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Effect of vitamin D on treatment of malignant tumor

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ABSTRACT:

Vitamin D is a group of steroid organic chemicals that are fat-soluble. The most important are two forms of vitamin D, which are ergocalciferol (vitamin D2) occurring naturally in plant organisms as well as yeast and cholecalciferol (vitamin D3) found naturally in animal organisms. This vitamin is known primarily for its effects on the skeletal system, where it affects the calcium-phosphate economy, and also constitutes a bone component. As a result, it is mainly used in the prevention and treatment of rickets or osteoporosis. Recent clinical and epidemiological studies suggest that vitamin D has other uses as well. More and

more research confirms that its deficiency increases the risk of malignant tumor and is associated with worse prognosis. Therefore, vitamin D supplementation may have an impact on reducing the number of cases and may increase the chances of recovery. It has been found that vitamin D inhibits the proliferation and formation of malignant tumor cells, can induce their apoptosis and has an effect on angiogenesis and metastasis. WHO estimates that in 2018 around 9.6 million people have died of malignant tumors and the number of patients in the world is constantly increasing. Therefore, the use of vitamin D in their treatment can be a breakthrough solution. Its low price, availability, or known and low toxicity speak for its use in the discussed purposes. Still, more research is needed to develop an effective anticancer drug with its participation.

KEY WORDS: vitamin D; neoplasms;

INTRODUCTION:

Ergocalciferol (vitamin D2) found in plants and yeasts as well as cholecalciferol (vitamin D3) found in animal organisms are the basic forms of vitamin D, which differ in the structure of the side chain. They do not have metabolic activity and are classified as prohormones, because thanks to their hydroxylation we get a biologically active form of vitamin D, which is 1α, 25-dihydroxyvitamin D (1.25(OH)2D) [1]. It works on a lot of systems for e.g. skeletal, muscular, cardiovascular, immune system; and receptors for the vitamin D are located in many tissues [2]. Low levels of vitamin D are associated with low calcium levels, resulting in rickets in children or osteoporosis in adults [3]. In the case of pancreas, this vitamin improves the synthesis and secretion of insulin, and is also associated with greater sensitivity of cells to this hormone [4]. It also causes a decrease in parathormone secretion by the parathyroid glands, as well as increased absorption of calcium by the kidneys or the gastrointestinal tract. More and more research proves that vitamin D also affects the cancer environment by inhibiting tumor proliferation, angiogenesis, migration, and metastasis, which prevents the disease from developing. It can induce apoptosis and autophagy, which causes a cancer reduction. Vitamin D has anti-inflammatory effects and may affect the suppression of cancer stem cells, as well as increasing the immune response. The indicator of vitamin D concentration in the body is 25(OH)D. Deficiency is demonstrated by a concentration below 20 ng/ml. The relative shortage is 20-30 ng/ml. While the concentration of 30ng/ml is a sufficient value [5].

According to the WHO in 2018 9.6 million people have died because of cancer and the number of cases is constantly increasing [6]. Therefore, the use of anti-cancer properties of vitamin D in the treatment of patients can have positive effects. In addition, the known toxicity (persistent concentration of 50ng/ml [7]), easy availability and low price are very beneficial factors. This work aims to demonstrate the anti-cancer properties of vitamin D, which will allow a better understanding of its role in the treatment of malignant tumors.

A REVIEW OF AVAILABLE RESEARCH:

In the regulation of tumor cell proliferation, 1.25 (OH) 2D3 was found to stop the cell cycle in most tumor cells, and the cell cycle distribution depended mainly on induction of p21 and p27 expression. Cell apoptosis caused by 1.25 (OH) 2D3 has been shown to be mediated by a mitochondrial-dependent pathway in which the release of cytochrome C protein from the BCL-2 family was involved, resulting in the suppression of anti-apoptotic proteins such as BCL-2 and BCL-XL and induction of apoptotic proteins: BAX, BAK, BAD [8]. Vitamin D may also prevent angiogenesis and metastasis by inhibiting VEGF (vascular endothelial growth factor) mediated by HIF-1α factor, which causes the formation of new blood vessels that nourish the tumor [9]. High level of vitamin D was also associated with low COX-2

concentration and inhibition of TNF-α, IL-6 and IL-8 factors, which are associated with inflammation. On the other hand, reduction of inflammation may contribute to suppression of tumor progression [10].

US Physicians' Health Study in the years 1982-2000 conducted a study on a group of 1066 men with prostate cancer and 1618 healthy men. It has been shown that increased sun exposure and vitamin D supplementation may reduce the risk of developing this malignant tumor. Especially in men with genotype FokI ff (gene encoding the receptor for vitamin D) [11]. In studies conducted on African-American men, who are more prone to aggressive forms of cancer, (ie> 7 on the Gleason scale), and Europeans with prostate cancer, it was shown that the higher molar ratio of 1.25(OH)2D /25(OH)D caused less risk of aggressive cancer. [12]

In the case of breast cancer, a cohort study from 2017 including 1666 women, showed that elevated serum 25(OH)D levels are associated with a longer survival time, especially in pre-menopausal women. In this case, the determination of the metabolite level could be a prognostic factor. Which is extremely important, because it concerns women at an early age [13]. In contrast, a study conducted on African Americans suggested that 25(OH)D deficiency increased the incidence of breast cancer by approximately 23%. In this case vitamin D could be a factor preventing cancer [14].

In a study of a group of 269 subjects, it was found that a low concentration of 25(OH)D increases the chance of adenoma and colon polyps seven times. And it is known that these cancers tend to be malignant. In patients with high levels of 25(OH)D (minimum 40ng/ml), mortality from colorectal cancer decreased by 37%. These studies suggest that restoring normal levels of vitamin D may be associated with better prognosis [15]. In the case of studies on two colon cancer cell lines - HCT116 and HT29, it was noted that Vitamin D-Nanoemulsion (NVD) induced cytotoxicity of colon cells. In addition, inhibition of tumor cell growth or apoptosis was found, depending on the dose. Research may indicate the healing properties of vitamin D [16].

Research at the Sun Yat-sen University in 2002-2006 on 197 patients with gastric cancer showed that over 90% (181 people) of patients had insufficient level (50-75nmol/l) or vitamin D deficiency (below 50 nmol/l). This was associated with an inferior clinical grade of cancer, lymph node metastases and a shorter survival time [17]. It is well known that chronic Helicobacter Pylori infection is a predisposing factor for gastric cancer. In our studies, the dosage of vitamin D3 resulted in the restoration of the lysosomal degradation function by activation of the PDIA3 receptor, resulting in increased release of Ca2 + from the lysosomes. The recovered lysosomal degradation function eliminates H. pylori through the autolysosomal pathway. The results of the study may indicate the antibacterial function of vitamin D, as well as its use in the prevention of gastric cancer [18].

Asthma is a predisposing factor for lung cancer [19]. Research suggests that supplementation of vitamin D improves lung function, and also reduces the risk of asthma in smokers and non-smokers, and thus, reduces the risk of cancer development. The results of the study may indicate that this vitamin may be a preventive factor in this disease [20].

CONCLUSIONS:

A lot of research suggests that vitamin D can have a huge impact on prevention, improved prognosis, or prolonged survival in the case of certain cancers. However, is still needed many studies confirming and proving its anti-cancer activity. Moreover, there is a need for studies on the therapeutic dose and possible additional substances in the medicine that would optimize the action of vitamin D as a medicine. However, based on many studies, it can be assumed that this vitamin may become the future

of treatment and prevention in some cases, and there is also a great chance for its therapeutic effectiveness.

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