129	2.021	0.046*	0.005	0.509
HbA1c	-0.125	0.273	-0.03	-0.46	0.646	-0.666	0.415
HOMA-β	-3.422	3.157	-0.068	-1.084	0.281	-9.676	2.832
FPG	1.024	0.208	0.327	4.921	0.000**	0.611	1.436
TG	0.492	0.263	0.118	1.869	0.064	-0.03	1.015

Note: *p<0.05, **p<0.01

TABLE 7: LINEAR REGRESSION ANALYSIS OF HbA1c

Variable quantity	B	SE	β	t	p	95 % confidence interval	
Constant quantity	6.613	1.589	-	4.161	0	3.465	9.76
KPS score	-0.015	0.016	-0.099	-0.9	0.37	-0.047	0.017
Average hospitalization days	0.114	0.063	0.178	1.797	0.075	-0.012	0.24
PPG	-0.02	0.031	-0.085	-0.667	0.506	-0.081	0.04
FPG	0.239	0.074	0.317	3.206	0.002**	0.091	0.386

Note: *p<0.05, **p<0.01

TABLE 8: LINEAR REGRESSION ANALYSIS OF KPS SCORE

Variable quantity	B	SE	β	t	p	95 % confidence interval	
Constant quantity	89.451	6.745	-	13.261	0	76.087	102.815
Average hospitalization days	-0.385	0.373	-0.089	-1.034	0.303	-1.124	0.353
PPG	-0.913	0.158	-0.56	-5.775	0.000**	-1.227	-0.6
FPG	0.422	0.424	0.083	0.995	0.322	-0.418	1.262
BMI	0.007	0.246	0.002	0.027	0.979	-0.48	0.493
LDL	-1.009	0.601	-0.123	-1.677	0.096	-2.2	0.183
HOMA-β	4.647	6.068	0.057	0.766	0.445	-7.375	16.668
Rehospitalization rate	-3.529	1.775	-0.15	-1.988	0.049*	-7.047	-0.012

Note: *p<0.05, **p<0.01

TABLE 9: LINEAR REGRESSION ANALYSIS OF THE REHOSPITALIZATION RATE

Variable quantity	B	SE	β	t	p	95% confidence interval	
Constant quantity	0.145	0.389	-	0.373	0.71	-0.624	0.915
Average hospitalization days	0.051	0.017	0.275	2.898	0.004**	0.016	0.085
KPS score	-0.005	0.004	-0.116	-1.22	0.225	-0.013	0.003

Note: *p<0.05, **p<0.01

TABLE 10: LINEAR REGRESSION ANALYSIS OF AVERAGE HOSPITALIZATION DAYS

Variable quantity	B	SE	β	t	p	95 % confidence interval	
Constant quantity	5.699	2.683	-	2.124	0.036	0.383	11.015
KPS score	-0.021	0.023	-0.09	-0.901	0.37	-0.066	0.025
Rehospitalization rate	1.385	0.428	0.255	3.232	0.002*	0.536	2.233
BMI	0.028	0.061	0.037	0.455	0.65	-0.093	0.148
FPG	-0.077	0.108	-0.065	-0.714	0.477	-0.291	0.137
PPG	0.151	0.042	0.402	3.604	0.000**	0.068	0.234
HbA1c	0.198	0.128	0.126	1.54	0.126	-0.057	0.452

Note: *p<0.05, **p<0.01

Adverse reactions were compared. There was no difference in total adverse reactions between patients in the liraglutide group (8.47 %) and those in the glargine group (12.90 %) (p>0.05). The hypoglycemia rate of patients in the liraglutide group (0 %) was significantly better than that in the glargine group (12.90 %) (p<0.05). The gastrointestinal symptoms of patients in the glargine group (0 %) were significantly better than those in the liraglutide group (8.47 %) (p<0.05) (Table 11).

In 2020, China's epidemiological survey showed that the number of patients with diabetes in China had exceeded 128 million[5]. According to the International Diabetes Federation, the number of patients with diabetes worldwide will reach 629 million in 2045. The number of patients in China will rise to 154 million[6]. Diabetes is becoming a disastrous disease in China. At the same time, China is also the country with the most malignant tumors. The latest statistical data suggest that approximately 10 000 people are diagnosed with malignant tumors every day and approximately 7 people are diagnosed with malignant tumors every minute. There is a close relationship between malignant tumors and diabetes. On the one hand, diabetes patients have a higher risk of developing malignant tumors, including liver cancer, renal cell carcinoma, pancreatic cancer, rectal cancer, bladder cancer and lung cancer[7]. On the other hand, patients with malignant tumors have a higher risk of diabetes. Treatment with antitumor drugs, radiotherapy and immune checkpoint inhibitors, such as glucocorticoids, paclitaxel, cisplatin and PD1/PD-L1 antibodies, may induce disorders of glucose metabolism, resulting in short-term or long-term elevated blood glucose[8]. Many studies have indicated that radiotherapy increases the incidence rate of diabetes[9]. At the same time, the blood glucose compliance rate of cancer patients with diabetes is lower than that of ordinary diabetes patients and the prognosis in such patients is even worse. According to the relevant guidelines, the traditional hypoglycemic therapy for patients with diabetes mellitus with malignant tumors is insulin injection[3]. Chemotherapy, especially glucocorticoid treatment, increases glucose and blood glucose, inhibits the utilization of peripheral glucose and increases insulin resistance[10]. Therefore, it is necessary to increase the dose of insulin according to the increase in blood glucose in patients and reduce the dose of insulin after glucocorticoids to avoid the occurrence of hypoglycemia. If glucocorticoids are given periodically, blood glucose may also fluctuate[5]. The sensitivity of different diabetes patients to insulin is different. When the dosage of insulin is increased during short-term therapy, the amplitude of the rise in blood glucose is different. There are great differences in individualized strategies in clinical adjustment of hypoglycemic programs and the ability of some nonendocrinology specialists to adjust blood glucose is deficient, leading to hyperglycemic crises such as Diabetic Ketoacidosis (DKA) during the use of glucocorticoids[11]. The risk of Hyperglycemic Hyperosmolar Syndrome (HHS) increases and with the cessation of glucocorticoid therapy, the risk of hypoglycemia increases due to insufficient reduction of insulin[12]. Studies have also demonstrated that the hyperglycemia rate is high in nonendocrinology departments of hospitals (approximately 40 %), with an average rate of 10 %[13]. A serious hypoglycemic event may offset the benefits of previous lifetime glucose control and even induce myocardial infarction and acute stroke[14]. Severe glycemic fluctuation does great harm to diabetes patients. It significantly increases the level of oxidative stress in diabetes patients and activates various pathways to participate in the progression of diabetic complications. It is an independent risk factor for chronic cardiovascular diseases and macrovascular events[15]. Therefore, a safer and rationale hypoglycemic regimen for type 2 diabetes patients with malignant tumors is needed in clinical practice.

Previous studies suggested that compared with

TABLE 11: COMPARISON OF ADVERSE REACTION RATES

Group	n	Total adverse reactions (%)	Hypoglycemia (%)	Gastrointestinal symptoms (%)
Glargine	60	8/12.90 %	8/12.90 %	0/0 %
Liraglutide	60	5/8.47 %	0/0 %	5/8.47 %
F	-	0.611	5.646	8.596
p value	-	0.436	0.019	0.004

intravenous injection of glucose, oral administration of the same amount of glucose increased insulin levels more. This phenomenon is known as the "incretin effect" and it occurs due to the production of peptide substances that regulate postprandial insulin secretion by gastrointestinal cells, such as incretin, GLP-1 and Gastric Inhibitory Polypeptide (GIP)[16]. The physiological effects of GLP-1 include promoting glucose tolerance and insulin secretion, slowing gastric emptying, regulating glucagon secretion, reducing liver glycogen synthesis, enhancing insulin sensitivity and inhibiting appetite. GLP-1 has been widely used in patients with type 2 diabetes mellitus. Liraglutide, a representative drug targeting GLP-1, is injected once a day. Compared with insulin injection, the glucose-dependent insulin secretary effect and dual regulation mechanism involving glucagon of liraglutide may avoid the increase in blood glucose during glucocorticoid treatment and the risk of hypoglycemia after the end of glucocorticoid treatment and reduce blood glucose fluctuation[17-20] and the dose of liraglutide does not need to be adjusted frequently, so it is convenient for nonspecialists and patients to use. It may be a more rational hypoglycemic regimen for type 2 diabetes patients with malignant tumors who receive periodic glucocorticoid treatment.

This study included 120 patients with type 2 diabetes mellitus with malignant tumors who were treated with periodic corticosteroids in our hospital from January 2019 to December 2020. They were randomly divided into the liraglutide group and the glargine group. The results suggested that the FPG and 2 h PPG of the liraglutide group were lower than those of the glargine group; HbA1c was also lower in the liraglutide group, which indicated that better glycemic management produced better results in patients with diabetes and tumors who received periodic glucocorticoid treatment. The HOMA-IR of the glargine group was lower than that of the liraglutide group, indicating that liraglutide alleviated the insulin resistance induced by glucocorticoids. The BMI of the liraglutide group was lower than that of the glargine group, which indicated that liraglutide had less effect on weight gain. Unlike before treatment, the fasting C-peptide and HOMA-β values after treatment in the control group were significantly higher than those in the liraglutide group and the results were statistically significant ($p<0.05$), indicating that liraglutide may have an effect on recovery of insulin function. Compared with the glargine group, the liraglutide group had an increased KPS score ($p<0.05$) and the rehospitalization rate and average hospitalization days were decreased in the liraglutide group ($p<0.05$). Compared with those in the glargine group, patients with type 2 diabetes mellitus with malignant tumors in the liraglutide group had significantly better KPS scores, rehospitalization rates and average hospitalization days.

Further correlation analysis suggested that BMI was significant positively correlated with FPG, PPG, TG and average hospitalization days and negatively correlated with HOMA-β and KPS score ($p<0.05$), indicating that improvement of BMI is closely related to fasting and postprandial blood glucose control and TG, as well as improvement of islet secretion function and the overall health status of patients. HbA1c was significantly positively correlated with FPG, PPG and average hospitalization days and negatively correlated with KPS score ($p<0.05$), indicating that long-term blood glucose control is closely related to fasting and postprandial blood glucose as well as improved overall health of patients and reduced average hospitalization days. KPS score was significantly positively correlated with HOMA-β and negatively correlated with BMI, FPG, PPG, LDL, rehospitalization rate and average hospitalization days ($p<0.05$), indicating that the overall health status of patients is closely related to islet function, BMI, fasting and postprandial blood glucose control, rehospitalization rate and average hospitalization days. The rehospitalization rate was significant positively correlated with average hospitalization days and negatively correlated with KPS score ($p<0.05$), indicating that the rehospitalization rate is closely related to the average hospitalization days and the overall health status of patients. Average hospitalization days was significant positively correlated with BMI, FPG, PPG, HbA1c and rehospitalization rate,

and negatively correlated with KPS score ($p<0.05$), indicating that average hospitalization days is closely related to BMI, fasting and postprandial blood glucose control, rehospitalization rate and the overall health status of patients.

Linear regression analysis suggested that the BMI had the greatest correlation with PPG ($p=0.039$) in patients with type 2 diabetes mellitus and tumors. We speculated that the improvement in BMI in the liraglutide group was mainly due to the control of PPG. FPG had the greatest relationship with PPG ($p=0.000$). We speculated that the improvement in FPG in liraglutide group was mainly due to the control of PPG. PPG had the greatest correlation with KPS score ($p=0.000$) and FPG ($p=0.000$). We speculated that the improvement in PPG in liraglutide group was mainly due to the control of FPG and KPS score (overall health status of patients). HbA1c had the greatest relationship with FPG ($p=0.002$). We speculated that the improvement in HbA1c in the liraglutide group was mainly due to the control of FPG. KPS score had the greatest correlation with PPG ($p=0.000$). We speculated that the improvement in KPS score (overall health status of patients) in the liraglutide group was mainly due to the control of PPG. Rehospitalization rate had the greatest correlation with average hospitalization days ($p=0.004$). We speculated that the reduction in rehospitalization rate in the liraglutide group was mainly due to the decrease in average hospitalization days. Average hospitalization days had the greatest correlation with PPG ($p=0.000$). We speculated that the reduction in average hospitalization days in the liraglutide group was mainly due to the decrease in the control of PPG. The above results suggested that the rehospitalization rate and the overall health of patients with type 2 diabetes mellitus with malignant tumors were significantly improved by reducing the average hospitalization days. The main reason for this outcome is that the reduction in average hospitalization days is dependent on glycemic control and the recovery of islet β-cell function, which may not be closely related to the improvement of BMI. It has also been revealed that glycemic control actively improves the prognosis of type 2 diabetes patients with malignant tumors. The adverse reaction analysis suggested that although liraglutide increased gastrointestinal symptoms in a small number of patients in this study, there were no hypoglycemic reactions; as such, the most intractable hypoglycemic side effects previously reported to be caused by insulin were effectively avoided.

In conclusion, compared with traditional glargine treatment, liraglutide treatment improved the quality of life and blood glucose management of type 2 diabetes mellitus patients with malignant tumors during periodic glucocorticoid treatment without increasing the incidence of adverse reactions or reducing the incidence of hypoglycemia. The regimen is worth promoting in clinical practice and the specific mechanism needs further exploration.

Our research has some limitations. First, the sample size was small and the follow-up time was short. Second, the study included only patients recruited from one hospital, so larger multicenter research with long-term follow-up is required.

Ethics approval:

The protocol was approved by the Chongqing University Cancer Hospital, School of Medicine, Chongqing University Institutional Review Board, conformed to the standards of the Declaration of Helsinki and is registered with Chinese Clinical Trial Registry (ChiCTR2100049169). All patients participated voluntarily and signed informed consent.

Author's contributions:

Pu Danlan and Jiang Juan contributed equally to this work. Pu Danlan, Jiang Juan, Song Cui, Xi Jiazhuang and Wu Qinan researched and analyzed the data. Pu Danlan and Wu Qinan contributed to the writing of the manuscript and helpful discussion. Song Cui directed the project and contributed to the discussion. Pu Danlan and Jiang Juan wrote and edited the manuscript. Xi Jiazhuang and Wu Qinan were the guarantors of this work and as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgements:

This work was supported by grants from the Joint Medical Research Project of Chongqing Science and Technology Bureau and Health Commission (2021msxm311); Chongqing Science and Technology Bureau and Health Commission of Chinese Medicine Technology Innovation and Application Development Project (2020ZY013540); Research Institute Performance Incentive and Guidance Project of Chongqing Science and Technology Bureau (cstc2019jxjl30006); General Project of Graduate Education and Teaching Reform of Chongqing University (cquyjg20329); Decision Making Consultation and Management Innovation Project of Science and Technology Bureau of Shapingba District (jcd202038); and 2019 Merck Diabetes Research Fund (g-x-2019-056).

Conflict of interests:

The author stated that there was no conflict of interest.

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This article was originally published in a special issue, "Trending Topics in Biomedical Research and Pharmaceutical Sciences" Indian J Pharm Sci 2022:84(1) Spl Issue "168-177"