Comparison of the influence of oral antidiabetic drug and combined with basal insulin treatment on diabetic control and micro-inflammatory state in type 2 diabetes mellitus patients

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ABSTRACT

Objective: To investigate the influence of oral antidiabetic drug and combined with basal insulin treatment on diabetic control and micro-inflammatory state in type 2 diabetes mellitus patients. Methods: From May 2014 to June 2015, 128 cases of Type 2 diabetes mellitus were recruited and divided randomly into two groups as observation group and control group. The observation group was given metformin (Glucophage, 0.25 tid) plus basal insulin (glargine) treatment, while the control group was given metformin (Glucophage, initial dose of 0.25 tid; the largest total dose of 2 g) plus other non-euglycemic OADs necessarily for 6 months to adjust dose and control blood glucose at target. The diabetic control indexes, islet function and micro-inflammatory factors were detected and analyzed. Results: After 6 months of medication, the observation group showed significantly lower level of FPG, and HbA1cthan the control group. While AUC_c-p, HOMA-β and HOMA-IR of the observation group showed significant difference compared to that of the control group after treatment. Also the micro-inflammatory indexes including hs-CRP, IGF-1, IL-6 and TNF-α of the observation group after treatment were significantly lower than the control group. Conclusions: Type 2 diabetes given metformin plus glargine not only could control and steady blood glucose, but also significant decrease the micro-inflammation state.

1. Introduction

In recent years, basal insulin treatment is taken more seriously in the type 2 diabetes mellitus. Basal insulin treatment is taken as a lifestyle combined oral antidiabetic drugs (OADs) according to American Diabetes Association (ADA) T2DM treatment consensus. After 3 months of treatment, the blood glucose below goal is preferred to the combined method. < Chinese type 2 diabetes prevention guide, 2010 edition > also suggests that the patients with poor diabetic control in the OADS treatment should be initiated basal insulin treatment as soon as possible. The efficacy and reliability of OADs combined basal insulin treatment has already been verified for adult patients with T2DM in many large clinical studies[1,2]. The study mainly investigates the influence difference of OADs and combined with basal insulin treatment on diabetic control and micro-inflammatory state in type 2 diabetes mellitus patients.

2. Materials and methods

2.1. Research object

From May 2014 to June 2015, 128 cases of type 2 diabetes mellitus were recruited approving by the ethics committee of our hospital. Criteria for the cases[3]: the patients with diabetes mellitus were diagnosed in accordance with < Chinese type 2 diabetes prevention guide, 2011 edition > and were diagnosed as T2DM according to classification criterion; the objects sought medical advice for the first time; the patients had no oral any OADs or...
injecting insulin in the past and the HbA1c was lower than 7.0%.
Exclusion criteria included the cases: co-infectious diseases, primary
hypertension, malignant tumor, hematological system diseases,
thyroid gland dysfunction, heart, brain, liver and kidney etc. organ
chronic underlying disease, diabetes mellitus acute complications
and gestational diabetes. Total of 128 patients were recruited, which
included 68 male cases and 60 female cases; the age range was 38-70
years old and mean age was (58.2±9.7) year old; body mass indexes
were 22.3-30.5 kg/m² and its mean values were (26.2±9.7) kg/m².
The recruited patients were divided into two groups as observation
group and control group using random number table. The general
data such as age, gender, the course of diabetes mellitus OADs treatment
and body mass index (BMI) between two groups had comparability
(P>0.05).

2.2. Research methods

2.2.1. Treatment methods
All the recruited research objects were performed a complete
routine inspection to exclude other possible existing diseases. The
objects were also performed diabetes education, and guided to
control diet and to do exercise training. The observation group was
given metformin enteric coat tablets (Glucophage, specification:
0.25; 0.25, tid). Insulin glargine was injected under the skin of
abdomen before breakfast (once-daily) and the doses of insulin
glarginne were adjusted individually. The control group was given
metformin enteric coat tablets (Glucophage, specification: 0.25;
the largest total dose of 2 g) plus other non-euglycemic OADs
necessarily. The blood glucose levels of two groups were detected.
After 3 days, the antidiabetic drug doses were adjusted according to
the level of blood glucose and the patients were treated continuously
after controlling blood glucose at an ideal level. The blood glucose
indexes, pancreas islet function and micro-inflammation status
after controlling blood glucose at an ideal level. The blood glucose
indexes, pancreas islet function and micro-inflammation status
indicators before and after treatment were compared for 6 months.

2.2.2. Blood glucose control indexes and detection method[4]
Fasting plasma glucose (FPG), 2 h plasma glucose (2hPG),
glycosylated hemoglobin A1C (HbA1c) fast plasma C-peptide
(PC-F), fasting insulin (FINS), postprandial C-peptide and 1, 2, 3, 4,
insulin C-peptide(C-P60, C-P120, C-P180) after a standard steamed bread
meal before and after treatment were observed. C peptide area under
the curve (AUC C-peptide) = 0.5 × (PC-F+PC-P180)+C-P120+C-P180 . Insulin
resistance index (HOMA-IR) was calculated by the level of insulin
and fasting plasma glucose and the detailed method was HOMA-
IR=20 FINS/FINS/FINS/FINS (22.5), BMI=body mass/kg / height² (m²). Pancreas
islet function was evaluated by the formula: HOMA-IR = 20 Fins/
(FPG-3.5).

2.2.3. Micro-inflammation status indicators and detection method
After standing 1 h, 6 mL venous blood was extracted on an
empty stomach before and after treatment respectively and 1 000
g venous blood was separated for 5 min to obtain serum. After
marking, the serum was stored in low temperature refrigerator
(-70 °C). IGF-1 (insulin-like growth factor-1), IL-6 and TNF-α
of a batch were detected by ELISA (Introvigen Company). High
sensitivity C-reactive protein (hs-CRP) was measured by using
immunoturbidimetry.

2.3. Statistical analysis
All data obtained were analyzed and processed by using IBM
SPSS20.0 and measurement data were expressed as Mean ± SD.
Mean values between groups were compared by using t-test and
χ² was used to test enumeration data. P<0.05 showed significant
difference.

3. Results

3.1. Comparison of diabetic control condition of type 2
diabetes mellitus OADs treatment and combined with basal
insulin treatment
The levels of FPG, 2hPG and HbA1c of observation group and
control group before and after treatment were compared and showed
significant difference (P<0.05). BMI had no significant difference
(P>0.05), and HbA1c (t=8.198, P=0.015) of two groups after
treatment were compared and showed significant difference (P<0.05)
respectively (Table 1).

3.2. Comparison of pancreas islet function of type 2 diabetes
mellitus OADs treatment and combined with basal insulin
treatment
Observation group combined with basal insulin before and after
treatment were compared and the differences of FC-P (t=1.236,
P=0.007), AUC-c-p (t=12.942, P=0.006), HOMA-β (t=11.342,
P=0.008) and HOMA-IR (t=10.048, P=0.010) were significant
(P<0.05), and AUC-c-p (t=7.589, P=0.012), HOMA-β (t=6.943,
P=0.011) and HOMA-IR (t=8.076, P=0.015) of control group after
treatment showed significant difference (P<0.05). FC-P (t=8.427,
P=0.010), AUC-c-p (t=9.134, P=0.013), HOMA-β (t=8.805,
P=0.011) and HOMA-IR (t=9.361, P=0.012) had significant
difference (P<0.05), compared with control group before treatment
(Table 2).

3.3. Comparison of micro-inflammation level of type 2
diabetes mellitus OADs treatment and combined with basal
insulin treatment
hs-CRP (t=13.532, P=0.005), IGF-1 (t=14.234, P=0.003), IL-6
(t=10.147, P=0.008), TNF-α (t=11.348, P=0.009) had significant
difference (P<0.05), compared with observation group combined
with basal insulin before and after treatment. hs-CRP (t=7.542,
P=0.015), IGF-1 (t=9.654, P=0.011), IL-6 (t=7.759, P=0.013), TNF-α
(t=6.935, P=0.017) had significant difference (P<0.05), compared
with control group after treatment. hs-CRP (t=9.65, P=0.012), IGF-1
(t=11.238, P=0.009), IL-6 (t=8.855, P=0.014), TNF-α (t=9.548,
P=0.016) had significant difference (P<0.05), compared with control
group before and after treatment (Table 3).
Comparison of micro-inflammation level of type 2 diabetes mellitus OADs treatment and combined with basal insulin treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>11.3±5.4</td>
<td>17.9±7.3</td>
</tr>
<tr>
<td>Control</td>
<td>11.5±4.7</td>
<td>17.8±8.1</td>
</tr>
</tbody>
</table>

4. Discussion

The study showed that unstable blood glucose is the risk factors of chronic vessel complication in type 2 diabetes mellitus patients and the stable blood glucose has become the new goal of blood glucose management in the course of diabetes mellitus treatment[5]. Some scholars recommend that preliminary type 2 diabetes mellitus patients use the basal insulin treatment and they believed that this treatment can quickly and effectively reduce blood glucose, relieve the damage of high blood glucose toxicity and remit the glucose toxicity of pancreas islet B cell from high glucose to prevent or postpone diabetes mellitus and its complications development[6]. Currently, basal insulin is mainly long-acting insulin analogues and isophand insulin. However, traditional isophand insulin cannot simulate the physiological basis of insulin secretion better and, is difficult to control FPG in a good way. The glucose fluctuation is also bigger[7]. Insulin glargine is the common use long-acting insulin analogues at presently, and it can simulate the secretion of basal insulin in human body and provide unlimited basal insulin for 24 h[8]. Clinical research showed that if the effect of insulin glargine can maintain for 24 h, it can produce a hypoglycemic effect and reduce hypoglycemia incident and it is commonly recommended to diabetes mellitus patients who cannot control the blood glucose in a good way for long time[9]. In this study, preliminary type 2 diabetes mellitus patients were given metformin combined with basal insulin (insulin glargine) treatment and the results showed that it can not only control blood glucose up to standard, but also control the level of FPG and HbA1c superior to the OADs treatment group. Moreover, after receiving metformin combined with basal insulin, the ranges of patients' AUCc-\( \beta \) and HOMA-IR decreased are superior to the control group. Several studies show that the use of exogenous insulin can not only eliminate high glucose toxicity, but also can recover pancreas islet B cell function to achieve blood glucose stability with no drug treatment for longer time[10]. Metformin can reduce patients' hyperinsulinemia, decrease the proinsulin secreted from pancreas islet B cell and relieve the burden of pancreas islet B cell by reducing insulin resistance[11]. The results of this study also verify that preliminary type 2 diabetes mellitus patients combined with basal insulin treatment can improve pancreas islet function and reduce insulin resistance.

In this study, we further detect and compare hs-CRP, IGF, IL-6 and TNF-\( \alpha \) etc. micro inflammation status indicators of two group patients, which showed that combined with basal insulin treatment can obtain inflammatory indicators with lower level. IGF-1 possesses a similar structure of insulin and physiological function, which not only can act to insulin metabolism, but also can reduce hypoglycemia incident and relieve hypoglycemia incident and is commonly recommended to diabetes mellitus patients. IGF-1 can reduce patients' hyperinsulinemia, decrease the proinsulin secreted from pancreas islet B cell and relieve the burden of pancreas islet B cell by reducing insulin resistance. IGF-1 can mediate the histological characteristics of diabetic nephropathy, which combine with intercapillary cells of glomerulus and stimulate

Table 1

Comparison of diabetic control condition of type 2 diabetes mellitus OADs treatment and combined with basal insulin treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>FPG (mmol/L)</th>
<th>2hPG (mmol/L)</th>
<th>BMI (kg/m²)</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>11.3±5.4</td>
<td>17.9±7.3</td>
<td>25.16±3.36</td>
<td>8.19±1.31</td>
</tr>
<tr>
<td>Control</td>
<td>11.5±4.7</td>
<td>17.8±8.1</td>
<td>25.57±3.74</td>
<td>8.24±1.23</td>
</tr>
</tbody>
</table>

*: \( P<0.05 \), compared with after treatment and before treatment within groups; **: \( P<0.05 \), compared with observation group after treatment and control group after treatment.

Table 2

Comparison of the influence of pancreas islet function of type 2 diabetes mellitus OADs treatment and combined with basal insulin treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>FC-P (pg/L)</th>
<th>AUCCc-( \beta ) (pg/L)</th>
<th>HOMA-( \beta )</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>1.63±0.56</td>
<td>8.92±2.31</td>
<td>32.35±8.31</td>
<td>4.58±1.16</td>
</tr>
<tr>
<td>Control</td>
<td>1.61±0.53</td>
<td>8.85±2.73</td>
<td>31.84±9.47</td>
<td>4.47±1.28</td>
</tr>
</tbody>
</table>

*: \( P<0.05 \), compared with after treatment and before treatment within groups; **: \( P<0.05 \), compared with observation group after treatment and control group after treatment.

Table 3

Comparison of micro-inflammation level of type 2 diabetes mellitus OADs treatment and combined with basal insulin treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>hs-CRP (ng/L)</th>
<th>IGF-1 (μg/L)</th>
<th>IL-6 (ng/L)</th>
<th>TNF-( \alpha ) (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>8.32±3.69</td>
<td>262.12±37.32</td>
<td>41.38±10.24</td>
<td>44.12±9.56</td>
</tr>
<tr>
<td>Control</td>
<td>8.53±3.72</td>
<td>258.63±34.52</td>
<td>42.34±11.15</td>
<td>45.78±10.45</td>
</tr>
</tbody>
</table>

*: \( P<0.05 \), compared with after treatment and before treatment within groups; **: \( P<0.05 \), compared with observation group after treatment and control group after treatment.
its proliferation can cause the enlargement and blood flow volume augment of kidney and the increase of glomerular filtration rate as well as can accelerate the development of diabetic nephropathy[13]. Macrophage inflammatory cytokines (TNF$\alpha$ and IL-6) can regulate and control the expression of resistin of adipose cell. TNF$\alpha$ and IL-6 of human monocytes can facilitate the expression of resistin of cells and mediate the form of peripheral insulin resistance. TNF$\alpha$ and IL-6 are the main medium of inflammatory response, which can activate the NF-κ B that regulates related gene expression in the inflammatory process, stimulate the secretion of inflammatory mediator of endothelial cells and induce hs-CRP expression of hepatic cell[14]. The results of this study showed that metformin plus basal insulin can effectively improve the micro-inflammatory state of diabetes mellitus patients and possible can contribute to prevent chronic complication.

In conclusion, type 2 diabetes given metformin plus glargine not only could control and steady blood glucose, but also significant decrease the micro-inflammation state and possible can contribute to prevent chronic complication.

Reference


