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Effectiveness and safety of a novel crosslinked hyaluronate canalicular gel occlusive device for dry eye

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Purpose: To evaluate the effectiveness and safety of a crosslinked hyaluronate (HA) canalicular filler (Lacrifill Canalicular Gel) compared with a commercially available hydrogel canalicular plug (Form Fit).

Setting: 5 sites in the United States.

Design: Prospective, multicenter, controlled, double-masked, randomized 2:1 (filler:plug).

Methods: Adults (≥22 years) with the Schirmer test (with anesthesia) ≤10 mm/5 minutes, presence of corneal staining, ocular surface disease index (OSDI) of ≥23 with ≤3 responses of "not applicable," patent lacrimal drainage system, and bilateral corrected distance visual acuity of 20/40 or better. Filler or plugs were instilled bilaterally in the inferior canaliculi. Primary effectiveness endpoint was noninferiority of the mean within subject change from baseline to month 3 in Schirmer score for patients receiving filler compared with plugs. The key secondary effectiveness endpoint was noninferiority of the proportion of patients with filler achieving improvement from baseline to month 3 in OSDI by a minimal clinically important difference. Additional endpoints included the mean change from baseline to 3 and 6 months in tear meniscus height, OSDI, corneal staining, tear breakup time, and safety.

Results: 157 patients were randomized; 99 patients with crosslinked HA filler and 52 patients with hydrogel plugs completed the study. Filler was noninferior to plugs in the mean Schirmer score change from baseline and in the proportion of patients achieving a clinically important improvement in OSDI.

Conclusions: Crosslinked HA filler is a safe, well-tolerated, and effective method to treat dry eye. Clinically and statistically significant improvements in signs and symptoms of dry eye were sustained through 6 months.

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Dry eye is characterized by a deficiency in the quantity and/or quality of tears or increased tear evaporation, tear film instability, ocular surface damage, ocular irritation, ocular inflammation, dryness, fatigue, and visual fluctuations.[1,2] In the general population, the prevalence of dry eye increases in contact lens wearers, older than 50 years, post menopause, with exposure to extreme environments (reduced humidity, increased wind, drafts, air conditioning, or heating), with use of certain systemic medications and glaucoma medications, and after cataract or refractive surgery.[1,3] The American Academy of Ophthalmology (AAO) Preferred Practice Patterns say that it is "imperative to treat any causative factors that are amenable to treatment."[1,2]

It is well known that dry eye disease (DED) can alter the results of cataract and refractive surgery.[4] The visual consequences of untreated dry eye before ocular surgery include inaccurate biometry, keratometry, and IOL type and power choice; increased higher-order aberrations; and worsening of preexisting dry eye, which result in patient dissatisfaction. The ASCRS Cornea Clinical Committee published a consensus-based practical diagnostic ocular surface disease algorithm recommending that DED and ocular surface disease be identified and treated preoperatively regardless of symptoms.[4]

Although the signs and symptoms of dry eye are not always sight-threatening, all severities of dry eye adversely affect quality of life, and dry eye becomes more burdensome

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as severity increases.[5–7] Dry eye is a chronic disease that can be psychologically debilitating. Thus, dry eye should be considered a serious disease worth treating.[6,7] The first step for managing DED is modifying the local environment and using topical aqueous enhancements (artificial tears, emulsions, gels, and ointments).[1,8] The limitations of these include the burden of frequent instillation, transient symptomatic relief, preservatives, cost, and that poor dexterity can cause insufficient instillation.[1,9] If aqueous enhancements are inadequate, topical or systemic prescription pharmaceutical approaches may be implemented. However, these too are limited by instillation burdens, significant and recurring costs, and added concern that topical steroids may increase intraocular pressure (IOP) and cause cataract formation and glaucoma.[1,10]

AAO and members of the Tear Film and Ocular Surface Society Dry Eye Workshop II recommend tear conservation through lacrimal occlusion as a second-line treatment option for managing dry eye.[1,8] Lacrimal occlusive devices improve dry eye by reducing tear outflow resulting in increased ocular surface moisture and are convenient for the patient. The plugs can be placed in the puncta or canaliculi and can be temporary (with a short or extended duration) or permanent. Punctal and canalicular plugs are available in a variety of shapes, designs, and materials, each with the objective to increase effectiveness and decrease adverse events (AEs).[11] They are made of collagen, silicone, hydrogel, polydioxanone, and acrylic depending on whether they are absorbable or intracanalicular.[8,11] Punctal plugs rest at the punctal opening, are able to be visualized, and are usually easy to remove, but may induce a foreign body sensation. Canalicular plugs are placed inside the canaliculus and are not visible but may not fully obstruct tear drainage because the canaliculus varies in diameter between patients. Early punctal occlusion preserves the tear film and may result in therapeutic benefits day-to-day and postcorneal surgery.[12,13]

The ideal canalicular occlusion device for dry eye would fully block the lacrimal drainage system; have straightforward placement; easy removal when necessary; and be comfortable, durable, biocompatible, and safe with a low potential for infection. Hyaluronic acid (HA) is a substance produced naturally in the human body as a component of the tear film, outer cornea, and vitreous humor, and has important functions throughout the body.[14,15] At the ocular surface, HA has lubricating, anti-inflammatory, antioxidant, and antitoxic effects.[14] Accordingly, HA is a useful component in artificial tears and has a proven safety record.[14] Crosslinking-free HA molecules form a durable gel that withstands degradation unless subjected to external shear force.[15] Thus, crosslinked HA is an excellent material for an intracanalicular occlusion device.

A new chemically crosslinked, particulate HA hydrogel intracanalicular occlusion device (Lacrifill Canalicular Gel, Nordic Pharma) has been cleared by the U.S. Food and Drug Administration. It is intended to block tear drainage by occluding the canalicular system and is indicated for up to 6 months of use in patients experiencing dry eye symptoms. The gel-like material completely fills the lumen, preventing tear flow through the lacrimal drainage system. It does not require custom sizing and can be removed through irrigation of the canaliculus.

The objective of this study was to evaluate the effectiveness and safety of the crosslinked HA filler compared with a commercially available canalicular plug. When this study was conceptualized, there were several permanent canalicular plugs commercially available (Form Fit, Oasis Medical; SmartPlug, Medennium Inc.; and Herrick plug, Lacrimedics). Form Fit is a semirigid rod of polyvinyl pyrrolidone-based hydrogel material that absorbs tears and expands to occupy the canalicular space. SmartPlug is a thermosensitive acrylic material that expands in diameter and shrinks in length after insertion. Herrick intracanalicular plug is silicone and shaped like a golf tee with a collapsable bell design. We chose to compare the crosslinked HA filler with the hydrogel plug (Form Fit) because of the design similarities.

METHODS

This was a prospective, multicenter, controlled, double-masked, randomized (2:1) study conducted at 5 sites in the United States. The study protocol was reviewed and approved by an Institutional Review Board in accordance with the tenets of the Declaration of Helsinki and the International Council for Harmonisation Guideline for Good Clinical Practice. All patients provided written informed consent, and HIPAA regulations were followed. The study was registered on www.clinicaltrials.gov (NCT0481785).

Included were adults 22 years or older with the Schirmer test (with anesthesia) ≤10 mm/5 minutes, presence of corneal staining, ocular surface disease index (OSDI) of ≥23 with ≤3 responses of "not applicable," patent lacrimal drainage system, and bilateral corrected distance visual acuity (CDVA) of 20/40 or better. Key exclusion criteria were use of ophthalmic cyclosporine within 6 months or lifitegrast (Bausch & Lomb, Inc.) within 3 months before day 0 because of the potential for a confounding effect; history of surgical punctal occlusion, canalicular infection, canalicular surgery, or ocular surgery within 6 months of day 0; and any ocular or systemic disorder that would interfere with study results.

Intervention Procedure

The crosslinked HA filler was instilled bilaterally according to the manufacturer's instructions.[16] In brief, following topical anesthesia, the lower puncta was flushed with saline to confirm patency. A cannula attached to a syringe prefilled with the crosslinked HA filler was inserted into the lower punctum, and 0.2 mL crosslinked HA filler was introduced into each canaliculus. To remove the plug at 6 months, the lower canaliculus was irrigated with sterile saline until it freely flowed through the drainage system and/or the patient reported swallowing or fluid sensation in the nose/throat. The hydrogel plug was placed bilaterally in the vertical portion of the inferior canaliculus according to the manufacturer's instructions.[17]

Outcome Measures and Data Analysis

Assessments occurred at baseline and months 3 and 6. The primary effectiveness endpoint was noninferiority of the mean measurement within subject change from baseline to month 3 in the Schirmer with anesthesia score for patients receiving the crosslinked HA filler compared with the hydrogel plug (noninferiority margin of 2.5 mm). The key secondary effectiveness endpoint was the noninferiority of the proportion of patients with the crosslinked HA filler achieving improvement from baseline to

month 3 in OSDI by a minimal clinically important difference (MCID) of 4.5 points for those with moderate baseline symptoms and 7.3 points for those with severe baseline symptoms compared with patients receiving the hydrogel plug (noninferiority margin of 20%).[18] Additional secondary endpoints were the mean change from baseline to 3 and 6 months in tear meniscus height (average of 3 measurements), OSDI (scale 0 to 100), corneal fluorescein staining (sum of all regions measured through the National Eye Institute scale 0 to 15), tear breakup time (TBUT, average of 2 measurements), and anesthetized Schirmer score. Safety was assessed by monitoring AEs, CDVA, biomicroscopy, and IOP. A dye disappearance test evaluated patency on a scale of 0 to 6, where >3 = occluded and <3 = patent.[19] Investigators rated plug insertion and removal through a questionnaire.

The effectiveness endpoints were tested in a hierarchical fixed sequence of both eyes averaged together to maintain the type I error rate and adjust for multiplicity. Each secondary endpoint was tested at 1-sided alpha = 0.025. The *P*-values for secondary endpoints were not interpreted after the first sequential secondary endpoint was found not significant. Any remaining untested secondary endpoints were then considered exploratory. Continuous and categorical variables were summarized with descriptive statistics, frequencies, and percentages. Data were analyzed using SAS (v. 9.4, SAS Institute, Inc.) and included linear mixed models with repeated measures, logistic regression models, Fisher exact test, and 2-sample *t* tests; significance was $P < .05$. To allow for 80% power to reject the primary null hypothesis and a 10% dropout rate, a sample size of 162 patients (108 with the crosslinked HA filler and 54 with the hydrogel plug) was targeted for enrollment.

RESULTS

A total of 157 patients were randomized; 99 of 103 (96.1%) patients (198 eyes) with the crosslinked HA filler and 52 of 54 (96.3%) patients (104 eyes) with the hydrogel plug completed the study. Four patients in the crosslinked HA filler group discontinued (1 lost to follow-up, 1 unable to instill, and 2 noncompliance), and 2 patients in the hydrogel plug group discontinued (voluntary withdrawal). Both groups had similar demographics and baseline characteristics (Table 1). The majority of women were postmenopausal (64.7%, 101/156). Ocular medical history included meibomian gland dysfunction (19.7%, 31/157), blepharitis (8.3%, 13/157), laser in situ keratomileusis (LASIK) (16.6%, 26/157), and cataract surgery (15.9%, 25/157).

At month 3, the crosslinked HA filler group was statistically noninferior and numerically superior to the hydrogel plug group in the anesthetized Schirmer test score change from baseline with a noninferiority margin of <2.5 mm, meeting the primary endpoint (LSMean difference [2-sided 95% CI] = 1.77 [−0.63, 4.18], $P = .0003$). The Schirmer score significantly improved from baseline to month 3 and month 6 in both groups (Figure 1). The change from baseline at 3 months was 3.9 ± 7.6 mm ($P < .0001$) for the crosslinked HA filler and 1.9 ± 5.0 mm ($P = .0047$) for the hydrogel plug groups. The change from baseline at 6 months was 3.8 ± 6.7 mm ($P < .0001$) for the crosslinked HA filler and 1.8 ± 4.0 mm ($P = .0009$) for the hydrogel plug groups.

The key secondary endpoint was met, the crosslinked HA filler was noninferior to the hydrogel plug in the proportion of patients achieving improvement from baseline to month 3 in the OSDI score by an MCID (84.3% [86/102] and

Table 1. Demographics and baseline characteristics (intent-to-treat population)

Parameter	Crosslinked HA filler (N = 102)	Hydrogel plug (N = 54)	Total (N = 156)
Age (y)			
Mean (SD)	61.9 (12.42)	64.9 (9.86)	62.9 (11.66)
Range	26, 84	47, 82	26, 84
Sex, n (%)			
Male	28 (27.5)	10 (18.5)	38 (24.4)
Female	74 (72.5)	44 (81.5)	118 (75.6)
Race, n (%)			
White	79 (77.5)	46 (85.2)	125 (80.1)
Asian	9 (8.8)	4 (7.4)	13 (8.3)
Black or African American	12 (11.8)	3 (5.6)	15 (9.6)
Multiple race	0	1 (1.9)	1 (0.6)
Anesthetized Schirmer test (mm)			
Mean (SD)	5.39 (2.630)	5.47 (2.452)	—
Total OSDI (0-100: higher is worse)			
Mean (SD)	48.8 (17.49)	46.4 (14.07)	—
Moderate symptoms,[a] n (%)	17 (16.7%)	11 (20.4%)	—
Severe symptoms,[a] n (%)	85 (83.3%)	43 (79.6%)	—
Tear breakup time (s) (lower is worse)			
Mean (SD)	3.007 (1.2975)	3.000 (1.3238)	—
Tear meniscus height (mm) (higher is better)			
Mean (SD)	0.941 (1.6102)	0.866 (1.5210)	—
Total corneal fluorescein staining (1-15: higher is worse)			
Mean (SD)	5.8 (3.16)	6.0 (2.97)	—

HA = hyaluronic acid; OSDI = ocular surface disease index
Mean of both eyes together
[a]Moderate symptoms were defined as having OSDI total score of 23 to 32 points, and severe symptoms were defined as having OSDI total score of 33 to 100 points

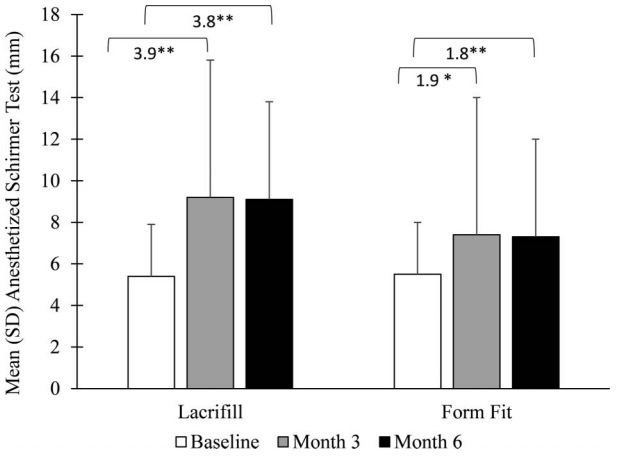

Figure 1. Mean change in Schirmer test score (mm) from baseline over time—intent-to-treat population. *P < .01, **P < .001.

83.3% [45/54], respectively, mean difference [2-sided 95% CI] = −0.009 [−0.121, 0.103], P = .0004). OSDI significantly improved from baseline to month 3 and month 6 in both groups (Figure 2). The change from baseline was 27.3 ± 20.30 (P < .0001) and 25.3 ± 16.24 (P < .0001) at month 3, and 25.3 ± 20.11 (P < .0001) and 23.9 ± 18.98 (P < .0001) at month 6 in the crosslinked HA filler and the hydrogel plug groups, respectively.

Secondary Endpoints

Neither group had a significant change from baseline in tear meniscus height; the change from baseline was 0.033 ± 0.6931 (P = .6837) and 0.002 ± 0.7681 (P = .5084) at month 3, and 0.084 ± 0.7951 (P < .8530) and 0.070 ± 0.8003 (P < .7354) at month 6 in the crosslinked HA filler and the hydrogel plug groups, respectively. Corneal staining significantly improved from baseline to month 3 and month 6 in both groups (Figure 3). The change from baseline was 2.0 ± 3.18 (P < .0001) and 2.3 ± 3.72 (P < .0001) at month 3, and 2.4 ± 3.51 (P < .0001) and 1.5 ± 3.70 (P = .0024) at month 6 in the crosslinked HA filler and the hydrogel plug groups, respectively. TBUT significantly improved

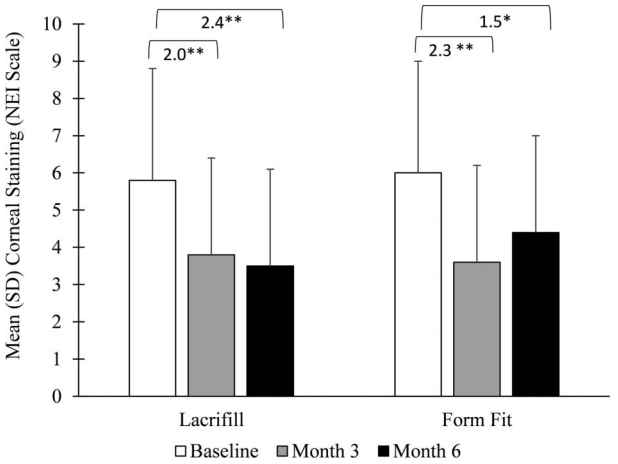

Figure 3. Mean change in total corneal fluorescein staining (NEI scale) from baseline over time—intent-to-treat population. NEI = National Eye Institute. *P < .01, **P < .001.

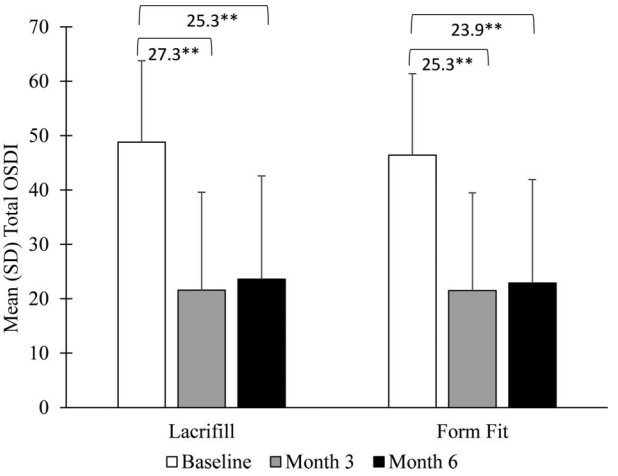

Figure 2. Mean change in total OSDI score (questions 1 to 12) from baseline over time—intent-to-treat population. OSDI = ocular surface disease index. **P < .001.

from baseline to month 3 and month 6 in both groups. The change from baseline was 0.787 ± 1.5032 seconds (P < .0001) and 0.787 ± 1.5032 seconds (P = .0063) at month 3, and 1.054 ± 1.5996 seconds (P < .0001) and 0.531 ± 1.7181 seconds (P = .0151) at month 6 in the crosslinked HA filler and the hydrogel plug groups, respectively.

Safety

Both groups had a similar rate of patients with ≥1 ocular device-related AEs (Table 2). No patient discontinued the study due to an AE. There were no ocular serious AEs. Increased corneal staining (reported as an AE) occurred in 7.8% (8/103) of the crosslinked HA filler group and 16.7% (9/54) of the hydrogel plug group. Neither group had a significant loss of CDVA, and there was no notable change in IOP. Dye disappearance mean scores increased from baseline and were maintained over the course of the study for both groups (crosslinked HA filler: 2.94 right eye and 2.91 left eye at baseline, 4.47 right eye and 4.54 left eye at month 3, and 4.42 right eye and 4.49 left eye at month 6; hydrogel plug: 2.81 right eye and 2.86 left eye at baseline, 4.28 right eye and 4.28 left eye at month 3, 4.48 right eye and 4.46 left eye at month 6).

Both plugs were easy to insert, with no to minimal pain during the procedure (Table 3). In 33.3% of cases, gel extruded from the upper punctum during insertion of the crosslinked HA filler through the lower punctum. In these cases, it seems that the cohesive properties of the crosslinked HA gel allowed it to track from the inferior to the superior canaliculus. Any excess gel was wiped away with a cotton tip applicator. Both the crosslinked HA filler and hydrogel plugs were easy to irrigate from the canaliculus, with minimal difficulties, and the patency of the drainage system was restored.

DISCUSSION

The crosslinked HA filler was statistically noninferior and numerically superior to the hydrogel plug in anesthetized

Table 2. Summary of adverse events (safety population)

Parameter	Crosslinked HA filler (N = 103) n (%)	Hydrogel plug (N = 54) n (%)	Total (N = 157) n (%)
No. of patients with ≥1 ocular device-related AE	26 (25.2)	14 (25.9)	40 (25.5)
Most common ocular device-related AEs			
Eyelid pain	5 (4.9)	1 (1.9)	6 (3.8)
Epiphora	8 (7.8)	3 (5.6)	11 (7.0)
Blepharitis	2 (1.9)	1 (1.9)	3 (1.9)
Procedural pain	7 (6.8)	3 (5.6)	10 (6.4)

AE = adverse event; HA = hyaluronic acid; N = total number of patients in the respective treatment group
Percentages were based on the total number of patients in each treatment group. AEs were coded using MedDRA 23.1. Patients experiencing >1 AE were counted once within that preferred term. Device-related AEs were those categorized as definite, probable, and possible.

Schirmer test score improvement from baseline to 3 months with a mean increase of 3.9 mm for the crosslinked HA filler group and 1.9 mm for the hydrogel plug group and the proportion of OSDI responders (84.3% for the crosslinked HA filler group and 83.3% for the hydrogel plug group). Compared with the hydrogel plug group, the crosslinked HA filler group had a trend toward superior increase of Schirmer score at 3 and 6 months (Figure 1) and had a numerically larger improvement in corneal staining at 6 months (Figure 3). The improvements in Schirmer score, OSDI, corneal staining, and TBUT were sustained over 6 months. This, along with the dye disappearance test, confirms that the crosslinked HA filler was in place for 6 months. The crosslinked HA filler was safe, well tolerated, easy to insert, and easy to remove at 6 months. The effectiveness and safety of the crosslinked HA filler are supported by a proof-of-concept study in 63 patients who received a different crosslinked HA intracanalicular gel (Restylane-L, Q Med).[20]

Tear Film and Ocular Surface Society Dry Eye Workshop II concluded that creating an adequate environment for ocular surface health can be accomplished by retention of tears through lacrimal occlusive devices.[8] Studies show that lacrimal occlusive devices can help improve dry eye associated with refractive surgery, contact lens wear, glaucoma, and menopause.[11] Patients with dry eye that has not been satisfactorily treated with lubricating eyedrops may benefit from lacrimal drainage occlusion, particularly patients with moderate dry eye.[21] Considering that approximately one-third of patients without preexisting DED develop dry eye after cataract surgery (surgical transient ocular discomfort syndrome) and contact lens discomfort attributed to dry eye is commonplace, it is anticipated that the crosslinked HA filler will be a useful tool for treating these patients.[3,22,23] In addition, the crosslinked HA filler did not cause alteration of IOP, which indicates that it may be useful for patients with dry eye and glaucoma by increasing the effectiveness of topical medications.[24]

Although the study concluded noninferiority, the crosslinked HA filler has some advantages over the hydrogel plug. The crosslinked HA filler completely fills the canaliculus up to the punctum, and in 33.3% of cases, gel extruded from the upper punctum during insertion. The benefit is that physicians have visual evidence that the punctum has been blocked, and complete blockage prevents the accumulation of stagnant tears within the canaliculus, which has been recognized as a potential source of infection. Permanent intracanalicular plugs (such as the SmartPlug, Form Fit, and Herrick plug) have been associated with pyogenic granuloma and canaliculitis, which required plug removal and in some cases have necessitated canaliculotomy and dacryocystorhinostomy.[21,25,26] These infections have been attributed to

Table 3. Plug insertion questionnaire at administration (safety population)

Question	Crosslinked HA filler (N = 102)	Hydrogel plug (N = 54)
Was gel extruded from the upper punctum during insertion into the lower canaliculus?		
Yes, n (%)	34 (33.3)	0
How easy was it to insert the plugs? (Score 1-5: higher scores indicate greater difficulty)		
Right eye, mean (SD)	1.8 (1.2)	1.4 (0.9)
Left eye, mean (SD)	1.6 (1.0)	1.4 (1.0)
Did the patient appear to experience any pain during the procedure? (Score 1-5: higher scores indicate more severe pain)		
Right eye, mean (SD)	1.4 (0.8)	1.3 (0.9)
Left eye, mean (SD)	1.3 (0.7)	1.4 (0.9)
Ask the patient to rate his or her pain level during insertion on a scale from 1 (no pain) to 10 (most severe pain)		
Right eye, mean (SD)	2.2 (1.9)	2.2 (2.1)
Left eye, mean (SD)	2.1 (1.8)	2.3 (2.0)

HA = hyaluronic acid

stagnant tears and accumulation of biomaterial.[27,28] SmartPlug may not completely fill the space, which can lead to stagnant tears and bacterial accumulation.[11,29] Herrick plug can also have a stagnant column of tears that fill the space between the plug and punctal opening.[11] In contrast to these intracanalicular plugs, the crosslinked HA filler completely fills the canaliculus and thus may provide better safety profile by design. In addition, it is noteworthy that reports of pyogenic granuloma and canaliculitis leading to occlusive device removal can occur several years post-occlusion; however the crosslinked HA filler is indicated for 6 months of use, then removal by irrigation and replacement for increased safety.[21,25,26]

The crosslinked HA filler also has advantages over punctal plugs. Punctal plugs can spontaneously extrude from the puncta. Punctal plugs can cause localized discomfort or corneal abrasion due to contact with the corneal and conjunctival surfaces. The crosslinked HA filler eliminates the potential for abrasion because there is no plug exposure. Punctal plugs can fall out prematurely. Spontaneous loss of punctal plugs has occurred in up to 60% of cases, with loss reported in 16% to 48% of cases 1 to 3 months postinsertion, depending on the punctal plug design.[8,30–32] By contrast, the crosslinked HA filler completely occludes the canaliculus and cannot spontaneously dislodge. In addition, the crosslinked HA filler does not require individualized sizing as needed by punctal plugs.

The study was not powered for superiority. However, the change from baseline in the Schirmer test score at 3 and 6 months and corneal staining at 6 months were numerically greater with the crosslinked HA filler group compared with the hydrogel plug group. Despite this study limitation, the study design was robust. This prospective multicenter, randomized, controlled, double-masked study included a diverse population of dry eye patients. The enrolled patients were 65% postmenopausal, 83% had severe dry eye, and 37% had a history of LASIK and/or cataract operation, supporting the use of the crosslinked HA filler in surgical patients.

This study demonstrates that lacrimal outflow occlusion with the crosslinked HA filler is a new, safe, well-tolerated, and effective method to treat dry eye. The crosslinked HA filler effectively occludes the canaliculi, maintaining lubricating natural tears on the surface of the eye. There were clinically and statistically significant improvements in both signs and symptoms of dry eye, which were sustained through 6 months, when the crosslinked HA filler was irrigated from the lacrimal system and could be replaced. The crosslinked HA filler will be useful in a wide population of patients with dry eye, including those undergoing surgery including cataract and refractive surgery.

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WHAT WAS KNOWN

- Lacrimal occlusive devices improve dry eye by preserving ocular surface moisture and are convenient for the patient.
- The ideal canalicular occlusion device for dry eye would fully block the lacrimal drainage system, has straightforward placement with easy removal when necessary, and is comfortable, durable, biocompatible, and safe with a low potential for infection. A crosslinked hyaluronic acid (HA) is an excellent material for an intracanalicular occlusion device.

WHAT THIS PAPER ADDS

- This is the first clinical trial to evaluate the chemically crosslinked, particulate HA hydrogel intracanalicular occlusion device (Lacrifill Canalicular Gel, Nordic Pharma).
- The crosslinked HA filler produced clinically and statistically significant improvements in both signs and symptoms of dry eye in a diverse group of dry eye patients, which were sustained through 6 months.
- The crosslinked HA filler is a new safe, well-tolerated, and effective method to treat dry eye.

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