THE ROLE OF VITAMIN D IN THE Wnt/β-catenin SIGNALING PATHWAY

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Background. The Wnt/β-catenin signaling pathway is a complex system involved in immune homeostasis, tissue regeneration, and various physiological processes. Aberrant activation of the signaling pathway, driven by genetic and epigenetic changes, developes various cancers: colorectal carcinoma, gastric, esophageal, nasopharyngeal, breast.
Objective of the study. To elucidate the biochemical mechanisms of action of vitamin D on the Wnt/β-catenin signaling pathway in order to develop effective methods of prevention and treatment in cancer. **Materials and methods.** A review of the literature from 2019-2024 was performed using 10 articles, including from the State University of Medicine and Pharmacy *Nicolae Testemitanu* Scientific Medical Library, Republic of Moldova, data from ScienceDirect, PubMed Central, Biomed Central, MDPI, Wiley Online Library, Febspress electronic libraries.
Results. The canonical Wnt/β-catenin pathway regulates cell differentiation, proliferation, and survival. Physiologically, this pathway is initiated by the binding of Wnt ligands to frizzled (FZD) receptors, that associate with low-density lipoprotein receptor 5 (LRP5) and LRP6. Without Wnt receptor activation, β-catenin is phosphorylated by the destruction complex (DC), including glycogen synthase kinase 3β (GSK3β), casein kinase 1α (CK1α), E3 ubiquitin ligase β-TrCP (SCFβ-TrCP), Axis inhibition protein (AXIN), and further degradation is carried out by proteasome. These processes prevent the accumulation of β-catenin in the nucleus and prevent further activation of the gene by the repressive complex containing theTCF/LEF family (T cell factor/lymphoid enhancer factor family). The Wnt/β-catenin pathway is activated when Wnt proteins bind to the FZD receptor, inhibiting DC and allowing β-catenin to accumulate in the cytoplasm, some of which translocates to the nucleus to activate TCF/LEF proteins. Abnormal expression of the signaling pathway causes excessive accumulation of β-catenin in tumor cells, which leads to tumor infiltration and metastasis progression. Calcitriol, $1,25(OH)_2D_3$, inhibits Wnt signaling in cancer cells through vitamin D receptor (VDR), blocking β-catenin from binding TCF and activating target genes.
Conclusions. Vitamin D administration significantly reduced Wnt and β-catenin expression, demonstrating its role in blocking β-catenin translocation. Currently, new strategies are being explored to develop effective drugs targeting this pathway for cancer treatment.
Keywords: Wnt/β-catenin, 1,25(OH)2D3, cancer, frizzled receptors, vitamin D receptor, destruction complex.