DOI: 10.53469/jcmp.2024.06(11).04

Exploring the Correlation between Five Chinese Medicine Organs and Osteoporosis based on Intestinal Flora

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Abstract: ***Osteoporosis (OP) is a common orthopedic disease, the incidence of which has increased dramatically, seriously affecting the quality of life of patients and causing a huge economic burden. The human intestinal tract hosts a large number of bacteria, fungi, and various viruses throughout the year, constituting an important part of the human body. In recent years, with the deepening of the understanding of intestinal flora, its related research has become a major hotspot. Based on the intestinal flora, this paper discusses the correlation between the five organs and osteoporosis, aiming to provide new ideas for the prevention and treatment of osteoporosis.***

Keywords: Intestinal flora, Osteoporosis, Five organs**.**

1. Introduction

Osteoporosis (osteoporosis) is a common and frequent systemic disease in the elderly population, which is characterized by a decrease in bone content, destruction of the microstructure of bone tissue, and an increase in bone brittleness, resulting in easy fracture after exposure to external forces [1]. With the rapid increase of the aging population in China, the incidence of OP will increase dramatically, seriously affecting the quality of life of patients and causing a huge economic burden, and must be given sufficient attention.GM has been a lifelong parasite in the human intestinal tract since the embryonic period, and has already become an important part of the human body, which is closely related to the physiology and pathology of the human body. With the development of molecular biology and modern medicine, it has been proved that GM is involved in a variety of life activities in the human body, and GM disorders can cause a variety of diseases, including OP [2]. According to the theory of holistic concept of Chinese medicine, the human body is a part of nature and itself is also a whole, physiologically cooperating with each other and pathologically influencing each other. In Chinese medicine, the treatment of diseases is mostly based on the identification and treatment of internal organs, and the organs within the internal organs, the internal organs outside, the two are interconnected, each other's surface, so the five organs have become the core of the treatment. Osteoporosis is the inevitable result of the life process of the human body, is a systemic disease, can be considered from the five organs for prevention and treatment. The five organs in Chinese medicine refer to functional states and their interconnections, which are different from the specific substantive organs in Western medicine, but we can still make use of the medium of GM to explore the correlation between the five organs in Chinese medicine and OP by discussing the relationship between GM and OP, so as to provide new clinical ideas for the prevention and treatment of OP in Chinese medicine.

2. Gut Flora and Osteoporosis

GM is a microbial community that has been parasitized in the human intestinal tract since the embryonic period and remains stable for a long period of time. These microbial communities include a variety of bacteria, fungi, and viruses, which play an important role in human growth, development, immune response, and other physiological activities, and are therefore generally regarded as important "hidden organs" of the human body. When the microbial community maintains an imbalance of homeostasis, various diseases will arise, affecting human health [3, 4]. GM and bone metabolism are closely linked, and studies have shown that GM can affect bone metabolism and cause OP by affecting calcium and phosphorus metabolism, regulating immune response, regulating estrogen secretion, and other pathways.

2.1 Influence on Calcium and Phosphorus Metabolism

GM produces many metabolites, among which short-chain fatty acids (SCFAs) are most closely related to calcium and phosphorus metabolism in the human body. The degree of phosphorylation of calcium ions is affected by PH, under the regulation of SCFAs, the intestinal pH decreases, the degree of phosphorylation of calcium ions in the intestine will decrease, SCFAs can also directly regulate the control of nucleosome localization and acetylation of histones [5]; the solubility of calcium ions and the expression of calcium-binding protein D9k are also affected by pH, SCFAs increase the solubility of calcium ions and the expression of calcium-binding protein D9k in the intestine by regulating the intestinal PH, and thus increase the solubility of calcium ions and the expression of calcium-binding protein D9k. The solubility of calcium ions and the expression of calcium-binding protein D9k in the intestine, and the passive transport of calcium cell bypass is also increased accordingly, causing calcium absorption, bone content and bone density to increase [6, 7]. The content of GM metabolites is closely related to the structure of bacterial flora, and the intestinal tract has a large number of probiotic bacteria such as bifidobacteria, bacillus subtilis, lactobacillus, etc., and the probiotic bacteria can make intestinal mucous membrane barrier intact, and when the content of the probiotic bacteria is

increased, SCFAs will be induced by SCFAs [8]. When their content increases, they will induce the secretion of SCFAs to increase, and synergistically exert anti-osteoporosis effects.

2.2 Regulation of Immune Response

GM balance is extremely important for the normal function of the immune system, when the GM is disturbed, the structure and number of intestinal flora changes and produces a large number of inflammatory factors, which cause local inflammation in the intestinal tract, and the inflammation in the intestinal tract further exacerbates the imbalance of the bacterial flora, and even systemic inflammation when the lesions are severe, causing bone metabolism disorders [8]. LPS-containing intestinal bacteria in the gut increase in content and release a large amount of LPS, T-cells are activated by LPS, then release a large amount of inflammatory factors, T-cells activated by the release of inflammatory factors to stimulate osteoclasts to proliferate, the number of osteoclasts increased leading to increased bone resorption and increased bone loss and cause OP. in addition, LPS can be directly involved in the regulation of osteoclasts, growth, maturation, secretion, LPS can be accelerated osteoclast formation, leading to the formation of osteoclasts. In addition, LPS can directly participate in regulating the growth, maturation and secretion of osteoclasts, and LPS can accelerate the formation of osteoclasts, leading to the acceleration of the OP process [9, 10].

2.3 Regulation of Estrogen Secretion

A variety of hormones are synergistically involved in bone metabolism, and estrogen plays the most important role. Under the action of estrogen, the apoptosis of osteoblasts is slowed down and the apoptosis of osteoclasts is inhibited, and therefore the probability of OP greatly increases in women after menopause [11]. Estrogen can play a biological role only after it enters the circulation as unconjugated estrogen, and estrogen metabolism is regulated by an enterohepatic cycle involving GM, which produces and secretes β-glucuronidase, which facilitates the conversion of conjugated estrogen to unconjugated estrogen and thus participates in bone metabolism [12]. Other studies have shown that related receptors can directly bind to estrogen, accelerate osteoclast apoptosis, slow down bone resorption, and delay the OP process [13].

3. The Relationship between the Five Organs and Intestinal Flora and Osteoporosis

3.1 Liver-gut Flora-osteoporosis

3.1.1 Liver communicates with the large intestine

Liver and large intestine are connected, which was first recorded in Huangdi Neijing (The Yellow Emperor's Classic of Internal Medicine). Suwen - The Sixty-Second Treatise on the Regulation of Menstruation (Suwen - The Sixty-Second Treatise on the Regulation of Menstruation) reads, "When there is an excess of ambition, there will be bloating and venereal emissions." Liver main drainage, regulating the body's qi activities, liver qi stagnation too much will affect the spleen and stomach qi operation, causing intestinal physiological dysfunction, abdominal distension, diarrhea and other symptoms. Suwen - to the true to be great theory of seventy-four" also contained: 'syncope yin Si Tian ..... cold leakage abdominal distension', that is, liver disease caused by intestinal disease. Liang Yu and others [14] believe that the theory of "liver and large intestine" is well-documented and detailed. Modern research has proved that the liver and intestines are originated from the same embryonic layer, and have many anatomical and functional connections [15]. Anatomically, the liver is connected to the intestine through the portal vein, and between the liver and the intestine, there is a section of peritoneal-hepatic colonic ligament; functionally, some of the material conversion of GM can only be carried out with the participation of the liver, which can regulate a variety of cytokines and immune cells in the intestinal tract through the hepatic-intestinal circulation pathway [16].

3.1.2 Liver-gut flora-osteoporosis

Hepatocytes can become cancerous when mediated by the intestinal microbiota, and when bile acid receptors function abnormally, they may cause liver damage and ultimately promote the development of hepatocellular carcinoma. Studies have shown that restoring bile acid metabolism to a normal state may be a reliable way to inhibit the evolution of hepatocellular carcinoma progression, which in turn needs to be predicated on correcting the imbalance of the gut microbiota [17]. The key to the gut-liver axis is the barrier role played by the gut, which is closely related to GM, and TCM can act on many targets, including the liver and GM, to improve liver function, reduce endotoxin levels, and minimize bacterial translocation in cirrhotic patients [18]. Modern medical research has shown that liver lesions can cause GM disorders, and GM disorders can lead to the occurrence of OP [19].

3.2 Heart-gut Flora-osteoporosis

3.2.1 Heart and Small Intestine

"Heart and small intestine" was first seen in the 'Ling Shu - this transmission': 'heart and small intestine, small intestine, the House of Sheng', which, together that is related, the meaning of the conjunction, that the heart and small intestine not only meridian connection, but also in the physiopathology has a close connection [20]. The spiritual center - this organ forty-seven "contained:" heart with the small intestine, the small intestine, the pulse of its response ". The relationship between the heart and the small intestine is clear. Pathologically, the heart fire will move down the small intestine, and the small intestine heat can also be disturbed in the heart, the heart and the small intestine will affect each other and interfere in the treatment of the symptoms and the root cause of the disease should be taken into account. In short, the heart and the small intestine are connected by meridians and channels, physiologically related and pathologically mutually detrimental [21].

3.2.2 Heart - intestinal flora - osteoporosis

Li Xingxing et al [22] proved that the "heart - intestinal axis" is a bidirectional interactions between the circulatory system and the intestinal tract, and cardiovascular disease is closely

related to the "heart - intestinal axis" interactions, heart disease will affect the balance of the GM, GM imbalance can accelerate the occurrence of heart failure and other diseases. Heart disease can affect the balance of GM, and GM imbalance can accelerate the development of heart failure and other diseases. Another study [23] showed that hypertension and atherosclerotic diseases are closely related to GM, and the inflammatory response and intestinal immune system dysfunction caused by GM metabolic imbalance can participate in the formation of hypertension and atherosclerosis. One of the mechanisms by which traditional Chinese medicine can be used to treat cardiovascular and cerebrovascular diseases is to regulate the composition and diversity of GM as well as the role of its metabolites [24]. Guo Lu et al [25] found that a variety of cardiovascular diseases, including coronary heart disease, cause abnormal lipid metabolism, which increases osteoclastogenesis and decreases osteoblast differentiation, leading to an increase in bone resorption and a decrease in bone density.

3.3 Spleen-Gut Flora-Osteoporosis

3.3.1 Spleen and Small Intestine Connection

It is well documented that the spleen is related to the small intestine. For example, the Suwen - Zangqi Fa Shi Lun Chuan: "If the spleen is sick ..... deficiency, then the abdomen will be full of intestinal tinnitus, and the food in the supper will be leaking and not being transformed," suggesting that symptoms of the digestive system such as abdominal distension and intestinal tinnitus will occur in spleen disease. Suwen - to the true to be a great theory of the chapter" said 'Taiyin Division of heaven ..... stool difficult', also indicates that the foot Taiyin spleen meridian lesions, will cause stool difficult and other diseases. From the point of view of meridian circulation, "Ling Shu - meridian" said, "the small intestine hand sun pulse ..... against the stomach, belongs to the small intestine," that is, the small intestine and stomach associated with the spleen and stomach, the small intestine and spleen there is a correlation. Yu Hanchuan et al [26] found that there was a significant difference in the level of monomorphic anaplasmosis between healthy people and patients with splenic disease by comparing the structure of the bacterial flora in the feces of the two.

3.3.2 Spleen-gut flora-osteoporosis

The physiological function of the spleen is related to GM, and a normal GM structure can lead to healthy spleen qi and adequate qi and blood biochemistry, thus effectively preventing colorectal cancer and other intestinal diseases [27]. Zhu Jiayuan et al. [28] found that GM was significantly imbalanced in mice with spleen deficiency and constipation compared with healthy mice in animal experiments, and the role of GM is similar to that of the spleen in the transportation of water and grains, so GM imbalance can be regarded as a microscopic manifestation of the loss of spleen transportation, which is also an enrichment and supplementation to the theory of the "spleen-intestines" in traditional Chinese medicine based on the modern research [29]. GM can regulate the immune response and affect the function of the spleen, and acquired immunity is based on the premise that spleen qi is healthy and functions normally. Both the spleen and GM have the function of regulating the organism, and the spleen is the "central earth to irrigate the four sides", i.e., the spleen is in the center of the human body and regulates the surrounding body, and is the regulatory center of the human body, while GM can also directly or indirectly regulate the distal organs through host-flora metabolism, signaling, and products of the immune-inflammatory axis [30].

3.4 Lung-gut Flora-osteoporosis

3.4.1 Lung and Large Intestine

The theory of the lungs and the large intestine can be traced back to the Yellow Emperor's Classic of Internal Medicine (HUNDI NEIJING): "The lungs and the large intestine, the large intestine, the skin, the skin should be ..... the lungs should be the skin, the skin is thicker, the large intestine is thicker," showing that the lungs and the large intestine are related to each other. Lung and colon in physiology and pathology affect each other, "Suwen - six sections of the Tibetan elephant theory" recorded: "the lungs, the gas of this", that the lungs main body of the function of the gas; "Suwen - cough theory" said: "the lungs cough has not been, then the large intestine affected by the", that is, the lung disease appears to be persistent coughing Can not stop will cause lesions in the large intestine; "Ling Shu - four hours of gas" said: "the abdomen is often ringing, the gas on the chest, wheezing can not stand for a long time, the evil in the large intestine, " suggesting that lesions in the large intestine is the cause of the ringing in the abdomen, the chest wheezing. In terms of embryonic development, the lungs originate from the foregut endoderm, and the epithelial cells and glands of the respiratory tract originate from the foregut endoderm [31]. Modern studies have shown that the lungs are most strongly correlated with the ileum and colon, pointing out that this anatomical segment mainly plays a role in intestinal operation, revealing the relationship between the conductive action of the large intestine and the lung's pronouncement and purgation [32].

3.4.2 Lung-intestinal flora-osteoporosis

Chronic obstructive pulmonary disease (COPD) is a frequent disease of the respiratory system, and during its development, there are phenomena such as lung tissue damage, lung function decline, and inflammatory response of the lungs, which will also affect the normal function of intestinal tissues, and GM imbalance or a certain degree of linkage with these phenomena, so that the lung's organization, structure, and function are all affected by GM [33]. The interaction of the "lung-gut" axis is based on the interaction between the lungs and GM, which also has an important impact on lung diseases, and clinical and experimental studies have suggested that disorders of GM and its metabolites can accelerate the development of a variety of lung diseases, such as chronic obstructive pulmonary disease (COPD) [34]. Lai Yitian et al. [35] found that the use of moxibustion to improve the inflammatory response of asthma model rats can simultaneously regulate the lungs and intestines, and that the "lung and intestines treatment" can more effectively regulate the level of intestinal short-chain fatty acids, and play a better therapeutic effect.2.5 Kidney-intestinal flora-osteoporosis

3.5.1 Connection between kidney and large intestine

Kidney-colorectal communication was first seen in the Yellow Emperor's Classic of Internal Medicine, such as "Su Wen - Jin Gui Zhen Shi", "the black color in the north, into the pass through the kidneys, opening the orifices in the two yin ....." In Chinese medicine theory, the kidney is the main two stools, the opening of the orifice in the two yin, dietary dregs through the intestines out of the body this process relies on its normal function. When the kidney metabolic function declines, toxic substances not metabolized by the kidneys accumulate too much in the body, leading to abnormal intestinal function; and intestinal pathology, intestinal microbial community disorders, pathogenic bacteria and endotoxins increase the impact of the intestinal mucosal immune barrier function, resulting in toxic substances through the intestinal tract to enter the bloodstream to affect the function of the kidneys, and the two have a mutual influence, constituting the "intestinal - kidney axis " [36].

3.5.2 Kidney-intestinal flora-osteoporosis

Xie Shiqin et al. [37] found that trimethylamine oxide is a harmful metabolite formed after GM metabolizes dietary substrates, and through its mediating role, GM can affect the intestines and kidneys in the "kidney-intestinal axis" and stimulate inflammatory responses to induce a variety of pathological changes in the kidneys and cause renal function damage. The composition and function of intestinal microorganisms are affected by renal diseases, chronic kidney disease (CKD) can cause GM disorder; and GM disorders can also cause damage to the intestinal barrier function, inflammatory response, endocrine disorders and other pathologies, resulting in renal failure, uremia and other diseases, and accelerating the development of a variety of renal diseases [38]. Through metabolic and immune pathways, the progression of CKD is interconnected with bacterial alterations in the gut and amplified in a positive feedback loop. When the number of commensal flora in the gut decreases and the number of conditionally pathogenic bacteria increases, the composition of the microbial community and the intestinal environment change, slowly transforming from a state of symbiosis to a state of dysbiosis, and the alteration of the bacterial flora has an important impact on the development and evolution of CKD and related complications [39].

4. Summary

In summary, there is a close correlation between the five TCM organs, intestinal flora, and osteoporosis. As a systemic disease, the essence of osteoporosis is the aging and degeneration of bone, which is inevitable and irreversible in the process of life just like other parts of the body, so it can be considered to be treated from a holistic and multi-faceted perspective. The treatment of osteoporosis in Chinese medicine is mostly based on the deficiencies of the spleen and kidneys, and most of the medicines are used to tonify the spleen and kidneys, while for the three organs of the liver, heart and lungs, the correlation with osteoporosis is seldom discussed directly. However, based on the systemic characteristics of osteoporosis and the classical theory of the holistic concept of Chinese medicine, it can be deduced that the five internal organs are closely associated with osteoporosis, and the pathology of the five internal organs can lead to the occurrence of osteoporosis.

In this paper, with the help of the latest research results of intestinal flora, the author elaborates the clear relationship between it and osteoporosis, i.e., intestinal flora can affect bone metabolism and cause osteoporosis through various ways; at the same time, the correlation between the five Chinese medicine organs and intestines and intestinal flora is also discussed, and it can be concluded that the lesions of the five Chinese medicine organs affect intestinal flora through the mediation of intestinal flora, which will ultimately affect the bone metabolism and cause the occurrence of osteoporosis, which is undoubtedly the best solution for the occurrence of osteoporosis. The occurrence of osteoporosis, which undoubtedly opens up a new path for the treatment of osteoporosis. For the prevention and treatment of osteoporosis, this study suggests that we should pay attention to systemic regulation when treating osteoporosis, that is, the lesions of the five viscera or other systemic diseases need to be treated in time, so as to avoid the prolongation and aggravation of osteoporosis, and at the same time, it also provides a new research direction for the prevention and treatment of osteoporosis by Chinese medicine.

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