



## Original article

# Effect of cervus and cucumis polypeptide combined with zoledronic acid on bone metabolic biochemical markers in glucocorticoids – Induced osteoporosis patients

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## ABSTRACT

**Objective:** To investigate the effect of cervus and cucumis polypeptide combined with zoledronic acid on bone metabolic biochemical markers in glucocorticoids - induced osteoporosis patients.

**Methods:** A total of 100 patients with glucocorticoids - induced osteoporosis admitted to our hospital from January 2015 to June 2017 were enrolled in this study. Patients were divided into observation group and control group by random number table method, 50 cases in each group. Patients in the observation group were treated with deer melon polypeptide in combination with zoledronic acid, and patients in the control group were treated with zoledronic acid alone. The patients in both groups were treated for 2 months. The changes of bone mineral density (BMD) and biochemical markers of bone metabolism in lumbar vertebrae L1-4, left femoral neck and large trochanter were analyzed before and after treatment.

**Results:** The pre- BMD at lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter had no statistic difference ( $P > 0.05$ ), the BMD at each sites improved after treatment, and the difference were statistical before and after treatment ( $P < 0.05$ ). BMD at above sites of two groups after treatment had statistical difference ( $P < 0.05$ ), and the BMD at lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter in the observation group was higher than that of the control group. There were no significant differences in PTH, 25-(OH) D<sub>3</sub>, TRACP,  $\beta$ -CTX and BGP levels between the two groups before treatment ( $P > 0.05$ ). The levels of 25-(OH)D<sub>3</sub>, TRACP,  $\beta$ -CTX and BGP in the two groups were significantly improved after treatment ( $P < 0.05$ ), and the levels of PTH, TRACP and  $\beta$ -CTX in the observation group were significantly lower than those in the control group. The levels of 25-(OH) D<sub>3</sub> and BGP were significantly higher than those of the control group ( $P < 0.05$ ).

**Conclusion:** The cervus and cucumis polypeptide combined with zoledronic acid can improve the BMD at lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter, and ameliorate the bone metabolic biochemical markers for patients with glucocorticoids - induced osteoporosis.

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Osteoporosis is mainly caused by decreased bone mass and bone structure degradation. Its clinical manifestations are low back pain, cramps, etc., easy to fracture, and difficult to heal. Osteoporosis occurs mostly in the elderly population (Cosman et al., 2016) and is referred to by the WHO as an “uninfected epidemic”.

According to epidemiological statistics in China, the number of patients in China in 2016 exceeded 200 million, and it is expected to reach 230 million in 2018 (An et al., 2016). Osteoporosis is mainly featured in reduction of bone mass and degradation of bone structure. Its clinical expressions include waist and back pain, spasm and so on. It is easily to cause fractures, which cannot be healed easily. Osteoporosis mostly occurs in senile population (Cosman et al., 2016) and has been called a “silent epidemic” by WHO. According to Chinese epidemiologic statistics, the patients in China were over 200 million in 2016 and have been predicted to reach 230 million in 2018 (An et al., 2016). Glucocorticoid-induced osteoporosis (GIO) is a metabolic bone disease, of which the patient's bone reduces due to big dose or long-term use of

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exogenous glucocorticoids and there are major expressions of damaged micro-bone structure, increased bone brittleness and fracture easiness. Its major mechanism is that glucocorticoids causes osteoporosis by promoting bone resorption and inhibiting bone formation (Cosman et al., 2016). Some studies indicate that the patients taking glucocorticoids have a high risk of bone fracture at the same level of bone mineral density. Current studies have verified that a small dose of glucocorticoids may also increase the risk of fracture (An et al., 2016). Because GIO occurs insidiously, has no well-defined symptom at early stage and only causes bone pain or fracture if it is serious, it may have been developed to serious osteoporosis when it is found, which increases invalidism and death rates of the patients. In China, after occurrence of osteoporosis hip fracture, the death rate is as high as 20% and the invalidism and abnormality rates are >50% among the survivors (Adler et al., 2016). GIO not only seriously threatens life safety of the patients, but also has great influence on their living quality. Therefore, it is quite significant to effective treat GIO. At present, the cervus and cucumis polypeptide and the zoledronic acid have remarkable curative effect on GIO, but there are fewer reports on combined use of the both. By comparing the changes of bone mineral density and bone metabolism of the patients treated with zoledronic acid or cervus and cucumis polypeptide combined with zoledronic acid, this study has assessed the effect of combined dose on bone metabolic biochemical markers of GIO patients.

## 1. Clinical data and method

### 1.1. Clinical data

A total of 100 patients with glucocorticoids - induced osteoporosis admitted to our hospital from January 2015 to June 2017 were enrolled in this study. Inclusion standards: the patients have been treated with glucocorticoids for over 1 year; have taken over 7.5 mg/d of glucocorticoids for continuously 3 months; the patient complies with the standards of the *Guidelines for Diagnosis and Treatment of Glucocorticoid-induced osteoporosis* (for discussion) (Adler et al., 2016); the patients and relatives have been notified. The study was approved by the hospital's ethics committee. Exclusion standards: the patients suffer from osteoporosis due to other reasons; the patients are sensitive to cervus and cucumis polypeptide or zoledronic acid; the women are pregnant and breast-feeding; the patients are with kidney incompetence; the patients with poor compliance cannot insist on follow-up survey; the patients are psychotic. According to the treatment modes, the patients were divided into an observation group (cervus and cucumis polypeptide combined with zoledronic acid) and a control group (zoledronic acid), each with 50 cases. The Observation Group consists of 23 males and 27 females with the age range of 36–74 and mean age of (55.7 ± 5.4); including 17 chronic obstructive pulmonary diseases, 14 rheumatoid arthritis cases, 11 asthma cases and 8 other diseases. The Control Group consists of 21 males and 29 females with age range of 34–75 and mean age of (54.7 ± 5.8); including 16 chronic obstructive pulmonary diseases, 15 rheumatoid arthritis cases, 12 asthma cases and 7 other diseases. Through statistical analysis, general data of the patients in both groups do not have difference ( $P > 0.05$ ) and are comparable. The study has been approval by local Ethics Committee.

### 1.2. Method

The patients of the Control Group were intravenously dripped with 5 mg/d zoledronic acid (H20041965, Yangzhou Aosaikang Pharmaceutical Co., Ltd.), which was mixed in 250 ml normal sal-

ine 0.9% for injection and should be dripped in 15 min. On this basis, the patients of the Observation Group were administered jointly with cervus and cucumis polypeptide (H20050950, Heilongjiang Jiangshi Pharmaceutical Co., Ltd.), and 10 mg cervus and cucumis polypeptide and 250 ml normal saline 0.9% for injection were uniformly mixed and intravenously dripped once per day. A period of treatment lasted for 1 month and all patients were continuously treated for 2 periods.

### 1.3. Observation indicators

- (1). Determination of bone mineral density (BMD): the BMDs of lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter were measured with dual-purpose X-ray bone mineral density instrument for the patients of both groups before and after the treatment, each item was measured for two times and the measured valued were averaged.
- (2). Determination of bone metabolic biochemical markers and relevant markers: before and after the treatment, venous blood was taken with an empty stomach for the patients of both groups in the morning and separated for the serum so as to determine parathormone (PTH), 25-hydroxy-vitamin D<sub>3</sub> (25-(OH)D<sub>3</sub>), tartrate resistant acid phosphatase (TRACP), delta sleep-inducing peptide (β-CTX) and γ-bone-carboxyglutamate protein (BGP); among the others, PTH, TRACP and BGP were measured by the radio-immunity method, 25-(OH)D<sub>3</sub> and β-CTX were tested with enzyme-linked immunosorbent assay, and the specific procedures should follow the reference instructions for use.

### 1.4. Statistical method

All experimental data of this study were statistically analyzed with SPSS21.0 software, the enumeration data were expressed in percentage and compared by  $\chi^2$  test, the measurement data were expressed in " $\bar{x} \pm s$ " and compared by *t*-test, the test level is indicated by  $P < 0.05$  and the difference of data comparison results are significant statistically.

## 2. Results

### 2.1. BMD comparison before and after treatment of both groups

Before the treatment, the BMDs of lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter of the patients in both groups were of no statistical difference ( $P > 0.05$ ). After the treatment of the patients of both groups, the BMD comparison results of the above positions had statistical difference ( $P < 0.05$ ), and the lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter BMDs of the Observation Group were obviously higher than those of the Control Group, and the difference was statistically significant ( $P > 0.05$ ), as shown in Table 1.

### 2.2. Bone metabolic biochemical markers

There were no significant differences in PTH, 25-(OH)D<sub>3</sub>, TRACP, β-CTX and BGP levels between the two groups before treatment ( $P > 0.05$ ). The levels of 25-(OH)D<sub>3</sub>, TRACP, β-CTX and BGP in the two groups were significantly improved after treatment ( $P < 0.05$ ), and the levels of PTH, TRACP and β-CTX in the observation group were significantly lower than those in the control group. The levels of 25-(OH)D<sub>3</sub> and BGP were significantly higher than those of the control group ( $P < 0.05$ ). See Table 2.

**Table 1**  
BMD comparison before and after treatment of both groups ( $\bar{x} \pm s$ ).

Group	Case	Lumbar spine L <sub>1-4</sub> (g/cm <sup>3</sup> )		Left femoral neck (g/cm <sup>3</sup> )		Great trochanter (g/cm <sup>3</sup> )	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation Group	50	0.59 ± 0.12	0.79 ± 0.16 <sup>*</sup>	0.58 ± 0.15	0.81 ± 0.16 <sup>*</sup>	0.76 ± 0.17	0.94 ± 0.18 <sup>*</sup>
Control Group	50	0.60 ± 0.11	0.68 ± 0.14 <sup>#</sup>	0.59 ± 0.14	0.69 ± 0.15 <sup>#</sup>	0.78 ± 0.16	0.87 ± 0.17 <sup>#</sup>
<i>t</i>	–	0.254	2.107	0.202	2.276	0.357	1.999
<i>P</i>	–	0.801	0.039	0.84	0.027	0.723	0.048

Note: Compared with the conditions before treatment.

<sup>\*</sup> *P* < 0.05.<sup>#</sup> *P* < 0.05.**Table 2**  
Comparison of bone metabolic biochemical markers before and after treatment in both groups ( $\bar{x} \pm s$ ).

Time	Group	PTH (pg/ml)	25-(OH)D <sub>3</sub> (ng/ml)	TRACP (U/L)	β-CTX (ng/ml)	BGP (μg/L)
Before treatment	Observation Group (n = 50)	51.52 ± 14.38	16.58 ± 8.24	4.89 ± 0.86	0.42 ± 0.29	30.54 ± 3.37
	Control Group (n = 50)	52.46 ± 15.24	17.73 ± 8.61	4.86 ± 0.84	0.41 ± 0.28	30.47 ± 3.39
<i>t</i>	–	0.317	0.682	0.177	0.175	0.104
<i>P</i>	–	0.752	0.497	0.860	0.861	0.918
After treatment	Observation Group (n = 50)	43.62 ± 12.86 <sup>*</sup>	27.56 ± 7.62 <sup>*</sup>	2.45 ± 0.25 <sup>*</sup>	0.22 ± 0.18 <sup>*</sup>	35.48 ± 4.15 <sup>*</sup>
	Control Group (n = 50)	49.27 ± 11.34	21.42 ± 9.01 <sup>#</sup>	2.97 ± 0.27 <sup>#</sup>	0.33 ± 0.22 <sup>#</sup>	39.23 ± 4.34 <sup>#</sup>
<i>t</i>	–	2.330	3.679	9.993	2.736	3.238
<i>P</i>	–	0.022	0.001	0.001	0.007	0.002

Note: Compared with the conditions before treatment.

<sup>\*</sup> *P* < 0.05.<sup>#</sup> *P* < 0.05.

### 3. Discussion

Previous studies have suggested that bones are “inert organs” and are important tissues that support body movement and participate in calcium and phosphorus metabolism. The bones continue to undergo metabolism and bone remodeling as well as other tissues in the body. Recently, studies have found that (Weaver et al., 2016), bone has a special biological vitality, which can be involved in the release of many factors such as bone protein and adipokines. The bones regulate the body's osteogenesis and bone destruction in an autocrine manner, maintaining multiple organ stability. Scholars like (Man et al., 2015) believe that bone is an important organ in the body, can induce a variety of active factors to promote bone development. Osteoblasts and osteoclasts in bone tissue play an important role in regulating the function of the body. It has been reported in the literature (Mafi et al., 2016) that bone tissue is involved in glucose metabolism, which can enhance the sensitivity of insulin and improve the sugar uptake function of peripheral tissues. A small number of active factors secreted by bones in pathological conditions are involved in the pathogenesis of bone diseases. Osteoporosis refers to the reduction of bone mass in the body of the skeletal unit, resulting in changes in local bone structure, increased bone fragility, and fracture. The main clinical manifestations of osteoporosis are thinning of the skin, reduction of trabecular bone, and easy fracture. According to the cause of the disease, osteoporosis can be divided into primary and secondary (Chapurlat and Confavreux, 2016). Primary osteoporosis is divided into senile osteoporosis and postmenopausal osteoporosis. Endocrine disorders, smoking, drinking, long-term consumption of carbonated drinks, liver and kidney diseases, medications, etc. can cause postmenopausal osteoporosis. Western medicine believes that bone reconstruction is a process of balance between bone resorption and bone formation. Existing studies have shown (Chavassieux et al., 2016) that osteoblasts are responsible for bone formation. Under normal circumstances, the bone has three stages: the first stage is that the osteoclasts are adsorbed on the bone surface, and the bone depression is formed after absorbing a small amount of bone. The second stage is the formation of new bone

by the osteoblasts entering the groove after the formation of the bone depression. The third stage follows the formation of new bones. If the groove is not filled with new bone, it means that the amount of new bone formation is out of balance with the absorbed bone mass, and the absorbed bone mass is increased, resulting in loss of total bone mass and causing osteoporosis (Chavassieux et al., 2015). The onset of osteoporosis is related to hormone regulation. A decrease in estrogen levels can cause menopausal osteoporosis. At present, Western medicine is mainly used to treat osteoporosis. First, drugs that inhibit bone resorption include estrogen, calcitonin, and the like. These drugs mainly inhibit bone resorption, increase the amount of new bone into the depression, inhibit the formation of osteoclasts, and reduce the total amount of bone loss. However, most patients with osteoporosis suffer from insufficient calcium absorption. Estrogen alone is not effective and may cause hypocalcemia. Therefore, a common combination treatment plan is used. The other is to promote bone formation drugs. The main mechanism of action of these drugs is to stimulate osteoblast activity, promote the formation of new bone cells, reduce brittle bone, improve bone mass, and increase ghost strength. These drugs mainly include androgens and parathyroid hormones. The third is the preventive drugs that promote bone mineralization, which are the basic drugs for the clinical treatment of osteoporosis (Uchiyama et al., 2015). Previous studies thought that skeleton was an “inert” organ and an important tissue supporting body motion and involving in calcium phosphorus metabolism. Like other tissues of the body, the skeleton involves in successive metabolism and remodeling. Recently, some studies found that (Kurland et al., 2016) the skeleton had specific biologos and could take part in release of various factors, such as bone protein, fat factor and so on. Through autocrine, the skeleton regulated osteogenesis and bone-resorbing of the body and maintained all organs steady. Pietschmann et al. (2016) believed that skeleton is an important organ in the body and could induce various active factors to promote bone growth. Osteoblasts and osteoclasts in bone tissues played an important role in regulating body functions. Some articles reported that (Weaver et al., 2016) bone tissues involved in sugar metabolism and could enhance sensitivity of

insulin and improve sugar-intaking functions of peripheral tissues. In a pathological station, the active factors excreted by some bones joined in the process of bone-related diseases (Man et al., 2015). Osteoporosis refers to reduction of bone mass in unit skeleton of the body (Mafi et al., 2016; Chapurlat and Confavreux, 2016; Chavassieux et al., 2016, 2015) and may result in changes of local bone structure, increase bone brittleness and even cause fractures. Main clinical expressions of osteoporosis include thinning of bone cortex, reduction of bone trabecula, easy fracturing and so on. According to onset causes, osteoporosis can be divided into primary osteoporosis and secondary osteoporosis (Uchiyama et al., 2015; He et al., 2016; Wei and Hua, 2016; Lucato et al., 2016; Yi et al., 2016; Miller et al., 2016). The primary osteoporosis can be further divided into senile osteoporosis and post-menopausal osteoporosis. Endocrine disorder, smoking, drinking, long-term intake of soda pop, liver and kidney diseases, drug administration and so on may cause post-menopausal osteoporosis. Western medicine thinks that bone remodeling is a balancing process between bone absorption and formation. Some current studies show that (Weaver et al., 2016) osteoblast is responsible for bone formation. Under normal conditions, bone remodeling includes 3 stages: firstly, osteoclast is adsorbed onto bone surfaces to form bone depression after a bit of bone has been absorbed (Papapoulos et al., 2016); secondly, osteoblast enters into recesses to form new bone after formation of bone depression (Papapoulos et al., 2016); thirdly, new bone comes into being. If the recess is not fully filled by new bone, it indicates unbalance between new bone formation and bone absorption and the increase of absorbed bone mass results in loss of gross bone mass, finally bringing about osteoporosis. Incidence of osteoporosis is related to hormone regulating. Among the others, decrease of estrogen level may lead to post-menopausal osteoporosis. At present, western medicines are mainly used clinically to treat osteoporosis. The first type includes drugs inhibiting bone absorption, including estrogen, calcitonin and so on. By inhibiting bone absorption, these drugs increase new bones into the recesses, inhibit osteoclast formation and reduce loss of gross bone mass. However, most osteoporosis patients also have deficiency of calcium absorption. So, estrogen cannot obtain a good effect and may also cause hypocalcaemia. Therefore, the combined treatment measures are normally adopted. The second type is the drug promoting bone formation, of which the leading acting mechanism is to stimulate osteoblast activity, promote formation of new osteocytes, reduce bone brittleness and improve bone mass and strength. These drugs mainly include androgen, parathormone, etc. The third type refers to the drugs preventing bone mineralization, which are basic drugs clinically used to treat osteoporosis. Glucocorticoids drugs have better therapeutic effect for immunologic derangement diseases and inflammatory diseases, but its large dose for a long period may affect the health of human (Kurland et al., 2016). GIO is a common complication after taking glucocorticoids drugs and its incidence rate was only secondary to senile osteoporosis (Pietschmann et al., 2016). Its main pathogenesis is that glucocorticoids can reduce intestinal calcium absorption, which further causes the increase of calcium in renal excretion, recuperative increase of bone absorption, reduction of bone formation and finally reduction of bone mineral density (Weaver et al., 2016). Glucocorticoids can directly inhibit reproduction of osteoblasts, activate functions of osteoclasts and cause osteoblasts to decrease and osteoclasts to increase (Man et al., 2015). In the bone metabolism, osteoclasts absorb old bone, while osteoblasts produce equivalent new bone, and both cells cooperate with each other to complete bone transformation. Therefore, reduction of osteoblasts may cause reduction of new bone formation and increase of osteoclasts can result in increase of old bone mass, reduction of bone stability, increase of bone brittleness and also increase of bone fracture risk. Found in

studies that bone tissues of a healthy adult are in a dynamic balance of successive remodeling. The dynamic process of bone remodeling is regulated by body hormone. Glucocorticoid can induce osteoporosis. Some studies found that osteoblast is covered by glucocorticoid receptors, which are important points where glucocorticoid acts on bone structure. Glucocorticoid of a healthy adult has an active stimulating function in maintaining osteoblast functions. Higher expression of glucocorticoid can thicken cortex surfaces and metalize and damage them. The glucocorticoid content higher than physiological concentration can inhibit osteoblast differentiation and proliferation, expedite osteoblast apoptosis and lead to delay of bone formation. This study found that glucocorticoid not only promotes osteocyte apoptosis but also reduce osteocyte synthesis. Found during research that, for the patients taking glucocorticoid drugs for a long period, their osteocyte apoptosis is 30% higher than that of normal adults. The osteocyte apoptosis leads to damage to network connection between osteocytes. The mechanical strength of bone decreases after bone change, finally leading to GIO.

Wei and Hua (2016) found that the bone tissue of healthy adults is in the dynamic balance of continuous reconstruction. The dynamic process of bone remodeling is regulated by the body's hormones. Glucocorticoids can induce osteoporosis. Studies have found that glucocorticoid receptors are distributed on osteoblasts, and this receptor is an important site for glucocorticoids to act on bone structure. Glucocorticoids in healthy adults play a positive role in maintaining osteoblast function. Excessive expression of glucocorticoids can thicken the surface of the bone, causing damage to mineralization. Glucocorticoids above physiological concentrations inhibit osteoblast differentiation and proliferation, accelerate osteoblast apoptosis, and lead to delayed bone formation (Lucato et al., 2016). This study found that glucocorticoids reduce bone cell synthesis while promoting bone cell apoptosis. Yi et al. (2016) found that patients with long-term glucocorticoids had 30% higher autologous bone cell apoptosis than normal people. Apoptosis of bone cells leads to impaired reticular connection between bone cells, and the bone mechanical strength decreases after bone changes occur in the body, eventually forming GIO.

At present, drug is a main treatment measure for GIO and common clinical drugs include antiresorptive drugs, calcimimetic agents, diphosphate drugs and cervus and cucumis polypeptide. Among diphosphate drugs, the representative one is zoledronic acid, which has good therapeutic effect for overall osteoporosis. The diazoimidazole heterocyclic structure unique to zoledronic acid can be combined with the bone surface of the patient to effectively precipitate hydroxyapatite crystals into bone-like substances, thereby promoting normal bone formation, increasing bone density and reducing bone formation. The pharmacological action of deer melon polypeptide mainly promotes bone formation and improves microcirculation. The main component of the deer melon polypeptide is the skeleton of the animal sika deer and the mature melon seed. After extraction, it is used as a solution to improve microcirculation and regulate bone metabolism (Miller et al., 2016). By inhibiting mevalonic acid paths, the drug breaks bone absorption and induces apoptosis of osteoclasts. The pharmacological actions of cervus and cucumis polypeptide are mainly to promote formation of bone mass and improve microcirculation. Among them, bone morphogenetic protein is a high-efficiency osteoblast-inducing substance, which can be used as the initial signal molecule for mesenchymal cells to differentiate into bone marrow cells, and plays a significant role in inducing the transformation of perivascular mesenchymal cells into bone cells. Deer melon polypeptide can regulate the composition of extracellular matrix and promote the formation of new bone. The mature seeds of the gourd melon in the deer melon polypeptide can reduce capillary permeability in the local tissue of the fracture,

reduce the exudation of inflammatory factors, relieve local pain, and improve local tissue blood supply. Deer melon polypeptide can also reduce the viscosity of whole blood and provide a stable blood supply environment for new bone formation (Weaver et al., 2016). Main constituents of cervus and cucumis polypeptide are bones of spotted deer and mature seeds of cucumis, which are extracted to prepare a solution to improve microcirculation and regulate bone metabolism. The cervus and cucumis polypeptide contains polypeptide-like biological factors and various free amino acids and has the functions of regulating bone metabolism and calcium phosphorus metabolism, stimulating osteocyte proliferation and preventing osteoporosis. Among the others, bone morphogenetic protein is high-effective osteocyte-induced substance, can be used as the initial signaling molecule for differentiation of mesenchymal cells towards osteocyte and has an outstanding action in inducing transformation of mesenchymal cells around blood vessels into osteocyte. Cervus and cucumis polypeptide can regulate stromal content outside osteocyte and promote formation of new bones. The mature seeds in the cervus and cucumis polypeptide can reduce capillary permeability in local fracture tissues, decrease exudation of inflammatory factors, release local pains and improve blood circulation in local tissues. The cervus and cucumis polypeptide can also reduce viscosity of whole blood and provide a stable blood circulating environment for formation of new bones. In this study, the cervus and cucumis polypeptide combined with zoledronic acid was adopted to treat GIO and to give play to advantages of both drugs to achieve synergetic treatment and realize optimum curative effect. In this study, the curative effect of the drug was comprehended by observing the changes of bone mineral density and bone metabolic biochemical markers. In the process of bone transformation, bone metabolic biochemical markers play an important regulating effect.

PTH is one of main hormones regulating blood calcium and phosphor and can inhibit re-absorption of phosphor by proximal convoluted tubule, promote re-absorption of calcium by distal convoluted tubule, improve intestinal calcium absorption and plays an important role in proliferation of osteoblasts and osteoclasts (Chapurlat and Confavreux, 2016). 25-(OH)D<sub>3</sub> is an important regulating hormone for intestinal calcium and phosphor absorption and beneficial to increase of bone mineral density (Chavassieux et al., 2016). With high dose, it can stimulate maturing of osteoclasts and promote bone absorption; with a physiological dose, it can promote proliferation of osteoblasts (Chavassieux et al., 2015). TRACP mainly has the functions of releasing osteoclasts and increasing activity of osteoclasts. β-CTX reflects absorptive activity of osteoclasts and is clinically used in testing curative treatment of diphosphate drugs (Uchiyama et al., 2015). BGP is the main component of non-collagenous protein in bone tissue and its main functions are to maintain mineralization speed of bone, take part in regulating bone transformation and act as a functional sensitive indicator of osteoblasts (He et al., 2016). The change of BGP content is unrelated to bone absorption, but reflects real-time change of bone metabolism (Wei and Hua, 2016). This study indicated that lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter BMDs, 25-(OH)D<sub>3</sub>, TRACP, β-CTX and BGP have been obviously improved after the treatment for the patients of both groups and the effect of drug combination was better than that of sole zoledronic acid, of which the difference was statistically significant ( $P < 0.05$ ). Meanwhile, the drug combination remarkably

reduced PTH level of the patient, which had statistical difference ( $P < 0.05$ ).

In conclusion, the treatment of glucocorticoid-induced osteoporosis patients with the cervus and cucumis polypeptide combined with zoledronic acid can remarkably improves lumbar spine L<sub>1-4</sub>, left femoral neck and great trochanter BMDs and ameliorate PTH, BMD, 25-(OH)D<sub>3</sub>, TRACP, β-CTX and BGP levels of the patients.

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