THE EFFECT OF METFORMIN COMBINED WITH SITAGLIPTIN ON TYPE 2 DIABETES MELLITUS AND THE ISLETS FUNCTION

Bo Hu*, Huihui Fan, Jinlei Yao
Department of Endocrinology, The People's Hospital of Fenghua, Ningbo, PR China

ABSTRACT

Objective*: To explore the effect of metformin combined with sitagliptin in the treatment of type 2 diabetes mellitus and its effect on the islets function.*

Methods: *A total of 84 cases of type 2 diabetes diagnosed in our hospital from December 2017 to December 2018 were selected for the present study. The patients were randomly divided into three groups. The sitagliptin group (n=28, recorded as group A) was only treated with sitagliptin, while patients in group B (n=)were only treated with metformin. Patients in the combined group (n=28, recorded as group C) were treated with both sitagliptin and metformin. The patients were randomly divided into three groups. Blood glucose control, islet β cell function [FBG (fasting blood glucose), 2-hour postprandial blood glucose (2hPG), HbAlc, HOMA-IR, HOMA-β], blood lipid, blood pressure, and metabolism (TG, TC, LDL-C, BIM, SBP, DBP) were compared among the three groups.*

Results: *The levels of FBG, 2hPG, HbAlc and HOMA-IR in the three groups decreased significantly (P<0.05), while the levels of HOMA-β in the three groups increased significantly (P<0.05). However, the differences between the indexes between groups A and B were not significant, while the levels of FBG, 2hPG and HbAlc in group C decreased significantly (P<0.05). While the level of HOMA-β increased significantly (P<0.05), there was no significant difference in HOMA-IR among the three groups after treatment (P>0.05). Moreover, the TG, TC, LDL-C, SBP and DBP values of the three groups were significantly lower after treatment (P<0.05); however, no significant differences in TG, TC, LDL-C, SBP and DBP values were observed between groups A and B, while the TG, TC, LDL-C, SBP and DBP values of group C after treatment were significantly lower than those of the other two groups (P<0.05). While BMI level in group A was not significantly different before and after treatment (P<0.05), there was a significant decrease in groups B and C before treatment (P<0.05), and between groups B and C before and after treatment (P<0.05).*

Conclusion: *Sitagliptin combined with metformin is beneficial in the treatment of type 2 diabetes and to the improvement of islet function, patient quality of life and the reduction of energy and financial costs associated with type 2 diabetes.*

Keywords: *Metformin, sitagliptin, type 2 diabetes, combination therapy.*

DOI: 10.19193/0393-6384_2020_6_575

Received *November 30, 2019;* ***Accepted*** *January 20, 2020*

Introduction

With the rapid development of China's economy, individual lifestyles have undergone tremendous changes, with people pursuing a higher quality of life. Diabetes has always been a serious disease, and with the improvement of quality of life in China in recent years, the prevalence of diabetes is also on the rise. Ironically, this trend is not conducive to the pursuit of a high quality of life and the creation of greater wealth. Therefore, it is of scientific significance to study the clinical treatment of diabetes. Type 2 diabetes accounts for 90% of all diabetic cases (type 1 and 2 diabetes)[1]. In China, type 2 diabetes has reached 97%[2]. Type 2 diabetes is due to the blockage of insulin secretion mechanisms in the body. Generally, patients experience symptoms at 35-40 years old[3]. The main reason for this trend is that the binding of insulin and its receptor is blocked, which leads to a disorder of the insulin system. In the treatment process, we primarily focus on the control of blood glucose[4]. A large body of clinical data shows that good control of blood glucose serves an important role in reducing related complications, which can not only play a certain role in controlling type 2 diabetes but also reduce the financial burden

of patients from complications[5]. At present, insulin, sulfonylureas and biguanides are mainly used in the clinical treatment of this disease[6]. The present study focuses on the clinical effect of metformin combined with sitagliptin in the treatment of type 2 diabetes, with the aim of exploring an improved treatment plan for type 2 diabetes.

Materials and methods

General information

A total of 84 cases of type 2 diabetes mellitus were diagnosed in our hospital from December 2016 to December 2018 and were randomly divided into two groups. The sitagliptin only group (group A) consists of 28 patients aged 34-69 years with an average age of 52.3±2.99, with 18 males and 10 females. The metformin only group (group B) consists of 28 patients aged 36-68 years with an average age of 51.7±3.01, with 16 males and 12 females. The sitagliptin combined with metformin group (Group C) consists of 28 patients aged 36-69 years, with an average age of 52.8±3.28 years old, with 17 males and 11 females. There was no significant difference in the economic status and education among the three groups (P>0.05).

Inclusion criteria:

• Meeting the World Health Organization (WHO) diagnostic criteria for type 2 diabetes;

• Not taking anti-diabetic drugs in the past three months or continuously taking drugs for no more than three months;

• Age 26-70 years old.

Exclusion criteria:

• Non-type 2 diabetes;

• Pancreatitis;

• Severe organ and tube disease;

• Diabetic acute complications.

All patients were informed and willing to participate in the trial.

Method

Group A was given 100 mg of sitagliptin (manufacturer: Merck sharp & Dohme Pty Ltd.) once daily; group B was given 500 mg of metformin (Hebei Samshi Pharmaceutical Co., Ltd.) three times daily; group C was given combination of sitagliptin and metformin, including 100 mg of sitagliptin once daily in addition to 500 mg of metformin three times daily. Groups A, B and C were treated for 3 months. During this period, other hypoglycaemic drugs could not be used, and the patients' lifestyle and eating habits were instructed.

Observation indicators

Blood glucose control and islet β cell function: including the detection of FBG, 2hPG, HbAlc, HOMA-IR, HOMA-β levels in the blood; blood lipid, blood pressure and other metabolic indicators: including the detection of TG, TC, LDL-C levels in the blood and the comparison of BI(BMI = body weight/height2 (kg/m2), SBP, DBP.

Statistical processing

The statistical software SPSS 22.0 was used to process the data, with count data expressed by (n, %). The χ^2 test was used. Measurement data was expressed by ($\bar{x}\pm s$), and the t-test was used. P<0.05 was considered statistically significant.

Results

Comparison of blood glucose control and islet β cell function before and after treatment

In the comparison of FBG, 2hPG, HbAlc and HOMA-IR levels, there was a significant decrease (P<0.05) in all three groups following treatment, while there was a significant increase in the HOMA-β level (P<0.05) in all three groups. However, no significant difference was observed between groups A and B after treatment.

When compared to the other two groups, the level of FBG, 2hPG and HbAlc in group C decreased significantly (P<0.05), and the level of HOMA-β increased significantly (P<0.05); however, the levels of HOMA-IR in groups A, B and C were not significantly different (P>0.05) (see Table 1 for details).

Group		FBG (mmol/L)	2hPG (mmol/L)	HbAlc (%)	HOMA-β	HOMA-IR
Group A (n=28)	Before treatment	8.1±0.9	13.3±1.8	7.2±0.7	43±18	3.3±1.3
	After treatment	6.6±0.7*	10.2±1.1*	6.6±0.4*	65±17*	3.0±0.7
	t value	6.961	7.776	3.938	4.702	1.075
	P value	<0.001	<0.001	<0.001	<0.001	0.287
Group B (n=28)	Before treatment	7.8±0.8	13.5±1.8	7.3±0.6	47±14	3.5±1.2
	After treatment	6.7±0.4*	9.9±1.0*	6.4±0.9*	64±23*	3.1±0.2
	t value	6.508	9.251	4.403	3.341	1.740
	P value	<0.001	<0.001	<0.001	0.002	0.088
Group C (n=28)	Before treatment	8.3±1.2	14.2±1.9	7.4±0.8	42±16	3.6±1.8
	After treatment	6.1±0.8*#	8.6±1.7*#	6.0±0.5*#	83±26*#	3.0±0.7
	t value	8.072	11.623	7.853	7.106	1.644
	P value	<0.001	<0.001	<0.001	<0.001	0.106

Table 1: Comparison of blood glucose control and islet β cell function before and after treatment.

*Note: *P<0.05, significant difference between the group before and after treatment; #P<0.05, significant difference between groups C, A and B after treatment.*

Metabolism indexes such as blood lipid and blood pressure

The TG, TC, LDL-C, SBP and DBP values of groups A, B and C decreased significantly after treatment ($P < 0.05$). However, no significant differences in TG, TC, LDL-C, SBP and DBP values were observed between groups A and B after treatment, while the TG, TC, LDL-C, SBP and DBP values of group C decreased more significantly after treatment when compared to the other two groups ($P<0.05$). Regarding BMI level, no significant difference ($P<0.05$) was observed before and after treatment in group A.

Notably, there was a significant decrease in BMI in groups B and C before treatment ($P<0.05$) and a significant difference in groups B and C after treatment when compared to group A ($P<0.05$) (see Table 2 for details).

Group		TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)	SBP (mmHg)	DBP (mmHg)	BMI (kg/m²)
Group A (n=28)	Before treatment	2.31±0.41	5.3±0.9	3.07±0.30	141±7	90±3	26.8±2.6
	After treatment	1.85±0.42*	4.9±0.3*	2.56±0.29*	136±4*	84±4*	26.7±2.6
	t value	4.147	2.231	6.468	3.282	6.350	0.144
	P value	<0.001	0.030	<0.001	0.002	<0.001	0.886
Group B (n=28)	Before treatment	2.27±0.28	5.4±0.6	3.06±0.42	143±4	89±6	26.8±2.5
	After treatment	1.84±0.15*	4.7±0.6*	2.55±0.41*	135±6*	86±4*	25.3±2.1*#
	t value	7.163	4.365	4.598	5.870	2.201	2.431
	P value	<0.001	<0.001	<0.001	<0.001	0.032	0.018
Group C (n=28)	Before treatment	2.54±0.87	5.4±1.1	3.01±0.62	148±8	89±7	27.3±2.6
	After treatment	1.53±0.56*#	4.1±1.2*#	2.29±0.41*#	131±5*#	80±4*#	25.3±2.5*#
	t value	5.165	4.226	5.126	9.535	5.907	2.934
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	0.005

Table 2: Metabolism indexes such as blood lipid and blood pressure.

*Note: *P<0.05, significant difference between the group before and after treatment; #P<0.05, significant difference between groups C, A and B after treatment.*

Conclusion

Metformin can improve the utilisation of sugar in the peripheral cells of islets of Langerhans, inhibit the metabolism of sugar, reduce the output of liver sugar, and reduce insulin resistance[7]. Metformin is the main drug use in the treatment of type 2 diabetes[8]. At present, the traditional oral drugs and insulin used in clinical treatment for type 2 diabetes increase or decrease the weight and blood glucose instability of patients. The alternation of high and low blood glucose can easily cause damage B cells and target organs of the islet of Langerhans, which can bring major inconvenience to patients and directly reduces their quality of life[9]. The L cells of the digestive tract can secrete GLP-1 and GIP, while GLP-1 and GIP can regulate insulin secretion[10].

Sitagliptin is a DDP-4 inhibitor, and GLP-1 and GIP will be inactivated by DDP[11]. DDP-4 inhibitors can inhibit the deactivation of GLP-1 and GIP, mainly because they compete with the activated site of DDP-4, which reduces the combination of DDP with GLP-1 and GIP-thus playing an inhibitory role[12]. Sharma et al. conducted a related study on sitagliptin and determined that sitagliptin can increase the activity of GLP-1 in normal human blood[13]. There are currently many DDP-4 inhibitors on the market. In 2006, the US approved sitagliptin as a treatment for type 2 diabetes[14]. In the treatment of type 2 diabetes mellitus, some scholars noted that, compared with metformin combined with placebo, metformin combined with sitagliptin has a better effect[15].

Moreover, the side effects of cigliptin are similar to those of placebo, while its safety and tolerance are better than other drugs and it can reduce the incidence of hypoglycaemia[16]. At present, the aetiology of diabetes is considered to be affected by genetics and environment. After analysing the statistical data of type 1 diabetes and type 2 diabetes, it was found that both types have obvious genetic properties; that is, people who have diabetes in their families are more likely to suffer from diabetes than those who have no diabetes in their family history[17]. In the study of type 2 diabetes, a variety of gene mutations have been found. Notably, irregular diet (mainly overeating) and an extreme lack of physical activity may lead to the occurrence of type 2 diabetes. In the treatment of type 2 diabetes mellitus alone, the blood glucose value of patients cannot reach a normal level, or the effective period is very short[18].

The combination of inhibitors and other hypoglycaemic drugs can not only reduce blood pressure and blood sugar but also control blood pressure and blood sugar to a certain extent—thus making the effective period longer than through the use of hypoglycaemic drugs alone.

In summation, sitagliptin combined with metformin is beneficial to the treatment of type 2 diabetes mellitus. When compared to a treatment using only hypoglycaemic drugs, the combined treatment has a better effect and is conducive to improving the function of islets of Langerhans and patient quality of life while reducing the energy and financial costs related to type 2 diabetes mellitus complications.

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Corresponding Author:
Bo Hu
Email: z882iy@163.com
(China)