Journal of Medical and Biomedical Discoveries

Nejat F, et al. J Med Biomed Discoveries 6: 127.

www.doi.org/10.29011/2688-8718.100027

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Research Article

# Innovative Solutions for Swift Enhancement: A Case Series on Filamentary keratitis treatment with Plasma Occlusion of Puncta

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**Citation:** Nejat F, Egdtedari S (2024) Innovative Solutions for Swift Enhancement: A Case Series on Filamentary keratitis treatment with Plasma Occlusion of Puncta. J Med Biomed Discoveries 6: 127. DOI: https://doi.org/10.29011/2688-8718.100127

**Received Date:** 20 May, 2024; **Accepted Date:** 29 May, 2024; **Published Date:** 11 June, 2024

## Abstract

**Purpose:** This study aimed to evaluate the effectiveness of plasma occlusion of punctum (POP) in treating filamentary keratitis (FK) secondary to severe dry eye disease (DED). **Methods:** This study included five patients diagnosed with FK secondary to severe DED, concurrent with immunologic disorders. Patients received three POP sessions at one-week intervals. The POP procedure involved applying one or two plasma spots on the punctum using the PLEXR PLUS device, leading to punctum stricture for about six months. Visual and dry eye parameters, including best corrected visual acuity (BCVA), tear meniscus height (TMH), tear break-up time (TBUT), corneal fluorescein staining (CFS), intraocular pressure, and the Ocular Surface Disease Index (OSDI), were measured before treatment, one week after the first session, and six months after the third session, and also slit-lamp examinations were conducted to assess FK signs and possible complications. **Results:** BCVA improved by two lines in two patients and by one line in another. The OSDI score showed a significant improvement, increasing by 65.26% over six months. The DED grade improved in all patients. TMH and TBUT showed significant increases, and CFS grades decreased, indicating enhanced tear film stability and ocular surface health. All patients showed significant improvement in FK symptoms, with four achieving complete healing after one session and one patient after two sessions. **Conclusion:** POP seems to be an effective treatment for FK associated with severe DED, providing swift improvements in tear film stability, and FK management.

**Keywords:** Punctal occlusion; Atmospheric low-temperature plasma; Filamentary keratitis; Immunologic disorders; Dry eye disease

## Introduction

Filamentary keratitis (FK) is introduced when filaments of epithelial, mucus, and cellular debris appear on the cornea secondary to aqueous deficient dry eye disease [1]. This ocular disorder is prevalent in females and elderly individuals [2]. In addition to dry eye disease, FK is associated with numerous conditions, including immunologic diseases, allergic conjunctivitis, recurrent epithelial erosion, chronic blepharospasm, ocular surgery, trauma, chemical injury, viral keratitis, and specific systemic medications such as diphenhydramine [3, 4]. Accurate treatment of FK is often ambiguous because the underlying condition must be cured first to avoid frequent recurrence in chronic filamentary keratitis [5]. Preservative-free Lubricant eye drops and gels, levofloxacin, autologous serum tears, corticosteroids, punctal occlusion, botulinum toxin injection, 10% N-acetylcysteine ophthalmic solution, 0.3% acetylcysteine, and cryopreserved amniotic membrane (CAM) are existing treatment modalities, but their efficacy remains controversial [5,6].

These filaments commonly manifest when individuals suffer from dry eye disease (DED) alongside conditions such as brain lesions, autoimmune diseases, and graft-versus-host disease, often due to the aggravating blink reflex, Additionally, given the promising

results of punctal occlusion with plasma in previous research for managing dry eye disease yielding swift improvement after a single session and long-term relief following three consecutive sessions, effectively treating DED with punctum stricture, the notion of its efficacy has inspired the present study[7-9]. This study aims to assess the efficacy of plasma occlusion of punctum (POP) as a prompt solution for filamentary keratitis (FK) in patients suffering from severe dry eye disease intensified by immunologic diseases, multiple ocular surgeries and traumas, and rheumatoid arthritis.

## Materials and Methods

### Study Protocol

This study has been approved by the ethics committee of Semnan Medical University of Science, Semnan, Iran. All participants signed the informed consent form after receiving a thorough explanation of the study conditions, possible side effects, and complications. All patients visited the Vision Health Clinic in Tehran between late 2023 and early 2024.

### Patient Selection

All participants diagnosed with filamentary keratitis secondary to DED by an expert ophthalmologist (F.N.). The grades of DED of our patients are based on the Oxford system (Figure 1), which is standardized with corneal and conjunctival staining [10]. All patients experiencing severe discomfort sensations were included in our study for plasma occlusion of punctum (POP).

Case 1 is a 61-year-old woman with a history of bone marrow transplantation and secondary Graft-Versus-Host Disease. She presented to the Vision Health Clinic with complaints of symptoms such as severe foreign body sensation, photophobia, and pain. She was diagnosed with severe DED in both eyes and FK in the left eye.

Case 2 is a 56-year-old woman referred to our clinic with rheumatoid arthritis, diagnosed with chronic FK in her right eye and severe dry eye, experiencing symptoms such as itching and foreign body sensation.

Case 3 is a 49-year-old man with a history of multiple intraocular surgeries after trauma included in our study, presenting with advanced dry eye disease and chronic FK in his left eye. He complains of intense foreign body sensation, photophobia, burning, tearing, redness, and irritation.

Case 4 is a 74-year-old woman with a history of multiple intraocular surgeries along with a medication regimen exacerbating dry eye disease. Severe dry eye caused FK in her right eye.

Case 5 is a 34-year-old woman with a history of recent chemotherapy and radiotherapy for breast cancer. She was diagnosed with severe dry eye accompanied by severe photophobia and discomfort in both eyes. FK was recognized in her right eye.

### POP Procedure

After local anesthesia using tetracaine eye drops 0.5% (Sina Daro, Tehran, Iran) applied 3 times at 5-minute intervals for the targeted eye, the patients were seated behind the slit lamp in a complete office-based manner. The surgeon applied one or two spots of plasma (depending on the need for occlusion with an instant slit-lamp check) on the punctum using the white handpiece of PLEXR PLUS (GMV, srl, Rome, Italy), which generates plasma by ionizing the air between the tip of the device's needle and the targeted tissue (Table 1). This occlusion remains for 2 to 5 days after the procedure, offering a critical time for healing filamentary keratopathy. However, these patients were diagnosed with severe and advanced DED, making it necessary to complete their DED treatment. The treatment plan included 3 sessions of punctal occlusion with plasma at 1-week intervals, resulting in punctum stricture for about 6 months. This stricture may help retain both natural tears and the artificial tears used by the patients on the ocular surface for a longer period. Non-preservative artificial tears and lubricant eye gel were continued alongside the POP procedure during the 6-month follow-up period.

### Measured Parameters

Visual parameters such as Best corrected visual acuity (BCVA), dry eye tests including tear meniscus height (TMH), tear break-up time (TBUT) using an ocular surface portable analyzer (OSA-VET, SBM Sistemi, Torino, Italy), and corneal fluorescein staining (CFS) using a photo slit-lamp (SL9900 ELITE 5X-D, CSO, Firenze, Italy) with an acquisition system (Phoenix, v.3.6), as well as the Ocular Surface Disease Index (OSDI)—a standard questionnaire containing 3 parts: OSDI-symptoms (ocular discomfort), OSDI-function (limitation of daily performance), and OSDI-triggers (environmental triggers), with 4 questions in each part, and a final score ranging from 0 to 100 (100 indicating the most severe dry eye disease and 0 indicating minimal signs and symptoms of dry eye disease)—and intraocular pressure (IOP) measured by a Topcon CT-80 non-contact tonometer (NCT) have been measured before, 1 week after one session of the POP procedure, and 6 months after the POP procedure with 3 sessions in a row. Table 1 shows the Oxford grading protocols used for this study and the DED grading of our patients based on CFS parameter. Slit-lamp examinations by an expert ophthalmologist were conducted at each visit to check for any possible side effects or complications of the POP procedure.

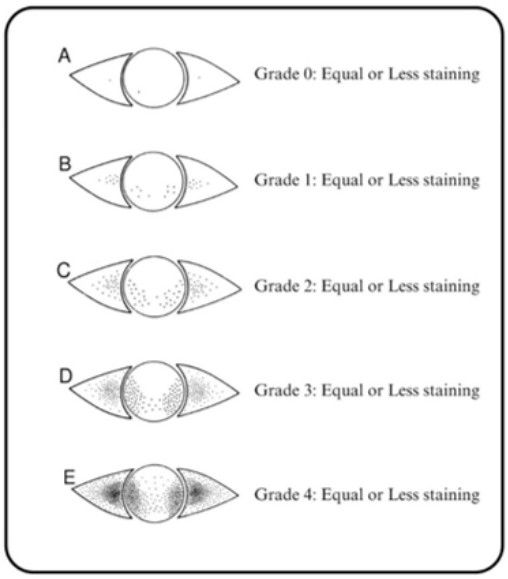


**Figure 1:** Oxford grading scheme of dry eye disease regarded corneal Fluorescein Staining of the total exposed inter-palpebral conjunctiva and cornea.

| | |
|---|---|
| **The device operates using air as the working gas.** | |
| White handpiece | Peak to peak voltage of 500 V |
| | Power of 0.7 W |
| | Frequency of 75 kHz. |
| Green handpiece | Peak to peak voltage of 600 V |
| | Power of 1 W |
| | Frequency of 75 kHz |
| Red handpiece | Peak to peak voltage of 700 V |
| | Power of 2 W |
| | Frequency of 75 kHz |
| **It is powered by a docking station with a voltage of 24 V.** | |
| Handpieces | The maximum power output of the devices are 2 W. |
| | The maximum working voltage is 1.3 kVPP. |
| It employs a sterile disposable needle made of stainless steel as the applicator electrode. | |

**Table 1:** PLEXR PLUS information

## Results

The Best corrected visual acuity (BCVA) improved by two lines in two cases and by one line in one case. In the two patients who had hand motion (HM) and no light perception (NLP), the BCVA remained unchanged. We hypothesized that treating severe dry eye disease and stabilizing more tear on the ocular surface could be the reason for these BCVA improvements. The intraocular pressure (IOP) did not show any significant change. The ocular surface disease index (OSDI) increased dramatically by 65.26% in the 6-month follow-up after 3 sessions of POP. One of our patients was at grade 4 of dry eye, which decreased to grade 2 after completing the treatment protocol. Four cases were at grade 3; two of them decreased to grade 0 (normal), and two of them decreased to grade 1 (Table 2).

The slit-lamp examination showed a significant improvement in FK signs and symptoms in all cases. Even though case three had a few filaments remaining on his ocular surface one week after the POP treatment, it is noteworthy that this FK healed after three consecutive treatment sessions. Given that this eye had chronic multiple filaments before the procedure and they became fewer after one session, this is also considered a success (figure 2).

The average difference in tear meniscus height (TMH) was 0.0675 mm one week after the first session and 0.135 mm six months after the third session. The average difference in tear break-up time (TBUT) was 5.3 seconds one week after the first session and 6.70 seconds, six months after the third session. For corneal fluorescein staining (CFS), there was a decrease of 1 grade one week after the first session in all patients and a decrease of 2 grades six months after the third session for three patients, and a decrease of 3 grades in two patients (Figure 3).

Surprisingly, four patients' FK was completely healed with only one session of POP therapy. Nevertheless, case 3 had multiple discrete filaments and required two sessions of POP to be completely healed. It is noteworthy that POP has a three-session protocol, and the surgeon performed punctal occlusion with plasma in three consecutive sessions to count as a treatment for severe dry eye disease. This protocol was followed for every single participant, despite the FK healing after one session.

| Demographic Characteristics | UCVA | | | IOP | | | OSDI | | | Grade of DED | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Before | After-1 | After-2 | Before | After-1 | After-2 | Before | After-1 | After-2 | Before | After-1 | After-2 |
| **Case 1-OS 61-year-old woman** | 2/10- | 04-Oct | 04-Oct | 10 | 10 | 11 | 84.5 | 46.1 | 32.1 | 3 | 2 | 1 |
| **Case 2-OD 56-year-old woman** | 08-Oct | 09-Oct | 09-Oct | 14 | 15 | 12 | 79.6 | 26.2 | 16.7 | 3 | 2 | 0 |
| **Case 3-OS 49-year-old man** | HM | HM | HM | 17 | 15 | 15 | 81.5 | 59.3 | 25.8 | 4 | 3 | 2 |
| **Case 4-OD 74-year-old woman** | NLP | NLP | NLP | 15 | 16 | 12 | 68.9 | 59.2 | 11.9 | 3 | 2 | 0 |
| **Case 5-OD 35-year-old woman** | 06-Oct | 07-Oct | 08-Oct | 15 | 13 | 13 | 77.3 | 56.2 | 49.2 | 3 | 2 | 1 |
| *Note: HM-Hand Motion, NLP: No Light Perception, Grade 0=Normal, Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Advanced DED, After-1: 1 week after 1 session of POP, After-2: 6 months after three sessions of POP | | | | | | | | | | | | |

**Table 2:** Patient's characteristics and measured parameters.

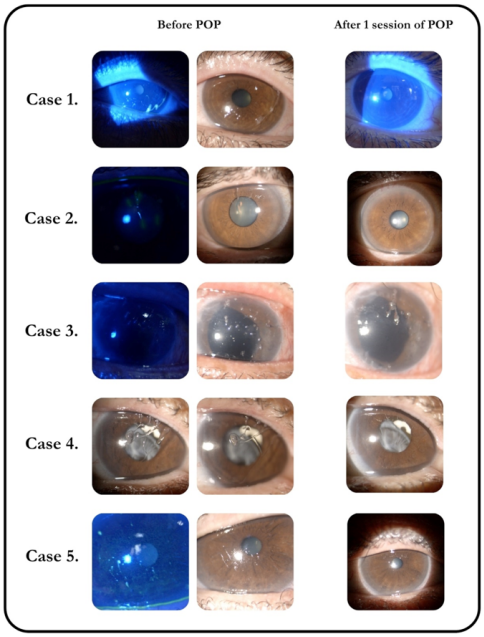


**Figure 2:** Photo slit-lamp images of five patients, before and after one session of POP procedure

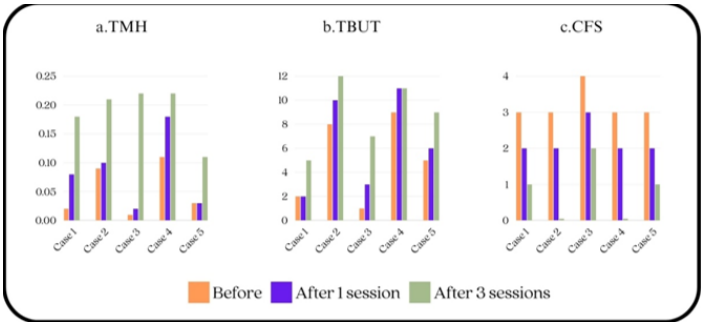


**Figure 3:** Dry eye parameters for five cases, before, 1week after first session of POP and 6 months after third session of POP, a.Tear Meniscus Height (TMH), b.Tear Break-up Time (TBUT), c. Corneal Fluorescein Staining (CFS) with grading of: No staining-Normal (Grade 0), Mild staining: Mild dry eye disease (Grade 1), Moderate staining: Moderate dry eye disease (Grade 2), Severe staining: Severe dry eye disease (Grade 4) [11-14].

## Discussion

Filamentary keratitis (FK) appears as 0.5 to 10 mm filaments on the cornea once the eye enters a cycle of tear instability, epithelial damage, and receptor site formation for mucin adhesion. Symptoms include foreign body sensation, severe pain, ocular discomfort, and photophobia, which vary from person to person [15-17]. Specific ocular and systemic conditions are known risk factors for FK, including immunologic disorders, dry eye disease (DED), ocular surgeries like cataract and strabismus and special medications [1]. Botulinum toxin injection, autologous serum tears, topical hypertonic saline, and corticosteroids are options for refractory dry eye disease [16, 18-20].

Ya-chi Huang et al. indicated in their published article in 2020 that the combined treatment of lubricants and steroids has a 79.4% remission rate for FK healing [2]. Cryopreserved amniotic membrane (CAM) was evaluated in a published article in 2018 involving 84 DED patients, 13% of whom had FK. The authors reported a significant healing rate of 88% [21].

Since 2019, a novel treatment modality named PANIS has been safely evaluated in animal studies. Atmospheric low-temperature plasma was applied to rabbit conjunctiva, and histopathological assessments revealed no persistent or deep effects of plasma on the eye at 1-month and 6-month follow-ups. [22, 23]. The concentration of seven different cytokines in tear and serum samples of rats exposed to plasma on the conjunctiva was measured. The results of flow cytometry indicated no persistent increase in the levels of the candidate cytokines [24]. These safety evaluations confirmed the initiation of human trials to use plasma technology for treating ocular surface diseases such as conjunctival cyst, conjunctivochalasis, pinguecula, pseudophakic bullous keratopathy, conjunctival concretion, pterygium, dry eye disease, and conjunctival nevus. A published case series about the PANIS modality (plasma-assisted noninvasive surgery) with an average follow-up of 6 months proved the safety and efficacy of this novel technique for treating common ocular surface diseases [7,25-32].

It is proven that FK generation depends on interactions between the stroma and tear film with various predisposing factors. Thus, Nejat et al.'s theory supports tear film stability with plasma occlusion of the punctum (POP). FK treatment can be challenging, but POP offers an office-based and effective adjunctive treatment to eye lubricant drugs for dry eye disease, which is a comorbidity of these corneal filaments. This new approach does not require the use of any contact lenses after the procedure. The FK progression mechanism is a robust debate in ophthalmic societies; however, our patients have drastically improved with POP, suggesting that this study can introduce an effective treatment for FK comorbid with refractory dry eye.

## Conclusion

It seems that POP can be an effective treatment for the swift enhancement of filamentary keratitis, regardless of its cause and risk factors. POP introduces a new approach for inducing punctum stricture for six months to stabilize the tear film, treat severe dry eye disease, and address possible filaments on the cornea.

**Author Contributions:** F.N. Conceptualization and methodology and supervision and finding acquisition, Sh.E. Data curation and writing (original draft and editing) and visualization and project administration. All authors have read and agreed to the published version of the manuscript.

**Funding**: No funding to declare.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Acknowledgments:** No one to declare.

**Conflicts of Interest:** The authors declare no conflict of interest.

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