AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 59, Issue 01, August, 2019

The role of the Vitamin D / parathormone system in the pathogenesis of bone metabolism disorders in rheumatoid arthritis

Huseynova A.S.[1], Kerimova I.A.[1], Rahimova R.R.[1]

Department of molocular microbiology, Science research Institute of Experimental Medicine, Russian Federation[1]

Keywords:
Cholecalciferol Parathyroid hormone Osteoporosis Rheumatoid arthritis

ABSTRACT

Osteoporosis is a well-established extra-articular feature of rheumatoid arthritis (RA). Systemic inflammation seems to play a crucial role in causing an alteration of multiple homeostatic systems implied in bone health, such as the RANK/RANKL/Osteoprotegerin and Wnt/ catenin pathways several other causal factors have been called into question, including the chronic use of corticosteroids. Since vitamin D exerts important immune-regulatory roles, it has been claimed that derangement of the vitamin D/parathyroid hormone (PTH) system, a well-known determinant of bone health, may play a pathogenic role in autoimmunity; animal models and clinical data support this hypothesis. Furthermore, RA patients seem to be relatively refractory to vitamin D-induced PTH suppression. Therefore, the link between RA and osteoporosis might in part be due to alterations in the vitamin D/PTH system. A better understanding of the pathophysiology of this system may be crucial to prevent and cure osteoporosis in patients with inflammatory/autoimmune diseases. A major clinical correlate of the strict cooperation and interdependence between vitamin D and PTH is that correction of the vitamin D deficiency, at least in autoimmune diseases, should be targeted to PTH suppression.

1. Introduction

Osteoporosis is a frequent complication of autoimmune inflammatory diseases, such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE) and multiple sclerosis (MS) [1]. The reasons why osteoporosis occurs in these diseases are multiple and not completely understood. The failure of several bone regulation systems has been claimed to be responsible for this complication of systemic inflammatory diseases even though this issue remain partially unresolved. The vitamin D/PTH system is a well-known determinant of bone health in the general population. Recently, a failure in Vitamin D metabolism has been described in patients affected by inflammatory rheumatic diseases [2] even though its relationship with the pathogenesis of autoimmune diseases and the consequences on bone health remain not completely understood. In this paper we will review the role of the vitamin D/PTH system in the pathogenesis of osteoporosis in autoimmune diseases and, in particular, in RA. To perform the present

review, we interrogated PubMed (accessed on-line on July 1st, 2013), limiting our search to papers published in English until June 30th, 2013, and using the following string: "(vitamin D PTH system) OR (vitamin D rheumatoid arthritis) OR (rheumatoid arthritis secondary hyperparathyroidism) OR (rheumatoid arthritis hypovitaminosis D)" yielded 856 articles. Eight-hundred papers were excluded for the following reasons: (a) dealt with topics non relevant for the present review, (b) letters, case reports, (c) small sample size, (d) unobtainable full text articles, or a combination of the above reasons. We reviewed all the remaining papers, plus additional relevant articles identified from the references of selected articles or through personal knowledge of the authors.

2. Conclusions

In the last few years the same definition of "vitamin D" has been debated and remains the subject of intense controversy. In fact, vitamin D is not only obtained by dietary intake, like the other vitamins, since its greater amount derives from endogenous synthesis. Importantly, the concept of "vitamin" is static, while vitamin D and PTH participate in dynamic system acting on several biological targets. For these reasons vitamin D is currently, more correctly, defined as "hormone D"; in fact the relationship between vitamin D and PTH shares many similarities with the other endocrine networks. Obtaining a normal vitamin D status is paramount in preventing RA related osteoporosis and the correction of a deficient vitamin D status should be suggested to each rheumatic patient. However, since the correlation between vitamin D and PTH is less linear in RA, this system is not correctly defined by the single evaluation of plasma 25(OH)D concentration. Many patients with a normal vitamin D concentration are affected by secondary hyperparathyroidism and present an inadequate vitamin D status. Therefore, we propose that in rheumatic diseases both Vitamin D and PTH are measured to establish the need for cholecalciferol supplementation, and that Vitamin D supplementation is targeted to the correction of hyperparathyroidism rather than to the normalization of plasma 25(OH)D concentration alone.

3. References

[1] Bultink IE, Vis M, Van der Horst-Bruinsma IE, Lems WF. Inflammatory rheumatic disorders and bone. Curr Rheumatol Rep. 2012; 14:224–30.

[2] Sainaghi PP, Bellan M, Antonini G, Bellomo G, Pirisi M. Unsuppressed parathyroid hormone in patients with autoimmune/inflammatory rheumatic diseases: implications for vitamin D supplementation. Rheumatology. 2011; 50:2290–6.

[3] Deodhar AA, Woolf AD. Bone mass measurement and bone metabolism in rheumatoid arthritis: a review. Br J Rheumatol. 1996; 35:309–22.

[4] Peel NF, Moore DJ, Barrington NA, Bax DE, Eastell R. Risk of vertebral fracture and relationship to bone mineral density in steroid treated rheumatoid arthritis. Ann Rheum Dis. 1995; 54:801–6.

[5] Kim SY, Schneeweiss S, Liu J, Daniel GW, Chang CL, Garneau K, et al. Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. Arthritis Res Ther. 2010;12: R154.

[6] Haugeberg G, Uhlig T, Falch JA, Halse JI, Kvien TK. Bone mineral density and frequency of osteoporosis in female patients with rheumatoid arthritis: results from 394 patients in the Oslo County Rheumatoid Arthritis register. Arthritis Rheum. 2000; 43:522–30.

[7] Vis M, Haavardsholm EA, Bøyesen P, Haugeberg G, Uhlig T, Hoff M, et al. High incidence of vertebral

ISSN: 0005-2523
Volume 59, Issue 01, August, 2019

and non-vertebral fractures in the OSTRA cohort study: a 5-year follow-up study in postmenopausal women with rheumatoid arthritis. Osteoporos Int. 2011; 22:2413–9.

[8] Epos Study Group. Incidence of vertebral fracture in Europe: results from the European Prospective Osteoporosis Study (Epos). J Bone Miner Res. 2002; 17:716–24.

[9] Nevitt MC, Cummings SR, Stone KL, Palermo L, Black DM, Bauer DC, et al. Risk factors for a first-incident radiographic vertebral fracture in women at least 65 years of age: the study of osteoporotic fractures. J Bone Miner Res. 2005; 20:131–40.

[10] Van Staa TP, Geusens P, Bijlsma JW, Leufkens HG, Cooper C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. Arthritis Rheum. 2006; 54:3104–12.

[11] Hsu H, Lacey DL, Dunstan CR, Solovyev I, Colombero A, Timms E, et al. Tumor necrosis factor receptor family member RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand. Proc Natl Acad Sci U S A. 1999; 96:3540–5.

[12] Geusens PP, Lems WF. Osteoimmunology and osteoporosis. Arthritis Res Ther. 2011; 13:242.

[13] Takayanagi H. Osteoimmunology and the effects of the immune system on bone. Nat Rev Rheumatol. 2009; 5:667–76.

[14] Kong YY, Yoshida H, Sarosi I, Tan HL, Timms E, Capparelli C, et al. OPGL is a key regulator of osteoclastogenesis, lymphocyte development and lymph-node organogenesis. Nature. 1999; 397:315–23.

[15] Schett G, Saag KG, Bijlsma JW. From bone biology to clinical outcome: state of the art and future perspectives. Ann Rheum Dis. 2010; 69:1415–9.

[16] Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. Lancet. 2011; 377:1276–87.

[17] Lories RJ, Luyten FP. Osteoimmunology: Wnt antagonists: for better or worse? Nat Rev Rheumatol. 2009; 5:420–1.

[18] Terpos E, Fragiadaki K, Konsta M, Bratengeier C, Papatheodorou A, Sfikakis PP. Early effects of Il-6 receptor inhibition on bone homeostasis. Clin Exp Rheumatol. 2011; 29:921–5.