Pharmacoeconomic evaluation of glimepiride combined with other drugs in the treatment of diabetes

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Abstract: The goal of diabetic drug treatment is to stabilize the blood sugar for a long time to close to the normal level, to correct the metabolic disorder and eliminate the symptoms. At present, glimepiride has become commonly used drugs for the treatment of diabetes with obesity. Compared with metformin, acarbose and rosiglitazone, glimepiride has different mechanisms of drug action, clinical combination showed synergistic hypoglycemic effect, good clinical curative effect. So, we use three treatments to study as group A (glimepiride and metformin); group B (glimepiride and acarbose); Group C (glimepiride and rosiglitazone). From the analysis of drug economics, glimepiride and metformin scheme is better, has the lowest cost per unit cost effect. From the comparison of scheme is efficient, the best curative effect is rosiglitazone plus glimepiride, effective rate as 96.7%. At the same time, the drug can be rationally used to reduce the occurrence of some drug-induced diseases and adverse drug reactions.

Keywords: Glimepiride, blood sugar, pharmacoeconomics, antidiabetic drugs, treatment scheme.

INTRODUCTION

Diabetes is one of the most common disease in the world, has become the third largest after tumor, cardiovascular serious threat to human health and non communicable diseases (Altorki *et al.,* 2016). Because diabetes often do not have typical symptoms, therefore, in China there are about 70% of diabetic patients failed to receive timely diagnosis and treatment effect, causing complications. In all diabetes related complications (Rosenthal *et al.,* 2015; Bergmann *et al.,* 2016). The risk of major vascular and micro vascular complications is an important cause of death and disability in diabetic patients (Chen *et al.,* 2015). Diabetes drug treatment goal mainly is the long-term stabilization of blood sugar levels close to normal levels, correcting metabolic disorder, eliminate the symptoms, prevent or delay complications, maintain good health and learning, the ability to work, to protect children's growth and prolong life, reduce mortality and improve the quality of life of patients (Chen *et al.,* 2009; Cahill *et al.,* 2015). The use of oral hypoglycemic agents is often effective in patients with type 2 diabetes, which can still not reduce blood sugar by controlling their diet (Dindo *et al.,* 2004). Clinical hypoglycemic drugs are mainly used insulin and insulin analogues, prandial glucose regulator such as repaglinide, double muscle like two armor double muscle, a glucosidase inhibitors such as acarbose, insulin sensitizing agents such as rosiglitazone (Emir *et al.,* 2014).

The most commonly used medications for the treatment of type 2 diabetes are oral hypoglycemic agents. According to the patient's condition and indications, single drug treatment can be used. For patients taking a single antidiabetic drug with poor blood sugar control, two and more than two drugs can be used in combination (Ghoneum *et al.,* 2015; Inzucchi *et al.,* 2015). Based on the principles and methods of pharmacoeconomics, we draw up a reasonable and effective treatment plan in the process of clinical drug treatment, which can provide an objective basis for scientization of rational drug use and treatment decision-making (Balmadrid *et al.,* 2015; Gunaldi *et al.,* 2015). If you only consider the cost without considering the results or results instead of only considering the cost are not desirable, how to get the maximum treatment effect with the limited cost, the effect of relative cost produced in the treatment of the most reasonable, the best, the best security scheme, is the main purpose of pharmacoeconomics research (Kargulewicz *et al.,* 2016). At present, glimepiride has become a common drug for the treatment of diabetes and obesity (Hu, 2013; Jean *et al.*2017). The drug is a new generation of oral hypoglycemic agents of sulfonylureas and its mechanism may be related to the recovery of the first phase secretion of insulin and the strong external effect of the pancreas (Hou *et al.,* 2015). The difference between traditional sulfonphthalein and urea is that it has little increase in insulin level and strong pancreatic function. The clinical study showed that glimepiride is only equivalent to 50% of the amount of glibenclamide can obtain the same hypoglycemic effect, patients with BMI Gregory pulse treatment group beauty also drops obviously (Liu *et al.,* 2013; Lu, 2014).

Effect of glimepiride and two armor double muscle, acarbose, rosiglitazone three drugs, clinical combination showed synergistic hypoglycemic effect, good curative effect, pharmacoeconomic evaluation of these three types

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of therapy has not been reported (Li *et al.,* 2015). So, we use three treatments to study: Group A as glimepiride and metformin; Group B as glimepiride and acarbose; Group C as glimepiride and rosiglitazone. In comparison with clinical efficacy, cost-effectiveness analysis was used to evaluate pharmacoeconomics, so as to provide basis for selecting appropriate treatment plan for patients with type 2 diabetes.

MATERIALS AND METHODS

Case selection

We randomly selected a total of 174 cases of patients with type 2 diabetes mellitus that treated in Yidu Central Hospital of Weifang in the year 2016. Complete clinical data, there were no complications of diabetes, the average age as 54.1±4.6 years old, Mean fasting blood glucose 10.5mmol/L, mean hemoglobin content of 13.1%. The data used in drugs and doses were complete. The basic situation of the patients in each group was basically no difference. All patients were approved by Ethics Committee of our hospital and signed on the informed consent.

Case exclusion criteria: (1) Pregnant or lactating women; (2) patient with obvious liver and renal dysfunction and blood system disease; (3) Has received blood pressure drugs after treatment by systolic pressure >170mmHg or diastolic pressure >95mmHg; (4) Combined heart disease, cardiac insufficiency, unstable angina, EGG indication of left ventricular hypertrophy, or severe anemia; (5) People who took other hypoglycemic drugs except the oral hypoglycemic drugs of the sulfonated vein were added in the test during the trial; (6) use of insulin.

Drug delivery scheme and grouping

Group A: glimepiride + metformin, Glimepiride for 1-2 weeks, once a day, 1 pills each time; in 3-12 weeks, two times a day, 2 pills each time; metformin, in 1-2 weeks, once a day, 1 pills each time; in 3-12 weeks, two times a one day, 2 tablets. *Group B:* glimepiride and acarbose; Glimepiride for 1-2 weeks, once a day, 1 pills each time; in 3-12 weeks, two times a day, 2 pills each time; acarbose, 1-2 weeks, 2-3 times a day, 1 pills each time; in 3-12 weeks, 3 times a day, 2 pills each time. *Group C:* glimepiride and rosiglitazone; Glimepiride for 1-2 weeks, once a day, 1 pills each time; in 3-12 weeks, two times a day, 2 pills each time; rosiglitazone, once a day, 1 pills each time.

The selected patients before and after treatment were performed following examination each time blood glucose, glycosylated hemoglobin, blood lipid, urine protein, serum creatinine and urine before and after treatment. Pay close attention to the conditions of the patients were recorded adverse reactions, especially patients with hypoglycemia, nausea, vomiting, flatulence, borborygmus, abdominal pain, diarrhea and other gastrointestinal reactions, erythema, rash and urticaria and other allergic skin reactions occur, weight loss or weight gain, edema and headache, dizziness, tiredness, fatigue and other symptoms.

Analysis of cost effect

The cost of this study includes only direct medical costs, and the direct non medical costs, indirect costs and intangible costs are omitted. The specific steps of incremental analysis is the first alternative cost calculation according to the order from small to large cost and less than the benchmark scheme cost effect ratio, determine the economy again to calculate the incremental cost effect between the adjacent cost amount larger than the scheme and plan. If the incremental cost effectiveness ratio is less than or equal to the baseline cost effect ratio, it shows that the incremental effect of incremental cost is economical, so eliminating the sub optimal high cost scheme and retaining the lower cost plan.

STATISTICAL ANALYSIS

Using the cost-effectiveness analysis method of pharmacoeconomics, all data processing and statistical analysis are carried out by SPSS analysis software. The experimental data is represented in x±s, using single factor analysis and variance of sample mean values of q test for statistical analysis. $P<0.05$ has statistical significance.

RESULTS

General situation of patients

In this study, a total of 174 cases were extracted, including 55 cases in group A, 57 in group B and 62 in group C. The demographic and related data of the selected cases were shown in table 1. There was no significant difference in gender, age, weight and blood pressure between the three groups. There was no significant difference in fasting blood glucose and postprandial 2h between the three groups before administration.

Comparison of curative effect

In group A, the blood glucose level of four time points decreased significantly after 2 weeks of administration. After 4 weeks treatment, postprandial blood glucose showed a more significant decrease. After 8 weeks, fasting blood glucose showed a more significant decrease (table 2). In group B, after 2 weeks of administration, the blood sugar values of four time points were significantly decreased, and after 4 weeks of treatment, blood glucose decreased significantly. Fasting blood glucose was also gradually reduced with the time of treatment. See table 3 In group C, the blood sugar values of the four time points were significantly decreased after 2 weeks of administration, and the decrease of fasting blood glucose and postprandial blood sugar was more obvious after 4 weeks of treatment. See table 4. The effective rate of the three groups of treatment weeks (table 5).

Table 1: Basic situation comparison

Category	Group A	Group B	Group C
Sex (male / female)	24/31	25/32	29/33
Age	52.1±7.5	50.4±9.2	53.7±8.4
Weight (kg)	75.4±6.4	72.1±7.3	73.4±6.8
BMI(body Mass Index)	25.1±1.4	26.3±1.5	26.0±1.3
systolic pressure	127.3±9.4	129.1±9.7	130.2±10.2
diastolic pressure	77.4±7.5	75.6±7.8	78.2±8.1
Fasting blood glucose	10.2±1.5	10.3±1.4	10.7±1.1
Postprandial 2h	14.5±1.8	14.2±1.3	14.6±1.8
HBAlc	11.5±1.2	12.3±1.7	11.9±1.5

Table 2: Effect of group A therapy on blood glucose in patients

Time	Fasting blood glucose	Postprandial 2h	HBAlc
Pre administration	10.2±1.5	14.5±1.8	11.5±1.2
2 weeks	9.6±1.1	12.4±1.3	10.3±1.1
4 weeks	8.5±1.0	10.5±0.8	9.4±0.9
8 weeks	8.2±0.8	10.1±0.6	8..5±0.8
12 weeks	7.8±0.5	9.8±0.4	7.4±0.6

Table 3: Effect of group B therapy on blood glucose in patients

Time	Fasting blood glucose	Postprandial 2h	HBAlc
Pre administration	10.3±1.4	14.2±1.3	12.3±1.7
2 weeks	9.9±1.2	12.6±1.0	10.9±1.5
4 weeks	8.8±0.9	11.4±0.8	9.4±1.2
8 weeks	8.1±0.7	10.5±0.7	8.5±1.1
12 weeks	7.5±0.5	10.2±0.4	7.1±0.8

Table 4: Effect of group C therapy on blood glucose in patients

Time	Fasting blood glucose	Postprandial 2h	HBAlc
Pre administration	10.7±1.1	14.6±1.8	11.9±1.5
2 weeks	9.5±0.8	11.8±1.3	10.1±1.2
4 weeks	8.2±0.6	10.2±0.9	9.0±0.9
8 weeks	7.3±0.5	8.8±0.7	7.8±0.7
12 weeks	6.6±0.5	8.4±0.5	6.4±0.5

Table 5: Efficiency comparison of scheme

Group	Cases	Effective case	Effective rate
A group	55	46	83.6
B group	57	48	84.2
C group	62	60	96.7

Table 6: The cost effect of the treatment scheme

Group	Cost	Average blood sugar decline rate	C/E	ΔC/ΔE
A group	455.6	27.1	16.48	--
B group	762.1	30.5	24.92	51.8
C group	1450.2	38.2	38.15	132.3

An analysis of cost effect

In pharmacoeconomics research, when there is no significant difference in the efficacy of different drug regimens, the cost-effectiveness analysis method should be used to compare the cost-effectiveness ratio (C/E) of different dosing regimens. In this study, the lowest cost solution as a reference for the incremental cost effectiveness analysis (ΔC/ΔE). The purpose of the cost-effectiveness analysis is to balance the cost and effect, to find an optimal combination between the two and to represent the cost of the unit effect. The C/E value of the A, B and C group has significant difference, and the A group is the least, that is, the cost of the scheme A is the lowest in the unit effect. Simply from the pharmacoeconomics analysis, the A scheme is the highest titer ratio.

DISCUSSION

Pharmacoeconomics is in recent years the rapid development of western economics and an interdisciplinary branch of pharmacy, research by means of modern economics, multidisciplinary research and epidemiology and biostatistics (Mellotte *et al.,* 2015). Comprehensive analysis of drug treatment alternatives includes non drug treatment costs, benefits and results evaluation the economic value of difference. While paying attention to the cost of drug treatment, it also pays attention to the output and results of drug treatment (Shim *et al.,* 2010; Qin *et al.,* 2015). In pharmacoeconomic analysis, cost-benefit analysis often ignores the evaluation of the efficacy itself, so it is seldom used in clinical research, and is often used in the evaluation of drugs by government agencies (Tokioka *et al.,* 2012). The purpose of cost-effectiveness analysis is to find the lowest cost treatment plan to achieve a therapeutic effect. The cost effectiveness ratio (C/E) is the organic integration of cost and effect two aspects. Cost effectiveness analysis is one of the most widely used evaluation methods in the evaluation of pharmacoeconomics.

The goal of diabetes drug treatment is to stabilize blood sugar near normal level for a long time, correct metabolic disorders, eliminate symptoms, prevent or delay the occurrence of complications, and improve the quality of life of patients (Tsiaras *et al.,* 2016). The use of oral hypoglycemic drugs is often effective in patients with diabetes mellitus after diet control and exercise therapy, which are still not ideal for blood glucose control. Oral hypoglycemic drugs are commonly used in treatment type diabetes, which can be treated by single drug or combined use. Single drug treatment can be selected: (1)Promoting insulin secretion drugs such as glibenclamide, glipizide, gliclazide, glimepiride, mainly used in newly diagnosed non obese patients with diet and exercise, the treatment effect is not ideal for patients; (2)Double arcing drugs, such as two a double muscle, suitable for patients with no apparent emaciation and patients with dyslipidemia, hypertension, or hyperinsulinemia; (3) Insulin sensitizer, thiazolidine two ketones, such as rosiglitazone and specific glipizone, are mainly suitable for obesity and insulin resistance. For patients taking a single antidiabetic drug with poor blood sugar control, two and more than two drugs can be used in combination.

Glimepiride is a new generation of iodine pulse oral anti diabetic drugs, with less stimulation of insulin secretion, pancreatic function, strong quick effect, long acting period, hypoglycemia and weight increased less (Zhu *et al.,* 2015). Combined with glimepiride and post receptor isolated rapidly, rarely cause hypoglycemia and has strong hypoglycemic effect of pancreatic islets, 1 times daily dosing regimens to improve patient compliance. Metformin sustained-release tablets release slowly, the plasma concentration is stable, prolong the duration of action, reduce the dosage and times, increase the compliance of patients, and significantly reduce the irritation of gastrointestinal tract. Gregory and beauty vein after combination can further improve the therapeutic effect of acarbose (Yoshio *et al.,* 2013). Not only can be used alone, can also be used in combination with other types of oral hypoglycemic agents and insulin. Because of its high safety factor, it is more beneficial for patients who are prone to nocturnal hypoglycemia, especially for elderly patients. Rosiglitazone can increase glucose uptake in peripheral tissues, significantly lower blood glucose, conducive to blood fatty acid, cholesterol and triglyceride three tended to be normal, can also cause the body fat redistribution, islet amyloid, and has anti-inflammatory effect, can help to protect the islet B cell function (Xuan, 2015). The mechanism of pulse and Gregory two armor double muscle, acarbose, rosiglitazone, clinical combination showed synergistic hypoglycemic effect, good clinical curative effect. In this experiment, glipizide combined with the other three kinds of therapeutic diabetic patients respectively. After 12 weeks of treatment, both fasting and postprandial blood glucose were significantly decreased. The extra hypoglycemic effect of GLM can be seen in enhancing the sensitivity of the surrounding tissues to insulin and stimulating the secretion of endogenous insulin, which has a unique way to save insulin.

CONCLUSION

Glimepiride has a strong external effect, combined with metformin can significantly increase the sensitivity of the peripheral tissue to insulin and significantly improve postprandial hyperglycemia. Three kinds of treatment can control the blood glucose in the ideal range, from the analysis of drug economics, glimepiride plus metformin scheme is better, the lowest cost unit cost effect; comparison from the solution efficiency, rosiglitazone plus glimepiride has the best curative effect. In conclusion,

the emphasis on the economics of medication is mainly to emphasize that the cost of unit effect should be as low as possible. At the same time, patients are allowed to spend as little as possible on the cost of drugs, in exchange for the greatest possible therapeutic benefits. At the same time, we should make rational use of drugs and reduce the occurrence of some drug-induced diseases and adverse drug reactions.

ACKNOWLEDGEMENTS

The authors would like to thank Yidu Central Hospital of Weifang for providing the experimental equipment.

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