Contribution of Vitamin D Insufficiency to the Pathogenesis and Prognosis of Multiple Sclerosis

Essay

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Loban El-Mohandess

Contents

List of Abbreviations

Abbrev.	Full term
ALS	: Amyotrophic lateral sclerosis
APC	: Antigen presenting cell
CD	: Cluster of differentiation
CIS	: Clinically isolated syndrome
CNS	: Central nervous system
CSF	: Cerebrospinal fluid
DBD	: DNA binding domain
EAE	: Experimental allergic encephalomyelitis
EBNA1	: EBV nuclear antigen 1
EBV	: Epstein-Barr virus
EDSS	: Expanded disability status scale
EVIDIMS	: Efficacy of vitamin D supplementation in multiple sclerosis
FasL	: Fas ligand
FMS	: Familial multiple sclerosis
GM-CSF	: Granulocyte-macrophage colony stimulating factor
GM-CSF	: Granulocyte-macrophage colony-stimulating factor
GWAS	: Genome-wide association study
HLA	: Human leukocyte antigen
ICAM-1	: Intracellular adhesion molecule 1
IFN	: Interferon
IL	: Interleukin
IMT	: Immunomodulatory therapy

List of Abbreviations *(Cont.)*

Abbrev.	Full term
LBD	: Ligand binding domain
LFA-1	: Lymphocyte function-associated antigen 1
MBP	: Myelin basic protein
MCP	: Monocyte chemotactic protein
MHC	: Major histocompatibility complex
MMps	: Matrix metalloproteinases
MOG	: Myelin oligodendrocyte glycoprotein
MRI	: Magnetic resonance imaging
MS	: Multiple Sclerosis
NAA	: N-acetyl aspartate
NO	: Nitric oxide
OLG	: Oligodendrocyte
PC	: Parental consanguinity
PGE2	: Prostaglandin E_2
PRMS	: Progressive relapsing MD
RCTs	: Randomized, controlled trials
RRMS	: Relapsing remitting MS
SD	: Standard deviation
SPMS	: Secondary progressive MS
TCR	: T cell receptors
TH	: T helper cells
TLR	: Toll-like receptors
TNF	: Tumor necrosis factor

List of Abbreviations *(Cont.)*

Abbrev.	Full term
UVB	: Ultraviolet B
VCAM	: Vascular cell adhesion molecules
VCAM-1	: Vascular cell adhesion molecule 1
VDR	: Vitamin D receptor
VDRE	: Vitamin D response element
VLA-4	: Very late antigen-4
WHO	: World Health Organization

List of Tables

List of Figures

List of Figures *(Cont.)*

Introduction

Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. The etiology of MS is unknown. It likely results from complex interaction between environmental and genetic factors ***(Tullman, 2013).***

Multiple sclerosis is considered a T cell mediated autoimmune disease of the central nervous system (CNS) that mainly affects young adults and lead to significant neurological disability as it affects both white and gray matters of the CNS, its neuropathology lead to loss of myelin, oligodendrocyte complex as well as neuronal and axonal degeneration ***(Franciotta and Tremolizzo, 2013).***

Low vitamin D status has been implicated in the etiology of autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, and inflammatory bowel disease ***(Dorr et al., 2013).***

Past sun exposure and vitamin D supplementation have been associated with a reduction in the risk of MS and the prevalence of MS was found to be highest where environmental supplies of vitamin D are lowest ***(Hatamian et al., 2013).***

Vitamin D is formed in human epithelial cells via photochemical synthesis and is also acquired from dietary sources. The major role of vitamin D in the human body is commonly related to calcium metabolism and bone structure. Apart from this non- classical effects of vitamin D have recently gained renewed attention ***(Yang et al., 2013).***

Vitamin D has numerous functions in regulation of nervous system development and function. The neuroprotective effect of vitamin D is associated with its influence on neurotrophin production and release, neuromediator synthesis, intracellular calcium homeostasis, and prevention of oxidative damage to nervous tissue ***(Wrzosek et al., 2013).***

Vitamin D metabolizing enzymes and vitamin D receptors are present in many cell types including various immune cells such as antigen-presenting-cells, T cells, B cells and monocytes, in addition to modulating innate immune cells vitamin D also promotes a more tolerogenic immunological status ***(Prietl et al., 2013).***

Vitamin D is a potent immune modulator, keeping the T-cell compartment in a more tolerogenic state. Multiple sclerosis (MS), a disease in which an autoreactive T-cell response contributes to inflammation in the central nervous system, has been associated with vitamin D deficiency. The

effects of vitamin D on the immune system are believed to be an important driver of this association ***(Pierrot- Deseilligny and Souberbielle, 2013).***

Low serum vitamin D levels may increase the risk of developing MS and patients with established MS and lower vitamin D levels are at higher risk for subsequent relapse, new lesion on magnetic resonance imaging (MRI) and disability compared to patients with higher vitamin D levels ***(Correale, 2013).***

Optimizing vitamin D levels have been shown to prevent a second demyelinating attack after a diagnosis of clinically isolated syndrome (CIS) or optic neuritis, which is an initial warning sign for MS. A dose of 20,000 IU of vitamin D3 once per week, alongside interferon beta-1b treatment, resulted in significantly fewer lesions on brain MRI, reduced disability scales and improved ability to walk ***(Post and Ernst, 2013).***

Aim of the Work

The aim of this work is to review updates about correlation between vitamin D deficiency and multiple sclerosis development, prognosis and impact as a therapeutic factor.