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Original Research Article

Vitamins A, D, E in the Primary Sjögren Syndrome compared with Control Group

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Abstract

Introduction: Sjögren's Syndrome is a complex and chronic autoimmune disease that affects the salivary and lacrimal glands, however the immunoregulatory and immunosuppressive effect of vitamins has been related to the disease. The objective was to know the vitamins related to the Sjögrens Primary Syndrome compared with a control group. ***Materials and Methods:*** A review was made in the PubMed database with the key words (Vitamin and Primary Sjogrens Syndrome and Primary Sjögrens Syndrome) without restriction of date until November 2, 2018, only studies conducted in humans and published in English were selected. ***Results:*** We identified 50 studies with the search criteria, 5 studies were conducted on animals and were excluded, 7 studies were written in a language other than English and were excluded, only 38 studies were eligible and 7 of them were included. The vitamins A, D, E, and 25 hydroxyvitamin D3 were analyzed in the pSS compared to a control group. ***Conclusion:*** The vitamins D are important to balance calcium, phosphorus for the development of bone tissue and in patients with pSS the musculoskeletal system may be affected.
Keywords: Sjögrens Primary Syndrome, Vitamins A, Vitamins D, Sjogren Syndrome, Patients, Syndrome

INTRODUCTION

Sjögrens syndrome (SS) is a complex chronic autoimmune disease that affects the salivary and lacrimal exocrine glands [11]. Primary Sjögrens Syndrome (pSS) is defined when it presents xerostomia and xerostalmia without systemic involvement and the Sjögrens Secondary Syndrome (sSS) when adjacent to a systemic disease. There is no specific cause of the disease, but there are several factors that can contribute to pSS among them; environmental, genetic, hormonal, alteration of B lymphocytes or innate immunity [14]. In Peru the prevalence rate of the SICCA Syndrome (Sjögrens) was reported 8.4 cases per 100,000 persons (95% CI: 7.99-8.91) and a prevalence of 0.0084% according to the international classification of diseases version 10, whose nomenclature was M035 for the disease [11].

Several criteria have been used to diagnose the disease, but the most used ones have been the 2002 European Consensus Group (EACG) [19] and recently the criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism have been approved. (EULAR) that are applicable to anyone with characteristics suggestive of pSS [15]. The disease presents extraglandular manifestations that affect the musculoskeletal system, lungs, liver, skin, kidneys, neurological [1] and neuropsychiatric [2] and may be related to low level of vitamin B12. Table 1 shows some common characteristics of pSS at the oral, extraglandular and systemic levels.

There are studies that have correlated a low level of vitamin D and neurological alterations and the presence of lymphoma [1], so that their consumption could contribute positively.

Baldini *et al.* reported that low levels of vitamin D and extraglandular manifestations were not associated, but it suggests that in some patients with subjugatory characteristics of pSS early, it could be beneficial [3]. However, Cermak *et al.* reported that nutrient intake is altered in patients with pSS [5]. The frequency of low iron and vitamin levels in the SS was also reported when a grade 1 lymphocyte infiltration occurs [9]. In the absence of consensus, a brief review of the literature was carried out in order to know the vitamins related to the Sjögrens Primary Syndrome compared to a control group.

Table-1: Manifestations of the Primary Sjögrens Syndrome

Author, Year of publication	Extraglandular and oral involvement	Systemic and social involvement
Wu y Carsons, 2014 [20]	• Extraglandular manifestations (mild-severe)	• Rheumatoid arthritis • Lupus erythematosus
Napeñas *et al.*, 2009 [13]	•Parotid and submaxillary glands swollen by 20% -30% • Xerostomia • Hyposialia • Symptoms of fatigue. • Vasculitis	• Rheumatoid arthritis (25% -35%) - older than 40 years.
Fazaa *et al*., 2014 [6]	•Oral dryness (lips, tongue and mucosa) • Fatigue	• Lymphoma (5%)
Stewart *et al*.,2008 [17]	• Xerostomia • Dysgeusia • Dysphagia • Mucositis •Fissured, depapilated and erythematous tongue •Angular cheilitis and labial fissures •Cervical or incisal caries (pH 5.5) • Erythematous candidiasis • Pseudomenbranose candidiasis • Periodontitis (in severe cases)	• Deterioration of quality due to difficulty eating, socializing, singing, speaking.
Klasser *et al*.,2007 [7]	• Alterations of the oral mucosa • Pathology of the salivary glands (hyposialia) • Temporomandibular disorders	• Sensory neuropathies • Headaches

MATERIALS AND METHODS

A review of the scientific literature was made in the PubMed/Medline database with the key words (Vitamin and Primary Sjogrens Syndrome and Primary Sjögrens Syndrome) without restriction of date until November 2, 2018, only studies conducted in humans were included. and published in English language. We selected all studies that analyzed any type of vitamin and that considered diagnostic criteria for the pSS and that compared the levels of vitamins with a control group. The characteristics of the studies that were considered were: author, year and country of publication, duration of the disease, number of patients, gender, age, gender of the pSS patients and control group, and the results of the levels of the vitamins analyzed when it was available.

RESULTS

We identified 50 studies, 5 studies were conducted on animals and were excluded, 7 studies were written in a language other than English and were excluded, only 38 studies were eligible, of which only 7 articles met the criteria and characteristics described and were included, all the others were excluded (Table 2). Due to the heterogeneity of the results, a quantitative synthesis was not analyzed and we only describe the data found.

DISCUSSION

In France, Vitamin B12 deficiency has been described in cases with pSS, although the use of validated and consensual diagnostic criteria for the disease is not clear [2]. We observed that serum concentrations of 25- (OH) D3 were analyzed in several studies with pSS patients compared with a control group [1,3,4,8,12]. 5 included studies used EACG-2002 diagnostic criteria [1,3,8,18,21] and only 2 studies used the Copenhagen 1986 criteria [4,10,12]. 3 studies showed complete data on age, gender and number of paceintes of the pSS group and control group [3,8,21].

Our study has limitations when considering a control group with osteoarthritis patients, SICCA patients and healthy volunteers. Therefore, the inclusion criteria of the control group may present some type of bias. There are studies that compared low levels of vitamin D in the pSS group with involvement of the peripheral nervous system p = 0.04. In addition, the low level of vitamin D was associated with the SS group that presented lymphoma [1]. Vitamin D has an immunomodular effect by its receptor [22] when it is located in the group of steroids that gives it various functions.

Szodoray *et al*. Analyzed vitamin D in the pSS group compared to a control group and found no significant difference in vitamin levels in both groups, a similar result found when comparing vitamin D levels and extraglandular involvement [18]. In counterpart Müller *et al.* reported that vitamin D3 may have an immunoregulatory function in vitro. Their results show that patients with pSS had a low level of 25- (OH) D3 compared with healthy volunteers, although the Gc phenotype did not differ significantly between both groups [12].

Table-2: Vitamins studied in patients with pSS compared to a control group

Author, Year, Country	Diagnostic Criteria for pSS	Duration of the disease median (range)	pSS Group i) Number of patients ii) Gender (w / m) iii) Age (m± SD)	Control Group i) Number of patients ii) Gender (w / m) iii) Age (m± SD)	Type of Vitamin	Vitamin levels in pSS vs CG
Zardi *et al.* 2016. Italy[21]	EACG 2002	8,2 years	i)25 pSS ii)25 w/0 m ii)68 ± 6.5 years	i)22 ostheoarthritic patients ii)22 w/0 m iii)66±7.3 years	Serum levels vitamin D	(20.93 vs 26.42) ng/ml) (p =0.005)
Lee *et al.* 2016. Korea [8]	EACG 2002	8.7±0.78 years	i)69 pSS ii)68 w/ 1m iii)56.7±1.32 years	i)22 SICCA patient ii)21 w/1 m iii)58.0±2.66 years	Serum levels of 25(OH)D3	(22.0±1.32) vs (28.0±2.69) p=0.036 ng/mL
Baldini *et al.* 2014. Italy [3]	EACG 2002	DN	i)30 pSS ii)30 w/0 m ii)median 54 years	i)46 SICCA patient ii)46 w/0 m iii)median 60 years	Serum concentrations of 25 (OH)D3	20 (9.3-26) vs 22.5(15.6-33) ng/ml (p= 0.50)
Agmon-Levin *et al.* 2012. Israel[1]	EACG 2002	DN	i)176 pSS ii)169 w/7m iii)DN	i)163 healthy individuals ii) 169 w/7m iii)DN	Serum concentrations of 25 (OH) vitamin D	(21.2±9.4) vs (22.4±10) ng/ml (p=0.2).
Szodoray *et al.*, 2010. Hungary[18]	EACG 2002	DN	i)25 pSS ii)22 w/3 m iii)56.4(9.4) years	i)15 healthy individuals ii)DN iii)DN	Serum levels vitamin A, E, D	Vitamin A: DN (p=0.522) Vitamin D:79.96 (37.87) vs 71.57 (23.01) nmol/l (p= 0.408) Vitamin E: 41.41(8.96) vs 33.68 (6.20) mmol/l, (p= 0.004)
Bang *et al.* 1999. Denmark[4]	Copenhagen 1986	18 (5-62) years	i)41 pSS ii) 39 w/2 m iii)62 (27-88) years	i)569 healthy individuals ii) DN iii)(18-60) years	Serum levels of 25(OH)-D	(20±10)vs (28) ng/ml
Müller *et al.*,1990. Denmark.[12]	Copenhagen 1986	DN	i)35 pSS ii)DN iii)51(27-69) years	i)DN ii)DN iii)18-60 years	Serum 25-(OH)D3	(median 9.0, (5.0-16.0) vs (28.2±12.4) ng/ml

pSS:Primary Sjögren's syndrome,DN: Data not available, EACG: European-American consensus group, OH=hidroxivitamina, w:women, m:mens, CG: control group

Analyzing vitamin D levels and their relation to pSS Zardi *et al.* studied the thickness of the intima-media layer, finding a positive association with the duration of the pSS [21]. On the other hand, Lee *et al.* and Baldini *et al* using the same diagnostic criteria for pSS and selecting SICCA patients as control group, evaluated levels of 25 hydroxyvitamin D3 reporting opposite results, this confirms the complex and heterogeneous effect represented by the etiopathogenesis of pSS [3,8].

CONCLUSION

Vitamins A, E, F and 25-hydroxyvitamin D3 were analyzed in the pSS when compared to a control group. These vitamins are important to balance calcium, phosphorus that allow proper development of bone tissue and in patients with pSS the musculoskeletal system may be affected. More conclusive studies are required that use the new diagnostic criteria for the pSS

and that consider potential biases in the selection of patients.

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