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Protective Effect of Ligustrazine on Osteoporosis in Diabetic Rats

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Abstract

To study the protective effect of Ligustrazine on osteoporosis in diabetic rats. Diabetic osteoporosis rat model was used. SD rats were half male and half female, 180-220g. 50 rats meeting the research conditions provided by the Institute were divided into two groups, with an average of 25 rats in each group. Group A did not take any intervention measures before treatment, group B was Ligustrazine intervention treatment group. Observe the general situation of rats, blood biochemical indicators, bone metabolism indicators and other related indicators, and carry out logical analysis, and finally statistical analysis of the data. In general, there was no significant difference between group A and group B in age before treatment, BMI, menopause age, blood Ca, P, Mg, PTH, BMD ($P > 0.05$). In the aspect of bone metabolism indexes, the bone metabolism indexes (OC, PINP, β- CTX, 25 (OH) D3) in group B were lower than those in group a before treatment, the difference was statistically significant ($P < 0.008$). There was no significant difference between the two groups before and after treatment ($P > 0.05$). From the perspective of protection effect, 68% of the protection effect is good, 20% of the protection effect is general, 6% of the protection effect is not good, and 6% of the protection effect is not good. Ligustrazine has a good protective effect on osteoporosis in diabetic rats. Bisphosphonates can reduce bone metabolism and enhance bone stability in PMOP and T2DM rats.

Keywords: Ligustrazine, Diabetes, Osteoporosis, Bone Protection

1. Research Background

Tetramethylpyrazine is an active alkaloid isolated from tetramethylpyrazine alkaloids, also known as tetramethylpyrazine [1-2]. In the early 1970s, ligustrazine was isolated from Ligusticum chuanxiong extract by Beijing Institute of pharmaceutical industry [3]. Now it's synthetic. According to traditional Chinese medicine, it can promote blood circulation and Qi and blood, and is suitable for qi stagnation and blood stasis [4-6]. Ligustrazine has the functions of dilating arterioles, venules, anti-platelet aggregation, changing hemorheology, improving microcirculation, reducing capillary permeability, enhancing hypoxia tolerance, scavenging hydroxyl radicals and anti-lipid oxidation [7]. Ligustrazine is widely used in the treatment of cardiovascular disease and cerebral ischemic disease because of its functions of expanding microvascular, anti-platelet aggregation, improving microcirculation and anti-oxidative damage [8-10]. The incidence rate of osteoporosis increases with the prolongation of human life span.

Osteoporosis has become an important disease affecting people's quality of life. The reason is osteoporosis, calcium and phosphorus metabolism [11-13]. Whether diabetes also has the disorder of bone metabolism, which leads to the decrease of bone mineral content, leading to osteoporosis [14]. How diabetes affects the occurrence and development of osteoporosis has been closely concerned by scholars [15-17]. To analyze the relationship between diabetes mellitus and bone density, osteoporosis, to determine whether diabetes can cause osteoporosis and the mechanism of osteoporosis, and to provide theoretical basis for the prevention and treatment of osteoporosis in diabetic patients. Bone mineral density (BMD) is a measure of bone mass [18]. Bone mineral density (BMD) is a common method to detect bone changes caused by chronic diseases. Dual energy X-ray bone mineral density is a more accurate instrument for bone mineral density measurement [19]. At present, the decrease of BMD is mainly related to the following factors:

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insufficient sex hormone, the decrease of calcitonin (CT), the increase of parathyroid hormone (hormone, thyroxine, 1,25 dihydroxyvitamin D. glucocorticoid, the factors regulating bone metabolism locally, the decrease of calcium absorption, etc. [20-21].

DM is a systemic metabolic disease, and its complications involve almost all parts of the body. With the continuous improvement of the treatment level, the threat of acute complications of diabetes is gradually reduced, and the impact of various chronic complications on the quality of life and health of patients with diabetes is increasingly prominent. Diabetic osteoporosis (do) is a secondary OP, which is the most common complication of diabetes in the skeletal system [22]. The continuous consumption of bone matrix (collagen, etc.) and bone salt (minerals, trace elements, etc.) will inevitably lead to the decrease of bone mass and the complex relationship between the occurrence of DM and bone metabolism and bone remodeling. It is related to many factors, such as systemic regulatory hormones, bone remodeling microenvironment, etc. [23]. Insulin deficiency and hyperglycemia are the main factors affecting bone metabolism, such as calcium (CA), phosphorus (P); insulin-like growth factor-1 may play an important role in the core of bone remodeling regulatory network, changing the whole microenvironment of bone remodeling [24-25].

2. Theoretical Basis

2.1. Osteoporosis

Bone metabolism is carried out through the process of bone reconstruction. Osteoclasts decompose and migrate. After the old bone was removed, osteoblasts formed osteoid and mineralized to form new bone. Their functional activities are regulated by a variety of systemic hormones and local bone microenvironment factors to maintain the balance of bone reconstruction. Biochemical indicators of bone metabolism in bone formation and absorption can often reflect the functional status and bone remodeling of osteoblasts and osteoclasts. Osteocalcin, also known as glutamic acid protein, has a positive correlation between serum osteocalcin level and bone regeneration rate, which can be used as a biochemical index to reflect the instantaneous changes of bone metabolism. It provides a new sensitive, accurate and specific method for the study of bone formation and turnover rate in recent years. The activity of osteoblasts and osteoclasts increased accordingly, so that the index reflecting the functional state of osteoblasts increased. It is considered that this is a reflection of early bone metabolism disorder. With the development of the course of disease, the process of bone formation can be reduced to normal. Under the compensatory mechanism, osteoblasts function is enhanced. Other factors such as ob synthesis of osteocalcin are mainly deposited in bone tissue and secreted into the blood, so the osteocalcin in the blood includes the newly synthesized part of osteoblasts and the components degraded by osteoclasts in the process of bone absorption. Whether bone resorption is active will also lead to the increase of osteocalcin. Light proline released from bone is no longer involved in collagen synthesis, but is excreted from urine. Therefore, light proline in urine is a more specific indicator of collagen degradation and bone regeneration. Bone is the largest calcium reservoir of human body, and Ca and P are the main components of bone salt. The excretion of Ca and P in urine increased, and the negative balance of Ca and P in vivo directly affected bone mineralization. The excretion of Ca, P and hop in urine was significantly related to the absorption of bone salt and bone matrix. The imbalance of bone reconstruction and the decrease of net bone mass are the basic pathological mechanism of osteoporosis. PTH, glucocorticoid, vitamin D and CT can stimulate the expression of c-fos gene. It is suggested that c-fos protein and its transcription factor ap-l are the key links in the regulation mechanism of bone turnover, and are one of the ways in which a variety of systematic factors affect the microenvironment of bone remodeling.

C-fos is highly expressed in the proliferation phase of ob, and low or no expression in the differentiation phase, which affects the proliferation and differentiation of ob, especially the proliferation and activation of osteoblasts. Transforming growth factor-p (tgf-p), igri and igf-11 gene sequences contain ap-l binding sites, which are closely related to bone remodeling and secreted by ob. IGF-1 is one of the most abundant growth factors in bone matrix. IGF-1 is closely related to the coupling of OB and OC functions, and can mediate the regulation of PGF, IL-6, TGF-1 and other cytokines on bone. At present, IGF-1 plays an important role in bone remodeling regulatory network. PTH, CT, VitD3, estrogen, insulin and other bone regulatory hormones may regulate IGF-1 level, c-fos protein expression and transcription factors. The expression of proto oncogene c-fos causes the expression of downstream or late genes such as IGF-1, which leads to a series of changes in

ob, OC and bone remodeling microenvironment, and plays an important role in bone remodeling. The surface of normal trabecula was covered with active and inactive osteoblasts except the absorption cavity. The final product of advanced glycosylation is a series of nonenzymatic glycosylation reactions between aldehyde or ketone groups of sugar and free amino groups of protein and lipid, which finally produces a kind of substance with characteristic fluorescence. First, sugar and protein combine to form a completely reversible Schiff base, aldmine. The Schiff base can then be rearranged slowly to form a stable reversible endomeric product (ketamine compound). The products of anladori are further rearranged, dehydrated and concentrated to form ages which irreversibly bind to proteins or some amines containing substrates. These processes do not need enzyme catalysis, and occur widely in vivo. Under normal circumstances, age is a necessary condition for tissue reconstruction and internal environment stability, but excessive accumulation will cause many lesions. The production of ges is mainly affected by two factors: the influence of blood glucose, its production rate is the second power of blood glucose concentration, so moderate increase of blood glucose can significantly increase the generation of age. Under the influence of contact time with high concentration sugar, the longer the half-life of protein, the more obvious the accumulation of non-enzymatic glycosylation products and long-lived proteins such as collagen and lens. Long term hyperglycemia in diabetes can promote nonenzymatic glycosylation of tissues and lead to the formation of a large number of glycosylation end products in vivo. Glycosylated hemoglobin (HBAI). This is an Amadori product made of red blood cells. Type C collagen accounts for 90% of bone matrix, rich in lysine and lysine, with long half-life. It is prone to over glycosylation and is more sensitive to the structural and functional changes caused by non-enzymatic glycosylation. Age: the cortical content of DM rats increased significantly. On the one hand, ages affect the properties and functions of modified proteins by changing the structure of modified proteins, on the other hand, it stimulates the synthesis and release of various cytokines by binding with ages receptors on the surface of various cells, thus playing an indirect pathological role. The age-related loss of osteogenesis may be related to the age of osteoblasts adhesion, the decrease of bone collagen ability and the influence of bone collagen structure on bone salt deposition. In vitro and in vivo experiments further proved that the high content of ages bone matrix inhibited the proliferation of osteoblasts, delayed the differentiation of osteoblasts, reduced the number and activity of osteoblasts, leading to the lack of bone formation. Bone is not only an important organ of human body, but also an important mechanical pillar of human body. From the biomechanical point of view, bone is a composite material composed of collagen fibers and inorganic crystals. Its organic components form a network structure, and inorganic components fill it, so that the skeleton has the strength, rigidity and stability needed to complete the important physiological functions of human body, such as load-bearing, lever, protection, etc. The so-called strength refers to the ability of materials to resist failure (fracture) under load, the rigidity refers to the ability of materials to resist deformation under external force, and the stability refers to the ability of materials to maintain their original equilibrium shape.

2.2. Diabetes

Diabetic osteoporosis (do) is a kind of systemic metabolic osteopathy. Some scholars think that do may be a kind of diabetic microvascular disease. There are many reasons for do, including insufficient insulin secretion, hormone imbalance, calcium and phosphorus metabolism disorder and so on. The high rate of disability and mortality caused by do has become an important cause of long-term physical and skeletal pain and dysfunction in diabetic patients. Estrogen plays an important role in bone metabolism. It can accelerate the differentiation and proliferation of osteoblasts and promote the formation of bone. Finally, when the absorption of bone is greater than the formation of bone, the quality of bone decreases and osteoporosis appears. The age of osteoporosis group was higher than that of non-osteoporosis group. This is because with the increase of age, the activity of osteoclasts will be stronger than osteoblasts, which will lead to the increase of bone absorption, the decrease of bone formation, the decrease of bone density, and then lead to osteoporosis. In addition, with the increase of age, the secretion of calcitonin, a calcium regulatory hormone, decreased gradually, while the secretion of parathyroid hormone increased gradually, which made bone metabolism active, bone absorption increased, and bone formation decreased. When the body mass index is large, the pressure on the bones is also large. In addition, poor blood glucose control will lead to the accumulation and deposition of age on bone collagen, affect the

differentiation and proliferation of osteoblasts, and reduce bone formation. When the balance between bone formation and bone absorption is destroyed, osteoporosis will occur. Poor long-term glycemic control increases age. The continuous accumulation of age can inhibit the differentiation of osteoblasts, promote the apoptosis of osteoblasts and the formation of osteoclasts, and reduce bone mass. The decrease of islet function can cause the decrease of OP: insulin level through many ways, which can activate collagen metabolism and enhance bone absorption through osteoclasts. The decrease of insulin secretion will reduce the number and activity of osteoblasts, slow down the maturation and transformation of bone matrix, and eventually lead to osteoporosis. The secretion of insulin-like growth factor (IGF) will also decrease due to the decrease of insulin secretion, and IGF plays an important role in the formation of bone matrix, which can stimulate osteoblast replication. When IGF secretion decreases, calcium deposition in bone decreases, and collagen synthesis also decreases.

Insulin like growth factor-1 (IGF-1) can promote the absorption of amino acids and the synthesis of collagen by regulating the metabolism and proliferation of osteoblasts and osteoclasts. The decrease of IGF-1 in diabetic rats may be related to the decrease of osteoblasts. With the prolongation of the course of the disease, the blood glucose control of the patients with diabetes will be worse. Proteins, nucleic acids and other macromolecules will react spontaneously with glucose to produce stable advanced glycation end products (ages). Ages can act on a variety of cells, leading to the inflammatory response of osteoblasts and osteoclasts after oxidative stress, thus participating in the pathogenesis of do. There are many inflammatory factors that affect OPL. At present, the main recognized ones are tumor necrosis factor (TNF) and interleukin-6 (IL-6). Tnf-tnf-can enhance osteoclasts. TNF mice can reduce calcium deposition and bone mineralization by increasing the proliferation and differentiation of osteoclasts. IL-6 can increase osteoclast gene expression, promote osteoclast differentiation and maturation, increase bone absorption and reduce bone formation. Leptin is encoded by osteoblast genes and is closely related to the function and quantity of osteoblasts. It was found that leptin coordinated body weight, bone mass and gonadal function through central nervous system and surrounding tissues. Leptin can weaken osteoclasts and enhance osteoblasts. It can maintain bone mass by stimulating bone formation. Insulin is closely related to leptin and can promote the secretion of leptin. In the later stage of DM, the content of leptin will decrease and the secretion of insulin will decrease, which will affect the function of osteoblasts, reduce bone formation, and eventually lead to the decrease of gene expression, bone morphogenetic protein expression and Runx-2, and the number of osteoblasts in the high glucose ho-1msc cells. In addition, nrf-2 can inhibit osteoblast differentiation by inhibiting runx-2-dependent pathway. DM is a chronic metabolic disease, which can reduce bone formation and increase bone absorption, leading to Op.

2.3. Bisphosphonate Treatment

Diabetes is an endocrine and metabolic disease. Its effect on BMD is mainly due to the following aspects: DM can affect the metabolism of calcium and phosphorus, which has been confirmed by a large number of clinical studies and animal experiments. The excretion of calcium, phosphorus and magnesium in urine was increased, positively correlated with blood glucose, and the content of calcium in blood was decreased. The main cause of osteoporosis in diabetic patients is the lack of INS. Insulin itself can promote the production of vitamin D, while lack of INS will reduce the production of vitamin D, reduce the absorption of calcium and bone mineralization in the intestine. In addition, there are insulin receptors on osteoblasts. Insulin can directly act on the receptor, promote the proliferation of osteoblasts, and directly promote the process of bone mineralization. When insulin is deficient, the effect is diminished. DM had significant effect on AKP, NGP, hop and PTH. The changes of calcium and phosphorus in plasma lead to the increase of parathyroid hormone. Diabetes can lead to a significant decrease in bone mineral density, and diabetes can lead to osteoporosis. Phosphonate (BPS) is commonly used in the treatment of osteoporosis. Bisphosphonates (BPS) are commonly used in the treatment of osteoporosis. At present, bisphosphonates have good therapeutic effect on diabetic osteoporosis. Bisphosphonates can prevent bone loss in type I diabetic rats in short-term treatment, and increase bone mineral density in type I diabetic rats in long-term treatment. Bisphosphonates can improve the bone mineral density of type II diabetic osteoporosis rats. At present, bisphosphonates mainly act on osteoclasts. It can inhibit the recruitment, differentiation, generation and bone absorption of osteoclasts by inhibiting the farnesyl pyrophosphate synthetase in the methylhydroxy acid signaling pathway, blocking the isoprene and

other proteins of small GTPase. Osteoporosis is a common disease of middle-aged and old people. It is characterized by excessive absorption of bone, which leads to decrease of bone mass, increase of bone fragility and easy fracture. Osteoporosis is divided into primary osteoporosis and secondary osteoporosis. Diabetic osteoporosis is a kind of secondary osteoporosis, which is mainly due to the absolute or relative lack of insulin in diabetic patients, resulting in the metabolic disorder of sugar, fat, protein, calcium, phosphorus, magnesium and other elements, resulting in the decrease of bone mass. More and more evidences show that bone metabolism is closely related to glucose metabolism.

Both type 1 and type 2 diabetes can lead to decreased bone turnover and an increased risk of fractures of the spine, hip, and foot. The main reason of osteoporosis is the imbalance of osteoblasts (responsible for bone formation) and osteoclasts (responsible for bone absorption), which are the main effectors of bone remodeling. The imbalance of osteoclast and osteoblast differentiation and functional activity will lead to osteoporosis, osteosclerosis, rheumatoid arthritis, periodontitis and other bone diseases. The diabetic rats with osteoblasts around the implants implanted into the oral cavity can degenerate in the osteoporotic bone microenvironment, resulting in the insufficient secretion of bone matrix components, the relatively low rate of incomplete calcification of bone matrix and bone binding, and the reduction of the success rate of transplantation, which limits the clinical application of the implants. Osteoblasts are derived from mesenchymal precursor cells, which are responsible for bone formation and play an important role in bone development and fracture repair. When osteocytes differentiate, they secrete osteoid and mineralize to form extracellular matrix of mature bone tissue. At present, the relevant literature shows that high glucose level has an effect on osteoblast differentiation and osteogenesis. In type I and type II diabetic rats, the number and activity of osteoblasts decreased, leading to a decrease in bone formation. High glucose can inhibit the proliferation and differentiation of bone marrow mesenchymal cells, inhibit the mineralization of osteoblasts, and promote the apoptosis of osteoblasts and osteoblasts. Osteoclasts are the only effective cells for bone resorption in vivo. They come from the monocyte / macrophage lineage of hematopoietic cells. Two important cytokines, macrophage colony stimulating factor and RANKL, are needed in osteoclast formation. In the process of cell proliferation, migration, fusion, osteoclast maturation and bone resorption, cell modification needs high metabolism and ATP production. As an intracellular sensor, adenylate activated protein kinase can regulate the energy balance of various tissues and cells. As a key regulator of intracellular energy homeostasis, it regulates various metabolic pathways of peripheral tissues through metabolic enzymes, and participates in gene expression related to energy metabolism, cell signal transduction, cell proliferation and differentiation, cell apoptosis, immunity and vascularization. In the liver, for example, AMPK acts as an energy control switch for metabolism.The activation of AMPK can inhibit energy consumption and stimulate ATP synthesis. In skeletal muscle, AMPK can improve energy production by regulating energy consumption during exercise. In the process of exercise, AMPK is involved in the transformation from glycolytic fiber to skeletal muscle oxidized fiber, and enhances glucose uptake by enhancing the expression of glucose transporter 4. It can repair and proliferate islet cells, increase secretory granules of sand cells, improve microcirculation of pancreatic tissue, enhance blood flow and complete perfusion, soften pathological fibrosis, improve sensitivity and quantity of receptor binding on the membrane of specific islet cells, inhibit antagonistic kinin and its derivatives, so as to reduce negative feedback on INS secretion. Bone biomechanics is a comprehensive reflection of bone mass, bone structure and bone quality. Therefore, bone biomechanics is one of the important methods to evaluate the effect of anti osteoporosis drugs. Stress and strain are two basic elements to describe the internal effects of bone. Strain refers to the deformation of the phalanx under the action of external force. Stress is the internal impedance of the deformation of bone to resist the external force, which is equal to the ratio of the external force acting on the cross section of bone to the cross section area of bone. In this experiment, the bone mechanics test method of bending test (three-point bending) was used to measure the elastic modulus, elastic limit, ultimate strength, maximum deflection and bending failure load of the femur of do rats. Microcirculation disorders include hemodynamic abnormalities, microvascular diseases and hemorheological changes. Hemorheology is the main manifestation of diabetic microcirculation disorder. Whole blood viscosity is the most important index of Hemorheology (influenced by blood cells, plasma, blood vessels and other factors), which is the comprehensive manifestation of many related indexes. This high

viscosity disease is called hyperviscosity. It is often manifested as the increase of hematocrit, the aggregation and hardening of red blood cells, the increase of plasma viscosity, and the hyperactivity of platelet function.

3. Experiment Design

3.1. Research Object

Using diabetic osteoporosis rat model, SD rats were half male and half female, 180-220g. The 50 rats that met the research conditions provided by the research institute were divided into two groups, with an average of 25 rats in each group. Group A was the pre-treatment group without any intervention measures, while group B was the treatment group with Ligustrazine intervention.

3.2. Experimental Plan

General data: collect and inquire the age and disease of all rats, whether they have fracture history, and collect relevant information (including the duration of diabetes, whether there are acute and chronic diabetic complications in blood glucose control), and calculate BMI. Detection of biochemical and bone metabolism markers: all rats were treated with blood before and 3 months after treatment. Give them a normal diet three days before blood collection to avoid stress and take special drugs. Fast for 8-12 hours before drawing blood. Venous blood was collected before 9 o'clock the next morning. Serum Ca, P, Mg and parathyroid hormone were measured. The indexes of bone metabolism such as OC, tpinp, β- CTX, 25 (OH) D3 were determined by electrochemiluminescence immunoassay. BMD measurement: BMD measurement was completed by the same person, and BMD measurement was conducted for all subjects. After the rats were killed, the right tibia was immediately peeled off, the fascia and soft tissue were taken out and soaked in normal saline for examination. The 1 / 2 boundary of the length of femur was used as the measuring point and measured by single photon bone densitometer. Before treatment, the BMD of lumbar spine (L2-L4, sum of lumbar vertebrae) and proximal left femur (including neck, neck and atrium triangle) was measured in g / cm2. During the treatment, adverse reactions included gastrointestinal reaction, mandibular necrosis, atypical femoral fracture and so on. If the rats had serious adverse reactions during the treatment, they would quit the experiment. Immunohistochemical staining (SP method) was used to detect the expression of c-fos protein in osteoblasts. DAB staining. After the rats were killed, the left femur was immediately peeled off, the fascia and soft tissue were removed, fixed and FFA for 48h, the solution was decalcified with EDTA, dehydrated with alcohol step by step, embedded and paraffin, cut into 4uxn thick parts of sliding microtome, dewaxed water, 0.1% Triton x-100-pbs, 20 minutes at room temperature, 3% H2O: 20 minutes at room temperature, 10% normal sheep serum sealed at room temperature for 30 minutes, serum was discarded, Immuno anti-c-fo: polyclonal antibody (diluted at 1:30) was added overnight. At room temperature, Sheep anti immune was (1:100) 37 ℃, horseradish enzyme labeled streptomycin was added for 40 minutes (1:100) 37 ℃, and the color was found to be satisfactory under the niab hzoz microscope for 40 minutes, then washed with tap water and washed with double steaming water. All the above steps were vibrated with PBS and smimx3. Conventional dehydration, transparency and sealing. PBS was used as negative control. Statistical methods: the measurement data were described by means of mean ± standard deviation, and the baseline data were compared by ANOVA. When there are differences, carry out layered comparison. T-test was used to compare the difference before and after treatment. The test level was 0.05, and the statistical software was SPSS 25.0.

3.3 Experimental Results

(1) General comparison

Table 1. **General comparison**

Group	Group A	Group B	F	P
Age	66.7±6.2	67.2±5.1	1.6	0.168
BMI	24.5±3.1	25.0±4.6	1.05	0.366
Ca	2.20±0.15	2.18±0.1	0.584	0.624
P	1.08±0.12	1.11±0.1	0.64	0.583
Mg	0.86±0.11	0.9±0.15	0.7	0.547
L2	0.81±0.1	0.80±0.1	1.13	0.333
L3	0.8±0.1	0.84±0.13	1.423	0.236
L4	0.82±0.12	0.83±0.1	1.011	0.388

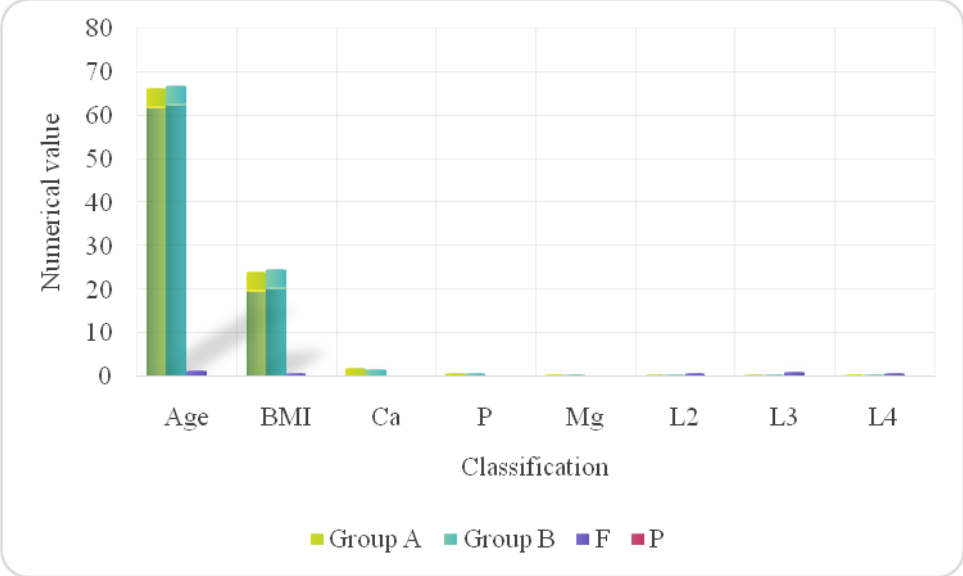

Figure 1. **General comparison**

According to the statistical analysis of data, as shown in Figure 1 and Table 1, there was no statistical significance (P > 0.05) in age before treatment, BMI, menopause age, blood Ca, P, Mg, PTH and BMD between the two groups.

(2) Comparison of bone metabolism indexes

Table 2. **Comparison of bone metabolism indexes**

Bone turnover index	Group A	Group B	F	P
OC	16.81±5.8	12.40±6.52	4.47	0.05
PINP	60.36±28.64	4.51±23.67	6.832	0.005
β-CTX	0.60±0.32	0.30±0.11	10.645	0.005
25(OH)D3	14.88±2.15	12.46±3.73	14.26	0.006

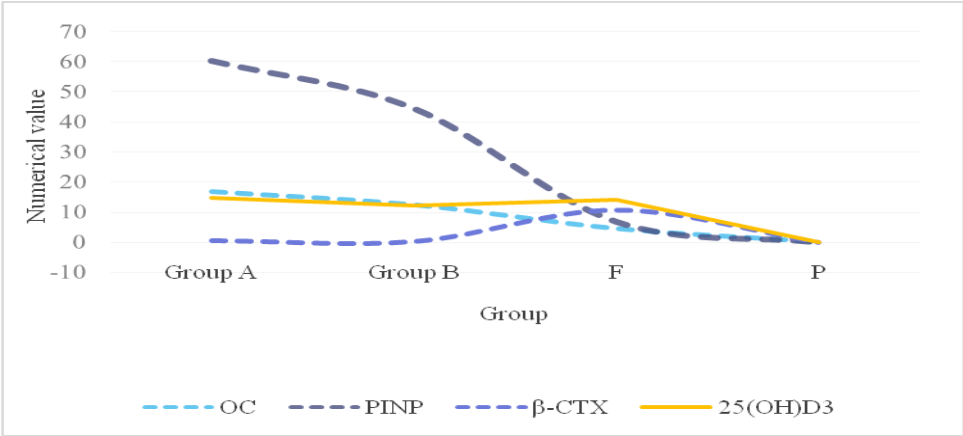

Figure 2. **Comparison of bone metabolism indexes**

According to the statistical analysis of data, as shown in Figure 2 and Table 2, the differences of bone metabolism indexes (OC, PINP, β - CTX, 25 (OH) D3) between the two groups before treatment were statistically significant. Before treatment, the bone metabolism indexes (OC, PINP, β - CTX, 25 (OH) D3) in group B were lower than those in group A (P < 0.008). There was no significant difference in bone metabolism indexes (OC, PINP, β - CTX, 25 (OH) D3) between the two groups before treatment (P > 0.05).

(3) Comparison of blood biochemical indexes

Table 3. **Comparison of blood biochemical indexes**

Blood biochemistry	Before treatment	After treatment
Ca	2.18±0.06	2.17±0.07
P	1.00±0.11	1.10±0.10
Mg	0.87±0.13	0.86±0.10
PTH	29.32±10.60	28.76±9.63

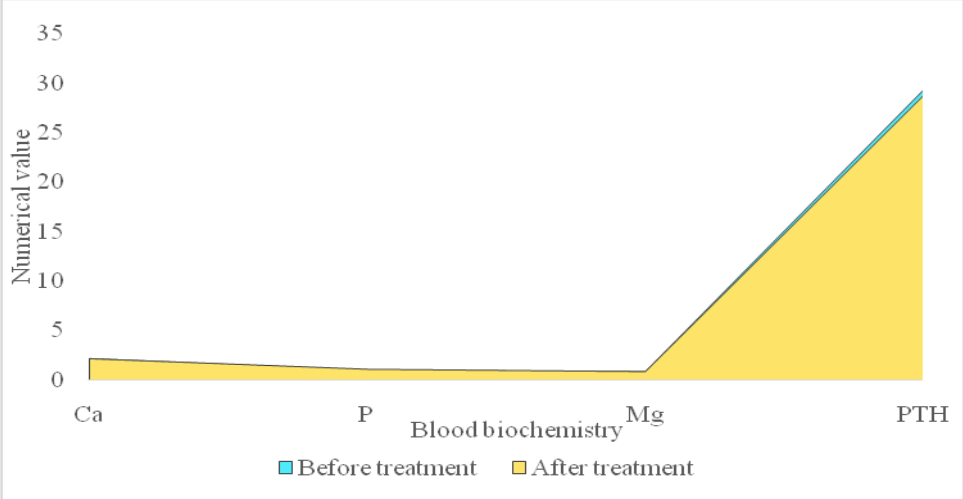

Figure 3. **Comparison of blood biochemical indexes**

According to the statistical analysis of data, as shown in Figure 3 and Table 3, there was no significant difference in blood biochemical indexes (blood Ca, P, Mg, PTH) between the two groups before and after treatment ($P > 0.05$).

Protection effect

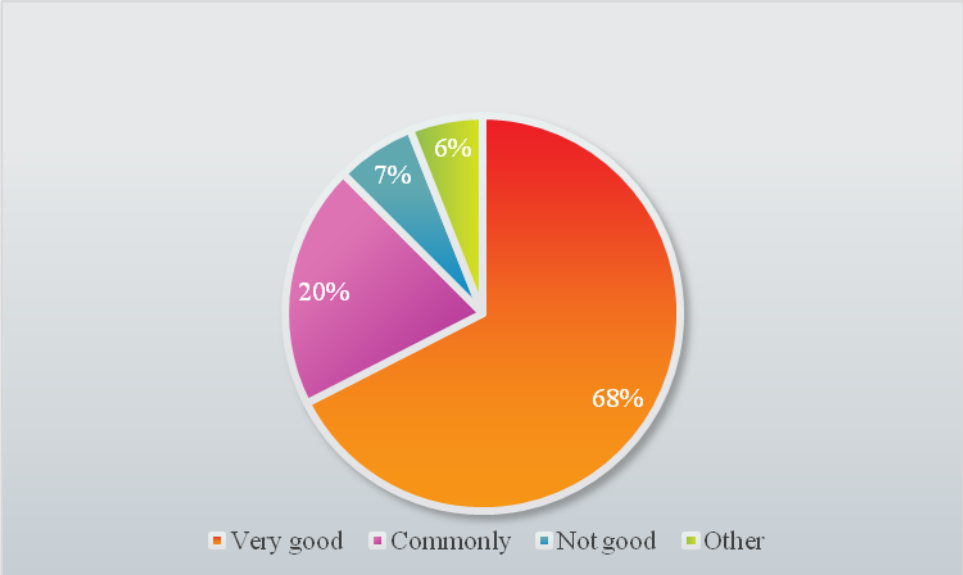

Figure 4. **Protection effect**

According to the statistical analysis of data, as shown in Figure 4, 68% of them have good protection effect, 20% of them have general protection effect, 6% of them have bad protection effect, and 6% of them have other situations.

3.4. Analysis and Discussion

Osteoporosis is a common disease of middle-aged and old people. It is characterized by excessive absorption of bone, which leads to decrease of bone mass, increase of bone fragility and easy fracture. Implant is the first choice in the treatment of tooth loss. As a fixed repair method that does not need to damage the adjacent teeth, the sick mice are comfortable to use, have a small sense of foreign matters, and do not need to be extracted, which is very popular in the edentulous mice. The key to the success of the implant lies in the formation of good bone integration between the host bone and the titanium implant, while osteoporosis will affect the bone integration of the implant and the success rate of the clinical implant. In order to improve the success rate of bone integration under osteoporosis, it is necessary to

improve the implant. At present, there are two ways: to find a good biocompatible metal material to replace titanium, and to improve the success rate of bone integration through the surface modification of metal materials.

Therefore, it has high endogenous growth potential. In addition, porous tantalum has the characteristics of low elastic modulus, high surface friction coefficient and excellent mechanical properties. In the medical process, it can avoid the "stress shielding" effect when implanted into human bone tissue, which is conducive to the normal conduction of biological stress. The concept of immediate implant, immediate repair and immediate load-bearing requires that the implant has good initial stability and can bear the early functional load. Diabetes mellitus and osteoporosis are two important public health problems in the world. There are many people suffering from two diseases at the same time, but the diagnosis rate, treatment rate and standard rate of the two diseases are not optimistic at present. With the deepening of understanding of diseases, we found that these two diseases are closely related and interact with each other. OC secreted by osteoblasts is an important bridge connecting the two, which can stimulate insulin secretion, improve insulin resistance and have a good effect on glucose metabolism. Diphosphonate is a kind of bone absorption inhibitor, which is the first-line drug to treat primary osteoporosis, especially PMOP rats. However, it is also often used in diabetic or diabetic osteoporosis rats.

4. Conclusion

Ligustrazine has clinical value in the prevention and treatment of diabetic osteoporosis. In vivo, ligustrazine can inhibit the interaction between cells and extracellular matrix, which is helpful to the stability of bone. The PMOP of bisphosphonates for T2DM can reduce the bone turnover rate without serious adverse reactions, and the safety is acceptable.

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