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Review Article

Advances in Vitamin D for the Treatment of Osteoporosis: A Review

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Abstract

This review systematically summarizes the latest research progress of vitamin D in the clinical treatment of osteoporosis to consolidate available evidence for its clinical practice, combined medication schemes and relevant mechanisms linked to adipokines, so as to provide valuable references for clinical medication and further scientific exploration of osteoporosis. Literature retrieval was performed across authoritative databases including PubMed and CNKI, covering research articles published in recent years before August 26, 2025. All eligible retrieved documents were managed, classified and screened via EndNote reference management software. The incorporated studies concentrate on three core dimensions: clinical efficacy observation of vitamin D monotherapy, diverse combination therapies with anti-osteoporotic agents, and the regulatory relationship between vitamin D and multiple adipokines secreted by adipose tissue. Existing research confirms that vitamin D possesses tremendous research and clinical application potential in osteoporosis intervention. Over recent years, abundant clinical trials and basic researches have made continuous explorations and innovative breakthroughs regarding its practical clinical performance, rational combined administration principles and adipokine-mediated bone metabolism pathways. These emerging findings have greatly expanded the applicable scenarios of vitamin D and further improved its clinical value in osteoporosis prevention and treatment. In summary, by sorting out cutting-edge research data, this paper integrates updated research conclusions on vitamin D against osteoporosis. It not only helps clinicians formulate more individualized and standardized therapeutic regimens in daily practice, but also lays a solid theoretical foundation for subsequent basic researches and clinical trials targeting vitamin D, bone metabolism and adipokine network regulation.

Keywords

Osteoporosis, Vitamin D, Calcitriol, Estradiol, Traditional Chinese Medicine, *Bifidobacterium longum*, Resistin

1. Introduction

Osteoporosis is one of the major epidemics of the 21st century, significantly weakening bone strength, compromising the integrity of bone microstructure, and increasing fracture risk. [1] The disease is categorized into primary and secondary types: primary osteoporosis results from aging and estrogen deficiency, while secondary osteoporosis stems from underlying diseases or medications [2, 3]. Among these, primary osteoporosis accounts for 80% of all cases [4]. Similar to osteoarthritis, the incidence of osteoporosis rises with age, affecting women more than men [5, 6]. As global aging intensifies, its

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prevention and treatment have become critical medical challenges [7].

Vitamin D itself is biologically inactive and must undergo two hydroxylation reactions in the liver and kidneys to be converted into the active form, calcitriol [8]. Calcitriol binds to vitamin D receptors (VDRs) in the intestines, kidneys, and bones, enhancing the synthesis of calcium-binding proteins. This increases the absorption of dietary calcium by the intestinal mucosa and the reabsorption of calcium and phosphate by the kidneys, significantly improving calcium absorption [9]. Calcitriol also induces the differentiation and mineralization of osteoblasts while stimulating the secretion of RANKL by osteoblasts, thereby enhancing osteoclast activity and completing bone remodeling [10, 11].

2. Analysis of Vitamin D Drugs

Vitamin D drugs have been applied clinically in China. Siyong Huang's team evaluated vitamin D and its analogues, calcitriol, alpha calcitriol, and eldecalcitol, based on Chinese guideline [12]. The selected drugs have the following three criteria: 1. Original drug; 2. Include in the national centralized procurement catalog; 3. Include in the National Essential Medicines List. There are five aspects to evaluate (100 points): pharmaceutical properties, efficacy, safety, economy, and others. A score greater than 70 is recommended for continued clinical use. The final scores for alpha calcitriol soft capsules were 73.17, calcitriol soft capsules I was 72.06, calcitriol soft capsules II was 71.52, and alpha calcitriol tablets were 71.29. These four drugs are strongly recommended for inclusion in the drug list [13].

3. Vitamin D Combination Therapy

3.1. Calcium Supplements

Vitamin D, calcium supplements, bisphosphonates, calcitonin, estrogens, and other traditional medications are used to treat osteoporosis. Among them, vitamin D promotes the absorption of calcium, while calcium supplements are used to supplement exogenous calcium. The combination therapy of calcium and vitamin D is the basic therapy for treating osteoporosis, which can improve bone density and reduce the incidence of fractures [14, 15]. At present, this combination therapy has been extensively studied in the treatment of glucocorticoid induced osteoporosis [16], postmenopausal osteoporosis [17, 18], and postmenopausal osteoporosis combined with osteoarthritis [19]. The main focus is on efficacy evaluation, with evaluation indicators including improved bone density and reduced fracture risk.

3.2. Estradiol

The latest research reveals a new mechanism by which the combination therapy of estradiol and vitamin D promotes the osteogenic process, which can prevent osteoporosis through the miR-351-5p/IRS1 axis and mTOR/NF κ B pathway. Overexpression of miR-351-5p inhibits the osteogenic process and targets the inhibition of IRS1; Overexpression of IRS1 can to some extent weaken the inhibitory effect of miR-351-5p overexpression on osteogenesis, restore ALP activity, BGP levels, and calcification nodule formation, and inhibit the mTOR/NF κ B pathway. The combination therapy of estradiol and vitamin D can downregulate miR-351-5p, relieve the inhibition of the target gene IRS1, reduce the expression of phosphorylated proteins (p-mTOR, p-NF κ B, p-I κ B) in the mTOR/NF κ B signaling pathway, inhibit pathway activation, and promote osteogenesis [20].

3.3. *Bifidobacterium longum* FSHHK13M1

Bisphosphonate drugs are traditional treatment drugs for osteoporosis, mainly targeting osteoclasts. By inhibiting the activity of osteoclasts, they reduce bone resorption, increase bone mass, and lower the risk of fractures. But this type of drug has nephrotoxicity and is not suitable for patients with liver and kidney function decline. *Bifidobacterium longum* FSHHK13M1 can regulate gut microbiota, increase vitamin D metabolism levels, and effectively alleviate osteoporosis. Animal experiments have shown that compared to the group supplemented with vitamin D alone, the combination of *Bifidobacterium longum* FSHHK13M1 significantly increases bone density, effectively reduces serum calcium and alkaline phosphatase, and has high research and application value in patients with liver and kidney dysfunction [21].

3.4. Chinese Herbal Medicine

Clinical research analysis shows that the combination of vitamin D with traditional Chinese medicine (such as Bushen Huoxue Tang, Xianling Gubao Capsules) and calcium supplements can increase bone density and reduce the risk of fractures in patients with osteoporosis. However, the specific mechanism of action of traditional Chinese medicine is still unclear [22].

3.5. Food

Vitamin D-fortified cheese (a cheese product with added vitamin D) [23]. The combination of fortified eggshell powder and vitamin D [24] in food therapy can enhance the absorption of vitamin D in the intestine, improve metabolic levels, significantly increase bone density, and reduce the occurrence of fractures. It has high clinical application value in preventing osteoporosis, especially osteoporosis caused by low vitamin D levels.

4. Vitamin D and Adipokines

Research data shows that adipokines can affect the process

of bone remodeling and are also related to the pathogenesis of osteoporosis [25]. Vitamin D is stored and metabolized in adipose tissue, which can release adipokines such as resistin, leptin [26]. Adipose factors can regulate bone metabolism, among which resistin can increase osteoclast activity and reduce bone density [27]. The Sundus Tariq team collected data from postmenopausal women (n=161) and divided them into three groups: vitamin D adequate (n=87), vitamin D deficient (n=64), and vitamin D deficient (n=10). Enzyme linked immunosorbent assay was used to measure serum resistin levels, and multiple stepwise regression (including weight, height, serum calcium, serum phosphatase, etc.) was used for data processing. The results showed a negative correlation between vitamin D and resistin [28].

5. Discussion

The clinical evaluation of vitamin D and its analogues drugs has resulted in many clinical drugs not being included due to their strict limitations; Due to inconsistent drug launch times, there are differences in the reported clinical efficacy. In the future, clinical analysis or tracking of drug reports for drugs not included can be conducted to update paper data in a timely manner.

The combination therapy of vitamin D aims to improve its in vivo activity and utilization rate. In the future, we can explore how to enhance the activity of nuclear receptors (VDR), design nano targeted vitamin D to enhance its binding with VDR, or conduct repeated experiments based on existing literature to refine its data and clarify its mechanism.

Fatty factors are a hot research topic. Adipose factors can regulate bone metabolism. In previous studies, only the relationship between adipokines and vitamin D, bone density was discussed, without considering factors such as age and BMI. The Sundus Tariq team provided multiple stepwise data analysis results to strengthen the argument for the negative correlation between vitamin D and resistin. In the future, multiple stepwise regression data analysis methods can be used to analyze a large amount of clinical data, in order to strengthen the argument for the relationship between adipokines, osteoporosis, and vitamin D. Cell or animal experiments can also be conducted to find new therapeutic targets.

Abbreviations

RANKL	Receptor Activator of Nuclear Factor-κB Ligand
VDR	Vitamin D Receptor
ALP	Alkaline Phosphatase
BGP	Bone Gla Protein
miR	microRNA
IRS1	Insulin Receptor Substrate 1
mTOR	Mammalian Target of Rapamycin
NF κB	Nuclear Factor Kappa B
IκB	Inhibitor of Nuclear Factor κB
ELISA	Enzyme Linked Immunosorbent Assay
BMI	Body Mass Index

Author Contributions

Wenbin Sun: Conceptualization, Resources, Writing – original draft

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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