The treatment of severe trachomatous dry eye with canalicular silicone plugs

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CLINICAL STUDY

Abstract

Purpose **To evaluate the effects of temporary canalicular occlusion with silicone plugs on trachomatous dry eye patients who were on maximal tolerable medical therapy.**

Methods **Forty-four trachomatous dry eye patients who had Schirmer testing with topical anaesthetic measuring 5 mm or less and a tear film break-up time of 5 s or less were included. After the lacrimal efficiency test with dissolvable collagen punctal plugs, silicone canalicular plugs were placed in 22 trachomatous dry eye patients. The other 22 patients in the untreated control group were allowed to continue their medical therapy. Pretreatment and post-treatment evaluations included subjective patient assessment, rose Bengal and fluorescein staining, tear film break-up time, Schirmer testing, conjunctival impression cytology and goblet cell counting.**

Results **Six months after plug placement, 18 eyes (82%) of 22 patients had subjective improvement and all these patients successfully wore plugs for at least 6 months. There were statistically significant differences between the pretreatment and post-treatment test results including rose Bengal and fluorescein staining scores, tear film break-up times and Schirmer testing measurements. Impression cytology showed improvement of squamous metaplasia in 17 eyes (77%). Eight of the patients (36%) were able to decrease dependency on topical therapy. Ten of the patients (45%) completely stopped using artificial tears. There were statistically significant differences between the two groups in the total symptom scores, staining scores, tear film break-up time, Schirmer testing, impression cytology scores and goblet cell counts.**

Conclusion **In cases where topical tear supplementation is insufficient to relieve the signs and symptoms of severe dry eye and the lacrimal puncta have not already been closed by the trachomatous cicatrising process, occlusion of the canaliculi may be useful to prevent drainage of both natural and artificial tears. Canalicular occlusion improves the objective signs and subjective symptoms and may significantly decrease dependency on tear supplements in selected patients.**

Key words Canalicular occlusion, Canalicular plugs, Dry eye, Impression cytology, Trachoma

The tear film plays an important role in keeping the epithelium of the cornea and conjunctiva in proper physiological condition and in forming a smooth optical surface. Observation of the ocular surface is essential to understanding the pathology of various abnormalities of the tear film including dry eye. Pathophysiologically the dry eye syndrome belongs to a larger group of diseases that may be named ocular surface disease. One common aspect of all dry states is the damaged corneal and conjunctival epithelium. Tear film insufficiency or instability invariably leads to some degree of cellular surface damage to the eye. In turn, ocular epitheliopathy adversely affects tear film stability. The vicious circle of tear film instability and ocular surface damage lead to a pathological condition most often referred to as a dry eye.[1,2]

Trachoma is a chronic ocular surface disease caused by *Chlamydia trachomatis* serotype A, B, Ba or C. *C. trachomatis* is essentially a pathogen of mucosal surfaces, infecting and replicating within epithelial cells. Attachments between conjunctival epithelial cells become loosened so the cells are often separate in conjunctival smears rather than in attached cell sheets. The conjunctival epithelial cells become irregular in size and may form multinucleated giant cells. Goblet cells in the conjunctiva are destroyed by the prolonged inflammatory reaction. Accessory lacrimal gland tissue and the ducts of larger lacrimal glands are compromised by subepithelial scarring. When tear secretion declines, several mechanism act to increase tear film osmolarity. Under these circumstances, increased tear film evaporation has a greater effect on tear film stability. Subsequent anterior surface drying accelerates the cicatrising process.[3–5]

In cases where topical tear supplementation is insufficient to relieve the signs and symptoms of severe dry eye and lacrimal puncta have not

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already been closed by the cicatrising process, occlusion of the puncta may be useful to prevent drainage of both natural and artificial tears. Canalicular blocking is specifically indicated in the aqueous-deficient dry eye, but, in fact, any type of dry eye may improve with canalicular blocking, because the deficits are interrelated, each affecting the other to some extent. The procedure increases the aqueous component of tears and mucin goblet cell density increases gradually following canalicular occlusion.[6,7]

No study has yet tested the efficacy of the different methods of canalicular occlusion to treat dry eye associated with cicatrising conjunctival diseases. We treated a series of trachomatous dry eye patients with removable canalicular plugs. These patients were not responding subjectively or objectively to topical tear supplements or lubricants. We favour less traumatic techniques and begin by inserting temporary collagen implants. If successful, this is followed by silicone plug insertion. This is an ideal method to establish whether the obstruction of lacrimal drainage is useful for the patient without having to remove the obstruction later on. The patients were evaluated before and after plug placement by clinical examination and conjunctival impression cytology.

Patients and methods

Forty-four eyes of 44 patients with severe trachomatous dry eye were included in this study. Twenty-two eyes of 22 patients were treated by mechanical canalicular occlusion. The canalicular occlusion group comprised 13 women and 9 men whose average age was 57.64 ± 7.64 years (range 48–81 years). In the control group the 22 eyes of 22 patients continued their medical treatment, which they had been applying for at least 3 months, until the end of the study. This untreated control group comprised 11 women and 11 men whose average age was 59.18 ± 8.86 years (range 51–76 years).

Inclusion criteria were as follows:

- The presence of *bilateral trachomatous scarring* (TS) according to the World Health Organization Trachoma Grading Scheme.[8]
- The presence of *functional signs of dry eye* for more than a year, with insufficiently effective conventional symptomatic treatment and no improvement despite what the patients considered to be maximum topical therapy.
- A *positive rose Bengal test* in the interpalpebral area, with a score of 4 or more. For the test of a drop of rose Bengal 1% was administered, which was washed with physiological saline 30 s later. Staining intensity was graded by slit-lamp examination from 0 for a normal eye to a maximum of 9.
- *Schirmer test* (after topical anaesthesia) *showing 5 mm or less* of strip wetting in 5 min. A 10 µl drop of fluorescein sodium 1% combined with oxybuprocaine chloride 0.4% was placed in each eye. Five minutes later, a strip of paper was hung from the lower eyelid, where it remained for an additional 5 min. The length of the wet portion was then measured, and the intensity of fluorescein staining was graded by slit-lamp examination from minimal possible score of 0 to a maximal score of 9.
- Tear *break-up time* (BUT) *of 5 s of less*. Ten microlitres of 1% fluorescein solution without preservatives or anaesthetics was applied in each eye. We measured the interval between the last complete blink and the appearance of the first black spot in the fluorescein-stained tear film without touching the eyelid. BUT estimation was performed three times on each eye and the mean value of the three measurements was calculated.
- *Squamous metaplasia in the conjunctival impression cytology samples*: large irregular epithelial cells with small nuclei (a decreased nucleus-to-cytoplasm (N/C) ratio), and few goblet cells, which tend to stain faintly.[9] After all other diagnostic assessments were performed the conjunctival impression cytology samples were collected in six zones (upper and lower bulbar, temporal and nasal bulbar, upper and lower palpebral) in each eye and stained according to the method described by Tseng.[10] Conjunctival epithelial cell changes were scored according to Nelson's grading system:[11]
  - 0 = small, round epithelial cells with scanty, eosinophilic cytoplasm. Large, basophilic nuclei with a N/C of 1:2. Plump, oval, intensely periodic acid–Schiff (PAS)-positive, abundant goblet cells.
  - 1 = slightly larger and more polygonal epithelial cells with eosinophilic cytoplasm. Nuclei smaller with a N/C of 1:3. Goblet cells maintain their plump, oval shape with an intensely PAS-positive cytoplasm but are decreased in number.
  - 2 = larger, polygonal and occasionally multinucleate epithelial cells with variable-staining cytoplasm. Small nuclei with an N/C of 1:4–1:5. Smaller, less intensely PAS-positive goblet cells markedly decreased in number and having poorly defined cellular borders.
  - 3 = large, polygonal epithelial cells with basophilic cytoplasm. N/C < 1:6. There are very few goblet cells, and often they are absent altogether.

In each patient, cyotological changes were scored separately in the six zones, then the sum of the scores of cytological changes in each patient was calculated as the 'total cytology score'. As goblet cell density was known to show large variations according to the conjunctival site, the average number of goblet cells was calculated from 10 representative high-power fields for the six impression zones.[12]

Subjects with the following conditions were excluded: senile lid laxity, trichiasis, entropion or ectropion, absence of nocturnal lid closure, punctal phimosis, punctal occlusion, canalicular occlusion, nasolacrimal duct obstruction.

Plug placement procedure

First a lacrimal efficiency test was carried out. Collagen punctal plugs (0.4 mm diameter and 2 mm long; Lacrimedics, Rialto, CA) were inserted by first anaesthetising the puncta with topical anaesthetic on a cotton-tip applicator. Dilation of the puncta is not usually needed prior to this procedure. These implants were used to predict results before punctal occlusion with a silicone plug.

Three weeks later, in patients who did not have epiphora when wearing collagen implants, hydrophobic silicone canalicular plugs (0.5 mm diameter, Herrick Lacrimal Plug, Lacrimedics, Rialto, CA) were inserted past the punctum, down the vertical canaliculus and into the horizontal canaliculus. Here the plug becomes lodged just in front of the common canaliculus. (These plugs requires no topical anaesthetic or dilation of the punctum for insertion.) Plugs were placed in upper and lower canaliculus.

Patients were examined before collagen plug placement and at 3 months and 6 months after silicone plug placement. The effectiveness of canalicular occlusion was checked at every examination. To be certain that the subjective improvement reported by the patients was not a placebo effect, one of us (M.G.) obtained an objective assessment of each patient. To minimise assessment bias, the results of the pre-placement evaluation were not available to the investigator at the time of the post-treatment examination.

The pre-placement and post-placement evaluations included the following:

- Changes in functional symptomatology: (a) foreign body sensation, (b) burning-stinging, (c) ocular fatigue, (d) photophobia (graded as 0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe). Each of the symptoms was rated separately, then the sum of the scores of symptoms in each patient was calculated as the 'total symptom score'.
- The amount of articificial tears required (the same, less or more).
- The amount of Schirmer test strip wetting after topical anaesthesia.
- The presence of fluorescein staining and rose Bengal staining in the bulbar conjunctiva nasally and temporally as well as on the cornea (minimal possible score of 0 and maximum score of 9).
- Conjunctival impression cytology (minimal possible score of 0 and maximum score of 18).

For statistical analysis of the results before and after plug placement, the total symptom scores, rose Bengal, fluorescein staining scores and impression cytology scores were analysed by Wilcoxon matched-pairs signed-ranks test. Schirmer test results, the average goblet cell counts and BUT values were analysed by *t*-test for paired samples. The Mann–Whitney *U*-test was used for the comparison of total symptoms, rose Bengal, fluorescein staining and impression cytology scores; a *t*-test was performed to compare the Schirmer test results, average goblet cell counts and BUT values in the treated and untreated group.

Results

The mean clinical follow-up period was 7.84 ± 2.05 months, with 14 months as the upper limit and a minimum follow-up of 6.25 months.

Eighteen eyes (82%) of 22 patients had subjective improvement. The improvement for plugged eyes versus their pre-placement values was highly significant by chi-square test ($p < 0.001$). Eight of the patients (36%) were able to decrease dependency on topical therapy. Ten of the patients (45%) stopped using artificial tears completely. Four patients (18%) who retained canalicular plugs did not experience any improvement in symptoms and none of these patients was able to decrease dependency on topical therapy. Total symptom scores decreased from a mean of 9.91 ± 1.60 to 4.14 ± 1.61 ($p < 0.0001$). When the plug-treated group and the untreated group were compared, significant improvement in ocular symptoms was observed in the treated group at 3 and 6 months, and there were significant differences between the total symptom scores of the two groups (Table 1, Fig. 1).

Rose Bengal staining scores decreased from a mean of 5.55 ± 1.77 to 1.55 ± 1.65 ($p < 0.001$). There were significant differences between plug-treated and untreated groups concerning rose Bengal staining scores at 3 and 6 months (Table 2, Fig. 2). Fluorescein staining scores decreased from a mean of 4.23 ± 1.82 to 1.32 ± 1.70 ($p < 0.001$). There were also significant differences between plug-treated and untreated groups in the fluorescein staining score at 3 and 6 months (Table 3, Fig. 3). Pre-placement Schirmer 1 test results were a mean of 3.90 ± 0.87 mm, and 6 months after plug placement were a mean of 9.18 ± 3.53 mm ($p < 0.001$). There were significant differences between plug-treated and untreated groups in the Schirmer test values at 3 and 6 months (Table 4, Fig. 4).

Impression cytology showed improvement of squamous metaplasia and increased goblet cells in 17 of 22 eyes (77%) (Fig. 5). Total impression cytology scores decreased from a mean 14.00 ± 2.89 to 5.27 ± 1.86 ($p < 0.0001$). There were significant differences between plug-treated and untreated groups in the impression cytology scores at 3 and 6 months (Table 5, Fig. 6). The average number of goblet cells increased from 8.92 ± 4.27 to 82.50 ± 40.40 ($p < 0.0001$). Significant increases were observed in the average goblet cell counts and there were significant differences between plug-treated and untreated groups concerning goblet cell counts (Table 6, Figure 7).

BUT values increased from 3.90 ± 0.92 to 12.68 ± 2.98 ($p < 0.0001$). Significant increases were observed in BUT values and there were significant differences between treated and untreated groups in the BUT values (Table 7, Fig. 8).

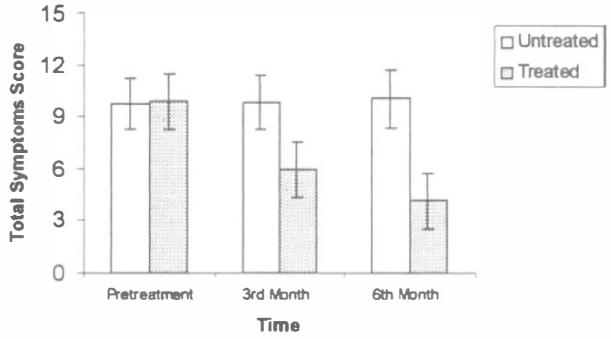

Fig. 1. *Total symptom scores for untreated and treated eyes.*

Table 1. *Total symptom scores for untreated and treated eyes*

	Total symptom score (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	9.77 ± 1.48	9.91 ± 1.60	>0.05
3rd month	9.82 ± 1.56	5.96 ± 1.62	<0.0001
6th month	10.05 ± 1.65	4.14 ± 1.61	<0.0001

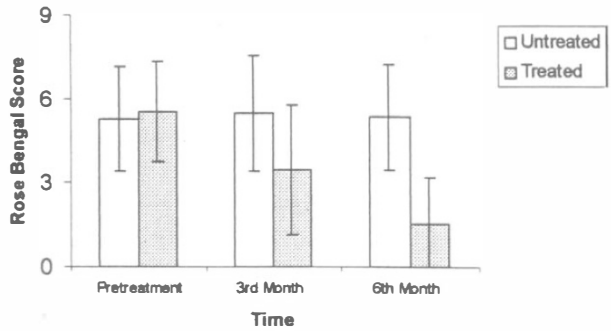

Fig. 2. *Rose Bengal staining scores for untreated and treated eyes.*

Table 2. *Rose Bengal staining scores for untreated and treated eyes*

	Rose Bengal staining score (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	5.27 ± 1.86	5.55 ± 1.77	>0.05
3rd month	5.46 ± 2.06	3.46 ± 2.32	<0.01
6th month	5.36 ± 1.87	1.55 ± 1.65	<0.0001

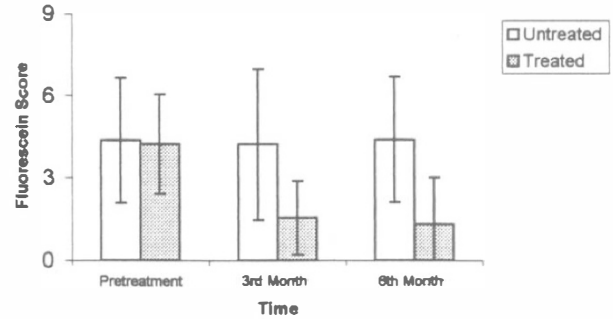

Fig. 3. *Fluorescein staining scores for untreated and treated eyes.*

Table 3. *Fluorescein staining scores for untreated and treated eyes*

	Fluorescein staining score (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	4.36 ± 2.28	4.23 ± 1.82	>0.05
3rd month	4.22 ± 2.76	1.55 ± 1.34	<0.01
6th month	4.41 ± 2.30	1.32 ± 1.70	<0.0001

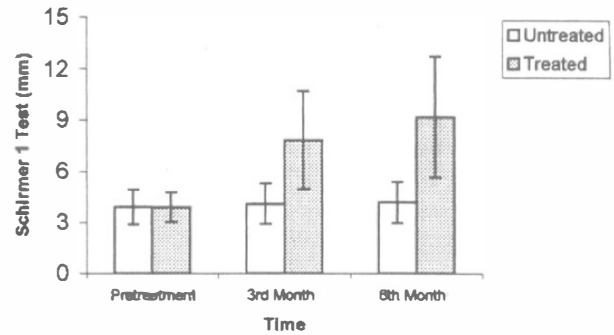

Fig. 4. *Schirmer 1 test values for untreated and treated eyes*

Table 4. *Schirmer 1 test values for untreated and treated eyes*

	Schirmer 1 Test (mm) (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	3.91 ± 1.02	3.90 ± 0.87	>0.05
3rd month	4.09 ± 1.19	7.82 ± 2.87	<0.0001
6th month	4.18 ± 1.22	9.18 ± 3.53	<0.0001

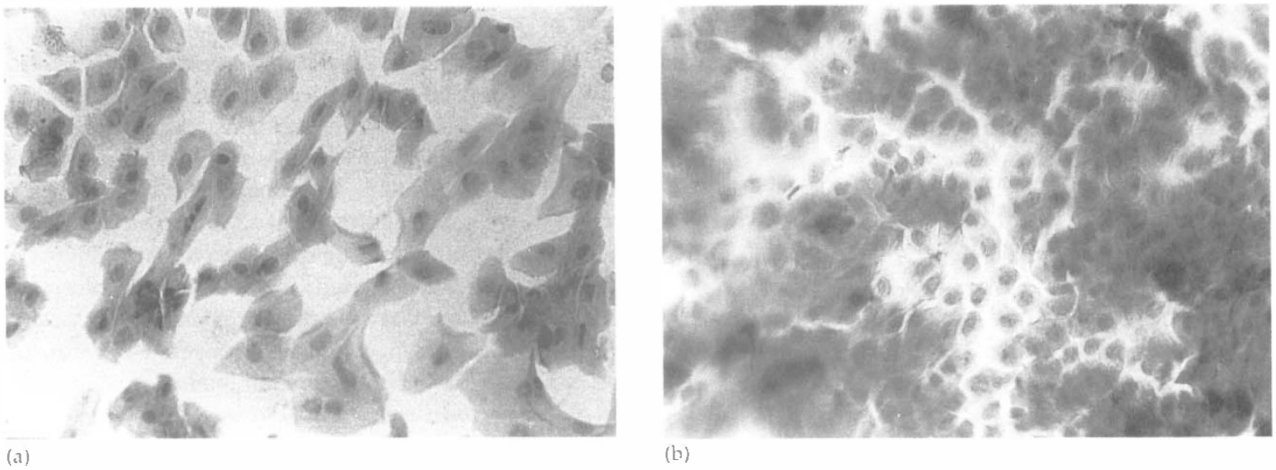

Fig. 5. *(a) Impression cytology of the inferior bulbar conjunctiva from a patient with trachomatous dry eye, demonstrating severe squamous metaplasia and total loss of goblet cells. The epithelial cells are large and polygonal in shape. (b) The same eye and location 6 months after punctal occlusion. Squamous metaplasia had almost completely resolved. Note the well staining goblet cells.*

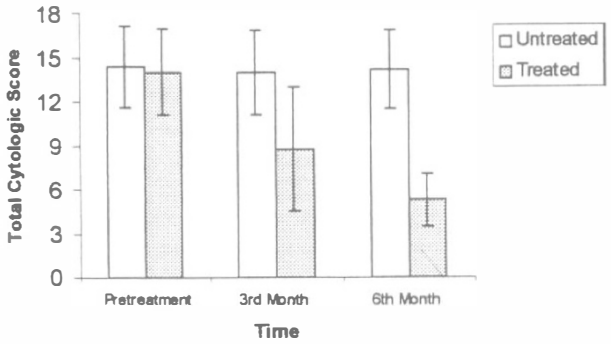

Fig. 6. *Total impression cytology scores for untreated and treated eyes.*

Table 5. *Total impression cytology scores for untreated and treated eyes*

	Total cytology score (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	14.36 ± 2.74	14.00 ± 2.89	>0.05
3rd month	13.95 ± 2.88	8.77 ± 4.20	=0.0001
6th month	14.14 ± 2.66	5.27 ± 1.86	<0.0001

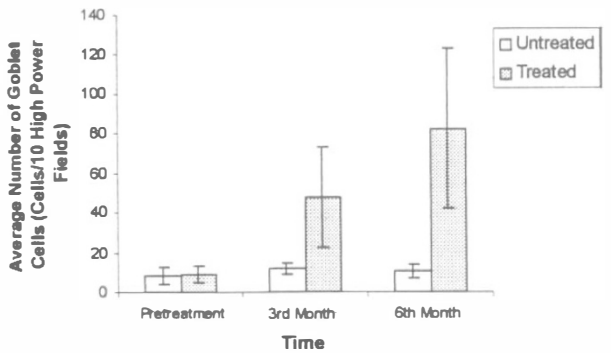

Fig. 7. *Average number of goblet cells for untreated and treated eyes.*

Table 6. *Average number of goblet cells (cells per 10 high-power fields) for untreated and treated eyes*

	Average no. of goblet cells (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	8.54 ± 4.11	8.92 ± 4.27	>0.05
3rd month	11.96 ± 2.80	48.10 ± 25.40	<0.0001
6th month	10.68 ± 3.39	82.50 ± 40.40	<0.0001

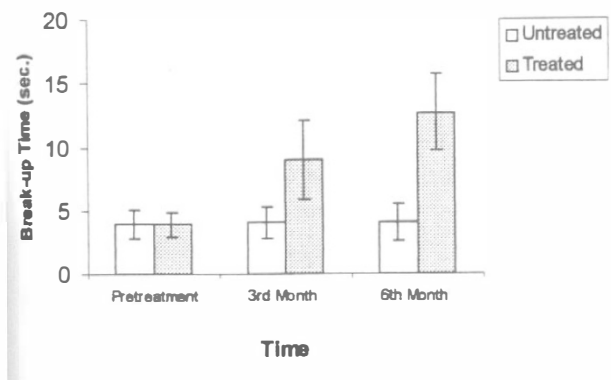

Fig. 8 *Tear break-up time values for untreated and treated eyes.*

Table 7. *Tear break-up time values for untreated and treated eyes*

	Tear break-up time (s) (mean ± SD)		
Time	Untreated	Treated	*p* value
Pretreatment	3.95 ± 1.09	3.90 ± 0.92	>0.05
3rd month	4.08 ± 1.27	9.00 ± 3.12	<0.0001
6th month	4.09 ± 1.48	12.68 ± 2.98	<0.0001

None of the patients in our study extruded canalicular plugs. It was observed that the canalicular occlusion continued effectively until the end of the study. The only complication associated with plug placement was mild epiphora in our study (14%).

Discussion

Dry eye is caused by a disease or injuries that affect tear production or composition, and it has an abnormal tear film. The maintenance of a normal tear film depends on the maintenance of a normal ocular surface. Lids, tears, mucous and epithelial surfaces interact to produce a complex physicobiochemical system that ensures an optimal corneal environment.[13] Cicatrisation of the conjunctiva may cause imbalance of this system resulting in changes which are incompatible with corneal clarity and normal eyesight. Trachoma is a conjunctival cicatrisation syndrome. Conjunctival cicatrisation destroys accessory lacrimal glands and goblet cells (basic secretory system) and obliterates lacrimal gland excretory ductules. All components of the tear film are therefore deficient, resulting in a dry eye.[14] Tabbara and Bobb[15] observed an increased incidence of dry eye syndrome among patients with severe inactive trachoma.

The most commonly used therapy for the dry eye is artificial tear instillation. Various artificial tear formulations are available that offer relief of symptoms, but, unfortunately, improvement is short lived because the tears drain through the lacrimal outflow channels and evaporate. The lacrimal outflow system can be closed by punctal or canalicular occlusion. Closure of the outflow system will preserve the natural tears and prolong the effect of artificial tears that are instilled. Therefore, occlusion increases tears in the conjunctival sac and replenishes the supply of mucus, protein, vitamins, and other chemicals to the cornea and conjunctiva.[16]

Punctal occlusion is the closure of the lacrimal outflow system at the level of the punctum or canaliculus. Some studies have indicated that punctal occlusion can decrease elevated tear osmolarity and rose Bengal staining of the ocular surface.[17,18] The success of punctal occlusion in the patients with dry eye is commonly predicted by the presence of conjunctival and corneal staining in the exposure zone and substantial tear film debris. A trial of temporary occlusion with collagen plugs and low Schirmer test results predict success, i.e. increased comfort and lack of epiphora.[16] During their wear, these implants reduce the flow through the canaliculus only partially, by 60–80%, and therefore dry eye patients who do not have epiphora when wearing collagen implants may have epiphora with total occlusion.[7,19]

The Herrick lacrimal plug is a blunt funnel-shaped or golf-tee-shaped silicone plug, commercially available since 1990. The insertion of the plug requires no topical anaesthetic or dilation of the punctum. Usually, the plug is well tolerated. If patients experience irritation or epiphora, the plug can easily be removed through saline irrigation or probing of the canaliculus.[7]

The anatomical effectiveness of punctal occlusion has been well established. Tuberville and co-workers[20] treated 27 patients with dry eye syndrome who underwent punctal occlusion of all four puncta. This reduced the pain and subjective symptomatic improvement was recorded in 97% of the 32 dry eyes treated. Epiphora did not occur after punctal occlusion. Sixteen patients (50%) completely stopped using artificial tears and 11 (34%) reduced the amount used. Tuberville *et al.*[20] observed a drop of 85% in rose Bengal staining scores, but found no significant improvement in Schirmer 1 test results after plug placement.

Willis *et al.*[21] reported parallel reduction in rose Bengal scores and functional signs in 5 of 11 patients (45%), and 1 case of anatomical improvement out of 3 (33%) without functional improvement. Willis *et al.* noted that in patients who showed functional improvement, Schirmer test results were better, with at least a 5 mm strip wetting (mean: 8 mm for 13 patients). The mucin goblet cell density increases gradually following canalicular occlusion. The increase is not appreciable after 6 weeks,[21] but it is evident after 2 or more years.[22] Rose Bengal staining and the Schirmer 1 test confirm the effectiveness of punctal plugging from the anatomical point of view.

The composition of tear becomes more normal and thickening of the conjunctival secretion is diminished, relieving symptoms dramatically in most cases of dry eye. Canalicular blocking preserves natural tears, which is better than artificial tears.[20,23] The tears also improve qualitatively, with diminished osmolarity.[16,17] Dohlman[16] hypothesised that punctal occlusion was therapeutic for dry eye by decreasing elevated tear film osmolarity, and Gilbard and associates[17] later demonstrated that punctal occlusion decreases elevated tear film osmolarity by increasing tear volume. With increase tear volume, evaporation has less of an effect on tear film osmolarity. Furthermore, freshly secreted tear fluid may have more of a dilutional effect on the tear film in the presence of decreased tear drainage.[17]

The one objective parameter that improved within 6 months with subjective improvement and improvement in Schirmer strip wetting and staining in our study was the impression cytology. In the study by Tseng *et al.*,[24] dry eye patients using retinoic acid ointment for 2 months showed improvement subjectively, clinically and cytologically. Wright[25] noted the disappearance of clinically detectable keratin plaques within 5 days of retinoic acid therapy. However, a previous study[22] of dry eye patients after punctal occlusion as monitored by conjunctival biopsy 2–5 years after treatment did show reversion to normal conjunctival morphology and restoration of normal goblet cell densities. Therefore, although the clinical response to both retinoic acid and punctal occlusion is rapid, reversal of cytological abnormalities may take longer for patients treated by punctal occlusion than for those treated by topical

retinoic acid. We were able to repeat the conjunctival impression cytological examination at extended intervals.

Canalicular occlusion has few or no disadvantages for most patients. Epiphora was the most frequent complication (22%) after complete punctal occlusion in Fayet *et al*.'s series.[18] Three of our patients (14%) eventually complained of epiphora. Each of these patients requested that one plug be removed from each eye, but all 3 patients later requested replacement of the plugs.

Lacrimal canalicular occlusion seems to be effective, and our patients were significantly satisfied with the results. This is a new approach for the treatment of severe trachomatous dry eye. Whereas permanent punctal occlusion methods, such as thermal cautery and argon laser, may also be applicable, the simplicity of the implantation procedure, and the good local acceptance observed, have reduced the importance of surgery and made it a secondary alternative. Canalicular occlusion can dramatically improve the quality of life in patients with severe trachomatous dry eye.

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