Int Ophthalmol (2019) 39:1345–1353
https://doi.org/10.1007/s10792-018-0953-8

ORIGINAL PAPER

Changes in ocular surface status after phacoemulsification in patients with senile cataract

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Received: 15 August 2017 / Accepted: 11 June 2018 / Published online: 20 June 2018
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Abstract
Aim To evaluate the signs and symptoms of dry eye after phacoemulsification; effects on the status of ocular surface using impression cytology; and associated risk factors.
Methods Prospective study included 50 eyes (50 patients) with no dry eye signs or symptoms, who underwent clear corneal phacoemulsification for senile cataract. Dry eye indices used included Ocular Surface Disease Index scoring, Schirmer I test, tear break up time, tear meniscus height, corneal fluorescein staining, lissamine green staining and goblet cell density (GCD) with the help of impression cytology. Primary outcome measures included post-operative changes in the dry eye indices. Secondary outcome measures included correlation of the dry eye signs and symptoms with various risk factors.
Results Aggravation of both the signs and symptoms of dry eye were noted in immediate post-operative period. The sharp deterioration was followed by a recovering trend towards the end of sixth week. A decrease in GCD was also noted. Risk factors for deterioration include age, duration of exposure to microscope light and effective phacoemulsification time. Diabetic status, socio-economic status and site of incision did not have any effect on dry eye status.
Conclusion There is a transient deterioration of "dry eye" status post-phacoemulsification. The patients should be carefully counselled about the evanescent nature of the disease. Incision can be given at the site of high corneal curvature to neutralize astigmatism without any fear of inducing dry eye. Minimum light exposure and ultrasound energy should be used during the surgery.

Keywords Phacoemulsification · Dry eye · Goblet cell density (GCD) · Impression cytology · Ocular Surface Disease Index (OSDI)

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Introduction

Ocular surface disorders are among the most common causes of ocular discomfort [1]. International Dry Eye Workshop (DEWS) defined "dry eye" as a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play aetiological roles [2]. The symptoms may range from mild eye strain to sight threatening complications.

Cataract surgery is one of the most cost-effective interventions in the field of medicine, resulting in immediate visual rehabilitation [3]. In spite of good visual gain, ophthalmologists come across a large number of unhappy and unsatisfied patients. Most patients complain of grittiness and soreness of eyes after the surgery. This occurs due to trauma to the ocular surface during the surgery [4].

Several authors have reported loss of corneal sensitivity after extracapsular cataract extraction (ECCE) and refractive surgeries associated with construction of flap [4–6]. However, incisions constructed during phacoemulsification are small, which theoretically spares the ocular surface [7]. Several publications report aggravation of dry eye after phacoemulsification; however, not many authors have reported its incidence [8–14]. Kasetsuwan et al. [8] reported, after 1-week after phacoemulsification, the proportion of patients (with 95% confidence interval) with abnormal Ocular Surface Disease Index (OSDI) to be 9.8% (3.6–16.0%), abnormal tear break up time (TBUT) to be 68.4% (52.9–83.9%), abnormal Oxford staining to be 58.7% (47.2–70.1%) and abnormal Schirmer I test (ST-I) to be 11.9% (3.4–20.4%). Only few studies have been done to evaluate the ocular surface, with the help of impression cytology, after phacoemulsification [11, 13, 15].

The literature yields meagre evidence on risk factors associated with the incidence of dry eye after phacoemulsification. The risk factors studied include the diabetic status of the patients; location of the corneal incision; and microscope light exposure time and cumulative dissipated energy during phacoemulsification. Diabetic status of the patient has been found to be a risk factor for the incidence of dry eye [16, 17]. All the studies have unanimously found that the location of the incision has no effect on the incidence of dry eye [10]. There have been contradicting findings on the correlation of various dry eye parameters with microscope light exposure time and cumulative dissipated energy [10, 14]. No study has been done to evaluate if the socio-economic status of the patient has any effect on the ocular surface status after phacoemulsification.

This study was done to evaluate the incidence of dry eye after phacoemulsification; and correlation with age, diabetic and socio-economic status of the patient; site of incision, duration of exposure to microscopic light and effective phacoemulsification time (EPT).

Materials and methods

This was a prospective study done after taking approval from the Institutional Review Board. The study adheres to the tenets of Declaration of Helsinki. It included 50 eyes of 50 consecutive patients, who underwent phacoemulsification with intraocular lens implantation for senile cataract between September 2014 and December 2014 by two surgeons (SKA and AR) at Government Medical College and Hospital, Chandigarh. The patients with any previous ocular surface surgery, presence of any ocular surface scarring or opacity, any sign(s) or symptom(s) of dry eye or history of use of any topical eye drops 1 month prior to the surgery were excluded from the study.

All the patients were operated under the same microscope, i.e. S7 OPMI VISU 160 (Carl Zeiss Meditec AG, Jena, Germany) with a halogen light source (12 V, 100 W). Also, both the surgeons followed the same surgical protocol. Clear corneal tunnel incision was made with the help of 2.8-mm disposable keratome blade, according to the keratometry values. Post-operative medications included topical moxifloxacin hydrochloride, 0.5% QID; nepafenac ophthalmic suspension, 0.1% TDS; and prednisolone acetate, 1% every 2 hourly in tapering dose. Further, patients were excluded in case of intra-operative complications like posterior capsule rupture, inability to put intraocular lens (IOL) in bag; post-operative complications like toxic anterior segment syndrome, endophthalmitis; accidental prescription of tear supplements or subjects lost to follow-up before 6 weeks.

Dry eye symptoms were evaluated by OSDI scoring, while dry eye signs were graded according to ST-I, TBUT, tear meniscus height (TMH), corneal fluorescein staining (CFS) and lissamine green (LG) staining. The Oxford Scheme was used to grade the staining pattern of both the dyes [18]. Goblet cell density (GCD) was measured with the help of impression cytology (IC). The study eye was anesthetized using one drop of 0.5% proparacaine ophthalmic solution. Lids were held away using an eye speculum. Topical anaesthesia was taken to be complete when the patient could open the eye comfortably with speculum inserted. Excess fluid from the eye was wiped off with a swab-stick. Nitrocellulose membrane strips with 0.22 mm pore size were placed on the inferior bulbar conjunctiva. Inferior site was chosen for specimen collection to minimize the effects of the incision used for the cataract surgery on the results of impression cytology [15]. The filter paper was brought into contact with the ocular surface, and uniform pressure was given for 10–15 s. The filter paper was then removed with peeling motion so that the goblet cells get attached to the filter paper. Filter paper was immediately transferred into test tube containing 95% alcohol for at least 2 h and then stained with periodic acid–Schiff (PAS) for identification of goblet cells. The number of goblet cells was counted in 3 adjacent rectangular fields under 10× magnification under light microscopy. The density of goblet cells was graded into 0+, 1+, 2+ and 3+ according to Nelson's classification of squamous metaplasia (Fig. 1) [19].

All the tests were performed pre-operatively and then at post-operative week 2, 4 and 6 by the same observer. All the tests were done at a 10-min interval to minimize reflex tearing secondary to the previous one [20]. Schirmer's test was done at the last as mechanical manipulation of the lid is extremely invasive and may create variability in the results of further tests [21]. Diagnosis of dry eye was considered in case of OSDI score $\geq$ 33, ST-I $\leq$ 10, TBUT $\leq$ 10 s, TMH $\leq$ 0.3 mm and CFS score $\geq$ 3 [22].

Primary outcome measures included post-operative changes in OSDI scoring, ST-I, TBUT, TMH, CFS, LG staining and GCD. Secondary outcome measures included correlation of the dry eye signs and symptoms with age, diabetic status and socio-economic status of the patient; site of the corneal incision; duration of exposure to microscopic light and effective phacoemulsification time (EPT) used during the surgery.

As the incidence of dry eye is higher in individuals above the age of 60 years, the patients were divided into two age groups [23–26]. Group A included patients below 60 years and Group B included patients above 60 years. The site of corneal incision was divided into superior, temporal and supero-temporal. Any incision given 20° on either side of the vertical axis was considered superior, 20° on each side of the horizontal axis was considered temporal, while area between superior and temporal was considered supero-temporal. Duration of exposure to microscopic light was calculated as the difference between the time from the start of surgery and the end of surgery. EPT was noted from the phacoemulsification machine. The socio-economic status of the patients was defined according to the most commonly used scale in India, i.e. the modified Kuppuswamy scale [27]. Based on the scale, we divided the patients into two classes, i.e. upper-to-upper middle and lower middle-to-lower on the basis of a score calculated on the basis of the education and the occupation of the head of the family and the monthly income of the family.

Statistical analysis

Statistical analysis was performed with STATA statistical software, version 11.1 (StataCorp, College Station, Texas, USA). Continuous variables were expressed as mean (± SD), and categorical variables were expressed as percentages. Any difference in continuous data between 2 groups was seen with help of Student's *t* test/Mann–Whitney test, while difference between more than 2 groups was seen with help of analysis of variance (ANOVA). Pearson and

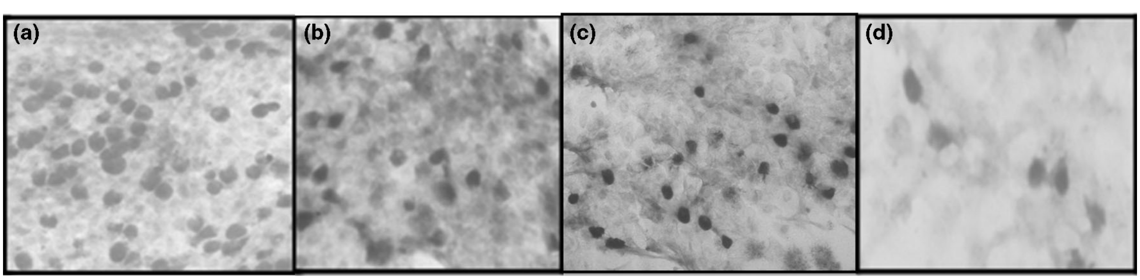

Fig. 1 Prototype of Nelson's classification of squamous metaplasia used for Goblet cell density grading with the help of impression cytology. The images were taken at 40× magnification. **a** Grade 0+, **b** Grade 1+, **c** Grade 2+, **d** Grade 3+

Spearman correlation test(s) were used to determine the association between parametric and nonparametric variables, respectively. A p value of less than 0.05 was considered to be statistically significant.

Results

The study group included 24 males (48.0%) and 26 females (52.0%). The average age was 60.60 ± 8.42 years (42–74 years). While 20 (40%) patients were ≤ 60 years of age, 30 (60.0%) were > 60 years of age. Seventeen patients (34.0%) were diabetics, while 33 (66.0%) were non-diabetics. Twenty (40.0%) patients belonged to lower-to-lower middle, while 30 (60.0%) belonged to upper middle-to-upper socio-economic status according to the modified Kuppuswamy socio-economical scale. The location of the corneal incision was superior in 20 (40.0%) patients, supero-temporal in 22 (44.0%) and temporal in 8 (16.0%) patients.

Mean EPT used during the surgery was 20.43 ± 8.89 s (4.8–43.1 s). Mean duration of light exposure was 28.66 ± 6.69 min. While 32 patients were exposed to the light of the microscope for ≤ 30 min, 18 patients were exposed to > 30 min. OSDI score ≥ 33 at week 2 in patients exposed to light for ≤ 30 and > 30 min was 25.0% (n = 8/32) and 50.0% (n = 9/18), respectively. SI-T score, i.e. ≤ 10 at week 2 in patients exposed to light for ≤ 30 and > 30 min was 28.1% (n = 9/32) and 83.3% (n = 15/18), respectively. TBUT ≤ 10 seconds at week 2 in patients exposed to light for ≤ 30 and > 30 min was 68.8% (n = 22/32) and 83.3% (n = 15/18), respectively. TMH ≤ 0.3 mm at week 2 in patients exposed to light for ≤ 30 and > 30 min was 21.9% (n = 7/32) and 55.6% (n = 10/18), respectively. TMH ≤ 0.3 mm at week 2 in patients exposed to light for ≤ 30 and > 30 min was 37.5% (n = 12/32) and 77.8% (n = 14/18) respectively.

All the dry eye signs and symptoms worsened after the cataract surgery (Fig. 2, Table 1). The percentage of patients with abnormal dry eye symptoms, i.e. OSDI score ≥ 33 was 32% at post-operative 2 weeks. However, the percentage of patients with abnormal dry eye signs like SI-T score, i.e. ≤ 10, TBUT ≤ 10, TMH ≤ 0.3 mm, CFS grade ≥ 3 and patients taking LG stain at second post-operative week was 48.0, 48.0, 34.0, 54.0, and 48.0%, respectively. The percentage of patients with OSDI score ≥ 33 was 14.0% at post-operative 6 weeks. However, the percentage of patients with SI-T score, i.e. ≤ 10, TBUT, i.e. ≤ 10, TMH ≤ 0.3 mm, CFS grade > 3 and patients taking LG stain at sixth post-operative week was 24.0, 28.0, 26.0, 22.0 and 30.0%, respectively. The mean GCD score increased from pre-operative value of 0.52 ± 0.76 to 1.60 ± 0.93 at second post-operative week and decreased to 0.78 ± 0.74 at sixth post-operative week (Table 1).

The percentage of patients below the age of 60 years with OSDI score ≥ 33, SI-T score, i.e. ≤ 10, TBUT, i.e. ≤ 10, TMH ≤ 0.3 mm, CFS grade > 3 and patients taking LG stain at second post-operative week was 15.0, 5.0, 50.0, 20.0, 15.0, and 15.0%, respectively. On the contrary, the percentage of patients above the age of 60 years with OSDI score ≥ 33, SI-T score, i.e. ≤ 10, TBUT, i.e. ≤ 10, TMH ≤ 0.3 mm, CFS grade > 3 and patients taking LG stain at second post-operative week was 46.7, 76.7, 93.3, 46.7, 76.7, and 73.3%, respectively (Fig. 3). However, there was no clinically significant correlation between worsening of the dry eye signs and symptoms with socio-economic status of the patient.

All the dry eye signs and symptoms correlated inversely with the EPT and the duration of exposure to light of the microscope at all post-operative visits (Table 2). However, there was no clinically significant correlation between worsening of the dry eye signs and symptoms with the site of incision. The mean GCD grade did not correlate with any of the factor(s) at any point of post-operative time.

Discussion

Phacoemulsification is the most commonly performed ocular surgery. Although the patients are restored with complete vision, few patients complaint about eye fatigue and foreign body sensation. This results in poor patient satisfaction, artificial tear drop abuse, as well as risk of drug-related epithelial toxicity. This study was undertaken to evaluate the incidence of dry eye after phacoemulsification using various dry eye indices; effects on the status of ocular surface using impression cytology; and associated patient-related and intra-operative risk factors.

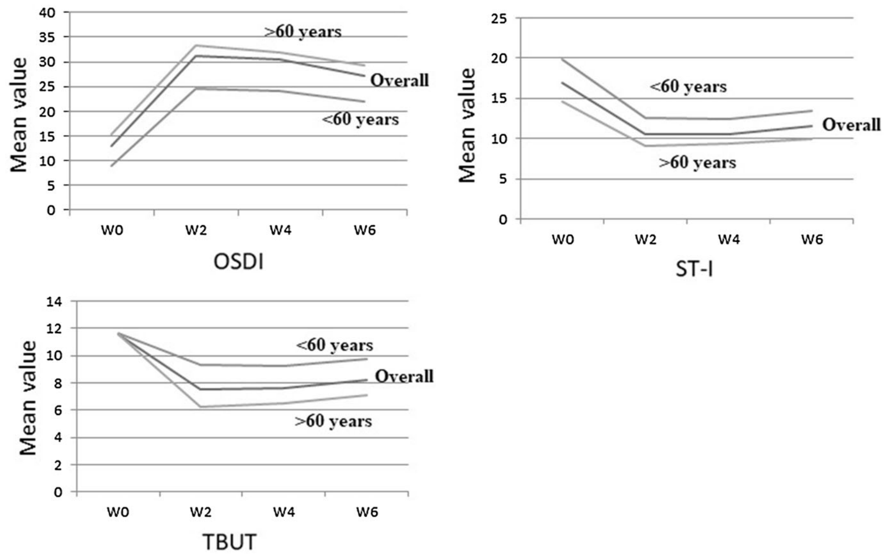

Fig. 2 Mean Ocular Surface Disease Index (OSDI) scores, mean Schirmer's test (SI-T) scores and mean tear break up time (TBUT) scores pre-operatively and at two, four and six post-operative weeks. There are 3 lines in each graph, showing the mean values of overall patients, patients above the age of 60 years and patients below the age of 60 years

Table 1 Change in dry eye indices after surgery

	Pre-operative	Post-operative week 2	Post-operative week 4	Post-operative week 6	*p* value (ANOVA)
Mean OSDI score	12.91 ± 4.73	31.25 ± 9.16	30.43 ± 8.66	27.27 ± 8.00	< 0.001
Patients with OSDI ≥ 33	0	16 (32.0%)	11 (22.0%)	7 (14.0%)	
Mean SI-T score	16.86 ± 2.01	10.60 ± 2.40	10.62 ± 2.28	11.50 ± 2.52	< 0.001
Patients with SI-T ≤ 10	0	24 (48.0%)	18 (36.0%)	12 (28.0%)	
Mean TBUT	11.58 ± 0.95	7.50 ± 2.50	7.62 ± 2.29	8.20 ± 2.17	< 0.001
Patients with TBUT ≤ 10	0	24 (48.0%)	18 (36.0%)	14 (68.0%)	
Patients with TMH ≤ 0.3 mm	0	17 (34.0%)	15 (30.0%)	13 (26.0%)	
Mean CFS grade	0	2.48 ± 1.01	2.18 ± 0.87	1.86 ± 0.77	< 0.001
Patients with CFS grade > 3	0	27 (54.0%)	16 (32.0%)	11 (22.0%)	
Patients taking lissamine green stain	0	24 (48.0%)	21 (42.0%)	15 (30.0%)	
Mean GCD grade	1.60 ± 0.93			1.14 ± 0.88	< 0.001

ANOVA analysis of variance, *OSDI* Ocular Surface Disease Index, *ST-I* Schirmer I test, *TBUT* tear break up time, *TMH* tear meniscus height, *CFS* corneal fluorescein staining, *GCD* goblet cell density

Similar to the previous studies, this study also noted an aggravation of both the signs and symptoms of dry eye after clear corneal incision phacoemulsification [8, 10–14, 23, 28, 29]. The creation of incisions in the cornea causes dry eye by destabilising the tear film by making the ocular surface uneven as well as decreasing the tear secretion by injuring the corneal nerve supply. This sharp aggravation of dry eye was followed by a recovering trend, starting from the sixth week. This trend is similar to that reported by other authors [8, 11–13, 17, 25]. This transient nature of the "post-surgery dry eye" may be explained by the fact that the inflammatory cytokines also induce the synthesis of a number of neurotrophic factors. This stimulates the regeneration of corneal nerves in few weeks [30].

In contrast to the incidence of post-phacoemulsification dry eye calculated by Kasetsuwan et al. [8], the proportion of patients with abnormal ST-I and OSDI were higher in our study, and the proportion of patients

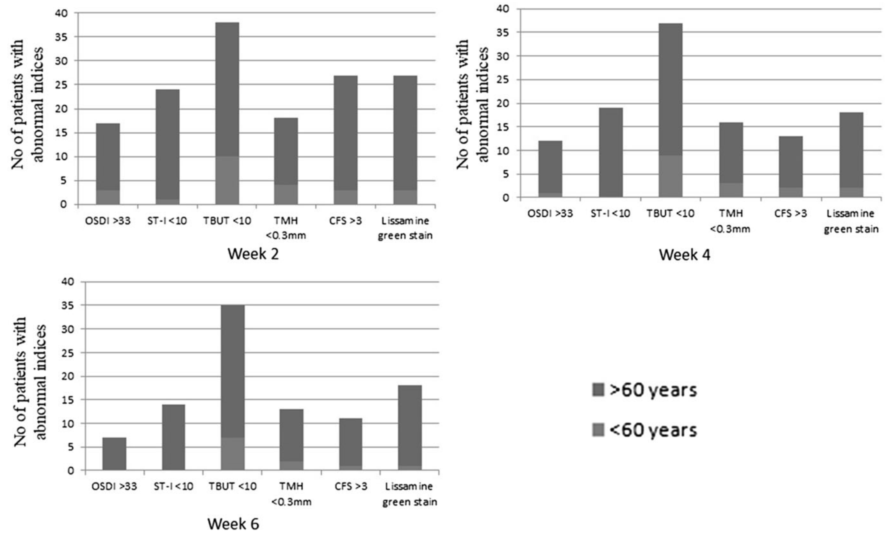

Fig. 3 Number of patients of with abnormal ocular findings at two, four and six post-operative weeks. The indices include Ocular Surface Disease Index (OSDI) score, Schirmer's test (SI-T) value and tear break up time (TBUT)

Table 2 The post-operative correlation of dry eye indices with effective phacoemulsification time and duration of exposure to microscope light

	Post-operative week 2	Post-operative week 4	Post-operative week 6	*p* value
Effective phacoemulsification time (EPT)				
Mean OSDI	0.337	0.328	0.356	< 0.020
Mean SI-T values	− 0.429	− 0.463	− 0.453	< 0.002
Mean TBUT values	− 0.528	− 0.569	− 0.516	< 0.001
Mean CFS grades	0.570	0.521	0.589	< 0.001
Duration of exposure to light of microscope				
Mean OSDI	0.349	0.395	0.396	< 0.015
Mean SI-T values	− 0.489	− 0.476	− 0.417	< 0.003
Mean TBUT values	− 0.355	− 0.397	− 0.368	< 0.011
Mean CFS grades	0.463	0.502	0.489	< 0.003

OSDI Ocular Surface Disease Index, *ST-I* Schirmer I test, *TBUT* tear break up time, *CFS* corneal fluorescein staining

with abnormal TBUT and Oxford staining were similar. The number of patients with abnormal dry eye signs was much higher than those reporting symptoms. Studies have proved that only half of the patients who show evidence of dry eye on the basis of signs have symptoms consistent with dry eye [31].

Several studies have found a higher incidence of dry eye in older population [23–26]. Similarly, we also found a higher incidence among the elderly population. Similar to Trattler et al. [32], we also found that the older patients had at least occasional symptoms of dry eye, but had OSDI score < 33. Further, we found that the patients with no signs and symptoms of dry eye and ≥ 60 years of age developed abnormal dry eye signs and symptoms more commonly than the patients ≤ 60 years of age, after phacoemulsification. Also, the pattern of recovery was much slower in the patients ≥ 60 years of age. This slower recovery among the older patients can be because of the reduced ability of tissue to regenerate with age.

Khurana et al. [33] found a higher incidence of dry eye among the patients belonging to poor socio-economic status. However, we found that there was no increased risk of dry eye in patients belonging to poor socio-economic status, after phacoemulsification. This presumptively indicates that nutrition plays an insignificant role in the development of dry eye after phacoemulsification.

We found that the diabetic status of the patient has no effect on the incidence of dry eye after phacoemulsification. This finding was different than found in the previous two studies [16, 17]. In the study by Liu et al. [16], the diabetic patients had a lower post-operative score of the various dry eye indices. However, the diabetic patients had lower pre-operative values of TBUT and ST-I than the non-diabetic ones. Jiang et al. reported a higher incidence of post-operative dry eye after in diabetic patients, on the basis of abnormal OSDI, SI-T and TBUT values, at 1-week and 1-month intervals. However, their criterion for dry eye had much lower threshold for all the indices as they diagnosed dry eye when OSDI score > 15, ST-I value < 7 and TBUT value < 7 [17].

Similar to other authors, no significant difference was found between the incidence of dry eye with respect to location of the incision [10]. Hence, the practice of constructing clear corneal incisions in the steeper meridian should be adopted to neutralize the astigmatism without any fear of inducing dry eye.

There have been contradicting findings on the correlation of various dry eye parameters with microscope light exposure time and cumulative dissipated energy [10, 14]. The light from microscope can cause dry eye due to the production of reactive oxygen species due to phototoxic effects of operating microscope, which can cause devitalization of corneal and conjunctival epithelial cells, squamous metaplasia of the conjunctival epithelium and decrease in conjunctival goblet cell density [34]. The phacoemulsification energy can aggravate dry eye due to free radical formation, which may cause damage to corneal structures such as the epithelium, stroma, keratocyte, endothelium and nerve plexuses [35]. We found a significant correlation between the dry eye test values and microscopic light exposure time as well as phacoemulsification energy used. Cho and Kim [10] found a significant correlation between microscopic light exposure time and dry eye test values, but no correlation between phacoemulsification energy and dry eye test values. On the other hand, Sahu et al. [14] found no significant correlation between dry eye test values and either of the two factors. The difference could be because of the fact that both the above-mentioned studies used a keratome of 3.2 mm while we used a keratome of 2.8 mm.

The IC results showed goblet loss and squamous metaplastic transformation of the conjunctival epithelial cells during the post-operative period. This occurs due to setting up of a vicious cycle of hypo-tearing leading to inflammation causing cell damage [4, 10]. The reduced tear production and increased evaporation due to damage to corneal nerve supply increases the osmolarity of the tear film. This starts an inflammatory process on the ocular surface, leading to release of multiple cytokines and chemokines causing cell damage. This cell damage further multiplies the inflammatory processes, setting up a vicious cycle. The inflammatory environment causes squamous metaplasia of ocular surface epithelial cells causing a decrease in goblet cell differentiation [10, 36]. Oh et al. [13] found a greater decrease in the GCD, if the duration of surgery was longer. However, we did not find such a correlation.

The results of this study give an idea about the incidence of "transient" dry eye and the effect on GCD after phacoemulsification. Further, it highlights the risk factors associated with a higher incidence of dry eye. The patients should be carefully counselled about the evanescent nature of the disease and the need for dry eye treatment. Limitations of the study were its small sample size, short follow-up and inability to evaluate the toxic effect of preservative-containing eye drops in the post-operative period as the patients who needed to use more than three eye drops were excluded.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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