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Editorial: Metabolic Bone Disease: From Basic Science to Clinical Frontier

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Introduction

Metabolic bone disease is defined as a diverse group of disorders that result in abnormalities of (i) bone mass, (ii) structure mineral homeostasis, (iii) bone turnover, or (iv) growth. The most prevalent form is osteoporosis, characterized by microstructural deterioration of bone tissue and decreased bone mineral density. 55% of the subjects aged $\geq 50$ years worldwide suffer from osteopenia or osteoporosis [1]. The link between the lifetime risk of fracture of the hip, wrist, or vertebral regions and osteoporosis has already been identified. Beyond compromising athletic ability, osteoporotic fractures severely impact daily functionality and mobility, resulting in personal and societal burdens [1-2].

Metabolomics is a new kind of omics developed after genomics, transcriptomics and proteomics. Its basic definition is "in the dynamic process of metabolism of organisms, through the systematic analysis of the changes in the spectrum of endogenous metabolites in the body fluids and tissues of organisms, to systematically study the biological status and regulatory function of organisms as a whole after external stimulation."[3] Metabolomics emphasizes the study of the body as a complete system, which coincides with the overall regulatory effect of traditional Chinese medicine (TCM). It can amplify the subtle changes in gene expression and protein expression on metabolites, so as to find the pathogenesis of osteoporosis and biomarkers after TCM treatment, and further analyze the metabolic pathways related to biomarkers, so as to clarify the mechanism of action of TCM in treating osteoporosis. In recent decades, significant progress has been made in pharmaceuticals and treatments for osteoporosis, particularly in bone homeostasis and bone remodeling [2].

The Metabolic disorders and osteoporosis
It mainly focuses on the lipid metabolism and osteoporosis, the fatty acid metabolism and osteoporosis, the amino acid metabolism and osteoporosis, the sugar metabolism and osteoporosis. Relevant studies suggest that the above plays an important role in the pathogenesis of osteoporosis [3].

Study on metabolomics of single herbal medicine for osteoporosis

Xia TS’s research [4] found that Morindae Officinalis Radix exerts its anti-osteoporosis effect mainly by regulating arachidonic acid metabolism in rats with glucocorticoid-induced osteoporosis, while Prepared rhizome of Adhesive Rehmanna exerts its anti-osteoporosis effect mainly related to steroid biosynthesis in osteoporosis. Pan S et al. Studied [5] the effects of Shortorned Epimedium Herb on serum and urine metabolites in glucocorticoid-induced osteoporosis model mice by NMR, and found that Shortorned Epimedium Herb could treat osteoporosis by regulating glycolysis, aerobic oxidation, lipid metabolism, phospholipid metabolism, energy metabolism, amino acid metabolism and intestinal flora disorder. Based on GC-MS technology, Wang FJ et al. [6] found that Eucommia Ulmoides Oliv could induce down-regulated glycine, lysine, docosahexaenoic acid, glucose and up-regulated tryptophan rollback in the serum of ovaricectotic osteoporosis model rats, and its mechanism may be related to regulating amino acid metabolism and oxidative stress. Huang Y et al. [7] have found that for the treatment of glucocorticoid-induced osteoporosis, rhizoma drynariae mainly plays a role by interfering with sphingolipid metabolism, anti-oxidation-oxidation balance and phenylalanine metabolism in the body, while for the osteoporosis model of rats induced by retinoic acid, rhizoma drynariae plays a role by regulating linoleic acid metabolism, glycerophospholipid metabolism and arachidonic acid metabolism[8]. The above studies show that a single Chinese medicine can achieve the purpose of treating osteoporosis by regulating multiple metabolic pathways, and for osteoporosis caused by different reasons, the metabolic pathways regulated by the same Chinese medicine are not exactly the same.

Metabonomics study on the treatment of osteoporosis by Chinese herbal
compound

Under the guidance of the theory of traditional Chinese medicine, TCM compounds play the role of multi-way intervention in diseases through drug compatibility. Li C [9] conducted a study on the treatment of retinoic acid-induced osteoporosis in rats with self-made Shen-Ling Jian-Gu Capsule (Shortorned Epimedium Herb, Dipsaci Radix, Salviae Miltiorrhizae, Polygonum Multiflorum Thunb, Prepared rhizome of Adhesive Rehmannia, Rhizoma Corydalis, et al.), and found that Shen-Ling Jian-Gu Capsule could inhibit osteoporosis by regulating amino acid metabolism, energy metabolism, sugar metabolism, fat metabolism and hormone levels. Luo D et al. [10] analyzed the plasma of primary osteoporosis mice treated by Zhen-Zhu Tiao-Zhi Prescription (Finger Citron Fruit, Fructus Ligustri Lucidi, Salviae Miltiorrhizae, Radix Notoginseng, Rhizoma Coptidis, Largehead Atractylodes Rhizome, Ligusticum wallichii, Eucommia Ulmoides Oliv), and found 12 potential biomarkers for anti-primary osteoporosis, the mechanism of which may be related to the regulation of phospholipid, arachidonic acid and energy metabolism. Shu-Gan Bu-Shen Formula is composed of Shortorned Epimedium Herb, Bupleurum falcatum L., Achyranthes bidentata Blume, Fructus Psoraleae, Eucommia Ulmoides Oliv, Dipsaci Radix, Curcumae Radix. Wu F’s research [11] found that it can reverse the plasma levels of four biomarkers: acetone, lactic acid, n-acetylglycoprotein and fatty acid in ovaries removed osteoporosis rats. Liu WJ et al. [12] found that the serum metabolic spectrum of ovariectomized rats was close to that of normal rats after treatment with Jian-Gu Granule (composed of Shortorned Epimedium Herb, Common Macrocarpium Fruit, Common Yam Rhizome, Pilose Asiabell Root, et al.) The analysis of differential metabolite-related pathways showed that Jian-Gu Granule may improve postmenopausal osteoporosis by regulating various metabolic pathways such as lipid metabolism, nucleic acid metabolism and amino acid metabolism. Based on the metabolomics of GC-MS, Yuan XM et al. [13] dug out the potential biomarkers of anti-osteoporosis of Gu-Shu Dan (Shortorned Epimedium Herb, Common Cnidium Fruit, rhizoma drynariae, Salviae Miltiorrhizae), including 11 biomarkers such as malic acid, malonic acid, adipic acid, glutaric acid and L-trilonic acid, which were
mainly related to amino acid metabolism, energy metabolism, fatty acid metabolism and oxidative stress. The above literature analysis found that traditional Chinese medicine compound in the treatment of osteoporosis mostly uses the herbal medicine of nourishing liver and kidney, through the compatibility of drugs, from multiple ways to regulate the level of metabolism to play a therapeutic role.

Metabolomics study on the treatment of osteoporosis by Chinese herbal extracts

Xu XX’s study [14] found that 9 biomarkers such as carnitine, 2-methylmalonic acid and 5-hydroxy-n-formylguanine in the serum of ovariectomized rats with osteoporosis were significantly up-regulated, while 20 biomarkers such as leukotriene F4 and PC (22:6/18:1) were significantly down regulated. After the intervention of Cistanche phenylethanoid glycosides (CPhGs), 23 biomarkers were significantly reversed, and the metabolic pathway analysis showed that they were mainly related to fatty acid metabolism, amino acid metabolism, phospholipid metabolism, et al. Zhang AH et al. [15] studied the intervention of acanthopanax lignin in ovarian osteoporosis removal based on LC-MS technology and found that the main metabolic pathways regulated by acanthopanax lignin include unsaturated fatty acid biosynthesis, linoleic acid metabolism, arachidonic acid metabolism, primary bile acid synthesis and tyrosine metabolism. Acanthopanthoside exerts its effects mainly by interfering with steroid hormone biosynthesis, primary bile acid biosynthesis, glutathione metabolism and tyrosine metabolism[16]. Si Z et al. [17] showed that the treatment of ovariectomized osteoporosis by Osthole is mainly related to 13 metabolic pathways such as linoleic acid metabolism, starch and sucrose metabolism, arachidonic acid metabolism, alanine, aspartate and glutamate metabolism. The above studies confirmed that in addition to single herb medicine and Chinese herbal compounds, Chinese herbal extracts can also play an anti-osteoporosis role by regulating different metabolic pathways.

Summary and conclusion

No matter it is single herbal medicine, Chinese medicine compound or Chinese medicine extract, it can effectively realize the anti-osteoporosis effect by regulating
the metabolic level of the body. With the continuous development of metabolomics
detection technology, more and more studies have been conducted on the treatment of
osteoporosis by Chinese medicine based on metabolomics. Through the study of
metabolomics, people can accurately find the potential targets of Chinese medicine in
the treatment of osteoporosis, and further reveal the mechanism of action of Chinese
medicine in the treatment of osteoporosis. Through the study of metabolomics, the
main metabolic pathways involved in TCM treatment of osteoporosis were found to
be lipid metabolism, fatty acid metabolism, amino acid metabolism, energy
metabolism, etc. At present, the methods used for differential metabolite detection
mainly include LC-MS, GC-MS and NMR. Different detection methods have their
own advantages and disadvantages. Due to the complex composition of biological
samples, different detection techniques can be used for detection according to the
properties and characteristics of different samples. At present, the samples used for
differential metabolite detection are mainly serum and urine, and there is a lack of
specific detection samples. Osteoporosis is a disease of bone metabolism. Synovial
fluid in the joint cavity is in direct contact with bone tissue and receives substances
from surrounding tissue, articular cartilage, synovial membrane, and bone. Therefore,
synovial fluid may contain important biological information and be a choice for
specific test samples. In addition, the studies on the treatment of osteoporosis with
Chinese medicine based on metabolomics are mostly at the animal level, including the
animal model of ovariectomized osteoporosis, the animal model of
glucocorticoid-induced osteoporosis, the animal model of retinoic acid-induced
osteoporosis and the animal model of primary osteoporosis. However, clinical studies
are lacking and further studies are needed.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for
publication.

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**REFERENCES**


Dear Editors,

I would like to submit an Editorial entitled “Metabolic Bone Disease: From Basic Science to Clinical Frontier” to the Journal Metabolism and Target Organ Damage.

I deeply appreciate your consideration of our manuscript. If you have any queries, please don’t hesitate to contact me at the address below.

Thank you and best regards.