The Role of Vitamin D in Menopausal Medicine

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Menopause is the time at which menstruation stops in women. After menopause, women are more susceptible to some diseases, especially osteoporosis and cardiovascular disease. Vitamin D has a protective effect against osteoporosis by facilitating the absorption of calcium and affecting parathyroid hormone. Vitamin D also affects cardiovascular function by lowering the blood pressure, which affects the renin-angiotensin system and alters the low-density lipoprotein receptor activity. This paper discusses supplemental vitamin D in postmenopausal women with osteoporosis and cardiovascular disease.

Key Words: Cardiovascular disease, menopause, osteoporosis, vitamin D

Menopause occurs when women stop producing female hormones and ovulating. Typically, it occurs in women older than 50 years. Women undergo many physiological changes during menopause, and some diseases are more prevalent in postmenopausal women, including osteoporosis, cardiovascular disease, cancers of the vagina and uterus, and altered cognitive function. Osteoporosis is associated with reductions in the integrity and strength of bone, which are accompanied by an increased fracture risk. The main causes of cardiovascular disease are arteriosclerosis, hypertension, degenerative changes, and heredity. Vitamin D can have a significant impact on postmenopausal women, potentially improving postmenopausal problems via several mechanisms. First, vitamin D promotes calcium absorption in the digestive tract, which affects bone density and bone metabolism.¹ It is also an intrinsic suppressor of the renin-angiotensin system (RAS) and is essential to maintain normal cardiovascular homeostasis because of lower blood pressures.² Calcium and phosphorus in skeletal muscle regulate the absorption of calcium and phosphorus mineralization in the metabolism of bone.³ Vitamin D is believed to benefit postmenopausal women.⁴,⁵
investigated the role of vitamin D in postmenopausal women.

**MENOPAUSAL SYMPTOMS**

Menopause is a time of great change when viewed in a social context, and postmenopausal women undergo physical and mental changes. Common symptoms are memory loss, facial blushing, and exhaustion in women at the menopause transition. Korean middle-aged women develop low-level depression, a slightly elevated degree of self-identity, and relatively fewer climacteric symptoms.\(^6,7\) A decrease in serotonin during menopause results in hot flashes.\(^8\) Despite recognizing the symptoms of menopause, many women do not seek treatment. Knowledge of menopause differs with age, and young women with more education tend to know more about menopause. Vitamin D has the potential to affect menopause symptoms because a lack of vitamin D results in failure of calcium binding in bone. In addition, vitamin D controls the calcium concentration in cells and improves muscle function. The risk of falling increases when there is insufficient vitamin D.

**OSTEOPOROSIS**

The incidence of osteoporosis increases after menopause, and the prevalence of osteoporosis is increasing with the recent increase in the elderly population.\(^9\) In patients with osteoporosis, the strength of bone is reduced and the risk of fracture increases. Enhanced estrogen during menopause can reduce the risk of postmenopausal osteoporosis. The primary role of vitamin D is maintenance of normal muscle mass and function, which reduces the risk of falling. The active form of vitamin D, 1,25-dihydroxyvitamin D3 \([1,25(\text{OH})_2\text{D}_3]\), stimulates the formation of intestinal intracellular calcium-binding proteins, opens calcium channels, and stimulates intestinal calcium and phosphorus absorption.\(^1\) When vitamin D is lacking, the 1,25(OH)\(_2\)D\(_3\) levels fall and less calcium is available for bone mineralization.\(^1\) A low serum calcium concentration stimulates increased PTH secretion,\(^10\) which stimulates bone turnover and leads to bone loss.\(^1,10\) Vitamin D deficiency also leads to secondary hyperparathyroidism, a calcium-induced increase in the secretion of parathyroid hormone, and high bone turnover, which leads to bone disease.\(^1\)

There is a relationship between bone mineral density (BMD) and serum 25-hydroxyvitamin D3 \((25(\text{OH})\text{D}_3)\).\(^11,12\) BMD is an index used to diagnose the risk of osteoporosis and fracture. A low BMD reflects a low bone density and an increased risk of osteoporosis.\(^13\) A study of postmenopausal women with osteoporosis in Amsterdam found a significant positive correlation between the vitamin D status and BMD,\(^11,12\) and the critical serum 25(OH)D3 level was 50 nmol/L.\(^14\) Vitamin D supplements reduce the risk of fractures by reducing PTH secretion and increasing bone density. In one study of healthy postmenopausal women, vitamin D and calcium did not significantly reduce hip fractures, although bone density had improved.\(^15\)
Hormone therapy for menopausal women can also affect bone density, and vitamin D should have a synergistic effect.\(^6\)

**JOINTS**

A gradual increase in joint symptoms is common in menopausal women via the influence of vitamin D, and joint symptoms can progress more quickly in vitamin D deficiency. One placebo-controlled clinical trial of the impact of vitamin D on joint symptoms in postmenopausal women found no difference in the incidence or severity of joint symptoms between vitamin D supplementation and placebo.\(^7\) Therefore, women taking calcium plus vitamin D should not expect an easing of joint symptoms.

**CANCERS**

The cause of pancreatic cancer is unclear. The risk of pancreatic cancer increases with an age of \(>45\) years: smoking history; history of head and neck, lung, or bladder cancer; diabetes; and high fat and food intake. Pancreatic cancer rates are increased in patients with chronic pancreatitis. One prospective cohort study examined whether vitamin D alters the risk and mortality of pancreatic cancer, but did not find a large difference between the study group and the group with insufficient vitamin D.\(^8\) Vitamin D deficiency has an adverse effect on colorectal cancer, while high vitamin D significantly lowers the risk of death from colorectal cancer. More research should be performed to examine the role of vitamin D in malignancy.

**CARDIOVASCULAR SYSTEM**

Lack of vitamin D inhibits the RAS, which negatively influences cardiovascular disease.\(^2\) In the RAS, the kidney secretes renin when the blood pressure drops, and renin is converted into angiotensin II by angiotensin-converting enzyme and then into angiotensin I in the liver, which increases the blood pressure. A knock-out study provided evidence that 1,25(OH)\(_2\)D\(_3\) is involved in regulating the RAS by inhibiting renin gene expression and reducing the activity of the cAMP response element.\(^9\)\(^,\)\(^10\) Numerous studies have found that serum 1,25(OH)\(_2\)D\(_3\) levels are inversely proportional to the blood pressure in normotensive individuals and hypertensive patients. 1,25(OH)\(_2\)D\(_3\) negatively controls the endocrine regulation of the RAS and cardiovascular function by interrupting the signal transmission path, reducing the synthesis of renin.\(^20\) If renin is suppressed, angiotensinogen is not activated by angiotensin I, which adversely affects blood pressure regulation.\(^21\) Vitamin D deficiency also has a negative effect on total cholesterol, LDL cholesterol (LDL-C), and insulin secretion in various ethnic groups.\(^22\) LDL-C is responsible for transporting liver-produced cholesterol to the tissues. When LDL-C levels increase, cholesterol builds up on the blood vessel walls, causing atherosclerosis. High-density lipoprotein cholesterol (HDL-C) prevents the accumulation of cholesterol. Therefore, vitamin D deficiency has a negative effect on LDL-C, increasing cardiovascular risk. Finally, vitamin D supplementation activates the RAS, re-
ducing LDL-C and positively affecting cardiovascular disease.

**UTERUS AND VAGINA**

Menopause-associated hormonal changes have many effects on the uterus and vagina. Vitamin D affects fertility and alleviates symptoms of vaginal atrophy, along with osteoporosis therapeutics. Vitamin D receptors (VDR) were expressed at a high level on uterus in postmenopause.

**HEALTH OUTCOME AND MORTALITY**

There has been recent interest in the effect of vitamin D on health. Supplemental calcium and vitamin D can have positive effects on hip fracture and colorectal cancer, but such supplementation does not reduce the risk of invasive breast cancer. A meta-analysis found that vitamin D alone does not affect mortality, but the risk of death was decreased if vitamin D was given with calcium.

In patients with osteoporosis, vitamin D supplementation increases the serum 1,25(OH)2D3 concentration, reducing PTH secretion and inhibiting osteolysis while increasing BMD. In patients with cardiovascular disease, vitamin D influences the RAS and has a positive effect on blood pressure. It also reduces LDL-C accumulation in the blood vessels. Consequently, vitamin D supplementation should lower the risks of postmenopausal osteoporosis, cardiovascular disease, and other diseases.

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**COMPETING INTERESTS**

The authors declare no conflict of interest.

**REFERENCES**

Peer Reviewer’s Commentary

Vitamin D supplementation increases the serum 1,25(OH)2D3 concentration, reducing PTH secretion and inhibiting osteolysis while increasing BMD. In patients with cardiovascular disease, vitamin D influences the RAS and has a positive effect on blood pressure.

In this review, the authors presented a number of function of the Vitamin D. Recently Several Research suggests that women with low levels of vitamin D have a higher risk of breast cancer. Vitamin D may play a role in controlling normal breast cell growth and may be able to stop breast cancer cells from growing. So it should be considered about the treatment level of Vitamin D.

(Editorial Board)