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VITAMIN D'S ROLE IN RHEUMATOLOGICAL, NEUROLOGICAL, AND IMMUNOLOGICAL PROBLEMS

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ABSTRACT

Over the past decade, more than 30,000 research papers worldwide have documented the numerous health benefits of vitamin D in managing a wide range of illnesses. The study aimed to review the crucial connection between vitamin D deficiency and its physiological role in neurological, rheumatologic, immunological, and other manifestations. Vitamin D is the primary hormone that regulates calcium, phosphate, and mineral bone metabolism balance. It controls calcium and phosphorus homeostasis, which is essential for maintaining and promoting the growth of healthy bone tissues. Vitamin D's effects on intracellular calcium homeostasis, neurotransmitter synthesis, neurotrophin production, and the prevention of oxidative damage to the nervous system are all linked to its neuroprotective properties. Another essential function of vitamin D is its role in regulating nervous system development. Deficiency in vitamin D can lead to atherosclerosis, causing vascular and endothelial abnormalities, rickets in development, and osteomalacia in adults. Vitamin D insufficiency is also associated with central nervous system disorders, such as schizophrenia, multiple sclerosis, anxiety, and dementia. Adequate vitamin D intake during pregnancy and the neonatal period can help prevent certain disorders.

Key words: *1, 25-dihydroxy vitamin D, bone development, central nervous system, Vitamin D deficiency*

INTRODUCTION

Vitamin D plays a crucial role in regulating the development of the nervous system. A deficiency in vitamin D can lead to atherosclerosis, resulting in vascular and endothelial abnormalities, rickets in development, and osteomalacia in adults. Additionally, vitamin D insufficiency is associated with central nervous system disorders, including schizophrenia, multiple sclerosis, anxiety, and dementia. (Sailike, et al., 2024). Adequate vitamin D intake during pregnancy and the neonatal period can help prevent certain disorders. Brain disorders such as depression, epilepsy, and Parkinson's disease are caused by vitamin D imbalance. Lower concentrations of vitamin D have been linked to atherosclerosis, endothelial dysfunction, hypertension, vascular inflammation, increased vascular myocyte proliferation, and secondary hyperparathyroidism, as well as other cardiovascular system problems. Research has also demonstrated a strong correlation between vitamin D and lipid metabolism, insulin secretion and sensitivity, and glycemic control, clarifying the connection between vitamin D deficiency and metabolic syndrome. Vitamin D deficiency contributes to the development of coronary artery disease, leading to arterial ageing, vascular calcifications, arterial stiffness, and atherosclerosis, decreased muscle fibre flexibility, and impaired functional performance.

When treating disorders of the bone and nervous tissue, vitamin D supplementation should be considered alongside other elements such as fibroblast growth factor, renin, parathyroid hormone, and phosphate levels. (Underland et al., 2020). Thus, the purpose of this review article is to explain how vitamin D functions as a hormone, neuroprotective agent, metabolic regulator, cellular growth regulator, and in a few other health-related ways.

CHEMISTRY

As a precursor to hormones, vitamin D regulates calcium absorption in the small intestine. It influences parathyroid hormone (PTH), which in turn affects blood calcium homeostasis and skeletal mineralization metabolism. Additionally, vitamin D impacts cytokines and immunological modulation. The recognized biomarker for vitamin D status is 25-hydroxyvitamin D, or calcidiol. Calcitriol (1, 25-dihydroxyvitamin D) measurements are only significant in cases of severe renal illness (Dusso et al., 2011).

VITAMIN D & VITAMIN D RECEPTOR (VDR)

It is now recognized that vitamin D is present in almost every tissue in the body, and its functions extend beyond controlling calcium and bone homeostasis. Vitamin D's activity is mediated by the Vitamin D Receptor (VDR). Recent epidemiological studies have sparked interest in a possible link between vitamin D and a variety of conditions, including ageing, autoimmune diseases, diabetes mellitus, hypertension, heart disease, and cancer. (Cooper et al., 2003). According to reports, vitamin D either directly or indirectly regulates around 3% of the human genome.

VITAMIN D AND MORTALITY

Due to its anti-inflammatory and immune-modulating properties, vitamin D may contribute to reduced mortality. In dialysis patients, it has been used to treat secondary hyperparathyroidism. Retrospective research suggests that vitamin D administration is associated with lower mortality rates among dialysis patients. In many patients with chronic renal illness before dialysis, low vitamin D levels are also linked to increased mortality, although no randomized trials have been conducted to examine this connection. Low vitamin D levels in non-dialysis patients are associated with higher levels of inflammation and antioxidant burden. Low vitamin D levels and cardiovascular mortality were positively correlated, according to a prospective study of over 3,000 male and female patients scheduled for coronary angiography. Individuals with inadequate vitamin D levels in the lowest quartile had a death rate ratio of 1.26, based on data analysis of survey data collected from over 13,000 people. A recent meta-analysis found that taking regular doses of vitamin D supplements is also associated with lower rates of all-cause mortality, suggesting that vitamin D plays a role in many causes of death. (Zhang, et al., 2019).

PHYSIOLOGICAL ROLE AND SOURCES OF VITAMIN D

After being exposed to sunlight, vitamin D is produced beneath the skin. The demand for vitamin D increases with ageing, pregnancy, and breastfeeding. It has been estimated that over one billion people globally are deficient in vitamin D. Pregnancy and lactation increase the need for vitamin D. Both the mother and the nursing child can avoid hypovitaminosis D by taking vitamin D supplements. Vitamin D supplementation is essential for women of reproductive age, according to a study conducted on African women. Foods such as cod liver oil, oily fish, milk, beef, eggs, yogurts, newborn formula milk, and margarine contain vitamin D. To address this issue, numerous nations have implemented various preventive measures.

In the human body, vitamin D serves a purpose. It facilitates the absorption of calcium and phosphorus. The skin produces cholecalciferol (D3), which the liver then transforms into 25-(OH) D3 and the kidneys into 1, 25-dihydroxycholecalciferol [1, 25-di (OH) D3]. 25-dihydroxycholecalciferol performs a number of bodily tasks. Vitamin deficiencies typically occur during wintertime due to reduced light exposure. Calcium and phosphorus levels in the blood are maintained by vitamin D.

(Çaykara, et al., 2020). Vitamin D is essential for the development and maintenance of bones. Conditions such as Crohn's disease, cystic fibrosis, coeliac disease, and surgical removal of a portion of the gut are associated with vitamin D malabsorption. Patients who take antiepileptic medications for an extended period of time may develop osteomalacia.

The kidney produces the active form of vitamin D following the hydroxylation process. Chronic renal illness prevents the kidneys from producing vitamin D in its active form. Vitamin D insufficiency is associated with multiple sclerosis. Vitamin D regulates

immune system responses. Overexposure to sunlight increases the risk of developing cancer. Vitamin D status is determined by measuring the blood's level of 25-hydroxycholecalciferol. People with dark skin have low vitamin D levels due to excessive melanin, which prevents UVB photons from being absorbed. When it comes to vitamin D production, white individuals are more effective than those with darker complexions. Compared to white individuals, people with darker complexions need more sun exposure to absorb and produce vitamin D. Compared to thin people; obese individuals are more likely to suffer from a vitamin D deficit. Vitamin D insufficiency impairs calcium and phosphorus absorption. A study on the culturing of rat neurons revealed that vitamin D raises the glutathione levels in these cells. In nerve cells, the reduced form of glutathione serves as an antioxidant and shields the cells from reactive oxygen radicals. (Averill-Bates et al., 2023). According to this study, vitamin D's neuroprotective properties are attributed to its ability to prevent oxidative damage to the central nervous system.

VITAMIN D STATUS

The active form of vitamin D, 25(OH)-D, is considered the most reliable indicator for determining serum vitamin D levels. Serum vitamin D levels typically range from 30 to 60 nanogrammes per millilitre (ng/mL). The Endocrine Society defines vitamin D deficiency as a level below 20 ng/mL and insufficiency as a level between 20 and 29.9 ng/mL.

PARATHYROID HORMONE

The control of calcium is influenced by parathyroid hormone (PTH). PTH indirectly stimulates osteoclasts, causing calcium to be released from bones (Feldman et al., 1980). It enhances calcium and magnesium reabsorption from distal tubules and thick ascending limbs. Additionally, it improves intestinal absorption of calcium. According to a report, parathyroid hormone affects the activity of the enzyme 1-α-hydroxylase, which converts 25-hydroxycholecalciferol into 1, 25-dihydroxycholecalciferol.

CAUSES OF VITAMIN D DEFICIENCY

The primary causes of vitamin D deficiency include inadequate exposure to sunlight, kidney transplantation, nephritic syndrome, decreased intestinal absorption, coeliac disease, gastric surgery, inadequate bile salt production, liver disease, pigmented skin, winter, obesity, advanced age, and a number of chronic diseases that affect vitamin D metabolism. Children with epilepsy have been shown to have poor bone health, and some of them have been discovered to have vitamin D deficiencies. Additionally, individuals on enzyme-inducing antiepileptic medications showed enhanced vitamin D catabolism.

INDIVIDUALS WITH LIMITED SUN EXPOSURE MAY EXPERIENCE VITAMIN D DEFICIENCY

Individuals with limited exposure to direct sunlight, such as those who work in offices during the day, sleep during the day, are housewives, or have occupations that limit their exposure to the sun, are more likely to acquire vitamin D deficiencies. The generation

of vitamin D from sunlight exposure is also influenced by the usage of sun blocking screens and the administration of protective cosmetic creams (Reichrath, et al 2025).

INADEQUATE INTAKE

Vitamin D deficiency is prevalent among both infants and older adults, largely due to inadequate dietary intake and insufficient cutaneous synthesis. Human breast milk contains approximately 22 IU L^{-1} of vitamin D, an amount insufficient to meet the needs of exclusively breastfed infants. Although some infant formulas are fortified, low vitamin D content remains a concern in certain preparations. In older adults, vitamin D deficiency is more frequent than in younger populations, driven by reduced dermal synthesis—owing to limited sunlight exposure—and suboptimal dietary intake. These factors contribute to an increased risk of bone demineralization and fractures in the elderly. Maternal supplementation at doses exceeding standard recommendations may be required to ensure adequate vitamin D transfer during lactation, while targeted supplementation strategies are essential for fracture prevention in aging populations.

GASTROINTESTINAL ABNORMALITIES AND FAT MALABSORPTION CONDITIONS CAN LEAD TO VITAMIN D DEFICIENCY.

In contrast to gastrointestinal diseases such as Crohn's disease, inflammatory bowel disease, and other malabsorption conditions that primarily impact fat absorption and ultimately lead to vitamin D insufficiency, healthy individuals absorb more lipids. Vitamin D supplementation may be necessary for people with a reduced ability to absorb lipids. (Lips et al., 2006). Numerous illnesses, including liver disease, Crohn's disease, coeliac disease, cystic fibrosis, and inflammation of the terminal ileum, have been linked to malabsorption of fats.

STEROIDS

Prednisolone and other corticosteroid medications, which are typically used to reduce inflammation, might also affect vitamin D metabolism and reduce calcium absorption. Bone loss and osteoporosis may develop as a result of long-term corticosteroid use.

LIVER AND KIDNEY DISEASE

Important enzymes in the kidney and liver convert food-based or sun-exposed vitamin D into the physiologically active form. Due to their low levels of these enzymes, patients with liver and renal illness are more likely to experience vitamin D insufficiency. Chronic renal disease and the latter stages of renal disease are associated with low vitamin D levels. Vitamin D treatment resolves the issue. Supplementing with vitamin D raises albumin levels, lowers bone turnover, and helps some people meet the KDOQI requirements for calcium and phosphorus. (Rysz et al., 2021). A lower amount of vitamin D increased cardiovascular risk, according to another study on peritoneal dialysis patients.

PATHOGENESIS

It is generally known that vitamin D, serum calcium, and parathyroid hormone are related. Bone metabolism is altered in the absence of activated vitamin D, resulting in the absorption of only 60% of phosphorus and

10% of calcium. Because osteoclasts demineralise bone to raise serum calcium, the skeleton serves as a primary basis for the body's calcium supply. In addition to causing osteomalacia, these activities also trigger and worsen osteoporosis and osteopenia.

VITAMIN D AND BONE DEFORMITIES

Worldwide, rickets, a disease caused by a lack of vitamin D, is still common. Due to inadequate nutrition, vitamin D insufficiency is still very common in several nations where solar exposure is an issue. According to a number of research studies, radiographs of the metaphyseal ends of long bones, typically at the wrist, show a distinctive look with cupping of the metaphyseal plate and broadening and fraying. (Caffey et al., 1970).

After a child is one year old, rickets develop as a result of costochondral junction edema. Alkaline phosphatase may rise while serum calcium and phosphorus may fall. The earliest radiological evidence is the lack of distinction between the growth plate and metaphysis. The hallmark signs of rickets at the ankles, knees, and wrists are splaying, fraying, and metaphyseal cupping. The hypertrophy of chondrocyte layers causes the gap between the metaphysis and epiphysis to widen. There is a thin white line of calcification at the junction of the growth plate and metaphyseal area during the early phases of healing, which thickens and becomes denser as the calcification advances. The bone's periosteum appears to be detached from the diaphysis as a result of osteoid unmineralization. Beginning in the first two months of life and continuing through adolescence, a minimum of 200 UD/day of vitamin D must be consumed. Research indicates that adolescents and children can safely consume 400 IU of vitamin D each day. Balanced sun exposure and protection can prevent vitamin D deficiency, and balanced sun exposure can lower the risk of skin cancer. In September through April, the best times to be exposed to sunshine are a few minutes before 10 am and after 3 pm every day. From May through August, two to three hours each week are spent in the sun. When UV levels are at their highest, children should be shielded from the sun by wearing clothing, sunscreen, and shade. Vitamin D and calcium should be included in children's diets. Foods high in vitamin D include liver, egg yolks, and oily fish, particularly mackerel, herring, salmon, and sardines (Lindsay et al., 1939). Enhancing the prevention of vitamin D deficiency in children can be achieved by combining fortified infant formula milk and vitamin D-containing margarines.

VITAMIN D AND THE HUMAN IMMUNE SYSTEM

Due to the presence of metabolising enzymes and vitamin D receptors in numerous immune cells, such as monocytes, B cells, T cells, and antigen-presenting cells, the immune system is extremely sensitive to changes in serum vitamin D levels. Vitamin D regulates the immune system, and vitamin supplements help the immune system, particularly when autoimmunity is present. Since the immune system depends on vitamin D for proper operation, a vitamin D deficit causes dysregulation of immunological responses. Research indicates that vitamin D boosts

innate immunity, which is demonstrated by the use of cod liver oil in tuberculosis treatment. Monocytes and macrophages are key effectors in the battle against Mycobacterium tuberculosis, and some research indicates that their actions against microorganisms are enhanced. Additionally, vitamin D contributes to improving the phagocytic and chemotaxis capacities of monocytes and macrophages. Vitamin D targets monocytes, innate antigen-presenting cells, and dendritic cells to influence the immune system. (Carlberg et al., 2019). By exposing B cells and T cells to an antigen, antigen-presenting cells promote the adaptive immune response. They can also influence these cells by immunogenic or tolerogenic cues, such as the production of cytokines and other co-stimulatory substances. Calcitriol inhibits T cell cytokines such as interleukin 1 and 17. Supplementing with large doses of calcitriol (1 µg twice daily for 7 days) dramatically lowers interleukin 6. Bergman et al. (2012) conducted a study to explore the connection of vitamin D with respiratory tract infections in immuno-deficient patients. In this study, 140 immunocompromised patients received 4000 IU of vitamin D each day. Comparing the test group to the placebo group, vitamin D significantly decreased the amount of pathogens in nasal fluid, infectious symptoms, and antibiotic use. Genetic predisposition, epidemiological risk factors, and environmental factors all contribute to the development of autoimmune disorders. Vitamin D insufficiency has been linked to autoimmune illnesses, including multiple sclerosis, RA (rheumatoid arthritis), SLE (systemic lupus erythematosus), and inflammatory bowel disease. Vitamin D reduced or avoided autoimmunity in animal models of inflammatory bowel disease, multiple sclerosis, autoimmune uveitis, and systemic lupus erythematosus. According to certain research, vitamin D plays a role in the development of type 1 diabetes mellitus, which is brought on by T cell-mediated death of the pancreatic beta cells. Early-life vitamin D supplementation protects against type 1 diabetes (Harris et al., 2005).

PSORIASIS

Vitamin D is applied topically in a synthetic formulation. Vitamin D inhibits the growth of keratinocytes and modulates the immunological system.

ROLE OF VITAMIN D AS A NEUROHORMONE

Myelination, neuroprotection, and brain function are all significantly impacted by this vitamin. It has recently been discovered that vitamin D regulates progesterone's ability to shield the brain from severe injury. In animals with low vitamin D levels, progesterone's protective impact is diminished. Additionally, combination therapy—such as vitamin D and progesterone—is more effective than progesterone alone at protecting the reference and spatial memory after bilateral contusions of the medial frontal cortex.

ROLE IN WEIGHT LOSS

Individuals seeking to lose weight are advised to take vitamin D. A study found that those who received vitamin D lost more weight than those who received a placebo. Extra calcium

and vitamin D are said to have appetite-suppressing properties (Stuby et al., 2019).

NEUROMUSCULAR FUNCTION

Vitamin D and neuromuscular function are strongly correlated. Vitamin D insufficiency is linked to postural instability. When youngsters with vitamin D insufficiency take vitamin D supplements, their body sways less.

DEPRESSION AND ANXIETY

Psychiatric and neurological disorders are brought on by vitamin D insufficiency. Depression and decreased cognitive function have been linked to vitamin D deficiency. Other research findings, however, have shown inconsistent data, most likely due to the fact that 1, 25 dihydroxyvitamin concentrations were measured rather than 25 hydroxyvitamin D concentrations. Genetic alterations in vitamin D receptors affect cognitive abilities and depressive symptoms in older adults (Kuningas et al., 2009). More than a thousand older persons participated in a study to measure vitamin D levels in depressed patients. The author came to the conclusion that, as compared to controls, patients with major and moderate depression had reduced vitamin D levels. Another study looked at the connection between vitamin D levels and the onset of depression in 7,970 young adults in the US between the ages of 15 and 39. It found that depression is common in those with low vitamin D levels. Winter and a lack of sunlight are thought to be potential causes of seasonal affective disorder. Vitamin D-containing supplements have shown promise in treating seasonal affective disorder. That suggests that vitamin D and depression are related. Research indicates that vitamin D supplements are more successful in treating seasonal affective disorders than phototherapy.

VITAMIN D AND COGNITION

Numerous studies have found that individuals with Alzheimer's disease have lower blood vitamin D levels compared to those without the disease. The antioxidant properties of this vitamin and the presence of vitamin D receptors in the hippocampus, observed in both humans and rats, support the biological validity of this connection. (Gáll et al., 2021). 225 patients were selected to investigate the relationship between Alzheimer's disease and vitamin deficiencies.

MULTIPLE SCLEROSIS

The presence of CYP27B1 and CDRs across a range of neurological and immune cells suggests that vitamin D may have been useful in multiple sclerosis (MS). A study on a sample of seven million US military veterans revealed that individuals with high blood levels of vitamin D were less likely to develop MS. MS is less common in populations where fish oil is a staple meal. Because it activates natural killer (NK) cells, vitamin D is crucial for immune regulation and the avoidance of autoimmune diseases. Patients with MS have lower levels of NK cells. MS develops as a result of environmental risk factors such as vitamin D insufficiency and Epstein-Barr virus infection (Correale et al., 2015). Children who engage in outdoor activities throughout the summer have been less likely to develop multiple sclerosis, and taking cod liver oil supplements is beneficial in regions with less sun exposure. The mother's vitamin D levels during

pregnancy and the month of delivery may affect the likelihood that her children may develop multiple sclerosis as adults. Those born in the spring have a higher prevalence of multiple sclerosis than those born in the autumn. In their 2010 study, McDowell et al. examined 927 US military personnel who had multiple sclerosis and found that individuals born in winter and in regions with low sun radiation experienced symptoms of the condition earlier than those born in the spring and in regions with high solar radiation.

EPILEPSY

Increasing school-age children experience vitamin D deficiency, leading to tetanyin or hypocalcemic seizures. Hypocalcaemia and electrolyte imbalances can cause seizures. Standard blood calcium levels are essential for neuronal activation. Parathyroid hormone and vitamin D help maintain normal calcium levels. (Adami et al., 2008). Vitamin D insufficiency is a major global public health concern, particularly in developing countries. Deficiency reduces intestinal calcium absorption, leading to hypocalcaemia—a condition most frequently observed during periods of rapid growth, such as infancy and puberty. Beyond its skeletal effects, vitamin D also modulates neuronal excitability. In a pentylenetetrazole (PTZ)-induced epilepsy animal model, pre-treatment with vitamin D (administered 30–180 min before seizure induction) attenuated seizure severity. Mechanistically, vitamin D suppresses interleukin-6, a pro-convulsant cytokine, while up-regulating neurotrophic factors such as glial cell line-derived neurotrophic factor (GDNF) and the anticonvulsant protein TN3. Deficiency disrupts this balance, impairing both pro-convulsant down-regulation and anticonvulsant up-regulation, thereby lowering the seizure threshold. Additionally, vitamin D influences the expression of calcium-binding proteins, further contributing to its neuroprotective effects.

SCHIZOPHRENIA

A meta-analysis of observational studies revealed a correlation between schizophrenia and low vitamin D levels. The exact mechanism underlying this association remains unclear. Schizophrenia patients exhibit elevated levels of inflammatory markers. (Upthegrove et al., 2019). Vitamin D modulates immune and neurodevelopmental processes implicated in schizophrenia pathophysiology. Cells with sufficient vitamin D produce fewer and less diverse inflammatory cytokines, whereas deficient cells exhibit a broader pro-inflammatory profile, suggesting an anti-inflammatory mechanism of action. At the molecular level, vitamin D regulates the transcription of genes involved in brain development, synaptic plasticity, and oxidative stress defense. In pregnancy, deficiency alters dopaminergic pathway development and dopamine metabolism in the fetal brain—mechanisms strongly associated with schizophrenia risk. Epidemiological studies indicate that low maternal vitamin D, particularly during the third trimester, correlates with increased incidence of schizophrenia in offspring. In one case–control analysis, 26 vitamin D-deficient mothers had children with schizophrenia, compared to 51 vitamin D-sufficient controls. The association

was especially pronounced among African-American mothers and their children. These findings support a role for maternal vitamin D sufficiency in reducing schizophrenia risk through both neurodevelopmental and immunomodulatory pathways.

CARDIOVASCULAR DISORDERS

Vitamin D supplements don't significantly lower the risk of heart conditions including myocardial infarction and stroke (Kotta et al., 2015). Blood pressure is not significantly affected by vitamin D supplements. Supplementing with calcium and vitamin D did not have a clinically meaningful effect on the risk of coronary heart disease or cerebrovascular disease, according to randomized clinical trials. A systematic review of randomized clinical trials found that vitamin D had only a small impact on cardiovascular outcomes and hypertension. Several studies suggest that vitamin D supplementation in deficient individuals may improve metabolic profiles and reduce cardiovascular risk. However, more research is needed to determine its proper location in treatment.

RESPIRATORY HEALTH

The inflammatory response in the lungs is reduced by vitamin D. The immune system of the lungs is strengthened against infections by vitamin D. Population-based researches have shown a link between lung function and circulating vitamin D levels. Although vitamin D is frequently given to patients with cystic fibrosis, there is little data to support its advantages.

INFECTIOUS DISEASES

Vitamin D receptors are found in immune system cells, including T and B lymphocytes, neutrophils, and macrophages (Skrobot et al., 2018). Current evidence establishes vitamin D as a critical modulator of immune function. A randomized controlled trial investigating vitamin D supplementation at 800 IU daily found no statistically significant association with self-reported infection rates or antibiotic utilization. Conversely, randomized clinical trial data demonstrate that vitamin D supplementation enhances immune responses in patients with tuberculosis.

A systematic review of randomized controlled trials evaluating vitamin D supplementation efficacy in influenza, tuberculosis, and various viral infections concluded that additional research is warranted to establish definitive therapeutic benefits. Epidemiological studies have identified vitamin D deficiency as a risk factor associated with tuberculosis reactivation. Comparative analyses reveal significantly lower serum vitamin D concentrations in tuberculosis patients relative to healthy control subjects. Furthermore, prolonged antitubercular therapy has been shown to further reduce circulating vitamin D levels.

Multiple investigations have characterized vitamin D as a pivotal immunomodulator of innate immune responses, functioning as an essential cofactor in the initiation of antimycobacterial immune mechanisms. These findings support the role of vitamin D in host defense against mycobacterial infections through modulation of innate immunity pathways.

ALOPECIA

Vitamin D is applied topically to alopecia patients undergoing chemotherapy. The effects of vitamin D on alopecia are poorly understood, despite its widespread use. Based on preclinical investigations utilizing animal models of chemotherapy-induced alopecia, vitamin D has been demonstrated to upregulate follicular receptors. Experimental studies in animal subjects have revealed that vitamin D supplementation promotes hair follicle development and growth throughout the integumentary system. However, these findings indicate that while vitamin D exhibits hair growth-stimulating properties, it does not possess the capacity to prevent or inhibit chemotherapy-associated hair loss in these experimental models. (Jimenez et al., 1996). Results from a few clinical trials have been inconsistent, most likely depending on the chemotherapeutic drug.

DIABETES

Epidemiological evidence suggests an inverse association between vitamin D status and diabetes incidence. Meta-analytic data have confirmed a significant relationship between vitamin D deficiency prevalence and type 2 diabetes mellitus risk. Additionally, observational studies have reported associations between neonatal vitamin D supplementation and reduced type 1 diabetes risk in later life.

However, clinical trial data examining the physiological effects of vitamin D supplementation on glycemic control remain limited and have produced inconsistent results, necessitating further investigation to establish causal relationships.

A prospective cohort study with 10-year follow-up in 524 non-diabetic subjects demonstrated a significant inverse correlation between baseline serum 25-hydroxyvitamin D [25(OH) D] concentrations and subsequent diabetes mellitus development. In a separate cohort study of 10,366 pediatric subjects, daily vitamin D supplementation at 2,000 IU was associated with a 78% reduction in type 1 diabetes risk compared to participants receiving lower supplementation doses.

These observational findings suggest a protective role for adequate vitamin D status in diabetes prevention; however, randomized controlled trials are required to establish definitive therapeutic recommendations and elucidate underlying mechanisms of action.

AUTOIMMUNE DISEASES

Improved immunological response is typically the result of vitamin D's positive effects, and this is linked to the complex control of acquired immunity (Bikle et al., 2022). Vitamin D deficiency has been implicated in the pathogenesis of numerous autoimmune conditions. Current research suggests that vitamin D and its analogues may serve dual therapeutic roles in autoimmune disease management: treatment of established conditions and prevention of disease progression.

Preclinical studies utilizing experimental animal models have demonstrated therapeutic efficacy of vitamin D supplementation across multiple autoimmune pathologies. These include systemic lupus erythematosus (SLE),

collagen-induced arthritis, autoimmune thyroiditis, type 1 diabetes mellitus, inflammatory bowel disease (IBD), and experimental allergic encephalomyelitis.

The observed therapeutic benefits in these animal models support the hypothesis that vitamin D functions as an immunomodulatory agent capable of attenuating autoimmune inflammatory responses. These preclinical findings provide a foundation for understanding the potential mechanisms by which vitamin D may influence autoimmune disease development and progression.

However, translation of these experimental results to clinical applications requires validation through well-designed human clinical trials to establish optimal dosing regimens, treatment duration, and patient selection criteria for vitamin D supplementation in autoimmune disease management. According to You et al. vitamin D support proper mating of impregnation (.

CANCER

The administration of vitamin D is used to cure cancer. It is crucial for preserving cell division and intercellular communication. Certain studies have shown that vitamin D can reduce metastasis and cell division, increase the death of cancer cells, and slow the growth and formation of new blood vessels. Low vitamin D levels are associated with an increased risk of developing cancer, according to observational studies (Heath et al., 2019). Current evidence regarding vitamin D supplementation in cancer patients remains limited and inconclusive. Observational studies demonstrate a correlation between elevated serum vitamin D concentrations and improved cancer outcomes, while vitamin D deficiency is associated with poorer prognosis across multiple cancer types.

Preclinical investigations have established that vitamin D exerts significant effects on various cancer cell lines through multiple mechanisms, including induction of apoptosis and cell cycle disruption. Meta-analyses of observational studies have consistently demonstrated an inverse association between high serum 25-hydroxyvitamin D levels and overall cancer incidence, with particular emphasis on breast, colorectal, and prostate malignancies.

Mechanistic studies have elucidated that vitamin D inhibits cellular proliferation and promotes terminal differentiation in both malignant and normal cells expressing vitamin D receptors (VDRs), including prostate cancer cells. Specifically, vitamin D has been shown to inhibit LNCaP (lymph node carcinoma of the prostate) cell growth and induce apoptosis in vitro.

Despite these promising preclinical findings and supportive observational data, randomized controlled trials evaluating vitamin D supplementation as a therapeutic intervention in cancer patients are insufficient to establish clinical recommendations. Further well-designed clinical studies are necessary to determine optimal dosing strategies, treatment duration, and patient selection criteria for vitamin D supplementation in cancer prevention and adjuvant therapy.

(Zhao, et al 2001). Apoptosis and disruption of the cell cycle are among the processes that have been identified.

COLON CANCER

Vitamin D receptors (VDRs) are extensively distributed throughout human tissues, including colonic epithelium. In vitro investigations have demonstrated that vitamin D exhibits anti-proliferative effects against colorectal cancer cell lines, suggesting potential therapeutic mechanisms.

However, clinical trial data present conflicting results regarding vitamin D's protective effects against colorectal malignancy. A randomized controlled trial evaluating moderate daily supplementation with calcium (1000 mg) and vitamin D (400 IU) demonstrated minimal impact on colorectal cancer incidence among healthy women at average risk. Conversely, case-control study data reveal a significant inverse association between serum vitamin D concentrations and colorectal cancer frequency.

These disparate findings highlight the complexity of translating preclinical mechanistic data to clinical outcomes. The observed discrepancies between controlled trial results and observational studies may reflect differences in study design, supplementation dosages, study populations, follow-up duration, or baseline vitamin D status among participants.

The current evidence base suggests that while vitamin D may possess anti-neoplastic properties against colorectal cancer at the cellular level, the clinical significance of supplementation for cancer prevention remains unclear. Additional large-scale randomized controlled trials with adequate follow-up periods and appropriate dosing regimens are required to resolve these conflicting findings and establish evidence-based recommendations for vitamin D supplementation in colorectal cancer prevention.

MANAGEMENT OF VITAMIN D DEFICIENCY

Alpha-alfacalcidol (1α-hydroxyvitamin D3), available as Cap-one leo in 0.25 µg and 1 µg formulations, represents a synthetic vitamin D analogue utilized in clinical practice. The recommended dosage range for alpha-alfacalcidol is 0.5 to 2.5 µg daily, with dosing individualized based on patient requirements and serum calcium monitoring.

Concurrent calcium supplementation is typically prescribed, with calcium carbonate administered at doses of 1.0 to 1.5 grams daily to optimize therapeutic outcomes and prevent hypocalcemia.

Standard vitamin D supplementation commonly employs cholecalciferol (vitamin D3), which represents the naturally occurring form of vitamin D synthesized in human skin upon ultraviolet B exposure. Cholecalciferol serves as the primary constituent in most commercial vitamin D preparations and requires hepatic 25-hydroxylation followed by renal 1α-hydroxylation to achieve biological activity.

The distinction between alpha-alfacalcidol and cholecalciferol lies in their metabolic requirements: alpha-alfacalcidol bypasses the initial hepatic hydroxylation step, requiring only renal 25-hydroxylation for activation, while cholecalciferol requires both hepatic and renal enzymatic conversions. This pharmacokinetic difference may provide

therapeutic advantages in patients with compromised hepatic function or specific metabolic disorders affecting vitamin D metabolism.

(Vieth et al., 2020). Some researchers claim that when taken as a supplement, it can be taken with meals. Enhanced absorption of fat-soluble vitamins occurs through stimulation of bile secretion into the intestinal tract following consumption of dietary fats and oils. This physiological mechanism facilitates improved bioavailability of lipophilic vitamins through bile acid-mediated emulsification and micelle formation, which are essential for optimal intestinal absorption of fat-soluble compounds.

MANAGEMENT OF PHOSPHATE DEFICIENCY

Improvements in nutrition are recommended. An oral phosphate supplement containing vitamin D is administered. Antacids that contain aluminium are prohibited. Human recombinant growth hormone may be added to the aforementioned regimen, as it reduces phosphaturia. (Reusz et al., 1997).

PREVENTION

400 IU of vitamin D should be given to every breastfeeding baby. Newborns can be provided with vitamin A, D, and C drops because they are produced at standard amounts. According to recommendations, breastfeeding mothers should get about 600 units of vitamin D daily. A daily intake of 1500–2000 units is advised based on the literature review.

CONTRAINDICATIONS

Vitamin D supplementation is contraindicated in patients with Williams's syndrome, sarcoidosis, metastatic bone disease, and granulomatous disorders due to increased risk of hypercalcemia and associated complications. Williams's syndrome patient's exhibit heightened sensitivity to vitamin D due to genetic alterations affecting calcium metabolism, predisposing them to severe hypercalcemia even with standard supplementation doses. Sarcoidosis and other granulomatous diseases are characterized by extrarenal 1α-hydroxylase activity within inflammatory granulomas, leading to unregulated production of active vitamin D metabolites and subsequent hypercalciuria and hypercalcemia.

Patients with metastatic bone disease, particularly those with osteolytic lesions, demonstrate increased calcium release from skeletal tissue. Vitamin D supplementation in this population may exacerbate existing hypercalcemia through enhanced intestinal calcium absorption, potentially precipitating life-threatening complications including cardiac arrhythmias, nephrolithiasis, and acute kidney injury.

These contraindications necessitate careful patient screening prior to initiating vitamin D therapy. Alternative approaches to maintaining bone health and managing vitamin D deficiency in these high-risk populations require individualized assessment and may involve specialized monitoring protocols or alternative therapeutic interventions under specialist supervision.

Healthcare providers must exercise clinical judgment and consider risk-benefit ratios when evaluating vitamin D supplementation in

patients with these underlying conditions (Gianella et al., 2020).

INTERACTIONS

Drugs that can affect vitamin D's function include lead, anticonvulsants, antifungal medications, and cytotoxic agents. Valproate speeds up the conversion of 25-OHD 2 to the inactive form of 24, 25-dihydroxyvitamin, which is used to treat epilepsy. It has been shown that taking medications raises serum vitamin D levels. Multiple pharmaceutical agents demonstrate significant interactions with vitamin D pharmacokinetics. Orlistat impairs intestinal vitamin D absorption through inhibition of pancreatic lipases, thereby reducing the bioavailability of this fat-soluble vitamin. Corticosteroid therapy interferes with vitamin D metabolic pathways, resulting in decreased biological activity. Anticonvulsant medications, including phenytoin and phenobarbital, enhance hepatic vitamin D catabolism through induction of cytochrome P450 enzymatic systems, leading to accelerated metabolite clearance and reduced serum concentrations. (Filippatos et al., 2008).

ADVERSE REACTIONS

Massive doses of vitamin D have little negative effects in clinical trials.

TOXICITY

Concurrent administration of calcium and vitamin D supplements, particularly in combination with fortified food products, may result in hypercalcemia and elevated serum vitamin D concentrations in susceptible individuals. Excessive calcium intake from supplemental sources has been associated with an increased risk of nephrolithiasis formation. These findings indicate the need for careful monitoring of serum calcium and vitamin D levels in patients receiving combination supplementation therapy, and consideration of total dietary calcium intake when prescribing supplemental regimens to minimize the risk of adverse outcomes.

(Curhan et al., 1993). Excessive vitamin D use can harm tissues and the lungs. More than 150 ng/mL of vitamin D is considered dangerous. Additional symptoms of poisoning include nausea, constipation, and weakness. Long-term sun exposure does not cause vitamin D to become contaminated. Thus, it is advised that people refrain from attempting to raise their vitamin D production by being in warm environments, as this will also raise their chance of developing skin cancer.

CONCLUSION

Vitamin D is a fat-soluble, hormone-like vitamin essential for bone development, immune function, neurological health, and metabolism. Global vitamin D deficiency rates are increasing due to factors including poverty, malnutrition, and lifestyle changes.

Deficiency is associated with multiple conditions including rickets, osteomalacia, osteoporosis, osteoarthritis, congenital malformations, and muscle pain. Adequate vitamin D status supports brain development and may reduce cancer risk and central nervous system disorders.

Public health strategies should promote appropriate dietary vitamin D intake and supplementation to address widespread deficiency and prevent associated health complications.

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