THE EFFECT OF VITAMIN D DEFICIENCY ON THE HEALTH OF YOUNG AND OLD AND PHARMACOLOGICAL TREATMENT

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Abstract:
The study's goal is to learn more about the significance of vitamin D, how it directly affects human health, and how crucial it is for the body to maintain enough levels of it. The study's goal is to learn more about the significance of vitamin D, how it directly affects human health, and how crucial it is for the body to maintain enough levels of it. Google Drive was used to create an electronic questionnaire, which was then disseminated via WhatsApp, a social networking app, to people in the city of Mecca who ranged in age from 16 to 65. A total of 1150 questionnaires were distributed. There were only 900 surveys that had responses.

Keywords: Vitamin D, deficiency, young and old, Pharmacological Treatment

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1- Introduction:

In addition to its numerous biological effects, vitamin D is a class of fat-soluble secosteroids that are responsible for increased intestinal absorption of calcium, magnesium, and phosphate [4, 5]. The most significant combination in this category for humans is vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) [4, 5, 6]. As a result of exposure to sunshine, particularly UVB rays, the skin's reduced layers assemble cholecalciferol, which is the primary natural exporter of the vitamin [7, 8]. Both the regimen and supplements contain ergocalciferol and cholecalciferol [9, 5]. Important levels of vitamin D are found naturally in just a few meals, such fatty fish flesh [10, 8]. Vitamin D is added to many cereal bowls for breakfast as well as cow's milk and plant-based milk substitutes in the US and other countries [4]. Dietary recommendations often assume that a person takes their vitamin D orally since sun exposure varies across individuals and many are cautious to determine the acceptable amount of sun exposure because of the risk of skin cancer [4]. Skin production or dietary vitamin D is not physiologically effective [15]. It functions by the hydroxylation of proteins in two stages, the first of which occurs in the liver and the second in the kidneys (8). Since most animals can manufacture adequate vitamin D when exposed to enough sunshine, vitamin D plays a crucial role in the metabolism and metabolism of calcium. His findings included the ability to identify the vitamin deficiency in children with rickets, a pediatric type of osteocalcin [12, 5]. Osteocalcin and vitamin D complements are used to treat or prevent rickets [5]. One definition of vitamin D insufficiency is having less vitamin D in the body than usual. People most frequently experience it when exposed to little sunshine, particularly ultraviolet B rays [13, 14]. Unrest that restricts vitamin D absorption and prevents the conversion of vitamin D into powerful metabolites, such as certain liver and kidney diseases, improper vitamin D food intake, and hereditary issues can also result in vitamin D insufficiency [13].

The study was attitude in the city of Mecca in Kingdom of Saudi Arabia from January 2022 to January 2022. The investigators used adjective analytical way which uses quantitative attributive or specific of the phenomenon of culture, which is look very significant in the humane and public part and is identify by this kind of research on analysis and cause, topically and linked reality, where attention by persons and proxies and foundations, regimen, countries and characterized the past, as is the depiction qualitative which adjectives the phenomenon painted the impacts of its non-attendance and the means used and the spread of their effect on the lives of the person and community and analysis are contributory changeable in the evolution and creation, as for quantitative idiom it gives us a specification digitally, shows how much the phenomenon, It will be the study of the changing, the health of the body, the social, the expander, and the prevalence of illness and their relationship to demographic inconstant such as age, genus, nationality, married cases, occupation, (1) to do statistical analysis such as locating the middle and statistics adjectival been used disparity between the averages analysis and use Excel program Office Group 2010 graphics histogram to tidy scores by pull them on the statistical plan (2).

2- The effect of vitamin D deficiency on teeth

Teeth are mineralized organs, surrounded by alveolar bone, and formed by three distinctive hard tissues: enamel, dentin, and cementum. The tooth mineralization process occurs parallel to skeletal mineralization, yet if mineral metabolism is disturbed then failures will occur similarly to those that occur in bone tissue. Vitamin D plays a key role in bone and tooth mineralization, and when levels are unregulated it can lead to the “rachitic tooth”, which is a defective and hypomineralized organ highly susceptible to fracture and decay [16]. The mechanisms by which VDD affects tooth mineralization are well debated elsewhere. The main biological basis relies on the fact that severe VDD (<10 ng/mL) causes hypocalcemia and hypophosphatemia with secondary hyperparathyroidism (driven by hypocalcemia) [17]. This hyperparathyroidism promotes intestinal absorption of calcium (Ca^{2+}), and renal production of 1 α,25-dihydroxyvitamin D (1,25[OH]2D), increasing bone turnover leading to elevated serum levels of Ca^{2+} and low serum levels of inorganic phosphate (Pi). The initial hypophosphatemia is then severely worsened. Ultimately, the loss of vitamin D signaling pathways in tooth cells with low concentrations of Ca^{2+} and phosphate ions inhibit proper mineralization of teeth and mineralization defects occur. Apart from its mineralization homeostasis role, circulating vitamin D can initiate a signaling pathway through vitamin D receptors (VDR). VDR is a ligand-activated transcription factor that controls gene expression through vitamin D elements (VDRE) [18]. For instance, some of these responsive genes affect bone, mineral metabolism, immune response, cell life cycle and migration, skeletal muscle, detoxification, and energy metabolism. Vitamin D upregulates VDR which, in turn, can induce structural gene products, including calcium-

binding proteins and various extracellular matrix proteins (e.g., enamels, amelogenins, dentin sialoglycoproteins, and dentin phosphoproteins), resulting in the formation of dentin and enamel. Beyond the typical VDD causes, nutritional deficiency or reduction of sunlight exposure, there are genetic deficiencies originating from mutations encoding elements of the vitamin D metabolic machinery. The main causes of VDD, second to genetic mutations, are abnormal enzyme secretion (i.e., vitamin D-dependent rickets type 1, VDDR-I) and anomalous VDR function or signaling (vitamin D-dependent rickets type 2, VDDR-IIa; hereditary defects in the vitamin D receptor-effector system, HDVDR) [19]. These genetic conditions cause defective mineralized tissues, despite normal vitamin D consumption or sunlight exposure and, ultimately, will increase the risk of mineralized tooth tissue hypoplasia (i.e., amelogenesis imperfecta, dentinogenetic imperfecta, enamel hypoplasia) or higher risk of caries. Remarkably, deciduous dentition can be influenced by maternal 25(OH)D levels, despite the influence of inherited defects of the fetus. Fetal serum-circulating levels of vitamin D follow the maternal concentration and can be used as a standard surrogate marker to the fetus. Therefore, if maternal 25(OH)D levels turn unbalanced, this may have direct repercussions on the baby's health [20] and, in particular, on tooth development. The pattern of mineralization defect depends on the specific week of gestation when maternal VDD occurred. For example, approximately at the 13th week from conception, the human primary maxillary central incisor begins its calcification, and if there is a VDD status, there could be a hypoplasia/mineralization defect on the incisal third of the crown. Nowadays, it is known that maternal VDD at 12–16, 20–32 and 36–40 weeks results in defects at the incisal third, middle third and cervical third, respectively [21].

In a randomized clinical trial (RCT), vitamin D supplementation during pregnancy revealed that pregnant women with < 15 ng/mL of vitamin D had a 14% higher risk of deciduous dentition [22]. In contrast, high-dose vitamin D supplementation during pregnancy was associated with an approximately 50% reduced odds of enamel defects. In another RCT, high-dose Vitamin D supplementation during pregnancy was linked to 50% lower risk of enamel defects in the newborn, underlying once more the likely preventive role of Vitamin D for enamel defects [23]. Furthermore, untreated caries in deciduous and permanent teeth were the most prevalent condition, affecting 9% and 35% of global population, respectively. Moreover, according to WHO, caries is the fourth-most expensive chronic disease to treat. This infectious disease has a complex and multifactorial etiology. Environmental factors, such as cariogenic diet with a high carbohydrate content, cariogenic bacteria, and poor oral hygiene were the most widely studied risk factors [24]. Nevertheless, when exposed to the same environmental risk factors, some patients are more susceptible or resistant to caries than others, so that environmental factors alone are insufficient to explain the prevalence and incidence of caries. Currently the evidence highlights the association of low levels of vitamin D and the high prevalence of caries in both children and adults, although the mechanism remains unclear [25].

Additionally, vitamin D exerts several roles in the control of the human immune system, and an optimal vitamin D concentration (≥75 nmol/L) is associated with lower odds for dental caries in children [26]. However, the studies' results are contradictory. A recent systematic review of controlled clinical trials, with data from 2827 children, investigated the impact of vitamin D supplementation on dental caries prevention. The results of this study show that vitamin D supplementation reduced the risk of caries in about 47%, but with low certainty [27]. Another research supports that caries-free children were twice as likely to have optimal vitamin D concentrations (≥75 nmol/L) and those with severe early childhood caries were at nearly three times the odds of having deficient levels (<35 nmol/L) [26]. On the one hand, it is important to clarify that serum vitamin D does not change the major structure of teeth since this structure remains constant until some extrinsic factor causes its wear. Notwithstanding, apparently vitamin D prevents caries lesions through immune regulation, promoting microbial eradication with peptide activity as discussed above. The roles of both UVB and antimicrobial peptides (AMPs) in cariogenic bacteria reduction have been studied [28]. The mechanism through which UVB reduces the risk of dental caries is likely to be through the production of vitamin D and followed by the induction of AMPs, which have antimicrobial properties [29]. AMPs are host defense peptides, mostly cationic and amphiphilic molecules, that are essential elements of the innate immunity against several bacteria, fungi and viruses [30]. Investigations seem to point to a combination of AMPs rather than a specific role of a single AMP [31], and they have been proposed as potential application for the prevention and treatment of dental caries [32]. Remarkably, Streptococcus mutans, a primary etiological agent of dental caries, may resist host salivary AMPs explaining its virulence in dental caries pathophysiology [33]. Hence, we can

conclude that vitamin D control levels prior to conception may be important to reduce the risk of enamel defects in deciduous teeth and should be controlled throughout pregnancy and after delivery.

3- Results and Discussion:

One important and practical method for obtaining information is reconnaissance. However, because the public refrained from assassinations at that time, researchers were unable to personally interact with participants based on their responses to the online questionnaire. This prevented participants from spreading the findings of the study to researchers, and vice versa. Additionally, since the questionnaire only includes twelve locked questions, answering it electronically was adequate. Additionally, the internet route has been utilized in Saudi Arabia and other countries to produce suitable specimens for the same purpose (3). The first question was about, did you check my vitamin D blood test? Those who answered yes were 75.3% and 22.1% with no, and the second question was about my suffering from pain in my bones and joints. Of those who answered yes 65.7% and 34.2%. The third question was about diversifying my food in order to maintain my health. Strongly agreeable was 28.3%, agree 50.5%, neutral 15.2%, disagree 7.8%, and strongly disagree 0%. As for the fourth question, how do I exercise daily in the day at a rate of half an hour a day? Strongly agree, agree, disagree, and neutral were equal to 22%, and strongly disagreed with 13.5%. The fifth question was about wearing long clothes and covering my head when I leave the house in the morning. Strongly agreeable and agreeable were equal at 34.7%, disagreeable and neutral were equal at 13.3%, and strongly disagreed was 0%. Sixth question: I weighed my body and found that my body mass index (BMI) is above 30 kg recently. Strongly agreeable and strongly disagree were equal at 7.5%, while neutral was 35.7% and disapproved at 28.2%. As for the seventh question, do I suffer from kidney and liver health problems and take medicines for them? 7.3% strongly agree, 0% agree and are neutral, 28.1% disagree and 65.2% strongly disagree, the eighth question: I feel tired and weak in my body? Where the strong agree and disagree were equal at 0%, agree at 35.3%, neutral at 28.4%, and disagree at 35.1%, Question 8: I feel tired and generally weak in my body. Where the agree strongly and disapproving were equal at 0%, agree at 34.9% and neutral at 29.1%, and disagree at 35.5%, Question nine I feel sleepy or lethargic in general? The answer was as follows: strongly agree 14.9%, agree 22.4%, neutral 28.1%, disagree 35.4%, and strongly disagree 0%. As for the tenth question, I suffer from hair loss and an increase in weight, and I often feel pain in the bones and joints. Strongly agreeable was 22.1%, agreeable 15.1%, neutral 35.4%, disagree 28.2%, and strongly disapproval 0%. As for the eleventh inquiry, do I suffer from depression, anxiety, and forgetfulness on a daily basis? Strongly agreeable and strongly disagreeable were equal to 15.3%, agreeable and disagreeable at 21.7%, and neutral at 28.4%. The twelfth (last) question was about, strongly agree 14.5%, agree 7.9%, neutral 21.1%, disagree 50%, and strongly disagree 7.1%.

4- Pharmacological Treatment:

Individuals with a measured 25(OH)D concentration below 20 ng/mL (50 nmol/L) should be treated with vitamin D supplementation, because their vitamin D requirements may not be met [34]. There is controversy in the scientific literature whether 25(OH)D concentrations between 20 ng/mL (50 nmol/L) and <30 ng/mL (75 nmol/L) justify vitamin D supplementation [35]. The recommended dose range of 800 to 2000 IU per day reflects various considerations underlying such treatment goals. When aiming for a minimum 25(OH)D concentration of at least 20 ng/mL (50 nmol/L), a daily vitamin D supplement dose of about 800 IU per day is sufficient for almost all individuals, even during the winter season, in Europe [36]. Data are less clear on which vitamin D doses are required to achieve a 25(OH)D concentration of ≥30 ng/mL (75 nmol/L) in almost all patients, but doses may be in the range of about 1500 to 2000 IU per day or even higher [37]. The classic rule of thumb that 100 IU of vitamin D per day increases serum 25(OH)D concentrations by about 1 ng/mL (2.5 nmol/L) seems to be a useful approximation, but several factors modulate the individual treatment response [38]. For example, increases in 25(OH)D are relatively high at low vitamin D supplement doses and low baseline 25(OH)D concentrations, whereas the dose-response curve flattens with higher vitamin D supplement doses and higher baseline 25(OH)D concentrations [39]. Evaluations of treatment success, by measurements of 25(OH)D, may be considered in certain patients, such as those with e.g., malabsorption or questionable adherence, but this should not be done earlier than 6 to 12 weeks after starting vitamin D supplementation, as this is about the time that it takes to reach a steady-state in serum 25(OH)D concentrations [40]. Although there is, of course, a seasonal variation in serum 25(OH)D concentrations, usually with higher levels during summertime, as a consequence of endogenous vitamin D synthesis in the skin, we do,

in general, recommend continuous and, usually, fixed doses of vitamin D supplementation throughout the year. The decrease in serum 25(OH)D during winter season is, in many patients, significant, but it is less than could be expected by the half-life of serum 25(OH)D concentrations of about 2 to 3 weeks because of a mobilization of vitamin D and its metabolites from various tissue stores (e.g., adipose tissue and muscle) [41].

If a rapid correction of vitamin D deficiency is clinically indicated, a regimen with a higher initial vitamin D dose, i.e., 6000 IU per day, and in certain cases, even up to 10,000 IU per day, followed by a maintenance dose with 800 to 2000 IU per day is recommended. Such doses of 6000 IU, or even up to 10,000 IU, per day for several weeks are usually safe and ensure a more rapid correction of vitamin D deficiency compared to lower doses [42]. Daily vitamin D doses are generally preferred over intermittent dosing schedules. The clinical indications for a rapid correction of vitamin D are, beyond osteomalacia, not clearly defined but may, according to our opinion, involve conditions such as extremely low 25(OH)D concentrations, osteoporosis patients with a very high fracture risk, patients with secondary hyperparathyroidism, and/or reduced serum calcium concentrations. Regarding treatment of vitamin D deficiency and its prevention, we want to emphasize that promoting a healthy lifestyle by preventing or reducing obesity, regular physical activity with moderate (cautious) sunlight exposure, and a healthy balanced diet are also effective measures to improve both vitamin D status and overall health. Promoting such lifestyle measures is, of course, also highly recommended, and it should accompany any vitamin D treatment.

As for the prevention of vitamin D deficiency, we recommend vitamin D3 (cholecalciferol) over vitamin D2 (ergocalciferol) for its treatment. Although parenteral, particularly intramuscular, vitamin D treatment can be considered in patients with malabsorption, e.g., inflammatory bowel disease, we primarily suggest to increase the oral vitamin D dose in such settings [43]. Clinicians have to consider that patients with inflammatory bowel disease frequently require higher vitamin D doses, but with daily oral vitamin D supplementation of about 5000 to 10,000 IU, even these patients usually achieve their 25(OH)D target concentrations [44]. If intermittent intramuscular vitamin D injections (e.g., 100,000 IU all three months) are used, the doses are roughly similar and slightly more efficient for intramuscular compared to oral doses, in terms of raising serum 25(OH)D concentrations, but the increase in serum 25(OH)D is slower for intramuscular versus oral vitamin D supplementation [44].

Some experts argue that calcifediol (=25(OH)D3, calcidiol) may also be used to correct vitamin D deficiency in certain conditions. The use of calcifediol seems to be more justified in obese people, people with malabsorption syndromes, people with liver disease, patients suffering from chronic kidney disease (stage 3 or 4), and those in all conditions where rapid correction of vitamin D deficiency is required [45]. Furthermore, calcifediol use may also be beneficial in patients taking medications that disrupt the hepatic cytochrome P-450 enzyme system, including those taking glucocorticoids, anticonvulsants, anticancer drugs, or antiretroviral drugs [46]. The increase in serum 25(OH)D is markedly reduced in patients with obesity (high BMI) and in patients with malabsorption syndromes treated with cholecalciferol, but with calcifediol, the 25(OH)D increase is not significantly different according to BMI or according to the presence, or absence, of malabsorption syndromes. Moreover, the increase in serum 25(OH)D is faster, and the dose-response curve is more linear with the use of calcifediol versus vitamin D3, and when stopping treatment, the decline in 25(OH)D concentration is faster after calcifediol compared to vitamin D3 [47]. While accumulating evidence suggests that calcifediol may be an attractive alternative to "native" vitamin D, due to the lack of experience with this molecule in Central and Eastern European countries, at this stage, we continue to recommend vitamin D3 (cholecalciferol). Cholecalciferol and calcifediol appear, so far, as equal molecules in the fight with vitamin D deficiency. However, RCT data are still missing on the superior benefit of calcifediol versus vitamin D, with reference to hard clinical outcomes, but more data on this topic may be available in the future [48]. Calcitriol (=1,25(OH)2D) and its analogues are used at much lower doses compared to vitamin D3, have a relatively high risk of hypercalcemia and a relatively narrow therapeutic window, and are not recommended for the treatment of common vitamin D deficiency [49]. Therefore, active vitamin D treatment is only indicated in certain diseases, such as chronic hypoparathyroidism, chronic kidney disease, or mineral and bone disorders (CKD-MBD) [50].

5- Conclusion:

here is no doubt that vitamin D is very important for a person and that controls his life in a very large way, as it is an essential element in the bones, joints, teeth, and controls the human mood, as it interferes with the psychological and emotional

state. This consensus statement covers various statements with relevance for the clinical practice in the treatment of vitamin D deficiency. We highlighted the relevance of vitamin D for public health and provided guidance regarding this issue by considering the totality of the available scientific evidence, including our personal experience and opinions.

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We would like to present this humble effort to all sincere people who wish to develop relevant health services for citizens and residents of the Holy Capital, asking God to grant us success in carrying out these works as we hope, Amen.

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