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Analysis of pharmacoeconomic value of sitagliptin in the treatment of diabetes mellitus

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Abstract. – OBJECTIVE: Diabetes mellitus is a chronic metabolic disease which has an adverse impact on the quality of patient's life, so patients often need to receive treatment for a long time. Selection of medications with high therapeutics effects and low cost is very important for patients to take medicine for a longer period of time. Sitagliptin is a drug which is widely used in clinics and can effectively control blood glucose level. This article explores the pharmacoeconomic value of Sitagliptin in the treatment of diabetes mellitus.

PATIENTS AND METHODS: A total of 100 patients with diabetes mellitus treated were recruited in this study. The patients were randomly divided into 4 groups with 25 cases in each group. Patients in group A were treated with pioglitazone, group B with Sitagliptin, group C with metformin and group D with glimepiride. The cost of the drugs, the treatment results and adverse effects were compared.

RESULTS: Compared with group A, C and D, the cost-effectiveness ratio of group B was low ($p<0.05$), and the therapeutic effect was high ($p<0.05$). In addition, the incidence of adverse reactions in group B was lower than that in group A, C and D ($p<0.05$). There was no significant difference in the levels of FPG, 2hPG and HbAlc in patients among the four groups before treatment ($p>0.05$). After treatment, the levels of FPG, 2hPG and HbAlc in group B were significantly lower than those in groups A, C and D ($p<0.05$). Finally, there was no significant difference in waist circumference and BMI among the four groups before treatment ($p>0.05$). After treatment, the waist circumference and BMI in group B were lower than those in groups A, C and D ($p<0.05$).

CONCLUSIONS: The application of Sitagliptin in the treatment of diabetic patients can effectively enhance the therapeutic effect. The cost effectiveness is satisfactory, and the blood glucose level can be maintained at a stable state.

Key Words:
Sitagliptin, Intervention treatment, Diabetes, Pharmacoeconomics, Value.

Introduction

Diabetes mellitus is a chronic metabolic disease while type 2 diabetes mellitus is the most common one[1]. Patients with diabetes often progress to severe complications, such as retinopathy, diabetic nephropathy, and diabetic foot. These complications will cause damage to important organs of the body, thus adversely affecting the patients' quality of life[2]. Because diabetes is a chronic disease, patients often need to receive treatment for a long time. The types of oral hypoglycemic drugs used in clinic are diverse, and there are great differences in the effects and costs of drugs. The key for most patients to take medicine for a long time is to choose drugs with curative effect and relatively low cost. Sitagliptin is a kind of drug which is widely used in clinic and can effectively control blood glucose level[3]. The aim of this study was to investigate the pharmacoeconomic value of Sitagliptin in the treatment of diabetes mellitus.

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Patients and Methods

General Information

A total of 100 patients with diabetes mellitus treated in our hospital from February 2019 to February 2021 were recruited in this study. The patients were randomly divided into 4 groups with 25 cases in each group. Group A included 17 males and 8 females, aged from 43 to 79 years, with an average of 59.8±1.2 years. The duration of illness ranged from 1 to 5 years, with an average of 2.5±0.3 years. Group B included 16 males and 9 females, aged from 45 to 78 years, with an average of 59.7±1.3 years. The duration of illness ranged from 2 to 4 years, with an average of (2.6 ± 0.2) years. Group C included 18 males and 7 females, aged from 44 to 77 years, with an average of 59.6±1.5 years. The duration of illness was 2-3 years, with an average of (2.3 ± 0.2) years. Group D included 15 males and 10 females, aged from 42 to 80 years, with an average of 59.3±1.7 years. The duration of illness ranged from 1 to 4 years, with an average of 2.1±0.4 years.

Inclusion Criteria

(1) The patients who participated in the study fully comply with the diagnostic criteria for diabetes mellitus according to the guideline for prevention and treatment of type 2 diabetes in China. (2) The patients do not suffer from serious mental diseases and can normally cooperate with relevant treatments.

Exclusion Criteria

(1) The patients have received other hypoglycemic drugs within 1 month before participating in the study. (2) The patients have malignant tumor or serious abnormality of liver and kidney function. (3) The patients are allergic to the drugs used in this study. (4) The patients suffer from serious infectious diseases or have abnormal water electrolytes. (5) The patients are pregnant or lactating or have a clear pregnancy plan in the near future.

Methods

Patients participated in the study are required to control their diet scientifically and reasonably in the process of treatment and formulate an exercise plan that meets the actual needs of the patients.

1. Patients in group A were treated with pioglitazone. The patients were given pioglitazone tablets (gyzz J20140082; specification: 15 mg×7S×1 plate; Tianjin Takeda Pharmaceutical Co., Ltd.) orally, with a dose of 30 mg once a day.
2. Patients in group B were treated with Sitagliptin. The patients were given Sitagliptin Phosphate Tablets [gyzz j20140095; specification: 100 mg × 7S × 2 plate; Merck Sharp & Dohme Italia SPA (Italy)] orally, with a dose of 100 mg once a day.
3. Patients in group C were treated with metformin. The patients were given metformin tablets (gyzz h20023371; specification: 0.85 g×20 tablets; Sino American Shanghai Squibb Pharmaceutical Co., Ltd.) orally, with a dose of 0.85 g three times a day,
4. Patients in group D were treated with glimepiride. The patients were given glimepiride tablets [gyzz h20057672; specification: 2 mg×15s; Sanofi (Beijing) Pharmaceutical Co., Ltd.] orally before dinner, with a dose of 4 mg once a day.

All patients were treated continuously for 12 weeks.

Observation Indicators

Cost Effectiveness

Cost Calculation

The total cost = unit price of drug * daily use amount of drug * duration of use of medicine * number of patients.

The therapeutic effect was analyzed and recorded as: remarkable effective, effective, and ineffective. Remarkable effective: after treatment, most clinical symptoms, and signs, such as fatigue, hyperglycemia and increased urine volume were completely eliminated, and the fasting plasma glucose (FPG) level was decreased to less than 6.1 mmol/l, and the 2hPG level decreased by more than 30%. Effective: after treatment, most clinical symptoms, and signs, such as fatigue, hyperglycemia and increased urine volume, were relieved to a certain extent, and the reduction of FPG level was in the range of 10%-29%. Ineffective: the patient's fatigue, hyperglycemia, increased urine output and other clinical symptoms and signs have not changed after treatment, and the condition is becoming more and more serious[4]. Total effective rate = significant efficiency + effective rate.

Table I. Comparison of cost-effectiveness in the 4 groups (n, %).

Group	COST (Yuan)	Treatment effect(E, %)	Cost effectiveness ratio (C/E)
A	24000	17 (68.0)	352.94
B	13500	23 (92.0)	146.74
C	15435	20 (80.0)	230.37
D	21000	16 (64.0)	328.125
F	6.563	6.218	6.326
p	< 0.05	< 0.05	< 0.05

We observed and analyzed the levels of FBG, 2hFBG and HbAlc. Before and after treatment, 5 ml fasting venous blood and two-hour postprandial venous blood were collected successively in the morning, centrifuged at the speed of 3500 r/min for about 25 min, and then the separated serum was taken out and stored at -70°C for subsequent use. The levels of glycated hemoglobin (HbA1c), fasting blood glucose (FBG) and 2 h postprandial blood glucose (2hPG) were measured by glucose oxidase method[5].

Observe and analyze the physical indicators. The body weight, height and waist circumference of the patients were accurately measured before and after treatment with a soft ruler, and then, the BMI value was calculated.

Statistical Analysis

All data in this study were analyzed by SPSS 18.0 (Chicago, IL, USA). X^2 (%) test was used for counting data, and *t*-test (x ± s) test was used for measurement data. $p<0.05$ was considered as significant difference.

Results

Comparison of Cost-Effectiveness

Compared with group A, C and D, the cost-effectiveness ratio of group B was relatively low ($p<0.05$).

The price of pioglitazone tablets is 80 yuan per 7 pieces, so a patient in group A need to cost 960 yuan, the total cost of group A is 24000 yuan. The price of Sitagliptin is 45 yuan per 7 pieces, so a patient in group B need to cost 540 yuan, the total cost of group B is 13500 yuan. The price of metformin is 49 yuan per 20 pieces, so a patient in group C need to cost 617.4 yuan, the total cost of group C is 15435 yuan. The price of glimepiride is 75 yuan per 15 pieces, so a patient in group D need to cost 840 yuan, the total cost of group D is 21000 yuan. The total effective rate of group B is 92%, which is higher than other groups. So compared with group A, C and D, the cost-effectiveness ratio of group B was relatively low ($p < 0.05$), as shown in Table I and Figure 1.

Comparison of Therapeutic Effects in the 4 Groups

Compared with groups A, C and D, the therapeutic effect of group B was relatively high ($p<0.05$).

The number of remarkable effective and effective persons in group A is 17; total effective rate is 68%. The number of remarkable effective and effective persons in group B is 23, total effective rate is 92%. The number of remarkable effective and effective persons in group A is 20, total effective rate is 80%. The number of remarkable effective and effective persons in group A is 16; total effective rate is 64%. So compared with other groups, group B had the best therapeutic effect, as shown in Table II and Figure 2.

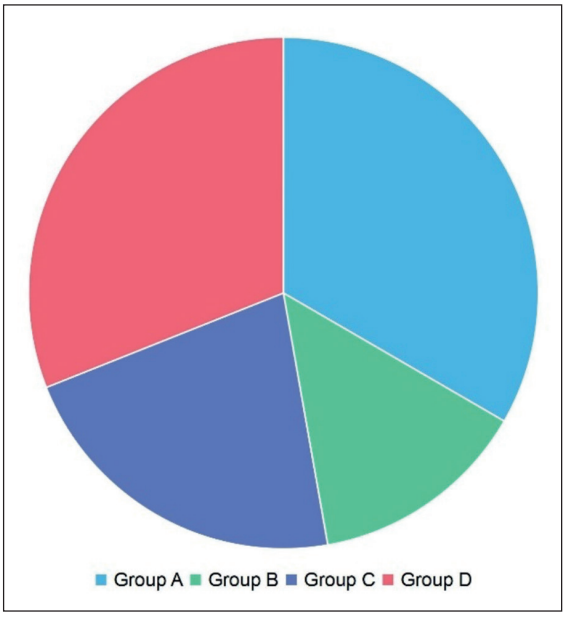

Figure 1. Cost effectiveness ratio (C/E).

Table II. Comparison of therapeutic effects among the 4 groups (n, %).

Group	N	Remarkable effective	Effective	Ineffective	Total effective rate (%)
A	25	11	6	8	17 (68.0)
B	25	15	8	2	23 (92.0)
C	25	12	8	5	20 (80.0)
D	25	11	5	9	16 (64.0)
F		6.107	6.256	6.317	6.153
p		< 0.05	< 0.05	< 0.05	< 0.05

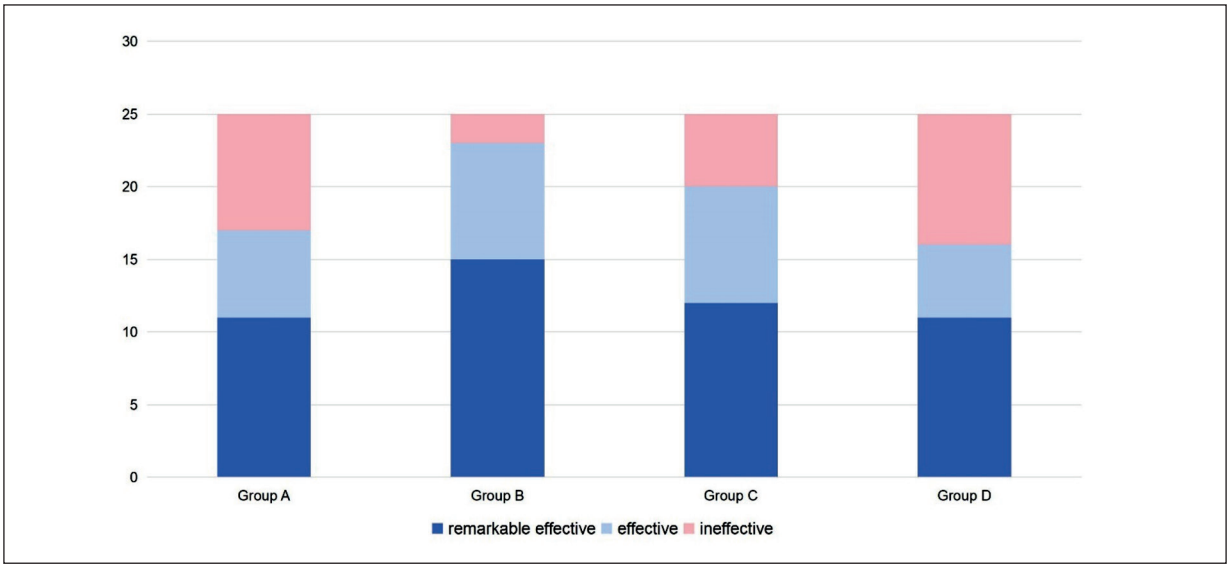

Figure 2. Therapeutic effects in all 4 groups.

Comparison of Adverse Reaction Rates in the 4 Groups

Compared with group A, C and D, the incidence of adverse reactions in group B was relatively low ($p<0.05$).

We compared the adverse reactions of abnormal liver and kidney function, nausea, diarrhea, and hypoglycemia in different groups. It was found that in group A, no one had abnormal liver and kidney function, 5 patients had nausea, 2 patients had nausea and 3 patients had hypoglycemia. In group B, no one had abnormal liver and kidney function, 2patients had nausea, no one had nausea and 1 patient had hypoglycemia. In group C, 2 patients had abnormal liver and kidney function, 1 patient had nausea, 1 patient had nausea and 3 patients had hypoglycemia. In group D, 2 patients had abnormal liver and kidney function, 3 patients had nausea, 2 patients had nausea and 2patients had hypoglycemia. The incidence of adverse reactions in group B was the lowest, as shown in Table III and Figure 3.

Table III. Comparison of adverse reaction rates between the two groups (n, %).

Group	N	Abnormal liver and kidney function	Nausea	Diarrhea	Hypoglycemia	Incidence rate (%)
A	25	0	5	2	3	10 (40.0)
B	25	0	2	0	1	3 (12.0)
C	25	2	1	1	3	7 (28.0)
D	25	2	3	2	2	9 (36.0)
F		6.236	6.158	6.219	6.305	6.117
p		< 0.05	< 0.05	< 0.05	< 0.05	< 0.05

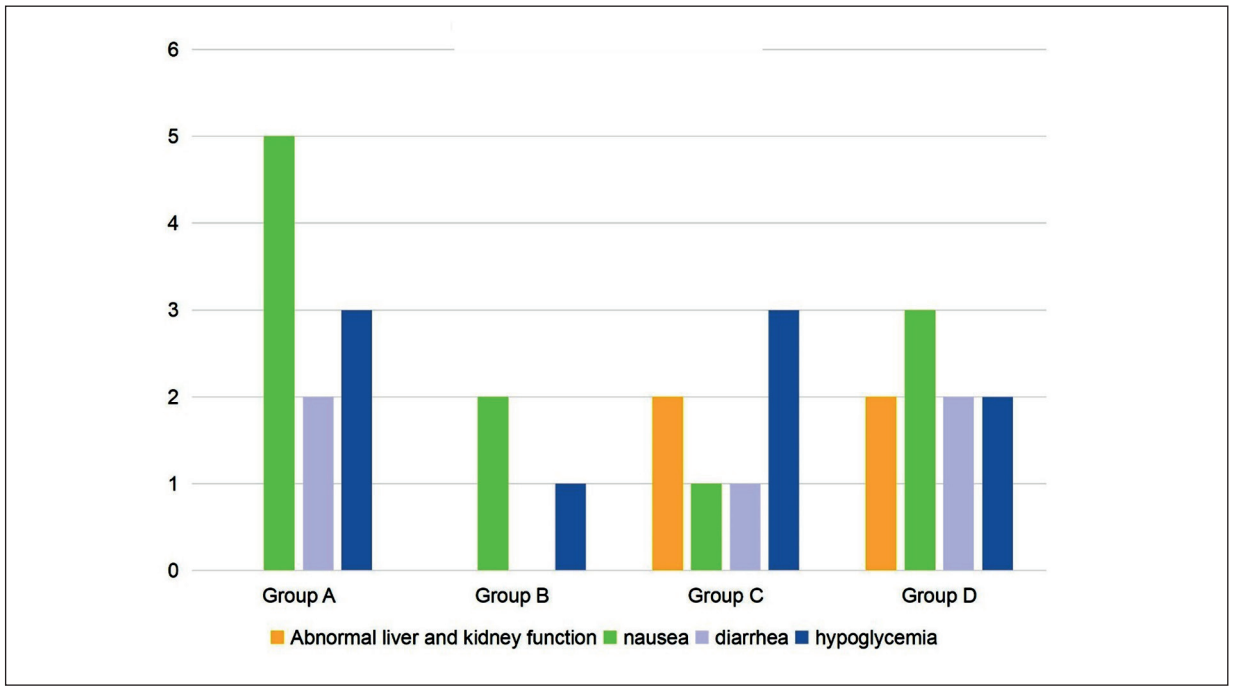

Figure 3. Adverse reactions noted for all groups.

Comparison of FPG, 2hPG and HbAlc

There was no significant difference in the levels of FPG, 2hPG and HbAlc before treatment ($p>0.05$). After treatment, the improvement of FPG, 2hPG and HbAlc in group B was significantly higher than that in groups A, C and D ($p<0.05$), as shown in Table IV.

Comparison of Physical Indexes in the 4 Groups

There was no significant difference in waist circumference and BMI in the 4 groups before treatment ($P > 0.05$). After treatment, waist circumference and BMI in group B were significantly lower than those in groups A, C and D ($p<0.05$), as shown in Table V.

Discussion

Type 2 diabetes is a common type of metabolic disease, mostly due to impaired insulin utilization or marked loss of insulin secretion[6]. Based on clinical studies, the morbidity and mortality of type 2 diabetes are high. Diabetes can lead to damage of multiple organs, that adversely affect the quality of life of patients. In recent years, with the increase of aging population and the continuous changes of living standards, the incidence of diabetes is increasing[7]. Therefore, we should adapt to China's medical insurance system, choose the therapeutic drugs with optimal curative effect and low cost for the treatment of diabetes.

Table IV. Comparison of FPG, 2hPG and HbAlc in the 4 groups ($\bar{x} \pm s$).

Group	N	FPG (mmol/L)		2hPG (mmol/L)		HbAlc (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A	25	10.5 ± 2.2	7.8 ± 1.7	15.3 ± 3.7	10.5 ± 2.1	11.4 ±1.3	8.3 ± 1.6
B	25	10.6 ± 2.1	6.1 ± 1.1	15.2 ± 3.8	8.1 ± 0.9	11.5 ± 1.2	6.1 ± 1.1
C	25	11.2 ± 1.8	7.6 ± 1.5	14.9 ± 4.1	9.7 ± 1.3	10.9 ± 1.5	7.2 ± 1.3
D	25	11.1 ± 1.9	8.1 ± 1.3	14.8 ± 4.2	11.2 ± 1.5	10.8 ± 1.6	9.1 ± 1.5
F		1.563	16.217	1.318	16.256	1.206	16.515
p		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Table V. Comparison of physical indexes between the two groups ($\bar{x} \pm s$).

Group	N	Waistline (cm)		BMI (kg/m^2)	
		Before treatment	After treatment	Before treatment	After treatment
A	25	92.5 ± 2.8	82.4 ± 5.6	29.7 ± 1.2	26.9 ± 2.6
B	25	91.3 ± 3.7	73.1 ± 3.5	29.6 ± 1.3	22.9 ± 2.1
C	25	91.8 ± 3.2	76.2 ± 3.7	28.9 ± 2.7	24.2 ± 3.5
D	25	94.3±1.5	84.2±3.2	29.5±1.4	27.6 ± 3.1
p		> 0.05	<0.05	> 0.05	< 0.05

Most of the oral hypoglycemic drugs have high safety and long-lasting effect. They can promote the improvement of pancreatic islet B cell function and effectively reduce insulin resistance in the body, therefore slowing down or reversing the progress of diabetes[8]. The α- Glucosidase inhibitors, biguanides, sulfonylureas, insulin sensitizers and non-sulfonylureas are the common types of hypoglycemic drugs that are widely used in clinic. Patients treated with these drugs can obtain an ideal hypoglycemic effect. However, there are differences in the cost of different drugs. From the points of drug economic benefits and other factors, some drugs with high cost might not be suitable for patients to take for a long time[9,10].

According to the analysis of pharmacoeconomic principles, the lower the cost-effectiveness ratio, the lower the cost required in the same unit efficacy. Therefore, drugs with low cost-effectiveness ratio are more in line with the specific principles of drug selection. From the two aspects of Pharmacoeconomics and pharmacodynamics, the two drugs pioglitazone and Sitagliptin in the treatment of patients with type 2 diabetes are the optimal drugs. However, compared with pioglitazone, Sitagliptin has more significant benefits and belongs to a class of clinical therapeutic drugs with high economic and ideal efficacy. In this study, we found that compared with group A, C and D, the cost-effectiveness ratio of group B was low, indicating that the application of Sitagliptin can further reduce the cost.

At present, many studies have shown that sitagliptin has ideal hypoglycemic effect. However, diabetes has the characteristics that accompany other diseases and long-term progression. Therefore, during the evaluation of different treatment options, it is critical to investigate some long-term indicators, that can accurately reflect the overall therapeutic effect and economic cost. The pharmacoeconomic analysis of Sitagliptin abroad shows that compared with pioglitazone, sitagliptin has ideal cost-effectiveness. Our study found that compared with group A, C and D, the treatment effect of B group was relatively high, indicating that the treatment of diabetic patients with Sitagliptin during clinical treatment can effectively enhance the therapeutic effect, thereby promoting the improvement of the patient's condition and clinical symptoms. The potential reason might be that Sitagliptin not only controls the blood glucose level of patients in a stable state, but also promotes the improvement of insulin resistance in vivo. Studies have shown that Sitagliptin can reduce the levels of FPG and 2hPG in patients and can also improve β cell function and insulin sensitivity. In addition, the overall tolerance of patients to the drugs is relatively ideal and will not cause adverse events such as hypoglycemia[11]. Finally, Sitagliptin is a second-class hypoglycemic agent for the treatment of type 2 diabetes mellitus. Its advantage is that it does not cause other diseases such as cardiovascular and pancreatic diseases, nor significantly increase body weight and other adverse effects[12]. DPP 4 inhibitor drugs can further reduce the direct medical costs caused by diabetes diseases, while other additional costs caused by complications can also be significantly reduced[13]. In addition, compared with groups A, C and D, the incidence of adverse reactions in group B was relatively low, indicating that Sitagliptin does not cause a variety of serious adverse reactions. The possible reasons are: only when there are abnormal changes in the blood glucose index level in the body, Sitagliptin will play an ideal role, so as to further reduce a variety of adverse reactions such as hypoglycemia. In addition, the metabolic site of the drug is eliminated in the kidney, which will not have a great impact on some patients with abnormal renal function[14].

FPG can accurately reflect the most basic blood glucose level in the body during the time of sugar free load. HbA1c reveals the control of blood sugar level in the recent period, which can accurately assess the blood glucose level of patients with type 2 diabetes mellitus[15]. Our study found that there was no significant difference in the levels of FPG, 2hPG and HbAlc in the 4 groups before treatment. After treatment, compared with A, C and D groups, the levels of FPG, 2hPG and HbAlc in B group improved significantly, indicating that diabetic patients receiving Sitagliptin had an ideal effect, which could improve the blood glucose level of patients. The reason may be that Sitagliptin has relatively strong affinity and selectivity for DPP4, which can inhibit the hydrolysis of intestinal islet stimulating hormone in vivo. Thus, the level of active intestinal islet stimulating hormone can be further increased, insulin can be stimulated to release, and the release of blood glucose can be effectively inhibited. Through effective combination with DPP4, the level of active intestinal islet stimulating hormone in the body can be significantly increased, the drug action time can be prolonged, and the utilization of glucose by patients can be significantly increased, to effectively control blood glucose. At the same time, there was no significant difference in waist circumference and BMI in these 4 groups before treatment. After treatment, compared with group A, C and D, the waist circumference and BMI of B group were decreased, indicating that the application of Sitagliptin in diabetic diseases can play an ideal role in reducing the waist circumference and BMI effectively. This study was conducted in a single center of a local hospital which is the main limitation of this study.

Conclusions

From the findings of this study, we can conclude that the application of Sitagliptin in the treatment of patients with diabetes can effectively enhance the therapeutic effect. The cost- effectiveness is satisfactory and the blood glucose level of patients can be maintained at a stable state. Sitagliptin could be a good choice for the treatment of diabetes.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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