Vitamin D – immunomodulatory actions and new potentialities

Abelha-Aleixo J[1], Fonseca R[1], Bernardo A[1], Mariz E[1], Costa L[1]

ACTA REUMATOL PORT. 2014;39:355-356

The authors intend to make a brief scientific review about the immunoregulatory potentialities underlying vitamin D providing an insight in areas such as multiple sclerosis, disorders of cognitive function, response to infection and neoplasia.

Active vitamin D (VD) plays homeostatic and immunoregulatory functions. The discovery of alpha-hydroxylase and vitamin D receptors (VDR) in other tissues beyond the kidney[1-4], raised attention to potential new effects that have been under investigation.

The VDR expression in activated lymphocytes, dendritic cells and macrophages has a crucial role in the inhibition of dendritic cell maturation, immunoglobulin secretion, suppression of activation and differentiation of T helper (Th) 1, Th17 and possibly Natural Killer (NK) lymphocytes and Th2 phenotype polarization. They are also important in the maturation of macrophages, regulation of chemotaxis and phagocytosis and in further enhancing an anti-inflammatory state by inhibiting pro-inflammatory cytokines (IL-2, INF-γ, IL-6, TNF-α)[1-5].

The immunoregulatory mechanisms described above have been studied in the treatment of various diseases such as multiple sclerosis (MS), disorders of cognitive function, response to infection and malignancies.

There are several premises that favor the relationship between the prevalence of MS and low levels of VD, such as: the prevalence of MS in the Nordic countries and the reduction of the risk in the population that migrates to lower latitudes; greater severity of the disease if the *ab initio* is in autumn/winter and an increased risk of MS in people born in the spring[3]. VD has been also described as a regulator of expression of HLA-DRB1*1501, involved in the development of MS[3]. Human and animal studies have shown that supplementation with VD reduces the incidence, severity and number of brain lesions in MS[3]. There are several ongoing clinical trials, which could definitely clarify the role of VD in the evolution of this disease (www.clinicaltrials.gov)[3].

Concerning the cognitive function, VD has been suggested as an important player in the brain information processing speed, attention and executive functions[5-6]. In Alzheimers dementia, lower scores on the mini-mental state questionnaire were found in patients with VD deficit, although the relationship is not fully established[2].

Regarding infectious processes it was verified that patients with deficit of VD are more likely to develop active *Mycobacterium tuberculosis* infection, and that they have increased rate of upper respiratory tract infections irrespective of the season[7]. In the presence of *Mycobacterium tuberculosis* monocytes and macrophages increase the expression of VDR stimulating the synthesis and activity of VD which in turn induces the production of antibacterial proteins and autophagosomes[4]. Finally, the production of cathelicidin in keratinocytes induced by VD confers protection against *S. aureus*[8].

VD also has potential anti-carcinogenic mechanisms: limits cell growth, regulates apoptosis, reduces angiogenesis and metastasis and decreases expression of cyclooxygenase 2, NFkB (nuclear factor kappa-light-chain-enhancer of activated B cells) and MAPK (Mitogen-activated protein kinases)[9]. In vitro and in animal models studies found an association between polymorphisms of the VDR and cancer, and that the expression of these receptors is reduced in later stages[9]. Is then VD chemoprevention justifiable in several cancers such as colon, breast and prostate? The studies are conflicting. While past meta-analysis of observational studies showed an inverse association between vitamin D levels and colon cancer, one most recent showed no differences in the incidence of colorectal carcinoma in patients with or without supplementation of VD[10].

Vitamin D appears to have many desirable actions beyond those already set forth in the prevention and treatment of osteoporosis. Ongoing studies will validate the supplementation of VD in numerous untapped potential that seem to exist.

1. Serviço de Reumatologia, Centro Hospitalar S. João, Porto

CORRESPONDENCE TO
Joana Abelha-Aleixo
Alameda Professor Hernâni Monteiro, 4200-319 Porto
Hospital de S. João, Serviço de Reumatologia
E-mail: abelha.aleixo@gmail.com

REFERENCES

1. Di Rosa M, Malaguarnera M, Nicoletti F, Malaguarnera L. Vitamin D3: a helpful immuno-modulator. Immunology 2011; 134:123-139.
2. Balion C, Griffith L, Strifler L, et al. Vitamin D, cognition, and dementia: a systematic review and meta-analysis. Neurology 2012; 79:1397-1405.
3. Dorr J, Doring A, Paul F. Can we prevent or treat multiple sclerosis by individualised vitamin D supply? EPMA J 2013; 4:4.
4. Christakos S, Hewison M, Gardner D, et al. Vitamin D: beyond bone. Ann NY Acad Sci 2013; 1287:45-58.
5. Wrzosek M, Lukaszkiewicz J, Wrzosek M, et al. Vitamin D and the central nervous system. Pharmacol Rep 2013; 65:271-278.
6. Constans T, Mondon K, Annweiler C, Hommet C. Vitamin D and cognition in the elderly. Psychol Neuropsychiatr Vieil 2010; 8:255-262.
7. Adams J, Hewison M. Update in vitamin D. J Clin Endocrinol Metab 2010; 95:471-478.
8. Bikle D. Vitamin D: newly discovered actions require reconsideration of physiologic requirements. Trends Endocrinol Metab 2010; 21:375-384.
9. Vanoirbeek E, Krishnan A, Eelen G, et al. The anti-cancer and anti-inflammatory actions of 1,25(OH)(2)D(3). Best Pract Res Clin Endocrinol Metab 2011; 25:593-604.
10. Fortmann S, Burda B, Senger C, Lin J, Whitlock E. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: An updated systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2013; 159:824-834.

AGENDA

WORKSHOP VASCULITES

Local e Data: Coimbra, Portugal, 30 a 31 de Janeiro de 2015

35TH EUROPEAN WORKSHOP ON RHEUMATOLOGY RESEARCH

Local e Data: Budapeste, 5 a 7 de Março de 2015

3RD INTERNATIONAL CONGRESS ON CONTROVERSIES IN RHEUMATOLOGY & AUTOIMMUNITY

Local e Data: Sorrento, Itália, 12 a 14 de Março de 2015

3RD INTERNATIONAL WORKSHOP ON ULTRASOUND IN LARGE VESSEL VASCULITIS & POLYMYALGIA RHEUMATICA

Local e Data: Kristiansand, Norway, 10 a 12 de Abril de 2015

3RD WORLD CONGRESS ON CONTROVERSIES, DEBATES AND CONSENSUS IN BONE, MUSCLE AND JOINT DISEASES

Local e Data: Montreal, Canada, 24 a 28 de Abril de 2015

4TH JOINT MEETING OF ECTS AND IBMS

Local e Data: Roterdam, Netherlands, 28 a 30 de Abril de 2015

1ST INTERNATIONAL SUMMIT ON SPORTS AND EXERCISE MEDICINE

Local e Data: Oeiras, Portugal, 30 de Abril a 02 de Maio de 2015

SIMPOSIUM: IMAGIOLOGIA EM REUMATOLOGIA

Local e Data: Póvoa do Varzim, Portugal, 14 a 16 de Maio de 2015