Vitamin D Role in Chronic Dacryocystitis

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Research Article

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Abstract

Introduction: Vitamin D deficiency has been associated with dry eye disease or Sjogren's syndrome. Due to the anti-inflammatory role of vitamin D in eye diseases, it has been proposed to study the role of this vitamin in chronic dacryocystitis, which is an infectious and inflammatory process affecting the nasolacrimal system.

Objective: Determine the association between vitamin D levels with the presence of chronic dacryocystitis.

Materials and Methods: A cross-sectional descriptive observational study analyzed a sample of 40 individuals, of whom had been diagnosed with chronic dacryocystitis. Biochemical tests for serum 25-hydroxyvitamin D (vitamin D) were subjected to the entire sample. The difference in the means was calculated using the T-test for associated data. The reference significance value was 0.05.

Results: Chronic dacryocystitis commonly occurs in the age group of 51 to 67 years. Women were more vulnerable to infection than men. No association was found between the presence of chronic dacryocystitis and vitamin D levels ($p=0.755$). It is recommended to use larger cohorts as well as multicenter studies evaluating this association, such as supplemental use of vitamin D on a large scale.

Conclusions: Low vitamin D levels are not associated with the presence of chronic dacryocystitis.

Introduction

Obstruction of the nasolacrimal duct leads to the excess overflow of tears called epiphora, a common complaint among ophthalmic patients. Physiologically, the mucosa of the lacrimal sac is very resistant to infection, occasionally distal obstruction of the nasolacrimal duct may occur, which can trigger inflammatory and infectious processes¹.

Pathologies of tear duct drainage account for about 3% of eye consultations, of which dacryocystitis is by far the most common cause of epiphora. Dacryocystitis is inflammation of the tear sac, and is classified according to the time of evolution in acute and chronic². Of these two varieties, chronic dacryocystitis is the most common, and is associated with nasolacrimal duct obstruction. Chronic dacryocystitis usually affects both children and adults more often women ≥ 40 years old.³.

The prevalence of chronic dacryocystitis exceeds acute infection, this is related to the microbiological pathogenesis of dacryocystitis, as well as the patterns of geographic variation of the etiological agents in these infections. Another influencing factor is the co-occurrence of nasal pathologies with the presence of chronic dacryocystitis^{1,4}.

Causes of chronic dacryocystitis range from idiopathic causes to secondary causes to infectious processes, local or systemic inflammations, nasal trauma, nasal polyps, nasal septum deviation,

hypertrophic rhinitis, lower corneal hypertrophy, congenital disorder or neoplasms, which triggers a buildup of tears in the sac, mucoid secretions and flaky cells, which cannot be drained to the nose, but usually overflow to the outside of the eye⁵. The accumulation of cell debris, mucus and tears leads to the arrival of bacteria and with it the origin of dacriocystitis⁶.

Chronic dacryocystitis associated with bacterial infections represents around 61–95% of all dacryocystitis^{6,7}. The causative agents of the infection colonize and multiply in the nasolacrimal duct and produce relevant symptoms such as epiphora, pyorrhea, ophthalmodynia and conjunctival hyperemia, among others, which affect the quality of life of patients. Delayed treatment can trigger infection extension to other tissues, such as orbital cellulitis, abscesses, meningitis, cavernous sinus thrombosis, and sepsis⁷.

Symptoms associated with chronic dacryocystitis include continuous epiphora, regurgitation of mucoid or mucopurulent secretions to digitopression in the tear sac or by infusing fluids into the tear drainage system².

Vitamin D is a known steroid hormone which can be endogenously synthesized or ingested in the diet. The role of vitamin D has been established at the eye level. Several studies describe the presence of vitamin D receptors in numerous eye structures, such as the corneal epithelium, lens, ciliary body, corneal endothelium and pigment epithelium, ganglion cells and retinal photoreceptors^{8,9}. Vitamin D hydrolase has also been shown to be present in various structures of the human eye, so a conversion of 25-hydroxyvitamin D to the active form 1.25-hydroxyvitamin D or calcitriol in the eye has been proposed. Similarly, epithelial limb cells, aqueous and vitreous humor and tear film could also be considered sources of origin of vitamin D in the eye⁹.

An improvement in cornea epithelial bore has been reported in patients with vitamin D supplementation, because it regulates narrow joints between cells¹⁰. In addition, vitamin D immunomodulatory mechanisms have been proposed in inflammatory eye processes, expressed in inhibition of inflammatory cell migration (Th1 and Th2 cells), increased interleucine synthesis (IL) 10, reduction of inflammatory cytokines such as IL6, C-reactive protein and tumor necrosis factor (TNF) alpha^{11,12}. Other described functions of this vitamin is act as a stabilizer of the eye surface, through the reduction of the osmolarity of tears¹². So vitamin D can influence the functions of the tear system¹⁰.

Normal levels of vitamin D in adults according to the Center for Disease Control and Prevention (CDC) range from 20–80 ng/ml, described as vitamin D deficiency at levels below 20 ng/ml and severe vitamin D deficiency for levels below 10 ng/ml). Tests to evaluate vitamin D may be total levels of 25 (OH) D (diagnosis and monitoring of vitamin D deficiency) and measurement of the 25 (OH) D2 and 25 (OH) D3 (treatment follow-up)¹³.

Human studies have determined a link between elevated serum vitamin D levels with improved symptoms in dry eye syndrome¹⁴, and highlighting that 25-hydroxyvitamin D deficiency linked to lack of

sun exposure are associated with dry eye syndrome¹⁰. That is, adequate levels of vitamin D have a positive impact on dry eye syndrome.

According to the review, this is the first study to evaluate the association between vitamin D levels in the presence of chronic dacryocystitis.

H0: There is no association between chronic dacriocystitis and vitamin D levels.

H1: Chronic dacriocystitis is associated with vitamin D levels.

Based on the background described, it is proposed to determine the association between vitamin 25-OH-hydroxyvitamin D levels in patients with chronic dacryocystitis.

Material And Methods

This study was a descriptive, retrospective and cross-sectional observational study, where vitamin D deficiency is to be checked as a predictive factor in the onset of chronic dacryocystitis. Consecutive patients with and without patent lacrimal drainage system were recruited prospectively from the Clinical University Hospital of Valladolid for a period of 12 weeks, from September 1, 2020 to November 30, 2020.

This study was approved by the ethics committee of the University Hospital of Valladolid and was carried out in accordance with the principles of the Helsinki Declaration.

Participants

Consecutive patients with and without permeable tear drainage were prospectively recruited at the Clinical University Hospital of Valladolid, from 1 September 2020 to 30 November 2020. Twenty patients with permeable tear drainage system and 20 patients without permeable tear drainage system. All patients with confirmed or minimally suspected vitamin D supplementation and paediatric patients were excluded.

Patients were diagnosed as chronic dacryocystitis based on their history of persistent epiphoria and regurgitation of mucoid or mucopurulent material at pressure over the sac area or tear duct test irrigation.

Data collection

Basal serum levels of 25-hydroxy vitamin D were measured by high-resolution liquid chromatography. All patients included were given a total serum level of 25-hydroxy vitamin D. Vitamin D deficiency was defined as 25(OH)D concentrations below 20 ng/mL, a level between 20-30 was considered a vitamin D insufficiency and a vitamin D level of 31 ng/mL or higher was adequate for good health, according to our laboratory guidelines. Serum levels of 25-hydroxy vitamin D were compared between patients with and without a permeable tear system.

The main result measure included the association between vitamin D levels and chronic dacriocystitis.

Statistical Analysis

All statistical analyses were performed by the SPSS version 25 statistical program. The mean was calculated for the age with standard deviation.

Pearson's correlation test was used to analyze the association between categorical variables (Healthy_sick and vitamin D levels).

Statistical significance was defined as a value of $p < 0.05$.

Results

Table 1 presents the demographic characteristics of including chronic dacryocystitis cases and healthy controls (with permeable tear system). A total of 20 cases of chronic dacryocystitis (3 men and 17 women) and 20 unmatched controls (6 men and 14 women) were included. The average age was $69.33 \pm$ years between the two groups, and ages ranged from 51 to 87 years, with differences in the female gender. The number of women was higher than that of men in both groups, with 31 (77.5%) women and 9 (22.5%) men. Furthermore, Table 1 reflects Pearson correlation data between categorical variables.

The average serum vitamin D in patients with chronic dacryocystitis was 20.55 ± 1.83 ng/mL, of which 55% (11/20) were normal (> 31 ng/ml), 40% (8/20) were insufficient (> 20 and < 30 ng/ml) and 5% (1/20) were deficient (< 20 ng/ml) in vitamin D. No statistically significant difference in vitamin D levels was observed between patients with dacryocystitis (20.55 ± 1.83 ng/mL) and healthy controls (19.54 ± 1.23 ng/ml) ($P = 0.508$) (Table 1).

In the current study, we categorized subjects according to their vitamin D status in three groups: less than or equal to 10 ng/ml as insufficient levels, range between 11 to 20 ng/ml as low vitamin D levels, and more than 20 ng/ml as normal vitamin D levels to better understand the association between vitamin D status and chronic dacryocystitis.

The data from the healthy group were not significantly different from those of the patient group.

Table 1
Descriptive statisticians

	Chronic dacriocystitis group (n = 20)	Control group (n = 20)	p
Age	71,75 ± 2,129	69,3 ± 1,674	0,998
Gender			
• Woman	n = 17 (42,5%)	34 (85%)	0,001
• Man	N = 3 (12,5%)	6 (15%)	
Serum 25 (OH) D			
< 10 ng / ml	5% (n = 1)	0	0,759
11 ~ 20 ng/ml	40% (n = 8)	10 (n = 50%)	
20 ~ 40 ng/ml	55% (n = 11)	10 (n = 50%)	0,759

In the group of patients with chronic dacryocystitis, low or insufficient levels of vitamin D were reported in 9 patients (45% of cases), while the group with tear sac permeability recorded a total of 10 people with low vitamin D levels (50%) (Table 2).

Table 2
Contingency table between study groups and vitamin D levels.

			Vitamin D levels.		Total
			Under	Normal	
Healthy_sick	Sick	Count	9	11	20
		% of the total	22,5%	27,5%	50,0%
	Healthy	Count	10	10	20
		% of the total	25,0%	25,0%	50,0%
Total		Count	19	21	40
		% of the total	47,5%	52,5%	100,0%

The bivariate correlation test was applied to the Pearson statistician, for dichotomized variables (low and normal vitamin D levels) and study groups (healthy group [with tear duct permeability] and sick group [without nasolacrimal duct permeability]).

There is a 75.2% chance of error between chronic dacryocystitis and vitamin D levels. So, the study hypothesis is rejected, and the null hypothesis is accepted.

Table 3
Chi Cuadrado test

	Value	df	Asymptotic (bilateral) significance	Exact (bilateral) significance	Exact meaning (unilateral)
Pearson's Chi-square	,100 ^a	1	,752		
Continuity correction^b	,000	1	1,000		
Reason for plausibility	,100	1	,751		
Fisher's exact test				1,000	,500
Linear-to-linear association	,098	1	,755		
N of valid cases	40				
a. 0 boxes (0.0%) have expected a count less than 5. The expected minimum count is 9.50.					
b. It has only been calculated for a 2x2 table					

Discussion

This study consisted of associating the presence of chronic dacryocystitis with vitamin D levels, compared with a control group of healthy patients, recruited in the same time period. There were not significant differences between the two groups for vitamin D levels.

Pearson's bivariate correlation with R showed an R-index of Pearson (0.050), reflecting a moderate correlation, however, the bilateral asymptotic significance data reflected a value of p-0.755 which, being a value greater than 5% of the significance posed for this work (margin of error of 5%) the independence of the variables studied was considered.

That is, vitamin D levels are not accepted to be associated with chronic dacryocystitis. Non-parametric tests with similar results were applied. This may be due to the low sample collected, vitamin D measurements, or that the variables have no significance in the inflammatory and infectious process of the tear sac, however, for this it is necessary to use larger study cohorts, as well as multicenter studies in order to generalize this data to the general population.

Other variables that accompany vitamin D values that complement these tests may also be analyzed.

No clinical trials were found in animals or humans to assess the association between vitamin D levels with chronic dacryocystitis, so this is considered a line of research to be expanded, to describe the possible association between this vitamin with diseases related to tear drainage.

Similarly, it is recommended to perform immunological tests associated with chronic dacryocystitis and correlate with vitamin D levels, to describe the immunomodulatory role found in other studies^{10,14}.

Although association of vitamin D levels has been reported in patients with dry eye syndrome, due to the immunomodulating role of vitamin D at the level of innate and acquired immunological responses^{13,15}. Still not studying the correlation of vitamin D levels with other eye disorders, in vitro studies indicate that vitamin D inhibits the release of pro-inflammatory cytokines from CD4 + T cells, and that it is able to induce a regulatory T-cell phenotype¹⁶. Other studies indicate the involvement of vitamin D in the release of cytokines from circulating monocytes^{13,15}.

The importance of studying this association between this disease and large-scale vitamin D levels is because of the prophylactic ability that can be achieved by using vitamin D as a supplemental for prophylaxis for the development of nasolacrimal duct obstruction.

The limitations of this study should be taken into account when interpreting their results. First, the entire sample was very low, and the selection of cases should be random in order to give greater objectivity to the results obtained. Second, measurements of vitamin D levels were total, no vitamin D2 and D3 measurements were used in either of the participants in both groups. And thirdly and finally, some variables that may have confused the results, such as socioeconomic level, caffeine intake, occupation, and exposure to sunlight, were not evaluated.

Despite these limitations, no association was found between study variables. Lower levels of vitamin D were present in both groups (healthy and sick), result probably biased due to lower sun exposure caused by motility limitations established in the Covid-19 pandemic.

Conclusions

Chronic dacryocystitis is an inflammatory and infectious disease of the tear sac, the causes of which range from infections to autoimmune diseases. This is the first study that raised the association between vitamin D levels with the presence of chronic dacryocystitis compared to a healthy control group. However, no association was established between these variables, due to external factors such as the total sample recruited, the evaluation of chronic inflammation variables along with serum vitamin D measurements is recommended, because a higher degree of inflammation can be associated with alterations in levels of vitamins and other substances, the behavior of vitamin D and the role in diseases by blockage of the nasolacrimal duct can be evaluated.

Declarations

Conflicts of Interest

The author declares no conflicts of interest.

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Figures

Figure 1

Frequency of vitamin D levels depending on healthy and sick patients.