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Correlation of PUFA with osteoporosis

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Abstract: The incidence of osteoporosis is high. Although the initial symptoms and effects are not prominent, if it is not effectively controlled, it will increase the risk of fracture, affect the role of bone tissue, and seriously reduce the quality of life of patients. At present, clinical studies have shown that its occurrence is related to age, endocrine, genetic, drugs and other factors, but there is no exact etiology and pathogenesis. With the continuous development of medical concept, some experts and scholars have studied the relationship between polyunsaturated fatty acids and osteoporosis, and believe that there is a close relationship between the two, but the specific mechanism is not clear. This is a brief analysis of the correlation between PUFA and this disease.

1. Introduction

Osteoporosis is a disease with high clinical incidence, which is relatively common in middle-aged and elderly people, and living factors have a great impact on its occurrence and development. The existence of this disease will cause the reduction of bone mass, bone tissue structure changes, increase bone fragility, make the body more prone to fracture, and fracture is easy to cause pain and bone deformation or other complications, seriously reduce the quality of life. Bone metabolism is affected, bone tissue function decreases, nutrient absorption capacity is reduced, the existence of diseases affecting bone metabolism, may induce this disease. Some studies believe that polyunsaturated fatty acids (PUFA) are related to the occurrence of this disease[1]. PUFA can protect the relative flow of cell membrane and ensure the full function of cells; reduce cholesterol and triglycerides in blood; reduce blood viscosity, accelerate blood circulation; and improve the activity of brain cells. From the analysis of the physiological role of PUFA, there is some theoretical support for the occurrence of this disease, but what is the specific role? What is the mechanism of action? The following review follows follows.

2. The PUFA is involved in the pathogenesis of osteoporosis

PUFA can affect bone metabolism from several pathways, which may then lead to the disease. There are three possible ways to play a role.

2.1 PUFA and PPAR γ

PUFA can exist as a specific ligand for the peroxisome bioactivated receptor γ (PPAR γ). After PUFA binding to PPAR γ, PUFA may induce accelerated differentiation of bone marrow adipocytes, thus affecting bone metabolism. PPAR γ is an endoreceptor and can bind to another endoreceptor, X receptor (RXR)[2]. There are three subtypes of PPAR, and PPAR γ is one of them, mainly in adipose tissue, which can be detected if it is rich in the bone marrow. PPAR γ can help to modulate adipocyte differentiation and play a critical role. If PPAR γ is activated and forms a heterodimer with RXR, the latter can act as a transcription factor that helping a variety of target genes undergo activation reactions. This will trigger a high expression of adipogenic genes and form fat through a series of reactions. Individuals with increased age, ovariectomy or other causal causes of osteoporosis have been shown to exhibit reduced bone mass and increased bone marrow fat. The origin of osteoblasts and adipogenic cells in the bone marrow has always been from the differentiation of progenitors-bone marrow stromal cells (MSCs). PUFA goes through PPAR γ to regulate the differentiation of osteoblasts and adipocytes in the bone marrow, and therefore has a role on the occurrence of this disease. For patients with this disease, MSCs were found to undergo lipoblastic differentiation and osteoblastic differentiation was inhibited. PUFA and its metabolites will specifically match with PPAR γ, and new products will be formed after combination. If the content of PUFA in the body increases, the expression level of PPARγ will also increase, which will increase the adipoblast differentiation of bone marrow stromal cells in the body and reduce the differentiation of osteoblasts, which will decrease the bone mass and induce the occurrence of this disease. However, the above specific mechanism is relatively complex, and further research is needed to deepen the understanding of this mechanism.

2.2 PUFA and inflammatory response cytokines

PUFA can also have a relative impact on the fluidity of the cell membrane, which may play the role of regulating inflammatory response cytokines, increase the formation of the latter, and then use the biosynthesis pathway of prostaglandin E2 (PGE 2) to regulate bone formation and bone reabsorption, affect bone metabolism, and then cause this disease. If the body develops an inflammatory response and is not effectively controlled for a long time, it will lead to an increased bone loss rate, resulting in osteoporosis and increasing the risk of fracture. PUFA can regulate the inflammatory response cytokines, reduce their expression level, control the bone loss problem caused by this, and appropriately increase muscle and bone absorption, thus affecting the occurrence of this disease. Tumor necrosis factor (TNF- α), interleukin 6 (IL-6), and PGE 2 are all affected by PUFA. Among them, it is believed that the effect of PGE 2 on bone is greatly related to its dosage. The high dose of PGE 2 can significantly inhibit the generation of bone matrix. At the same time, the low concentration of PGE 2 can accelerate the production of the body, including in vitro experiments are also concluded. During metabolism, the PGE 2 biosynthesis work in bone tissue is influenced and regulated by various factors. Among them, the most prominent role is the level of cyclooxygenase (COX-2). Studies have shown that PUFA can regulate the expression level and activity degree of COX-2, and then indirectly affect the generation of PGE 2, and finally have an effect on bone tissue, causing the occurrence of this disease.

N-3 PUFA can downregulate the expression of COX-2 and reduce the generation of PGE 2, which can accelerate the formation of bone matrix, while n-6 PUFA can up-regulate the expression of COX-2 and increase PGE 2 generation, so it can inhibit the formation of bone matrix[3]. Some studies established a rat model, fed high n-3 PUFA diet and high n-6 PUFA diet, and found that high n-3 PUFA diet showed low COX-2 expression. No study selected in vitro cultured chondrocytes and n-3 PUFA was added to the medium. After culture, COX-2 mRNA showed low

expression level, thus reducing the generation of PGE 2 and promoting the formation of bone matrix. Therefore, dietary PUFA can affect bone metabolism through the PGE 2 biosynthesis pathway, thus regulating bone formation and bone reabsorption[4].

2.3 PUFA with bone marrow microcirculation

PUFA can reduce the blood viscosity, have an impact on the blood microcirculation, and then may therefore affect the occurrence of the bone marrow microcirculation, and then play a certain role in the metabolic capacity of bone cells, and eventually cause this disease. PUFA may cause ischemia and hypoxia in the bone marrow by affecting the microcirculation of the bone marrow, which can cause bone tissue dystrophy, reduce the metabolic capacity of osteocytes, and eventually lead to osteoporosis. Possible causes of this condition include: increased PUFA. To reduce the level of nitric oxide and improve the vasoconstrictor factor, endothelial cytosol may cause dysfunctional vasoconstriction and endothelial cell damage, altering the permeability of blood vessels, making it easy to develop thrombosis, which can block bone marrow microvascular circulation. Additionally, increasing PUFA may also cause a rise in triacylglycerol in the blood. When this rising level exceeds the liver's transforming capacity, triacylglycerol accumulates in hepatocytes, leading to the formation of fatty liver. In turn, this can lead to inadequate emulsification of VLDL in the blood, causing lipid particles to polymerize and cause increased pressure in the osseous system and bone marrow microcirculation disorders. Furthermore, hyperlipidemia caused by increased PUFA may lead to increased blood viscosity and reduced red cell deformation function, causing microvascular blockage and bone marrow blood flow disorders[5].

3. n-3 PUFA is associated with osteoporosis

Studies have found that n-3 PUFA is beneficial in maintaining the stability of calcium in bone, and in promoting the maintenance and improvement of bone density. Especially for the elderly with dietary calcium deficiency, n-3 PUFA has significant benefits in maintaining bone health. Therefore, nutritionists recommend that people eat fish rich in n-3 PUFA at least twice a week, which is not only beneficial to the heart and blood vessel function, but also helps to increase bone firmness. The study compared the relationship between protein, n-3 PUFA and n-6 PUFA and energy intake and bone mineral density, and found that high levels of PUFA are beneficial to increase bone mineral density, especially large amounts of n-3 PUFA, which plays an important role in maintaining bone mineral density in the elderly. As n-3 PUFA may promote skeletal growth by regulating PGE 2 synthesis, it may act by affecting COX-2 and may directly inhibit this enzyme activity by competitively inhibiting the metabolic pathway of its substrate — arachidonic acid (AA). Therefore, increasing the ratio of n-3 PUFA in the diet can effectively compete to inhibit AA and reduce PGE 2 production, thus promoting the generation of bone tissue[6].

The obligatory fatty acid — Omega-3 PUFA series, composed of linolenic acid and its derivatives, has been shown to have an important protective utility for alleviating bone loss in postmenopausal women. Scientific-research research confirmed that Omega-3 PUFA showed obvious effect in reducing bone mass in postmenopausal female rats. The experiment showed that Omega-3 PUFA and rats with the maximum load, stress resistance, elastic pressure, and elastic energy storage, and flexibility, thus enhancing the efficacy of impedance fracture. Also, the use of Omega-3 PUFA treatment of female ovarian rats, the femur fracture surface slope and no fragmentation, this suggests that after this means of rats on the bone biological attribute has been strengthened, increased ability to prevent fracture, the effect is similar to the results of estrogen replacement treatment. The study further revealed that ovariectomized rats rich in Omega-3 PUFA fish oil showed a mild and slow bone loss compared with a diet containing corn oil. In addition,

Omega-3 PUFA could effectively inhibit the effect of antitartrate-resistant acid phosphatase activation in osteoclasts cultured in vitro. Based on this, it can be speculated that inhibition of osteoclast formation and function is perhaps one of the potential mechanisms for Omega-3 PUFA to relieve bone loss due to ovarian removal surgery. The intensive study found that after 48 hours of Omega-3 PUFA treatment to the osteoblast precursor cell line MC3T3-E1, the observed amount of alkaline phosphatase significantly exceeded the group treated with AA, highlighting the great potential of Omega-3 PUFA in enhancing osteoblast effects.

4. n-6 PUFA is associated with osteoporosis

It was found that a higher intake of n-6 PUFA may lead to osteoporosis. On the one hand, n-6 PUFA promotes the transformation of bone marrow stromal cells into adipocytes, which restricts their development to osteoblasts, and then reduces the formation of bone tissue; on the other hand, these fatty acids stimulate the production of inflammatory cytokines and activate osteoclasts to enhance bone resorption. In particular, AA, a long-chain n-6 PUFA, drives bone marrow stromal cells into adipocytes and hinders osteoblast formation; AA generates inflammatory pion PGE 2 catalyzed by COX-2. The effect of PGE 2 on bone depends on its concentration, promoting osteoclasts, accelerating the degradation of bone, and blocking the formation of new bone matrix, while facilitating DNA replication and enhancing alkaline phosphatase activity at low concentration, which facilitates the formation of bone structure. Therefore, AA regulates the bone through its metabolite PGE 2: increased AA levels can lead to increased PGE 2 and increased bone resorption, which may lead to osteoporosis.

5. n-6 / n-3 ratio to osteoporosis

It is found that adjusting the ratio of n-6 and n-3 PUFA in food can effectively reduce the AA content and the production of PGE 2 in vivo, and have a positive effect on the metabolism of bone bones. Some authorities in some fields have explored the changes in rat bone metabolism caused by different n-6 and n-3 PUFA ratios for tail suspension through comparative experiments. Five groups of rats were established: the ratio of n-6 and n-3 PUFA in the first group was 7.79 in the second group and 1.47 in the third group; the tail hanging control group (SC group) and the free movement control group (FAC group); compared with the SC group, the mechanical properties of the femur were greatly increased. As the ratio of n-6 to n-3 decreased, the amount of AA in the rat liver decreased, while the n-3 PUFA content increased. Since AA is the synthetic precursor of PGE 2, the decrease of AA content leads to the decrease of PGE 2, which helps the absorption and excretion of calcium, and promotes the deposition of calcium in bone, effectively reducing osteoporosis and the resulting risk of fracture. Therefore, it can be seen that reducing the ratio of n-6 to n-3 PUFA in the diet is important for improving bone metabolism and enhancing bone structure, and helps to improve the biomechanical properties of bone.

6. Conclusion

In conclusion, there is a close relationship between PUFA and the occurrence of osteoporosis. Most studies show that n-3 PUFA has a certain osteogenic effect, while n-6 PUFA has a certain osteoclastic effect. Some in vitro studies and animal experiments also confirmed that n-3 PUFA is very beneficial in the prevention and treatment of this disease, and n-3 PUFA can improve BMD in patients with this disease and reduce the risk of fracture. However, some studies suggest that n-3 PUFA does not improve BMD in OP patients. Therefore, the specific role and related mechanisms of different species of PUFA in the occurrence of osteoporosis need to be further explored.

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