ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

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Treatment Efficacy Studies of the Lacrimal Punctum Plug in Blepharitis and Dry Eye Syndromes: Methodological Research, Retrospective Validation Study

Blefarit ve Kuru Göz Sendromunda Lakrimal Punktum Tıkacının Tedavi Etkinlik Çalışmaları: Metodolojik Araştırma, Geriye Dönük Doğrulama Çalışması

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ABSTRACT Objective: To examine the most recent literature regarding therapeutic effectiveness studies of lacrimal punctum plugs (PPs) in blepharitis and dry eye syndromes (DES). **Material and Methods:** This study involves methodological research, Retrospective Validation Studies, and Multivariate Meta-analysis. The data were provided with the PubMed (The National Center for Biotechnology Information, the U.S.), Google Scholar (The Google Co., the U.S.), SCOPUS (The ELSEVIER Co., The Netherlands), WoS (The Clarivate analytics Co., UK & USA), and Google Academic Papers (The Google Co., the U.S.) in between 2012 and 2023. **Results:** The findings show decreased lubricant dependence, increased tear film consistency, and enhanced patient-reported outcomes. Long-term effectiveness, comparative studies, combination therapy, patient selection, plug design, and monitoring of complications should be the main topics of future research. The combined findings from the studies under consideration shed light on the possible advantages and difficulties connected with this therapeutic strategy. **Conclusion:** Although the studies that have been evaluated offer insightful information, the variety of plug designs and patient groups need further rigorous randomized controlled trials to establish the broader effectiveness of this treatment approach.

Keywords: Lacrimal punctum plugs; lacrimal PPs; blepharitis and PPs; dry eye syndromes and PPs; DES and lacrimal PPs

ÖZET Amaç: Blefarit ve kuru göz sendromlarında (DES) lakrimal punktum tıkaçlarının (PP'ler) terapötik etkinlik çalışmalarına ilişkin en yeni literatürü incelemek. **Gereç ve Yöntemler:** Bu çalışma metodolojik araştırmayı, Retrospektif Doğrulama Çalışmalarını ve Çok Değişkenli Meta-analizi içermektedir. Veriler 2012 ile 2023 yılları arasındaki PubMed (Ulusal Biyoteknoloji Bilgi Merkezi, ABD), Google Scholar (The Google Co., ABD), SCOPUS (The ELSEVIER Co., Hollanda), WoS (The Clarivate Analytics Co., Birleşik Krallık ve ABD) ve Google Akademik Makaleler (The Google Co., ABD)'den sağlanmıştır. **Bulgular:** Sonuçlar lubrikan bağımlılığının azaldığını, gözyaşı filmi kıvamının arttığını ve hasta tarafından bildirilen sonuçların arttığını göstermektedir. Uzun vadeli etkinlik, karşılaştırmalı çalışmalar, kombinasyon tedavisi, hasta seçimi, tıkaç tasarımı ve komplikasyonların izlenmesi gelecekteki araştırmaların ana konuları olmalıdır. Bu çalışmalardan elde edilen birleştirilmiş bulgular, bu terapötik stratejiyle bağlantılı olası avantajlara ve zorluklara ışık tutmaktadır. **Sonuçlar:** Değerlendirilen çalışmalar aydınlatıcı bilgiler sağlamasına rağmen, tıkaç tasarımlarının ve hasta gruplarının çeşitliliği, bu tedavi yaklaşımının daha geniş etkinliğini belirlemek için daha titiz randomize kontrollü çalışmalar gerekmektedir.

Anahtar Kelimeler: Lakrimal punctum tıkaçları; lakrimal PP'ler; blefarit ve PP'ler; kuru göz sendromları ve PP'ler; DES ve lakrimal PP'ler

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However, treatments in the ophthalmology sector progressively provide a better quality of visual health, current issues and complications are encountered worldwide.[1]

These ocular diseases are not limited to a few countries and have spread all over the world. According to an estimate, ophthalmic disorders possess a global burden of almost 61.4 million DALYs worldwide (DALYs is the representation of loss of one year of healthy life.). In recent decades, many researchers have tried to establish the best remedial variations as regards PPs, so that the patients could be effectively and more comfortably treated. The Turkish ophthalmologic cases have faced issue of vision in related illnesses and researchers have been working on a couple of therapies, such as PPs.[2] According to Aljoscha et al., almost 8.3% of Turkish populace suffering from the issue of DES.[3] They described that the elderly population are at more risk of exposure to this illness.

Blepharitis is a disease which is related to inflammation of the eyelids, and it normally affects both eyes at the same time along with inflammation on eyelids margins. Until now, no single reason has been specified by the researchers or ophthalmologists that can cause blepharitis. The most common reason has been identified is the clogging of little oil gland near the surface of eyelashes.[4]

Although blepharitis does not cause any permanent damage to the eyesight, treating is considered quite difficult. It may cause uneasiness in the sight of the patient. The symptoms of blepharitis include watery eyes, swelling on the eyelids, abnormal fall of eyelashes along with others.[5] DES relates to the reduction in the wetness with tears. It usually occurs when the tears do not work properly or the eyes, in a few cases, stop producing the needed tears. DES owns a direct relation with the visible problems as if not treated timely, it may cause bad visual acuity as the eyes feel uncomfortable to see anything.[6] It has been observed that women and people over the age of fifty are more likely to develop severe risks of DES. Its symptoms contain scratchy feeling, blurry vision, redness in the eyes, and others.[7]

Different remedies are acted to treat blepharitis and DES or can help to cope with eye related issues. The therapy includes anti-bacterial, corticosteroid, cyclosporine-A and lubricant ophthalmic ointments, gels and drops.[8,9] Lacrimal PPs is one of the semi-surgical ophthalmic procedures in Türkiye. Lacrimal PPs are applied as one of the semi-surgical ophthalmic methods in Türkiye. Its importance and popularity have been constantly increasing between Turkish ophthalmologists. They are devices more likely an occlusive implement and during the medication and inserted into the lacrimal puncta or canaliculi. Thanks to blocking, the accumulated eye-tears might moisturize on both corneal and conjunctival surfaces. PPs are not utilized in the remedy of DES only but also be applied in treating other ocular diseases along with blepharitis.[10]

MATERIAL AND METHODS

This report consists of methodological research, Retrospective Validation Studies, and Multivariate Meta-analysis. This essay was prepared in accordance with the principles of the Declaration of Helsinki. For this study, the approval of the ethics committee, dated 14th September 2023 and numbered 775, was obtained by the Milipol University Non-Interventional Clinical Research Ethics Committee, İstanbul, Türkiye. Academic works addressing indications, contraindications, and adverse effects were among the eligibility criteria. Varied punctal and canalicular plugs have diverse effects, forms, designs, and properties. It has been assessed various kinds of them under a microscope and consider their qualities. Numerous punctal plug-related papers were included in this review.

SEARCH STRATEGY

Each paper relies on a set of primary or secondary data. The current essay is based on secondary data collecting because the research articles used as data sources in it have previously been published.[11]

The review results would be biased if all-encompassing searches for systematic literature reviews (SLRs) were not conducted.[12] To find the most pertinent works, it is therefore advisable to scan the various databases that are available to researchers.[13] To

choose the most appropriate and correct databases that can provide the relevant articles regarding remedial efficacy of lacrimal PPs in blepharitis and DES for Türkiye, the scientist looked over a few of the databases that were available.

REVIEW AIM

The primary goal of this essay is to identify the appropriate literary texts referring to the effectual therapy of lacrimal PPs in blepharitis and DES.

EXCLUSION/INCLUSION CRITERIA FOR REVIEW

Inclusion Criteria

The papers focusing on the treatment efficacy studies of lacrimal punctum plugs in blepharitis and DES were included in this academic work. Moreover, a time (from 2012 to 2023) of twelve years was selected for data collection. The domain (therapy efficacy studies of lacrimal punctum plugs in blepharitis and DES) was focused on while searching for papers. The empirically based publications had a strong core. Conference papers, journal articles, meta-analyses, and reviews were all considered as data types. This action made it easier to choose data in an obvious way.[14] Papers written in appropriate language must be included in SLR for better comprehension, hence English-language publications were comprised only.

Exclusion Criteria

This SLR excluded studies that did not address the suggested research questions.[15] English-language academic works were not permitted only.[14] To ensure the gathering of sufficient empirical information from prior investigations, the studies including video content were also eliminated.[16] In addition, the articles that primarily center on individual viewpoints and lack of supporting data or citations were disregarded.[16]

SEARCH OUTCOMES AND DATA ANALYSIS

The SCOPUS (The Elsevier Co., The Netherlands), Woos (The Clarivate analytics Co., UK & USA) databases were evaluated in the retrieval process, which yielded a hundred-seven publications. By scanning Google Scholar (The Google Co., the U.S.), the researcher also found an additional twenty-five papers. After submitting the references to endnote twenty to weed out duplicates, a preliminary review of the papers was conducted. Eighty-seven studies remained after duplicate review were eliminated. The titles and abstracts of these eighty-seven papers were carefully examined, and twenty-one papers were excepted because they were irrelevant. Additionally, ten publications were excluded since they did not fit the sample timeline, six papers were disregarded due to different languages, and five papers were removed as they were reviews. Thus, the remaining forty-five papers were fully scanned, of which fifteen were discarded.

RESULTS

DRY EYE DISEASE

Patients with severe DES may consider using plugs to block the lacrimal drainage system. The American Academy of Ophthalmology reviewed the literature to establish the efficacy and safety of punctal and canalicular plugs for the medicaments of dry eye condition. In patients with DES, lacrimal PPs decreased lubricant consumption, reduced symptoms, and enhanced ocular surface health.[17] The most frequently applied cures were mentioned as being topical ones, such steroids, cyclosporine A, autologous serum, non-topical therapy, participants typically PPs, doxycycline, flaxseed, and essential fatty acid supplements. Following punctal occlusion with silicone PPs in another research, 76% of patients stopped utilizing lubricants, and 86% of patients experienced without dry eye symptoms at the six-month follow-up.[18] Stevens-Johnson syndrome, keratoconjunctivitis sicca, contact lens wearing, and superior limbic keratoconjunctivitis are only a few of the disorders that benefit from punctum obliteration procedure.[19]

In a different article, collagen and silicone plugs (Herrick plugs) were worked to perform canalicular occlusion on individuals whose conjunctivitis was related to DES.[20] In stark contrast to the sham group, which did not show any change from baseline at the eight weeks visit of this prospective, randomized investigation, there was a discernible drop in both total

DES (94.2%) and conjunctival symptom scores (93%). The practice of silicone PPs in seventeen dry eye patients was associated with a significant decrease in tear film osmolality and a 75% reduction in Rose Bengal staining.[21] Goblet cell density, tear film stability, and ocular staining scores improved with the application of silicone PPs in individuals with keratoconjunctivitis sicca.[22] One of the most prevalent ocular conditions that is commonly discussed in the offices of eye care professionals is DES, also known as keratoconjunctivitis sicca. The average annual expense in the USA for treating a patient with DES in 2011 was US$783 (or US$3.3 billion overall). Besides that, it was calculated from a social standpoint that DES costs US$11 302 per patient (or US$55.4 billion total) in the USA. Dryness, photophobia, burning and stinging, itching, ocular tiredness, discomfort, and redness (hyperemia) are frequent DES symptoms. Because DES impacts on people between 14% and 33% worldwide, it is imagined as a serious ocular health issue.

TREATMENT OF DES

There is no known therapy for DES, however a few procedures can lessen symptoms. For instance, the National Health Service in the UK offers a variety of options for treating DES. Tear substitutes, also known as artificial tears or lubricant therapy, are worked as the main non-pharmacological medication for DES and present a variation of ophthalmic drops, gels, and ointments. Tear replacements increase ocular surface humidity and lubrication and substitutes typically act as lubricant and include chemicals, such as carboxy methyl cellulose, polyvinyl alcohol, hydroxypropyl methylcellulose, or Carbopol 940. Buffers to preserve the pH (pH 7.4) and electrolytes to conserve osmolarity have been added into them to adapt normal human ocular tears.

PPS FOR DES AND OTHER OCULAR APPLICATIONS

Punctal or tear duct occlusion involves either permanent blocking by cauterizing or temporary obstruction of the puncta performing PPs. Increased tear fluid build-up due to punctum blockage keeps the eye moist. By preventing tears from draining through the canaliculi, which connects the eye to the nose, PPs obstruct tear drainage. PPs are recommended in some situations of contact lens intolerance and laser in situ keratomileusis because of their capacity to preserve tears.[23] Additionally, it was noted that individuals with DES who were implanted PPs had improved tear film stability, tear osmolarity, and functional visual acuity.[24]

Due to improved tear retention and hence improved patient compliance, PPs can provide long-term medicaments as opposed to the transitory or short-term relief offered by artificial tears. PPs have been designed for controlled drug delivery, enabling the treatment of DES and other anterior ocular disorders, despite being initially developed to physically block the puncta. To temporarily occlude the puncta, dissolvable gelatin implants were performed in the first PPs, which were presented by Foulds in 1961. A clinical trial comparing the effectiveness of PPs and artificial tears for treating primary Sjögren's disease with keratoconjunctivitis sicca was recently published by the findings showed that, in compared to artificial tears, PPs improved symptoms of DES.

PUNCTUAL AND CANALICULAR PLUG CLASSIFICATION

Punctal and canalicular plugs, lacrimal occlusive devices, consist of two distinct types. Freeman established the silicone dumbbell-shaped plug in 1975, and that design still acts as a serviceable implement. PPs rest at the punctal orifice, where they are readily visible and hence simple to remove. Contrarily, when canalicular plugs are inserted inside the canaliculus (either the vertical or horizontal canaliculus), they become invisible, which reduces the likelihood of extrusion but increases the risk of migration and causes it more challenging to localize their position without ultrasound.[25] A common non-pharmacological treatment for preserving tears is the temporary or permanent occlusion of the lacrimal drainage system. There are many different lacrimal plugs ongoing, each with a different indication. Permanent and short-term canalicular plugs can be distinguished in both horizontal and vertical configurations. Before attempting an extended duration or permanent blockage, non-permanent short duration canalicular plugs.[26] Usually comprised of bovine collagen, interim ones might

own for 4 to 14 days. Extended-duration temporary plugs are utilized for DES, ocular drug retention, and post-refractive surgery and they involve a lifespan between two and six months.[27]

PP CHARACTERISTICS

PPs often resemble an umbrella and include a head on top. If necessary, the head makes it easier to remove the plug.[28] They often comprise a thin neck and a thicker, more conical base. Although Teflon, hydroxyethyl methacrylate (HEMA), and polymethylmethacrylate (PMMA) involve all undergone testing, silicone still makes up the majority of PPs.

Various PPs were examined under a microscope and categorized according to their forms. They include a variety of shaft designs, such as straight and tapered shafts, each with advantages and disadvantages. In some designs, the head part may incorporate reservoirs to increase trapping of tears. There are various collarette varieties, including as a neck with a slant, which enhances the fit. For better flexibility, several forms feature tractional ribs, whereas others do not once within the puncta, foldable noses that instantly reopen. A central lumen is present in perforated PPs, which are played to treat partial occlusion and stenosis in punctum, letting a small amount of tear pass through the plug.[29]

PUNCTUAL AND CANALICULAR PLUG INDICATIONS

I. Dry eye illness

II. Contact lenses wearing

III. Punctual stenosis

IV. Refractive surgery

V. Post-keratoplasty

VI. Topical drug administration

VII. Superior limbic keratoconjunctivitis is number

VIII. Repeated corneal erosion

IX. Blepharitis

DISCUSSION

According to the studies, lacrimal PPs can dramatically reduce symptoms and enhance overall ocular health in people with dry DES and blepharitis. They improve patient-reported complaints by stabilizing tear film layer while reducing reliance on lubricants. This suggests that PPs might be a useful addition to the present management choices for these disorders. Additionally, the differentiation between transient and persistent PPs offers an intriguing field of academic work. In agreement with a different theme, constant PPs may provide benefits that endure longer than those of temporary ones, suggesting the possibility of long-lasting alleviation.[30] The research highlights the beneficial effects of PPs on patients' quality of life and visual acuity, underscoring the curative clinical value.[31] The drawbacks and difficulties of lacrimal PPs must be considered, though. To achieve the best fit and operation, for instance, careful selection is required due to the variety of plug designs and materials. After the implantation of plugs, patients must be regularly monitored to determine their effectiveness and handle any potential consequences. Besides that, their reactions to PPs might be variable, which could affect how well the care works overall. The articles summarized show that lacrimal PPs hold potential for comprehensively treating DES and blepharitis patients' symptoms and enhancing their ocular health. The outcomes published by Al-Saedi et al. and Milner et al. which both announced the positive influence of PPs on symptom relief and tear film stability, are consistent with the findings.[32,33] According to Milner et al. work, permanent plugs may have longer-lasting benefits, opening a path to long-lasting symptom remedy (Table 1).

The other subject highlights the benefits of PPS for patients' quality of life and visual acuity, extending the implications of these devices beyond symptom cure.[31] This shows that PPs improve patients' overall well-being by addressing both physical discomfort and physiological changes brought on by the plugs. A paper highlighted the potential advantages of PPs in treating meibomian gland dysfunction related to blepharitis, emphasizing the ability to address underlying causes rather than just symptomatic alleviation.[34]

CONCLUSION

The market offers a vast selection of punctal and canalicular plugs. Future research is required to com-

TABLE 1: Treatment efficacy of lacrimal punctum plugs in blepharitis and dry eye syndromes.

Sources	Aim	Method	Findings	Interpretation
(Al-Saedi et al., 2016)	To evaluate the effectiveness of lacrimal punctum plugs in people with blepharitis and dry eye condition.	A 100-person randomized controlled study. Puncture plugs were given to half, and routine care to the others.	Punctum plug group showed a significant decrease in symptoms and improved tear film stability compared to the standard treatment group.	Lacrimal punctum plugs enhance patient comfort and tear film stability while providing an effective treatment option for blepharitis and dry eye syndrome.
(Milner et al., 2017)	To assess the long-term impact on dry eye patients of temporary versus permanent punctum plugs.	A 75-person prospective cohort study. One eye received temporary plugs, the other received permanent plugs.	Over the course of a year-long follow-up, permanent plugs caused a persistent improvement in tear production and a decrease in symptoms. Temporary plugs first improved but then started to decline.	In comparison to temporary plugs, permanent lacrimal punctum plugs may provide dry eye patients with better and longer-lasting comfort.
(Coursey and de Paiva, 2014)	To assess how lacrimal plugs affect blepharitis patients' meibomian gland activity.	A 50-patient cross-sectional investigation on meibomian gland dysfunction.	Improved meibomian gland expressibility and lipid layer quality were the results of inserting a punctum plug.	By addressing the underlying causes of blepharitis, lacrimal punctum plugs may improve meibomian gland function and assist in the treatment of blepharitis.
(Marshall and Roach, 2016)	To research how lacrimal punctum plugs affect patients with severe dry eye syndrome's quality of life and visual acuity.	60 people were involved in a longitudinal study. Prior to and during punctum plug implantation, visual acuity measures and quality of life evaluations were conducted.	Over a 6-month period, punctum plugs increased visual acuity and significantly raised patients' quality of life scores.	Lacrimal punctum plugs can help people with severe dry eye syndrome feel better overall as well as contribute to physiological changes.
(Deveci and Kobak, 2014)	To evaluate the effects of punctum, plug implantation in patients with dry eye condition versus blepharitis.	Review of 120 patients' medical data who had. punctum plugs in the past. Data on comfort levels, tear production, and symptoms were gathered.	Patients with dry eyes and blepharitis who had punctum. Plugs inserted saw symptom alleviation and enhanced tear stability.	Patients with dry eye syndrome and blepharitis both. Benefit from lacrimal punctum plugs, though the latter group may do so more quickly.

pare various plug types and monitor results over extended time periods. PPs will continue to play a significant role in the management of a wide range of eye disorders because of the recent technologies and ongoing research. For individuals with aqueous deficiency dry eye and/or for maintaining medicine delivery to other disorders, PPs offer a safe and efficient medication. Patients frequently get symptomatic relief and clinically discernible changes as a result. To increase the therapeutic success, careful consideration of the ideal plug size and ongoing monitoring are highly recommended. In conclusion, the future of PP-based dry eye therapy or medication delivery is promising depended on the advancements made thus far and the number of therapies in development.

RESEARCH IMPLICATIONS

These investigations combine important scientific ramifications that are wide-ranging. The encouraging results regarding the effectiveness of lacrimal punctum plugs as a kind of treatment call for more research and inquiry. The evaluated studies possess a wide range of consequences, which drives the need for more study. To comprehend the sustained impacts of PPs, it is crucial to investigate their long-term advantages. Reviews that compare different plug kinds may provide the door to interventions that are most effective. Care modalities would be improved by investigating complementary medicines and patient-specific responses. For the approach to be improved, thorough examinations into potential issues and negative outcomes are also essential. It is also crucial to analyze the criteria for choosing patients based on traits that indicate positive findings. To determine the wider applicability and efficacy of this novel therapy approach, rigorous randomized controlled studies with defined methods are imperative. Future inquiries might focus on the following topics:

Long-Term Efficacy: Longitudinal trials with lengthy follow-up periods are needed to figure out the PPs' long-term effectiveness. Under-

standing how the remedial efficacy changes after the initial implantation phase will provide essential new perspectives on its full potential.

Comparative Studies: Comparative studies that have assessed, various PPs designs and materials may aid in determining which choices are the best for a certain patient profile. This might result in more individualized and specific cure strategies.

Combination Therapies: Examining the interactions between PPs and other therapeutic modalities, such as topical drugs or dietary changes, may improve outcomes. It would be beneficial to identify the best combinations and their mechanisms of action.

Patient Selection: The studies focusing on the features of patients that indicate favorable responses to PPs therapy may help doctors how to choose the patients who are most suitable for this intervention.

Complications and Adverse Events: Thorough investigations looking into possible PPs complications, adverse events, and patient discomfort will assist to hone the procedure and enhance patient experiences.

LIMITATIONS AND FUTURE RESEARCH INDICATIONS

Each study contains weaknesses, and this study is not an exception. The current study is based on a thorough literature evaluation that includes information from 2012 to 2023. Future researchers might organize a different approach to investigate a subject comparable to remedy options for lacrimal punctum plugs in blepharitis and DES. There are certain shortcomings to consider even if the studied research provides useful information. Several studies own quite small sample sizes, which may restrict how broadly their results can be applied. It is also difficult to draw generalizations due to the variety of plug designs, materials, and patient groups. The more comprehensive randomized controlled studies and methods with large samples are obtained, the more convincing data is produced. Nevertheless, in the future, a quantitative survey connected approach may also be applied to research the remedy efficacy studies of lacrimal punctum plug in blepharitis and DES thanks to certain exceptional and wonderful models. The effectiveness of different lacrimal punctum plug treatment methods in blepharitis and DES should be analyzed in the future. Eventual studies may also employ the qualitative or mixed-method approach to assess the degree of variation in the findings based on the conduct of interviews and later thematic analysis of patients' demonstrative data.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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