Original Article

The Efficacy and Safety of 0.3% Acetylcysteine Eye Drops in Filamentary Keratitis

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Purpose: To determine the safety and efficacy of 0.3% Acetylcysteine eye drops for the resolution of symptoms and signs of filamentary keratitis.

Study design: Quasi experimental study

Place and Duration of Study: This study was conducted at a tertiary care centre (Envision, Squint & Oculoplastics Centre, Lahore) from April 2016 to October 2018.

Material and Methods: Fifty two consecutive cases (104 eyes) with mild to severe filamentary keratitis, from 9-72 years (mean 49 ± 8.6) were included. Cases with active ocular surface infection, uveitis, recent ocular surgery (< 1 month) and pregnant/lactating patients were excluded. All cases were prescribed lubricants, anti-inflammatory therapy (Tacrolimus skin cream 0.03%) and tetracycline eye ointment for meibomian gland disease (MGD). Alternate cases were divided into two equal groups of 26 cases; Group A received Acetylcysteine eye drops 0.3%, four times daily, Group B cases received placebo eye drops (distilled water in a bottle). Clinical symptoms on ocular surface disease index (OSDI), corneal filaments, corneal fluorescein staining, Tear Film BUT and Schirmer's test were recorded at the beginning of the study and every two weeks, for the next 12 weeks.

Results: Primary Outcome Measure was reduction of symptoms (OSDI score) and absence of filament formation after treatment. The patients were followed-up for a mean duration 12 ± 2 weeks. A marked subjective and objective improvement (100%) was noted in all cases that received Acetylcysteine 0.3% eye drops as compared to the placebo group.

Conclusion: Acetylcysteine 0.3% eye drops efficiently dissolve filaments and offer quick resolution of symptoms even in severe cases of filamentary keratitis.

Key words: Filamentary keratitis, dry eyes, Acetylcysteine eye drops, mucolytic agents.

Filamentary keratitis is a chronic, recurrent and functionally debilitating condition in which mucous strands or filaments are present over the ocular surface. With each blink, the eyelids pull upon the filaments and the traction/pull exerted on the underlying corneal epithelium results in a lot of ocular discomfort, pain and a constant foreign body sensation in the eye[1]. It occurs in association with a

number of ocular surface diseases like Sjögren syndrome (SS), non-Sjogren's Dry eyes syndrome (non-SS), Stevens Johnsons syndrome, vitamin A deficiency, lacrimal gland tumour/dacryo-adenitis, superior limbic keratoconjunctivitis, chronic Vernal keratoconjunctivitis, post-herpetic keratitis, recurrent corneal erosions, neurotrophic keratitis, thyroid eye disease (TED), facial palsy, bullous keratopathy, and prolonged patching following ocular surgery.

Normally, there is a certain fixed ratio of aqueous: mucin in the tear-film[2]. The mucin molecules float freely in the aqueous component of the tear-film and act as scavenger molecules, and secondly, it forms a smooth, uniform coating over the glycocalyx of the corneal apical cells thus making the normally hydrophobic cornea hydrophilic, and allow the aqueous component of the tear-film to spread uniformly over the cornea.

The basic mechanism for filament formation is an increased ratio of mucin to aqueous. Excess mucin accumulates in the lower conjunctival fornix and is joint together by disulphide bonds, thereby forming mucous strands. The free mucin molecules are no longer available to coat the glycocalyx over the apical corneal epithelial cells so the corneal surface becomes hydrophobic. The reduction of aqueous component increases the osmolarity of the tear-film; the increased concentration of solutes in the tear-film produce chemical inflammation of the ocular surface. This affect is exaggerated in the hot, dry climate, as a part of the ageing process (androgen deficiency) and in diabetes. The hyper-osmolar tears lead to sloughing of the desiccated corneal surface epithelial cells thus producing epithelial defects that act as high-energy pits or a nidus to which mucous strands adhere firmly. The corneal epithelium grows around the mucous to form a filament. In addition, the inflammatory cytokines and enzymes released from eosinophils and lymphocytes in VKC, Sjogrens syndrome, viral keratitis etc, further increase the osmolarity of the tear film, thereby creating a chronic inflammation[3] and ocular surface damage.

The filaments are gelatinous structures, refractile in appearance, consisting of a focal "head" firmly adherent to the compromised areas of corneal epithelium and a freely floating "tail" of varying length[4]. The head is made up of a central core of desquamated corneal epithelial cells, surrounded by degenerating conjunctival epithelial cells and a thick layer of mucin. They vary in size from 0.5 mm sessile adhesions to 10 mm long strings. With each blink, vertical friction causes a lot of ocular discomfort and pain[5], while further shearing of the corneal epithelium results in increased inflammation of the underlying exposed stroma. Mechanical removal of filaments increases the inflammation and promotes further filament formation. To manage filamentary keratitis[6], the treatment needs to be targeted towards treating the underlying cause, the associated ocular surface

inflammation and preventing further epithelial degradation, to remove/treat the filaments.

In order to address all these issues, the therapeutic drug armamentarium must include topical lubricants (to reduce the mechanical stress and ocular discomfort by diluting inflammatory cytokines, and also stabilise the tear film) and topical anti-inflammatory drugs (tacrolimus, cyclosporin A, corticosteroids and non-steroidal agents). In order to dissolve the filaments, oral (Acetylcysteine, carboxymethyl cysteine, bromhexine) as well as topical mucolytic agents like 5-10% Acetylcysteine eye drops have been used in various studies. They dissolve the filaments efficiently but the main problem with these eye drops is the severe ocular irritation, burning and stinging upon their instillation that persists for 10-30 min. This results in a reduced patient compliance to therapy. Unless the filaments are dissolved efficiently, the vicious cycle of further filament formation cannot be broken. In Pakistan, commercially preparation of Acetylcysteine eye drops are not available. With the help of a dispensing pharmacist, we prepared a diluted preparation of 0.3% Acetylcysteine eye drops for our patients. This study was conducted to analyzse whether such a diluted preparation can efficiently dissolve the filaments and whether it is better tolerated than the 5-10% preparation by the patients.

MATERIAL AND METHODS

A prospective interventional study was conducted at a tertiary care centre, for a period of two and a half years, from April 2016–October 2018. An approval from the centre's ethical committee was obtained and there was no conflict of interest to conduct this study. During this period, 52 consecutive cases (104 eyes) which presented with mild to severe filamentary keratitis were included in the study. They were between the age of 9-72 years (median 49 ± 8.6), with 31 females and 21 males. A detailed history was taken regarding the duration and severity of symptoms, systemic illness (arthritis, thyroid dysfunction, psoriasis, vitiligo and other auto-immune disorders), recent ocular surgery and a detailed list of all topical and systemic medications being used by the patient. The time spent on digital screens per day, occupation and smoking was also noted. The baseline characteristics of the 52 cases are shown in Table 1. Cases with an active ocular surface infection, uveitis and recent ocular surgery (< one month) and pregnant/lactating patients were excluded from the study.

A detailed ophthalmic examination was performed in order to assess the underlying cause of the patient's problems and to grade the severity of disease before initiating the specific therapy. Facial appearance regarding brow droop, increased frequency of blinking, blepharospasm, dermatochalasis, position and contour of the eyelids was noted. Presence or absence of meibomian gland dysfunction was assessed by looking for lid margin thickening, telangiectasia, hyperemia, keratinization or frothing at the angles; noting the quality of meibum, the ease with which it could be expressed, position of the meibomian duct orifices, their clogging or notching (indicating absence), trichiasis/distichiasis.

Table 1: Baseline characteristics of 52 cases.

Age	**Range: 9 – 7 Years**		**Mean : 41.20 Median: 55**	
Sex	Males: 21 (40.38%)		Females 31 (59.61%)	
Severity of Dry eyes	Moderate: 16 cases (30.76%)		Severe 36 cases (69.23%)	
Severity of Filaments	Mild: 4 cases (7.7%) Moderate: 12 cases (23%)		Severe 36 cases (69.23%)	
Underlying Cause	Post-cataract Surgery: VKC : Facial palsy: Thyroid eye disease;	4 cases 6 cases 4 cases 4 cases	Non-SS dry eyes: SS dry eyes: Stevens Johnsons:	23 cases 5 cases 8 cases

The lower tear meniscus height and its clarity was noted; the presence of corneal filaments, their number/site, as well as that of corneal epithelial punctate staining with fluorescein, corneal epithelial defect, scarring, pannus formation was also noted.

The primary parameters assessed for the purpose of the study were OSDI, fluorescein staining score (FSS) of the ocular surface, TFBUT, and Schirmer's 1 test. The patients were asked to fill in the Ocular Surface Disease Index questionnaire[7], OSDI, which is a 12-question survey that was developed by the Outcomes Research Group at Allergan Inc;

To record the FSS[8], the ocular surface was divided into three zones: the nasal bulbar conjunctiva, temporal bulbar conjunctiva, and the cornea. Each zone was evaluated on a scale of 0-3, with 0 = no staining, 1 = a few separated spots, 2 = many separated spots, 3 = an area of confluent staining; the maximum score possible was 9. The severity of filamentary keratitis was graded by counting the number of filaments on the cornea as grade 1 (mild) = 1-4 filaments, grade 2 (moderate) = 5-9 filaments, grade 3 (severe) = filaments scattered over the whole surface of cornea.

The Schirmer's test readings were recorded after instillation of one drop of topical anaesthetic (0.5% proparacaine hydrochloride). In a silent room, away from the fan, a filter paper strip (35 × 5 mm, bent at 5 mm) was placed at the lateral one-third of the lower lid margin. Care was taken to prevent the paper from touching the cornea, by asking the patient to look up while placing the strip. The patient was instructed to keep the eyes closed, and not to talk during the test. After 5 minutes, the strip was removed and the level of strip wetting (in mm) was measured. The tear secretion was considered abnormal if the reading was equal to or less than 15 mm.

All cases were prescribed the regular dry eyes treatment protocol[9] comprising of lubricant eye drops 1 – 2 hourly during the day (depending upon the disease severity), lubricant eye ointment (lacrilube, Allergan pharma) at night, anti-inflammatory therapy as Tacrolimus skin cream 0.03% (Crolimus, Valor Pharma) applied in the evening into the lower conjunctival fornix by a cotton-tip. For the associated meibomian gland dysfunction, tetracycline eye ointment (Xinoxy, Remington pharma) was prescribed, to be massaged into the lid margins at night and application of a hot, wet towel to lid margins for 10 minutes in the morning followed by gentle scrubbing of closed eyelids with baby shampoo. All patients were instructed to quit/reduce smoking and drink at least 8 glasses of water daily.

In addition, the compounding pharmacist was instructed to divide the alternate cases into two equal groups; the odd number of cases, from 1-51 were included in Group A, and even number of cases from 2-52 were included in the Group B, so that each group consisted of 26 alternate cases. The Group A cases received Acetylcysteine eye drops 0.3%, freshly prepared by the compounding pharmacist, to be instilled four times daily, whilst the Group B cases received placebo eye drops (distilled water in a bottle). Patients were instructed to keep the bottle refrigerated in between instillation, discard them after a month and get a fresh bottle from the pharmacist. Only the compounding pharmacist had the list of cases who received either the Acetylcysteine or the placebo eye drops. The list was disclosed to the examining

ophthalmologist at the end of the study for analyzing the results. The manual removal of filaments or application of a bandage contact lens was not performed in any case.

The severity of clinical symptoms (OSDI), the number of corneal filaments, corneal fluorescein staining, Tear Film BUT, Schirmer's test readings were recorded at baseline and then at each follow-up visit which was conducted every 2 weeks for 12 weeks. For statistical analysis, the SPSS software version 20 was used. The data was expressed as mean and standard deviation (frequency distributions ± SD) for the OSDI score while it was expressed as median and range for the FSS, TFBUT, Filament grade and Schirmer's test. A "paired" t-test was used to assess the scores from the same set of patients (for both group A and Group B cases) at baseline and then at the 12 week follow-up. The final 12 week score obtained by Group A and B cases was analyzed separately to see which indices improved significantly between the two groups, and $p < 0.05$ was taken to indicate statistical significant. The efficacy analysis population included all cases that completed the study. The safety analysis population included all cases that were enrolled in the study. The statistical analyses included data for the worst affected eye.

RESULTS

The baseline demographics of the 52 consecutive cases (104 eyes) included in the study are demonstrated in Table1; there were 21 males (48.38%) and 31 females (59.61%), with an age range of 9 - 72 years (mean 41.20, and median 55 years).

S*evere dry eyes* were noted in 36 cases *(69.23%)*out of the total 52 and were due to non-Sjogren's syndrome (SS) (23 cases) or SS (5 cases), and the filaments were present in the inter-palpebral region of the cornea along with punctate corneal staining in the same region. The 8 cases due to chronic Stevens Johnson's syndrome also had severe dry eyes, with the corneal filaments and staining diffusely scattered all over the cornea. The remaining 16 cases (30.76%) had dry eyes of a *moderate severity*. They included 6 cases with acute-on chronic VKC, the filaments were present next to the area of limbitis, while the 4 cases with exposure keratopathy due to chronic facial palsy and 2 cases of thyroid eye disease had filaments at the lower limbus. The 4 post-cataract surgery cases had a mild dry eye with a few filaments at the incision site while one had mucous plaques around the corneal sutures.

The presenting complaints of all 52 cases are shown in Table 2; the most common presenting complaints were ocular discomfort, photophobia and a foreign body sensation in the eyes in all 52 cases (100%). Corneal filaments were present in all 52 cases (100%); the site of filaments was determined by the underlying cause while the number was related to the severity and chronicity of the disease.

Table 2: Frequency of symptoms in 52 cases.

Symptoms	Baseline
Photophobia	52 cases (100%)
Foreign body sensation	52 cases (100%)
Eye pain	52 cases (100%)
Eye discomfort	52 cases (100%)
Itching	47 cases (90.38%)
Blurred vision	31 cases (59.6%)
Blepharospasm	28 cases (53.84%)
Watering	47 cases (90.38%)
Discharge	12 cases (23%)

The primary parameters assessed for the purpose of the study are demonstrated in Table 3, and their response to therapy in both groups from baseline till 12 weeks of regular two weekly follow-up. In all **group A cases**, the OSDI score gradually improved from a mean score of 41.5 ± 5.26 to 4 ± 1.5 over the 12 weeks of continued therapy with Acetylcysteine. Even the diluted preparation of 0.3% efficiently removed corneal filaments in all cases within 2-4 weeks of therapy. A recurrence of filaments was noted only in 3 cases who had stopped using Acetylcysteine abruptly. Therefore, the remaining patients were instructed to continue with Acetylcysteine therapy for at least one more month after the total clearance of filaments. All 26 cases in group A completed the 12 weeks follow-up and showed excellent compliance to therapy. Only 2 patients (7.7%) complained of mild discomfort on instillation of Acetylcysteine drops, but no pain or stinging.

The fluorescein staining score (FSS), as shown in Table 3, improved in group A cases from a median of 2 (range 1 – 4) at baseline, to 0 at 12 weeks follow up which was highly statistically significant ($p < 0.00001$). The TFBUT increased from 4 (range 1-7) sec to 9 (range 7-13) sec at 12 weeks, indicating a marked improvement ($p < 0.0001$). The Schemer's 1 readings gradually improved in all cases from 2.5 (range 0-4) mm at baseline to 8 (range 5-12) sec ($p < 0.001$), though very slowly in cases with Stevens Johnson's syndrome.

In **group B cases**, the OSDI score improved very slowly and gradually from the baseline score of 40.67 to 28.5 ± 3.4 over the 8-10 weeks, despite the continued use of lubricants and tacrolimus therapy. This was much less improvement as compared to the group A cases (improved to 4 ± 1.5). It was due to the persistence of corneal filaments and the resultant ocular discomfort, because of which 3 cases did not complete the 12 weeks follow up and dropped out of the study. A statistically significant difference (p = 0.05) between Acetylcysteine therapy and the placebo group was found for the OSDI score as well as all the objective parameters assessed i.e. the FSS, TFBUT and Schirmer's score, which showed only a slight improvement in the placebo group, as demonstrated in Table 3.

Table 3: Results: Comparison between group A & B.

Parameter	Group	Baseline	2 wks	4 wks	6 wks	8 wks	10 wks	12 wks	p value
OSDI	A	41.5± 5.26	32 ± 6.97	24.5 ± 5.50	18 ± 3.26	11 ± 4.50	7 ± 4.60	4 ± 1.5	0.00001
	B	40.67	37 ± 3.42	33 ± 5.55	31.5 ± 5.15	30.20 ± 4.42	28.5 ± 4.52	25 ± 3.4	0.01
Filament grade	A	3 (1-3)	2 (1-3)	0.5 (0-1)	0	0	0	0	0.00001
	B	3 (1-3)	3 (1-3)	2 (1-3)	2 (1-2)	2 (1-2)	2 (1-2)	2 (1-2)	> 0.5
FSS Score	A	2 (1-4)	2 (1-3)	1 (1-2)	1 (0-1)	0 (0-1)	0	0	<0.00001
	B	2 (1-4)	2 (1-3)	2 (1-3)	2 (1-2)	1 (0.5-2)	1 (0-1.5)	0 (0-1)	<0.5
TFBUT sec	A	4 (1-7)	4 (3-7)	5 (4-8)	7 (4-9)	8 (5-11)	8.5 (5-13)	9 (7-13)	< 0.0001
	B	4 (1-6)	4 (1-7)	4 (2-8)	5 (3-7)	5 (3-8)	5.5 (4-9)	6 (5-9)	< 0.01
Schirmer Test mm	A	2.5 (0-4)	3 (1-4)	4 (2-5)	5 (4-7)	6 (4-8)	7 (5-9)	8 (5-12)	< 0.001
	B	2 (0-4)	2 (0-4)	3 (1-5)	3 (1-6)	4 (2-6)	4 (3-6)	5 (3-7)	< 0.01

FSS (Fluorescein Staining Score), TFBUT (Tear-film Break up Time), Schirmer's test readings: shown as median and range (minimum to maximum).

DISCUSSION

Filamentary keratitis is a sight-threatening and a functionally debilitating complication of a number of ocular and systemic conditions, as already mentioned. The site of filament formation depends upon the underlying cause. In our study, the cases with aqueous deficient dry eyes (SS and non-SS = 5 + 23 = 28 cases) and exposure keratopathy due to facial palsy (4 cases) and proptosis due to thyroid eye disease (4 cases), the filaments were noted in the inter-palpebral area. This was due to an excessive evaporation of aqueous from the most exposed area of the ocular surface. The additional factors noted in these patients were smoking, working in an indoor environment, air pollution, prolonged staring at digital screens (computers, mobile phones[10], television) or prolonged reading which reduces the blinking rate and replenishing the tear film.

The 4 post-cataract surgery cases in our study complained of watery eyes, intermittent blurring of vision and grittiness that gradually worsened over 2-6 months after the surgery, which was performed in both eyes one after the other. Corneal filaments were noted at the site of corneal incision in 3 cases and around the corneal sutures in one case. This was due to a pre-existing mild to moderate tear film instability that generally exists in the elderly population due to androgen deficiency and was missed pre-operatively. The added surgical trauma[11,12] destroyed the nerve plexus at the incision site and reduced the corneal sensitivity and the TFBUT. Moreover, the mechanical injury from surgical instrumentation, chemical toxicity of medicines (particularly the preservatives) used pre-operatively, intra-operatively and during the post-operative period, and the co-existent meibomian gland dysfunction in this age group, further aggravated the ocular surface inflammation mainly at the site of corneal incision/suture (due to suture irritation) and filaments formed in the late postoperative period at that site. It takes a long time for the composition and

production of the tear film to recover post-operatively. However, all our cases responded well to the dry eyes therapy and the 0.3% Acetylcysteine eye drops; their vision cleared up as well as the ocular discomfort.

In VKC (6 cases) and autoimmune disorders (Sjogren's syndrome 5 cases), the filaments were noted at the limbal area. This is because the corneal limbal tissue is vulnerable to inflammatory mediators, antibodies, and complement released by the activated eosinophils and lymphocytes present in the peri-limbal vascular arcade[13]. The perilimbal swelling results in tear-film instability and filaments are formed in that area. Additionally, the autoimmune disease process often affects the secretion of lacrimal gland, conjunctival goblet cells, and meibomian glands resulting in a severe form of dry eyes. Ultimately, the filaments are distributed over the whole cornea. According to various studies, allergic conjunctivitishas been found to be accompanied by dry eyes with an incidence of 62.5% to 83.3% while itching of eyes have frequently been noted as a symptom of dry eyes.

Systemic medications[14] like diuretics, anti-histaminics and anti-depressants reduce the production of aqueous and can alter the balance between aqueous: mucin in the tear film, thereby precipitating filamentary keratitis. One patient in our study with VKC was on oral anti-histaminic and two were on diuretics. When these were stopped, their OSDI improved rapidly.

In this study, 38 cases were already on topical lubricants for months and they still developed the corneal filaments. Therefore, the addition of anti-inflammatory medicines topically was mandatory. Tacrolimus[15,16] has been used in various studies as a potent anti-inflammatory agent when applied topically as 0.03% eye drops. Similar to cyclosporin eye drops [17], it is a potent calcineurin inhibitor, known to reduce the ocular surface inflammation by inhibiting the T cell-mediated immune responses. They both promote corneal healing and improve secretion and quality of all the three components of the tear-film. They are safe drugs with minimal side effects (stinging and burning upon instillation) after prolonged usage, in comparison to the topical steroids that can be safely used for dry eyes for only 1-2 weeks. Since the tacrolimus eye drops are not available commercially, the 0.03% skin cream (Crolimus by Valor pharma) was prescribed to all cases, to be applied into the lower conjunctival fornix twice daily.

Patients with associated meibomitis[18] were advised warm wet towel application to closed eyelids twice daily; the heat melts the thick meibum and opens up the clogged duct orifices. They were also instructed to scrub the lid margin with baby shampoo, after the hot fomentation, so as to remove the melted toxic meibum and massage tetracycline eye ointment into the lid margins at night to control the associated inflammation of the meibomian glands and the eyelids. For the severe cases of MGD, oral tetracyclines (Doxycycline 100 mg/day for 6 weeks) were also prescribed. In patients with severe ocular pain or discomfort, topical diclofenac sodium 0.1% eye drops three times a day was added to the therapeutic armamentarium; this not only reduces the ocular discomfort but has an additive anti-inflammatory affect.

Filaments on the ocular surface can be dissolved by using topical or oral mucolytic agent like N-Acetylcysteine[19] which is a derivative of the natural amino acid L-cysteine. It is frequently used in acute and chronic broncho-pulmonary disease. It exerts its affects by opening up the disulfide bonds in mucoproteins, thereby lowering the viscosity of mucous, inhibiting collagenase enzymes that are secreted by inflammatory cells and cause corneal thinning by melting collagen, by chelating calcium or zinc, it inhibits MMP-9 secretion, thereby inhibiting the inflammatory cytokine responses and reducing ocular surface inflammation.

Hence, Acetylcysteine has multiple beneficial effects in filamentary keratitis. It is available in Europe and USA commercially. A recent preparation, Chitosan-N-Acetylcysteine[20] has been used in various studies with remarkable results in dry eyes associated with filamentary keratitis. Unfortunately, no commercially prepared eye drops are available locally in the market, and it has to be prepared on request by a compounding pharmacist. It is readily available as tablets and in sachets containing powder (Mucolyte 200 mg) that is water soluble. It is a relatively strong acid and cannot be applied directly to the ocular surface, but only after being suitably neutralised. The prepared solution should have a neutral pH between 6.6-7.5. The solvent used for preparing the solution and neutralisation should not increase the osmolarity from an initial value of 241 mOsm/kg (of the powdered form) to more than 300 mOsm/kg. The 5% or 10% N-Acetylcysteine solution that has been used in various studies had a much higher osmolarity of > 1000 mOsm/kg. We previously used 0.5% preparation but that also caused a lot of stinging in the eyes upon instillation. It is due to the high osmolarity

of these preparations which irritates the inflamed, irritable ocular surface. The 5% eye drops cause a lot of ocular surface irritation (manifested as stinging, burning on instillation of eye drops and an increase in punctate epithelial erosions) and potential corneal damage as the tear fluid is already hypertonic in patients with the dry eyes syndrome.

In this study, we used a diluted preparation of 0.3% Acetylcysteine eye drops, freshly prepared by our compounding pharmacist. The pH was kept at 7 and osmolarity of the prepared solution at 300 mosmol/litre. The patients were instructed to keep the freshly prepared eye drops refrigerated at 2-8ºC. to avoid decomposition of the solution. It not only dissolved the corneal filaments efficiently within 2-4 weeks in all group A cases but helped in restoring the quality of mucin, so that further formation of filaments was not noted in cases that continued using it for at least 6-8 weeks even after the filaments had cleared up. Recurrence was noted in only 3 cases who abruptly stopped Acetylcysteine. It also helped in improving the overall OSDI score, the tear-film BUT and corneal staining in all group A cases. This was because the diluted preparation was well tolerated with no ocular discomfort or stinging, thus ensuring a good patient compliance. The marked improvement in patient's symptoms and clinical signs was particularly noticeable early within 2-4 weeks in cases with VKC, post-cataract surgery and exposure keratopathy due to facial palsy and Thyroid eye disease.

This was in comparison to the 26 group B cases in which despite the usual treatment protocol for dry eyes, the absence of a mucolytic agent delayed the clearance and further production of filaments. The filamentary keratitis persisted for 8-10 weeks despite using lubricants, Tacrolimus and tetracycline eye ointment so the ocular discomfort failed to show a remarkable improvement. The other parameters assessed also failed to show as much improvement as in Group A cases. There was no possible bias in the study as the lead ophthalmologist conducting the study was totally unaware as to which cases were using 0.3% Acetylcysteine eye drops or placebo.

Manual debridement of filaments can be performed under topical anaesthesia, using a fine-tipped forceps at the slit lamp. But it was not done in any case in our study as pulling upon the corneal filaments causes traction on the corneal epithelial cells, resulting in more damage to the underlying epithelium with shearing of their basal lamina; this increases the ocular surface inflammation (by the release of cytokines from the damaged epithelial cells) and further promotes the adherence of mucus as well as recurrent filament formation.

CONCLUSION

Filamentary keratitis is a chronic, recurrent, and debilitating condition. With the correct and a systematic approach to diagnosis and management, the acute condition can be effectively controlled and the incidence and severity of recurrences minimised. Certain important points highlighted by this study need to be kept in mind while managing such patients:

1) Acetylcysteine eye drops constitute an integral part of the therapy of filamentary keratitis due to any cause. 0.3% Acetylcysteine eye drops efficiently clear up the filaments and are well tolerated by the patients, thus ensuring a better compliance to therapy. Manual removal of corneal filaments should be avoided.
2) The therapy has to be continued for at least 6 weeks even after the filaments have cleared up, to avoid recurrence.
3) Filamentary keratitis can be induced or exacerbated by systemic medications and ocular surgery, particularly in the elderly age group. Therefore, a pre-operative assessment for dry eyes should be considered in the surgical planning of such patients by tear film break up time and Schirmer's test.

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