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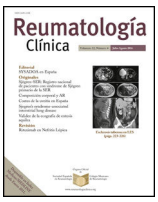

Letters to the Editor

Vitamin D and Autoimmune Rheumatic Diseases☆

Vitamina D y enfermedades reumáticas

To the Editor,

We were highly interested in the editorial "*Vitamina D y enfermedades autoinmunes reumáticas*" ("Vitamin D and autoimmune rheumatic disease"), published recently in Reumatología Clínica.[1] At the present time, it is well-known that vitamin/hormone D has an essential role in the regulation of the immune system,[2] and that its deficiency is related to the presence of inflammation, autoimmunity, cancer and atherosclerosis.[3] This is especially interesting, when we learn that the levels of vitamin D are substantially reduced in western countries and in the Spanish population in particular.[4]

As the authors of the editorial do point out, the deficiency or insufficiency of vitamin D is related not only to the coexistence of autoimmune diseases like systemic lupus erythematosus or rheumatoid arthritis (RA), but also to the activity of some of these diseases.[5–7] The role that vitamin/hormone D may have in other chronic inflammatory diseases, like ankylosing spondylitis (AS) or psoriatic arthritis (PsA), is less well-known.

Recently, we published the baseline data on cardiovascular morbidity and levels of vitamin/hormone D in patients included in the CARMA ("CARdiovascular in rheuMAtology") project.[8,9] The proposal is a prospective Spanish study, promoted by the Sociedad Española de Reumatología (SER), in which we evaluate the risk of developing a fatal cardiovascular event after 10 years in patients with RA, AS and PsA, compared to a cohort of patients with no inflammatory diseases, followed in rheumatology clinics of 67 Spanish hospitals. The study includes a total of 2234 patients: 775 RA, 738 AS and 721 PsA, in addition to 677 noninflammatory individuals, with degenerative or soft tissue diseases.[8,9]

In the baseline analysis, we found that the patients with inflammatory diseases had a more marked deficiency of D (25-OH-vitamin D < 20 ng/mL), than the noninflammatory patients (40.5% in RA; 40% in AS; 41% in PsA; and 26.7% in the control group; [P<.001]). The mean levels of 25-OH-vitamin D were: 20.4 ng/mL in RA; 20.9 ng/mL in AS; 20 ng/mL in PsA; and 24.8 ng/mL in the control group. We should point out that the controls included, mostly, patients with osteoarthritis, osteoporosis, low back pain or soft tissue disease, in which vitamin/hormone D is usually reduced, as we confirmed, although with fewer percentage points of deficiency.[9]

With respect to the activity and severity, the bivariate study demonstrated a significant association between the vitamin/hormone D deficiency and certain parameters for aggressive disease. This association disappeared in the adjusted model, although there persisted a certain associative trend between the vitamin/hormone D deficiency and the presence of anti-cyclic citrullinated peptide antibodies (adjusted odds ratio [OR]: 1.45; 95% confidence interval [CI]: 0.99–2.12; P=.056) and Bath AS Functional Index (adjusted OR: 1.08; 95% CI: 0.99–1.17; P=.070)[9] in RA and AS, respectively. However, we also point out that patients with inflammatory diseases are closely controlled in hospital rheumatology units, and between 40% and 47.4% are receiving biologic therapy, with activity reduced to their inclusion in the study (disease activity score 28 joints–erythrocyte sedimentation rate of 3.2 in RA and 3.0 in PsA; Bath AS Disease Activity Index 3.5 in AS).[9]

Although our work has certain limitations and there are still doubts concerning supplementation in patients with vitamin/hormone D deficiency, in particular, those with chronic inflammatory diseases, as to, whether, it improves their health and reduces inflammatory activity.[10] We feel, like the authors of the editorial, that it is important to monitor and supplement these patients, especially those with a moderate/serious deficiency, because of the possible pathogenic role that vitamin/hormone D may have in the course and comorbidity of their underlying disease.

Finally, it must still be determined whether the maintenance of low vitamin D levels increments the incident of cardiovascular events in our cohort. This is one of the objectives of the CARMA study, and is to be analyzed in the next few years.

Acknowledgements

All of the patients and participating centers, whose role in the follow-up and collection of clinical data is being fundamental for the development of the project. The list of participating centers and authors appears in the addendum of the respective publications. Likewise, we wish to thank the SER and Abbvie España for promoting and sponsoring the project.

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Response to: Sjögren's Syndrome and Halitosis: A Case Report☆

Respuesta a: Síndrome de Sjögren y halitosis: descripción de un caso clínico

Dear Editor:

I read very carefully the publication of Ruiz Serrato et al.[1] in Reumatología Clínica, where the authors report a case of halitosis secondary to Sjögren's syndrome (SS). I would like to express a few considerations, which I hope will contribute to a better understanding of this association.

Sjögren's syndrome is a systemic, autoimmune disease, with a prevalence that ranges between 0.1% and 0.5%, with a predominance of women (4th and 5th decades of life).[2] Histopathological studies show it to be characterized by lymphocytic infiltration at the level of the exocrine glands.[2] This syndrome can be primary or secondary (associated with systemic lupus erythematosus, rheumatic arthritis and scleroderma).[2] The destruction of the exocrine glands leads to "sicca syndrome" (xerostomia and xerophthalmia).[2] However, SS can show extraglandular manifestations, including general, cutaneous, musculoskeletal, respiratory, urogenital, thyroid, gastrointestinal and hepatobiliary.[2] The association between halitosis and SS is multifactorial.

First: Parotid gland dysfunction results in xerostomia and a decrease in salivary flow that leads to periodontal diseases due to *Treponema denticola, Porphyromonas gingivalis* and *Bacteroides forsythus*, which produce mercaptan and sulfur that are associated with the level of halitosis (oral cause of halitosis).[3] Saliva has antimicrobial properties; thus, the amount and quality of saliva are essential to prevent halitosis. Therefore, in patients with SS and xerostomia, the production of saliva is reduced, increasing the possibility of generating volatile sulfur compounds (VSC), the result of the degradation of proteins with sulfur-containing amino acids from the exfoliation of human epithelial cells, leukocytes and the remains of food, and with it, oral malodor.[3] Volatile sulfur compounds are associated not only with halitosis, but can enter into a vicious circle of pathogenesis of gingivitis and periodontitis.[3]

Second: Extraglandular manifestations are factors that trigger halitosis in SS. Patients with SS are more predisposed to develop chronic rhinosinusitis (a perioral cause of halitosis) and bronchiectasis (an extraoral cause of halitosis). Among the gastrointestinal manifestations, they may present esophageal dysfunction, chronic gastritis, *Helicobacter pylori* infection and bacterial overgrowth, which also cause halitosis (extraoral cause). Primary biliary cirrhosis, as a hepatobiliary manifestation, is an extraoral cause of halitosis.

Third: Diseases associated with secondary SS play their own role. For example, gastroesophageal reflux (an extraoral cause) in SS secondary to scleroderma produces dental erosion and dysphagia that provoke halitosis.[4] Moreover, patients with SS have an elevated risk of developing non-Hodgkin's B-cell lymphoma, which can be an extraoral cause of halitosis. On the other hand, the symptomatology of halitosis in SS patients can, subjectively, be worse (not genuine), by psychosomatic halitosis, halitophobia or because the xerogenic medicine they take (antidepressant and nonsteroid anti-inflammation drugs). With respect to the case reported by Ruiz Serrato et al.,[1] as the authors, reasonably explain, it is true halitosis due to oral causes (xerostomia), with a favorable response to pilocarpine. However, we recommend follow-up, to screen for possible perioral and/or extraoral causes related to SS, in the case of therapeutic failure or recurrence. I conclude that, halitosis is a prevalent entity (up to 50% of the general population), and has been studied little in SS. Although, it is considered more a problem related to poor dental hygiene or to diseases of the oral cavity (87%), on occasions, it may be a manifestation of the disease at other levels—perioral—or even of a psychiatric or systemic disease—extraoral—(13%).[3] Therefore, an initial approximation should include a complete history (diet, drugs, poor habits and dental hygiene), a thorough examination, a complete analysis, as in screening. The therapeutic management requires a multidisciplinary evaluation, with hygienic, dietetic, pharmacological (pilocarpine hydrochloride) and/or etiological—oral, perioral, extraoral or mixed, as in the case of SS.

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