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CHRONIC BLEPHARITIS: REVIEW OF INCIDENCE, PREVALENCE AND TREATMENTS

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ABSTRACT

According to statistical data, Chronic Blepharitis has the highest incidence of eye diseases. In a survey conducted in the United States (USA), 37% to 47% of patients seen by respondents were diagnosed with blepharitis. In 2014, blepharitis accounted for 700,000 patient visits in the USA. There are few epidemiological data estimate that the true prevalence of blepharitis. In the past, there has been considerable confusion over the pathophysiology, and thus the definition of blepharitis. Because of these uncertainties, an accurate assessment of the prevalence and incidence of the disease has been difficult to achieve. The objective of this study was to review the literature to present and contribute to the readers information on the incidence and prevalence of chronic blepharitis in the world, and to identify the best medical treatments and interventions. Based on the literature review, there are still many information gaps regarding the best treatment for chronic blepharitis as well as dysfunction of Meibomian gland (DMG). In conclusion, it is imperative to create multicenter randomized studies to better understand what is the best treatment for these diseases in order to at least ensure improved quality of life throughout the entire treatment.

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INTRODUCTION

According to statistical data, Chronic Blepharitis has the highest incidence of eye diseases. In a survey conducted in the United States (USA), 37% to 47% of patients seen by respondents were diagnosed with blepharitis (Duncan *et al.*, 2015; Nakamura *et al.*, 2015). In 2014, blepharitis accounted for 700,000 patient visits in the USA. In a study conducted in the San Francisco and Texas, staphylococcal blepharitis had higher incidence in women with an average age 42 years. Moreover, it was postulated that staphylococcal blepharitis occurs more often in warmer climates, and about 25% to 50% of the cases were associated with keratoconjunctivitis sicca (Duncan *et al.*, 2015; Nakamura *et al.*, 2015 and Hirsch-Hoffmann *et al.*, 2015). Added to this, the study reported that chronic blepharitis is the most common condition among

patients looking for an eye exam by discomfort or eye irritation. The three most commonly diagnosed medical conditions were later blepharitis 24% (276/1148), dry eye 21% (241/1148) and anterior blepharitis 12% (138/1148) (Merdler *et al.*, 2015). Interestingly, in 54% of cases, the treatment was not consistent with the diagnosis at the time of examination, it was inappropriate and led to poorer results in 60% of cases (4,5). Moreover, the prevalence of Meibomian gland dysfunction (MGD), which causes blepharitis, is greater in the Asian population, over 60%, while ranges from 3.5 to 19.9% among Caucasians.

Thus, a study by Hom *et al.* (MGD, 2015) found an existing pattern of meibomian gland dysfunction in a sample of randomly selected patients, from normal appearance. Of 398 patients, 38.9% showed meibomian gland dysfunction. Factors such as the patient's sex, age, allergies, wear contact lens were evaluated to determine the correlation with meibomian glands. Only advanced age was positively correlated with the prevalence of meibomian gland dysfunction (MGD, 2015);

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Ianchenko *et al.*, 2014; Back *et al.*, 2012). Based on the context of the incidence and prevalence of blepharitis in an attempt to mitigate the negative impact of this disease, treatment for blepharitis is performed by two situations, the treatment of the acute form of the disease or to make prevention the same (Nakamura *et al.*, 2015; Nelson *et al.*, 2011; Knop *et al.*, 2011). The staphylococcal blepharitis may be or seborrheic and while the first, the treatment must pass flap antibiotics and anti-inflammatory drugs, in seborrheic is usually sufficient to use anti-inflammatory and cleaning of the eyelids (Utine *et al.*, 2011; Nichols *et al.*, 2011; Nelson *et al.*, 2011). In addition, the natural palpebral daily treatment involves the long term care, keeping the edge of the eyelids as clean as possible using through compresses soaked in warm water, wiping well eyelids and then placing on a whole surface ointment containing antibiotic and anti-inflammatory (Kim *et al.*, 2011; Filho *et al.*, 2011).

The local heat helps to remove the crust and greasy secretions through the moistened pads in hot water, placed on the eyelid several times daily, for 3 minutes to 2 times per day. The gentle massage of the base of the eyelashes allows fluidize secretions of gland, being very effective in the treatment of blepharitis (Zhu *et al.*, 2011). Other forms of treatments for blepharitis are used artificial tears for the treatment of discomfort and eye irritation and may be used eye drops or ointments for local treatment of palpebral infection (Knop *et al.*, 2011; Liu *et al.*, 2010; Bernardes *et al.*, 2010 and Divani *et al.*, 2009). In more serious situations may be necessary to use systemic antibiotics. However, patients may be oversensitive to blepharitis preservatives eye drops. Since treatment with antibiotic ointment are used especially in staphylococcal blepharitis. The corticosteroids are used for treating the most serious inflammation, there are, however, care in their use, since they may cause side effects such as cataracts and glaucoma. The treatment of blepharitis is simple, yet quite laborious, because the patient must be disciplined to achieve a good quality of life (Bambury *et al.*, 2009; Brewitt *et al.*, 2008; Lemp *et al.*, 2008).

Furthermore, there is little epidemiological data to estimate the true prevalence of blepharitis (Duncan *et al.*, 2015). In the past, there has been considerable confusion over the pathophysiology, and thus the definition of blepharitis. Because of these uncertainties, an accurate assessment of the prevalence and incidence of the disease has been difficult to achieve. Blepharitis is a common chronic condition whose etiology is poorly understood. Commercial products are available and sold to patients, but it is unclear whether they are effective (Nakamura *et al.*, 2015). Thus, the literary findings show how the treatment for blepharitis is diligent, as an example, a study selected 5,000 adult patients randomly in the US to analyze the prevalence of blepharitis symptoms in the general population. Ophthalmologists report that patients diagnosed with blepharitis, only 34% sought treatment for blepharitis symptoms, while 41% sought treatment for dry eye symptoms, 16% surgical evaluation and 6% routine complaints examination / vision (Duncan *et al.*, 2015; Zhu *et al.*, 2011).

In the same study, when consulted on the age and sex of patients predisposed blepharitis / meibomian gland

dysfunction, and 33% of ophthalmologists cited that men had the age of 65 and that 27% of ophthalmologists cited that women were ages between 46 and 65 (Zhu *et al.*, 2011). Moreover, the majority of ophthalmologists agreed that the condition of dry eye is a common co-morbidity with meibomian gland dysfunction and 74% of ophthalmologists agreed that meibomian gland dysfunction is the most common cause of dry eye (McCulley *et al.*, 2003). Blepharitis has a large impact on quality of life. Its signs and symptoms are nonspecific and include eye irritation and itchy, red eye, burning, photophobia, redness and crust on the eyelid margin (Hirsch-Hoffmann *et al.*, 2015; Asano-Kato *et al.*, 2001).

If not handled properly, could evolve with chalazion, stye, dry eye and falling eyelashes. The greatest benefit observed after 30 days of treatment with tacrolimus ophthalmic ointment was the improvement in the patient's symptoms with persistence only slight foreign body sensation. (Hirsch-Hoffmann *et al.*, 2015). For refractory blepharitis, the use of corticosteroids alone or in combination with antibiotics is a therapeutic option, provided that the treatment is controlled with minimal doses and for short periods. Among immunomodulatory agents, there is a possibility of the treatment with cyclosporin A and tacrolimus, both with the same mechanism of action, however Tacrolimus has a greater effectiveness in vitro 10-100 cyclosporin A (Zhu *et al.*, 2011). The objective of this study was to review the literature to present and contribute to the readers information on the incidence and prevalence of chronic blepharitis in the world, and to identify the best medical treatments and interventions.

Methodology and Study Design

Descriptive study which was carried out literature in the database PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) (Figure 1). In this case, they selected original and review articles, regardless of the date of publication and mention information about chronic blepharitis. The following keywords were used: chronic blepharitis, treatment, information gap, incidence and prevalence (Figure 2). The primary outcomes were subjective improvement in symptoms as judged by the patient, symptom report measured by questionnaire, interview or visual analog scale (VAS), including but not limited to, irritation, burning, tearing, itching, sticking eyelids, photophobia and increased flicker frequency, improvement in the clinical examination findings as judged by investigators, including but not limited to: the injection / eyelid margins erythema, scaling, change of cilia, abnormalities in quality or quantity of tear film abnormalities and the rear lid margin and meibomian orifices. Since there are no standardized diagnostic criteria for blepharitis and without standardized scales on which to judge the severity of symptoms, clinical improvement of the symptoms expected range between studies. Although it would have been ideal for studies using validated scales, all scales used in the included studies were considered for inclusion provided standardized information was unavailable. Secondary outcome measures were: eradication measures or decrease in the number of colonies of positive bacterial cultures, adverse events measured by the patient or change the report on clinical, quality of life measures, economic costs and benefits of different interventions.

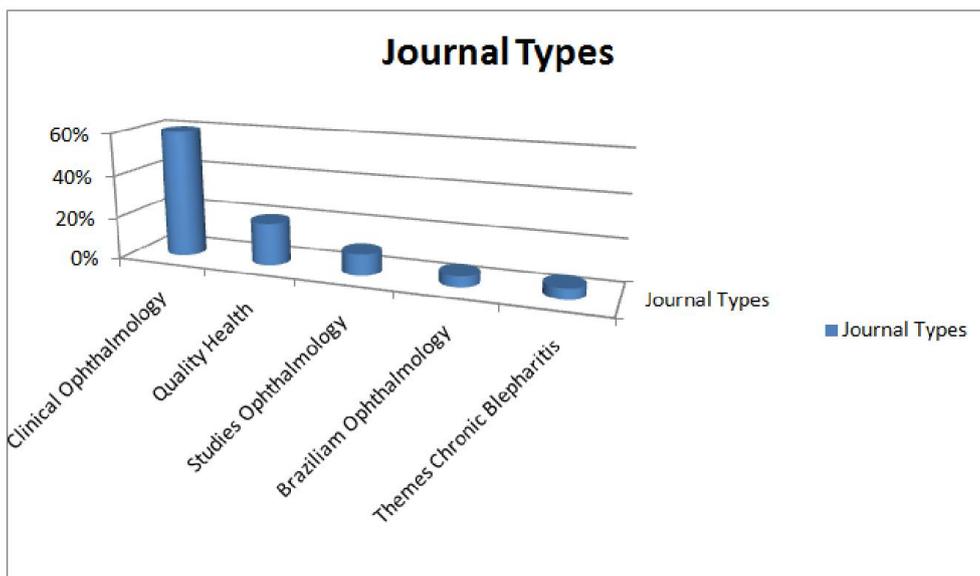


Fig. 1. Main types of newspapers that publish on Chronic Blepharitis and were research targets for this work

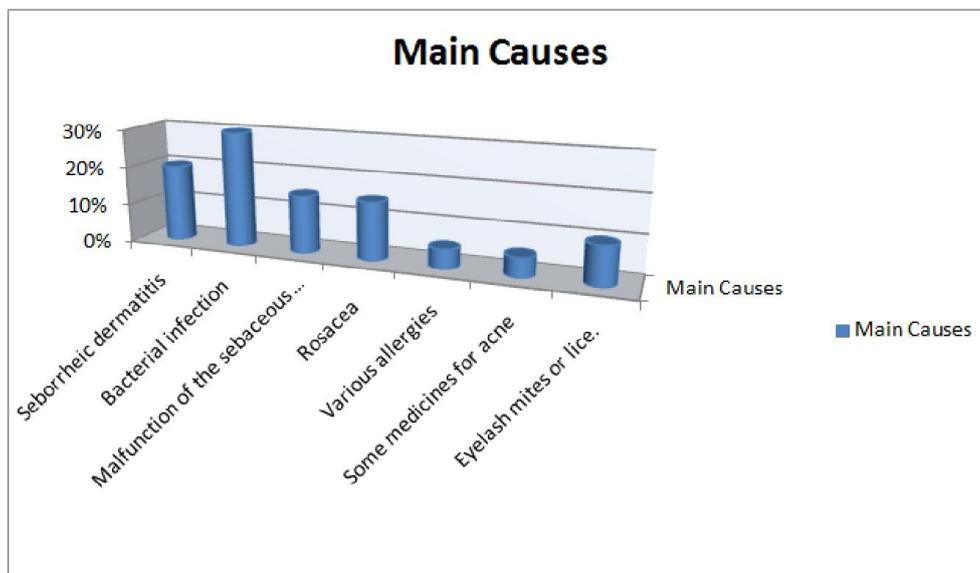


Fig.2. Graph showing the main causes and the incidence of Chronic Blepharitis

Literature Review – Development

Staphylococcal blepharitis believed to be associated with staphylococcal bacteria on the ocular surface (Duncan *et al.*, 2015). However, the mechanism by which bacteria cause symptoms of blepharitis is not fully understood. Comparisons between normal bacterial flora eyes and those diagnosed with staphylococcal blepharitis have identified some differences (Duncan *et al.*, 2015; Nakamura *et al.*, 2015). Only 8% of normal patients had positive cultures for *S. aureus*, compared with 46% to 51% of people diagnosed with staphylococcal blepharitis (Nakamura *et al.*, 2015; Hirsch-Hoffmann *et al.*, 2015). Furthermore, hordeolum is an inflammatory nodular eyelid resulting from hair follicles or meibomian gland is associated with staphylococcal blepharitis (Hirsch-Hoffmann *et al.*, 2015; Merdler *et al.*, 2015; Arrúa *et al.*, 2015).

On the other hand, in two studies, 92% to 97% of patients had blepharitis Cultures positive for *Staphylococcus*. Quantitative or qualitative deficiencies in meibum may be responsible for the symptoms experienced in blepharitis. Furthermore, the hyperkeratinizationmeibomian gland epithelial may lead to clogging and reduction in the amount of meibomian gland secretions (Arrúa *et al.*, 2015; MGD, 2015; Ianchenko *et al.*, 2014; Back *et al.*, 2012 and Friedland *et al.*, 2011). Qualitative differences in the composition of meibum has been investigated. Thus, it was found that patients with blepharitis significant differences in free fatty acids in the secretions of their meibomian glands, compared to controls (Friedland *et al.*, 2011; Nelson *et al.*, 2011). It is not known if these differences are present in the endogenous secretion or bacterial enzymes may modify the secretions on the eye surface.

Changes in these tear film protection portions may decrease its effectiveness and contribute to inflammation and irritation (Nelson *et al.*, 2011).

Added to this, there were also variations in the interventions. Four studies compared topical antibiotics or anti-bacterial agents placebo. Three other studies compared ciprofloxacin ophthalmic solution with a topical antibiotic another, one of which used the same dose for each treatment a different used doses and doses not reported (Knop *et al.*, 2011; Utine, 2011; Nichols *et al.*, 2011). Still, a study investigated a topical antibiotic and an oral antibiotic, using topical and oral placebos as controls (Nelson *et al.*, 2011; Kim *et al.*, 2011 and Filho *et al.*, 2011). Furthermore, studies have analyzed five combinations of topical antibacterials / antibiotics and corticosteroids, with the same dose of topical antibiotics or anti-bacterial agents and corticosteroids alone or placebo. Another study showed the combination of topical antibiotic and corticosteroid (Utine, 2011; Zhu *et al.* 2011).

Three other studies have investigated pharmacological interventions compared to placebo topical antifungals and the same dose of topical antibacterial agent (Kim *et al.*, 2011; Filho *et al.*, 2011). In addition, 14 studies, including 12 randomized controlled trials evaluated the effectiveness of interventions among participants with chronic blepharitis. There was considerable variation in the types of interventions investigated (Zhu *et al.*, 2011; Knop *et al.*, 2011). Two studies treatment with antibiotics: A study of topical antibiotics in addition to hot compresses hot packs per se and the other lower studied and high doses of oral antibiotic versus placebo. Two studies, one immunosuppressive agent compared to placebo topical or more steroids with topical antibiotics. A study evaluated a treatment regimen more topical antibiotics and steroids hot compresses and artificial tears with or without supplementation with an oral mucolytic agent. The topical mucolytic agent was compared with artificial tears in another study. The latest study investigated an automatic heater and massage device with or without additional manual expression of meibomian gland (Liu *et al.*, 2010; Bernardes *et al.*, 2010).

In an open study, 33 patients with meibomian gland dysfunction were treated with azithromycin ophthalmic solution 1.0% twice a day for two days, then every night, for a total of 30 days. As a result 26 of 33 patients completed the study (Divani *et al.*, 2009). Tear break up time and Schirmer score increased by 52.7% and 24%, respectively. There was a reduction in staining of the cornea and conjunctiva for 83.2 and 67.9%, respectively. In conclusion, the results showed clinically and statistically significant improvement in signs and symptoms associated with blepharitis. Based on these results, 1% azithromycin ophthalmic solution provides a viable option for the treatment of blepharitis. In a randomized prospective study with placebo, patients with impaired Meibomio gland and blepharitis, which had stopped all topics and tetracycline drugs, received dietary supplementation of omega-3 orally (Bambury *et al.*, 2009). The patients were examined every 3 months for 1 year with the ocular surface disease index (OSDI). The results showed that in one year, the omega-3 group had a 36% reduction and 31% with the use of omega-6, while the placebo group showed no change.

Conclusion

Based on the literature review, there are still many information gaps regarding the best treatment for chronic blepharitis as well as dysfunction of Meibomio gland (DGM). Thus, it becomes imperative to create multicenter randomized studies to better understand what is the best treatment for these diseases in order to at least ensure improved quality of life throughout the entire treatment.

Disclosure of potential conflicts of interest

The authors declare that they have no conflicts of interests.

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