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Effect of insulin combined alendronate sodium on bone mineral density and levels of serum BAP, TRAP−5b and BGP in aged patients with type 2 diabetes mellitus with osteoporosis

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ABSTRACT

Objective: To explore the effect of insulin combined alendronate sodium on bone mineral density and levels of serum BAP, TRAP-5b and BGP in aged patients with type 2 diabetes mellitus with osteoporosis. **Methods:** A total of 136 patients with type 2 diabetes mellitus with osteoporosis in January 2014 to January 2016 in our hospital for the treatment were selected, and randomly divided into 4 groups, each of 40 cases. Caltrate D was given as a basic treatment to all the patients, and the control group was given the treatment of insulin, and the metformin group was given the treatment of metformin, and the combination group was given the treatment of metformin combined alendronate, and the experiment group was given the treatment of insulin combined alendronate. BMD of the femoral neck and the serum levels of BAP, TRAP-5b and BGP were detected and recorded before the treatment and after one year's treatment. **Results:** On index of bone mineral density, the control group and the metformin group showed no significant differences; the combination group was slightly improved, but showed no statistical significance; After the treatment, the bone mineral density of the experiment was significantly improved. On index of bone turnover, the levels of serum BAP and BGP all had been improved and the level of TRAP-5b all was reduced then before the treatment in the control group, the combination group and the experiment group, but only the experiment group showed significant differences; On index of bone turnover, the experiment group were better than other groups, the differences were statistical significant. **Conclusions:** It has greater clinical curative effect that insulin combined alendronate sodium in the treatment of aged patients with type 2 diabetes mellitus with osteoporosis, it can effectively balance the metabolism of bone, safe and reliable, and it is worthy of application.

1. Introduction

Diabetic osteoporosis (DOP) is a kind of systemic metabolic bone disease caused by diabetes complications which make bone mineral density (BMD) reduce, bone strength weaken and bone microstructure change, It is also a kind of chronic complication of diabetes[1−3]. With the modern lifestyle changes and the serious aging population structure, the incidence of diabetes increased year by year, and as its complications, the incidence of diabetes osteoporosis also increases. The main reason is a lack of insulin in diabetic patients, causing metabolic disorders of sugar, protein and fat, then causing metabolic disorders of calcium, phosphorus, magnesium, reducing the bone density, damaging the bone tissue microstructure, and therefore easily leading to fractures and other diseases[4]. Alendronate applies to men with osteoporosis or postmenopausal women. This study combined with insulin and alendronate, by observing bone turnover markers of the patients to explore the clinical efficacy of the two drugs used in combination, so as to provide a basis of guiding clinical practice. Now the details are reported below.

2. Materials and methods

2.1. General information

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A total of 136 patients with DOP in our hospital for the treatment from January 2014 to January 2016 were selected, with 71 male patients, 65 female patients. Ages were from 68 to 88 years old. They were randomly divided into 4 groups, respectively 34 cases. In the control group there were 17 male patients, 17 female patients, aged 68 to 82 years old; In the metformin group, there were 18 male patients, 16 female patients, aged 69 to 88 years old; In the combination group there were 19 male patients and 15 female patients, aged 70 to 84 years old; In the experiment group there were 17 male patients, 17 female patients, aged 69 to 87 years old. There was no significant difference in basic information, age, gender, weight and so on of two groups' patients (P>0.05).

2.2. Inclusion criteria

All patients met the criteria: (1) Diagnostic criteria for diabetes was established by World Health Organization in 1999[5], fasting blood glucose 7.0 mmol/L; glucose tolerance test glucose 2 h 11.1 mmol/L. (2) Osteoporosis diagnostic criteria made by the World Health Organization[6], is that bone mineral density was lower with 2.5 standard deviations in the peak bone of the same gender the same race and the same age (T -2.5). (3) Glucocorticoids were not used within six months, bone metabolism of drugs had been unused for over a year, naturally menopausal women had spent over five years. (4) excluding the diseases can cause osteoporosis except diabetes: Exclude adrenal, thyroid, parathyroid, gonads, pituitary and primary renal disease, and exclude lumbar disc herniation, bone metastasis and bone ankylosing spondylitis and other diseases that affect bone metabolism[7].

2.3. Treatment methods

All patients equally took the same amount of Caltrate D 600 mg/d as a basis drug. The patients of the control group were treated with subcutaneous injection of ultrashort-acting insulin Biasp30 (Novo Nordisk (China) Pharmaceutical Co., Ltd., J20100037). Consumption was selected according to the actual needs of the patients with 0.5-1.0 units per kilogram of body weight for treatment once a day; The patients of the metformin group were treated with oral metformin hydrochloride tablets (Sandoz (China) pharmaceutical Co., Ltd., H20013054). At first the amount was 0.25 g/times, 2-3 times a day, gradually increasing the amount of 1-1.5 g/d at last, no more than 2 g based on the actual effect. In order to achieve good effect, each medication with a full glass of water to service, the patients could not lie down and eat anything within 30 min after taking; The patients of combination group were treated with metformin combined with alendronate , taking 70 mg alendronate tablets once a week (Yunnan Maxyee Pharmaceutical Co., H20073959), in combination with metformin hydrochloride tablets; The patients of experiment group were treated with insulin combined alendronate, daily subcutaneous injection of right amount of Biasp30, taking 70 mg alendronate tablets once a week. BMD of the femoral neck and the serum levels of bone-specific alkaline phosphatase (BAP), tartrate-resistant acid phosphatase-5b (TRAP-5b) and BGP of all patients were detected and recorded before treatment and after one year′s treatment.

2.4. Therapeutic effect evaluation and detection index

Venous blood of all fasting patients in the morning were collected, injected into anticoagulant tube and centrifuged at 3 000 r/min for 15 min. Then the upper layer of the serum was separated and placed into refrigerator at -70 ℃ stored. Enzyme-linked immunosorbent assay produced by Linco co., LTD.was used to test serum BAP, TRAP-5b and BGP levels.

Bone mineral density of all patients were detected before and after a year's treatment, DPX-LBMD dual-energy X-ray bone densometer produced by LUNAR was used to determinate the femoral neck bone mineral density.

2.5. Statistical method

SPSS 19.0 statistical software was used, measurement data were expressed as mean ± standard deviation. t test and χ^2 test were used to compare measurement data and count data. Their differences were statistically significant at P<0.05.

3 Results

3.1. Changes of bone mineral density

The BMD and bone turnover markers of four groups′ patients were not significantly different before treatment (P>0.05); After treatment the patients of the control group and metformin group showed no significant difference in bone mineral density indicators (P>0.05); The combination group was improved slightly, but the difference was not significant (P>0.05); BMD of the experiment group was upgraded significantly after treatment (P<0.05) (Table 1).

3.2. Changes of bone turnover markers

Serum BAP and BGP levels of the control group, the combination group and the experimental group were improved before treatment. But only in the experiment group it was significantly different (P<0.05). Compared the experiment group to other groups, bone turnover markers were significantly better than other groups after treatment (P<0.05) (Table 2).

4. Discussion

Diabetic osteoporosis is mainly due to the relative lack of insulin of the patients leading to the imbalance between bone augmentation and bone resorption. Bone augmentation decreased, but bone resorption remained increasing at the normal rate, therefore causing bone metabolic imbalance, decreasing bone strength and increasing Brittleness. Impacts of diabetes on bone metabolism are multifaceted, high calcium, high blood sugar, the increase of advanced glycation end products, inflammation, the decline of IGF-1 and other factors can affect the normal bone metabolism[8–10]. High blood sugar can cause increase of osteoblast blocked and osteoclast bone resorption, resulting in a reduce to bone augmentation. There are also studies showing that bone marrow fat accumulation and osteoblasts pimelosis also lead to reduced bone mass and osteoporosis[11]. While high blood sugar can lead to the accumulation of advanced glycation end products in collagen, leading to changes in the physical properties of the collagen, expression of osteoblastic phenotype hindered and increased bone resorption, eventually leading to decreased bone strength[12].

TRAP-5b is a good indicator to measure bone resorption and osteoclast activity, produced from osteoclasts, being a specific and highly sensitive indicator of bone metabolic reactions. The role of BAP and osteocalcin (BGP) is opposite to TRAP-5b, they are index of a group of highly specific reaction of bone formation and osteoblast activity[13]. As one of the synthetic hormone, insulin not only involved in the metabolism of sugar, protein and fat, also associated with the metabolism of calcium, phosphorus, magnesium and other minerals. More importantly, it is the only hormone to

Table 1

Changes on BMD before and after treatment (g/cm^2).

Time (month)	Control group	Metformin group	Combination group	Experiment group
0	0.697±0.104	0.676±0.122	0.695±0.110	0.689±0.114
12	0.701±0.117	0.675±0.125	0.702±0.117	0.789±0.238$^{*\#}$

Ps: Compared before treatment, $^{*}P$<0.05; Compared with other groups after treatment, $^{\#}P$<0.05.

Table 2

Changes serum BAP, TRAP-5and BGP levels before and after treatment.

Groups	Time (month)	BMD (g/cm^2)	BAP (μg/L)	TRAP-5b (ng/mL)	BGP (U/L)
Control group	0	0.697±0.104	7.501±3.211	3.327±1.153	6.209±2.211
	12	0.701±0.117	7.508±3.212	3.321±1.141	6.218±2.212
Metformin group	0	0.676±0.122	7.497±3.276	3.298±1.164	6.214±2.189
	12	0.675±0.125	7.421±3.280	3.321±1.187	6.203±2.176
Combination group	0	0.695±0.110	7.501±3.301	3.320±1.159	6.243±2.201
	12	0.702±0.117	7.505±3.302	3.317±1.157	6.251±2.195
Experiment group	0	0.689±0.114	7.502±3.298	3.324±1.158	6.241±2.208
	12	0.789±0.238$^{*\#}$	9.367±3.257$^{*\#}$	2.467±1.208$^{*\#}$	7.721±2.317$^{*\#}$

Ps: Compared before treatment, $^{*}P$<0.05; Compared with other groups after treatment, $^{\#}P$<0.05.

lower blood sugar in the body, increasing bone amount and avoiding bone loss. Existing studies know[14,15], bisphosphonate drugs can induce osteoblast secretion inhibitor, inhibiting bone resorption signal, which can weaken the strength of bone turnover, reduce bone resorption, and therefore commonly used in clinical hyperthyroidism treatmeat. This study showed that the bone density had no significant difference in the control group and metformin group. It improved slightly in the combination group, but the difference was not significant. BMD significantly improved after treatment in the experiment group. And in the bone turnover markers, clinical effect of insulin combined with alendronate for diabetes osteoporosis was significant. This showed that metformin can indirectly protect the bone tissue and, not just unilaterally supple calcium, control blood sugar and increase bone density for the treatment of diabetes osteoporosis. Apart from other reasons caused by diabetes, elderly patients physiological decline in renal function, primary osteoporosis can also lead to osteoporosis[16]. Diabetes osteoporosis mainly occurs in the elderly population, with ages increasing, decline of islet function, bone cells secrete osteocalcin blocked, bone turnover slowing. Therefore in the actual clinical treatment relevant treatment programs should be made based on individual circumstances[17–20]. In general, insulin is the preferred on clinical application for the treatment of diabetic patients with osteoporosis, the use of insulin balance in bone metabolism coming before hypoglycemic drugs.

In summary, It has great clinical curative effect that insulin combined alendronate sodium in the treatment for diabetes osteoporosis, it can effectively balance the metabolism of bone, safe and reliable, and it is worthy of application.

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