



## **Vitamin D Intake and its Protective Role in Multiple Sclerosis: The Checkmate to Survivin?**

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Vitamin D has long been speculated to reduce the risk of multiple sclerosis (MS). However, its role in development and modulating the course of MS has yet to be clarified. To date, there is no scientific evidence for the use of vitamin D as monotherapy for MS in clinical practice and perplexities still exist on potential disadvantages of Vitamin D intake. MS is one of the most common disabling neurological disorders of the Central Nervous System (CNS) in young and middle-aged adults. The pathogenesis of MS has long been thought to be an immune mediated disorder of the CNS. It has been verified that failure of autoreactive T cells to undergo apoptosis may contribute to the pathogenesis of MS. Studies of lymphocytes from patients with active relapsing-remitting MS have suggested a potential role for survivin in MS pathology. Survivin is the smallest member of the inhibitor of apoptosis protein family. Abnormal up-regulation of survivin has been involved in the inability to remove autoreactive lymphocytes in MS. Over-expression of survivin in mitogen stimulated T lymphocytes from patients with active MS has been correlated with cellular resistance to apoptosis and with features of disease activity, such as disease duration and the number of enhanced lesions on cranial magnetic resonance. Survivin is widely expressed in fetal tissue and over-expressed in cancer cells where it is described as a biomarker predictive of aggressive cancer. Vitamin D has been found to suppress cell proliferation and induce apoptosis in a variety of cancer cell models such as human colon carcinoma, breast cancer, prostate cancer and Kaposi sarcoma. A large body of data indicates that Vitamin D promotes inhibition of cancer cell proliferation by suppression of survivin. Although survivin level is considered as an unfavourable risk factor for cancer and MS, it plays an important anti-apoptosis role in vascular cell responses to injuries. Even if survivin is scarcely detectable in normal adult tissues, its expression can be reactivated by a number of pro-survival stimuli such as ischemia and hypoxia. Upregulation of survivin seems to have valuable effects on heart and brain ischemia-reperfusion injury limiting tissue damage and improving functional outcome. Survivin myocardial expression after acute myocardial infarction (AMI) has been linked to survival of at risk myocardium and favorable remodeling after AMI. Furthermore, survivin has been shown to be a key determinant in enhancing neural cell survival after a traumatic brain injury and in response to hypoxia/ ischemia conditions such as stroke. Re-endothelialization represents an important therapeutic strategy for repairing injured blood vessels. Survivin has been reported to control the proliferation of endothelial progenitor cells (EPC) that are implicated in the prevention of restenosis after vascular injury. EPC are the major source of cells related to endothelium repair and re-endothelialization. The DNA binding 1 (Id1)/ PI3K/Akt/nuclear factor kappa B (NFκB)/survivin signaling pathway has been described as a critical player in EPC proliferation after vascular injury. Of note, patients affected by MS have been supposed to be at high risk for cardiovascular diseases (CVDs) and a careful surveillance and CVD preventive health measures are recommended. All these contentions led us to hypothesize that vitamin D may be effective against MS inhibiting survivin gene expression and thereby affecting the development and progression of the disease. However, decreased levels of survivin may lead to worse outcomes during the acute phase of cardiovascular conditions such as AMI and stroke taking into account the highest-risk status of patients with MS. Thus, vitamin D should be administered to patients with MS after excluding potential associated risk factors for CVD and defining threshold Vitamin D levels above

which supplementations might negatively influence recovery from AMI and stroke.

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