Original Research Article

Conjunctival impression cytology as an assessment of ocular surface changes following manual small incision cataract surgery

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Abstract

Purpose: To determine the changes inocular surface following manual small incision cataract surgery. **Setting:** Department of Ophthalmology, Sri Venkateswara Medical College, Tirupati. **Design:** A prospective study **Methods:** The study was conducted in 100 eyes of 100 patients. All selected patients without dry eye symptoms preoperatively and who underwent uncomplicated cataract surgery were included in the study. They were studied for tear film breakup time (TBUT), ocular surface staining by Rose Bengal (RB) staining method, and conjunctival impression cytology (CIC) from inferior bulbar conjunctiva. Tests were performed 1 day before and 1wk, 1month and 3months after manual small incision cataract surgery (SICS). **Results:** Majority of the study participants were aged between 51- 60 years (51%) with the female predominance. In 8 % of the patients, lower TBUT values were recorded at 3 months postoperative follow up, with statistical significance ($P<0.01$). There was a statistically significant difference in ocular surface changes with RB staining between preoperative and postoperative 1 week, 1 month, and 3 months follow up ($P<0.002$). On CIC, 12%, 49%, 46% of patients showed abnormal grades (grade2 or 3) at 1 week, 1 month, and 3 months postop respectively with a statistically significant value ($P < 0.03$). **Conclusion:** Patients undergoing manual SICS without having dry eye preoperatively, showed changes in ocular surface and tear film stability. Positive test with RB staining and abnormal grading of goblet cells studied by CIC during the postoperative period had shown that compromised ocular surface health after SICS, which can produce dry eye.

Keywords: CIC, TBUT, SICS, Ocular surface, Impression cytology

Introduction

Dry eye is a common condition affecting the tear film and ocular surface. The 2007 International Dry Eye Workshop stated that ‘‘dry eye is a multifactorial disease of the tear film and ocular surfacethat results in symptoms such as ocular discomfort, visual disturbance, and potential damage to the ocular surface”. [1] Conjunctival Goblet cells, the chief source of mucinis most dense nasally, least dense in the upper temporal fornix and absent at the palpebral mucocutaneous junction and limbus. “The density of goblet cells is 10±3 cells/mm^2 [2]. In developing countries like India, manual SICS with intraocular lens implantation is considered as a safe surgical procedure which provides good postoperative outcomes.However, after cataract surgery, many patients complain of irritation, foreign body sensation, redness, blurring of vision which is considered as unwanted effects of the surgery [3].

Although the precise mechanism(s) for postoperative dry eye is not completely understood, past studies have suggested that eyes with this type of abnormality have a short TBUT [4], a decrease in the density of goblet cells [5], as seen in eyes with conventional dry eye syndrome [6], A decrease in goblet cell density will also reduce mucin secretion and disrupt the tear film stability consequently lead to dry eye.

Purpose of this study was to determine the effects of small incision cataract surgery on the ocular surface assessed by conjunctival goblet cells with impression cytology, causing the tear-film instability and dry eye.

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Materials and methodology:

Study setting- The study was conducted in the Department of Ophthalmology, Sri Venkateswara Medical College, Tirupati.

Study Design- A prospective study

Study period- The study period was between December 2014 and June 2016. Ethical committee approval was obtained from the institutional ethical committee (IEC). Written informed consent was taken from all patients included in the study.

Inclusion criteria: All patients who were above 50 years of age and who underwent uneventful manual SICS were included in the study.

Exclusion criteria: The patients with pre-existing dry eyes, rheumatoid arthritis, Sjogren's syndrome and other autoimmune disorders and patients with pre-existing ocular diseases like uveitis, glaucoma, ocular allergies, disorders of the lid or the nasolacrimal pathway, pterygium and previous ocular surgeries and patients with surgical complications were excluded from the study.

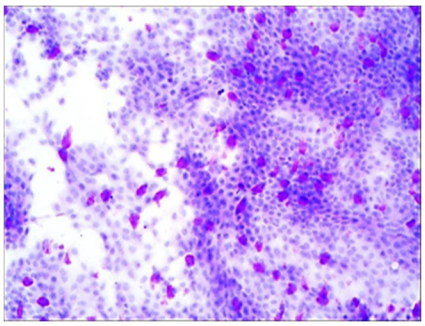
Clinical examinations included comprehensive and extensive anterior segment evaluation done under slit lampto excludeany pre-existing ocular surface disease. TBUT, RB staining, and CIC were done. The patients were started on topical and systemic antibiotics one day before surgery. On the day of surgery, 0.8mg tropicamide, and 10% phenylephrine eye drops were used to dilate pupils 90 minutes before cataract surgery.

Manual SICS was performed under 2 point peribulbar block. The standard incision was 6 to 6.5 mm in length and 1.5 to 2 mm from the limbus. Implantation of a rigid PMMA intraocular lens was done in all the patients. A standard postoperative regime was followed for all the patients. It included the use of steroid-antibiotic combination in tapering doses for eight weeks. Postoperative evaluation was done at 1week, 1month, and 3 months. At each visit TBUT, RB staining, CIC was done.

Tear film break up time measurement (TBUT): The TBUT measures the interval between the last complete blink and the first appearance of the dry spot over cornea using cobalt blue filter after application of 2% fluorescein dye under slit-lamp biomicroscopy. Three TBUT readings were noted, and an average of the readings was calculated.If TBUT less than 10 seconds it is considered as adry eye.

Rose Bengal stain (RB): It is a measure of assessing ocular surface change using the Rose Bengal dye.A commercially available, sterile Rose Bengal strip moistened with 4% Xylocaine solution was applied to the inferior cul de sac.The eye was examined after15 sec for staining of conjunctiva and cornea under a bright light or red-free light under the slit lamp. Van Bijsterveld scoring system was used to grade, based on a scale of 0-3 in 3 areas: cornea, nasal conjunctiva, and temporal conjunctiva. A quantitative scale of 0 to 3 was used in each area of the eye. An additive score of 4 or more in the eye considered a positive test for dryness of ocular surface.

Conjunctival impression cytology (CIC): Conjunctival impressions were taken from inferior bulbar conjunctiva. **Procedure***:* The test was conducted using cellulose acetate strips having a pore diameter of 0.45 µm with the patient in supine position.A drop of 4% lignocaine was instilled in the eye. After inserting a wire speculum, Millipore cellulose acetate filter strips were cut into 3x10mm size pieces with a diagonal edge and were applied on the inferior-nasal bulbar conjunctiva with the help of a blunt smooth-edged forceps. The specimens were collected from the inferior bulbar conjunctiva. The rough surface of the paper was used, and it was pressed gently by a smooth glass rod. The strip was removed with a peeling motion after 5 seconds. The papers were fixed in a fixative solution (absolute alcohol + glacial acetic acid + 40% formaldehyde in 20:1:1 respectively) and stained with PAS (periodic acid Schiff‟s) and counterstained with hematoxylin. The filter paper was mounted and examined under the microscope and graded. Nelson grading system [7] was followed for staging. **Interpretation:** The eyes having grade 2 or 3 changes were considered positive for dry eye. Eyes with grade 0 or grade 1 change were considered negative [Figure 1, 2, 3].



Figure–1: Microscopic picture showing grade 1 goblet cells

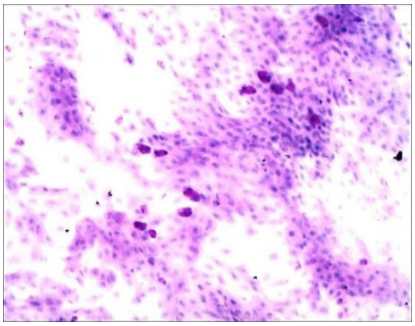


Figure-2: Microscopic picture showing grade 2 goblet cells

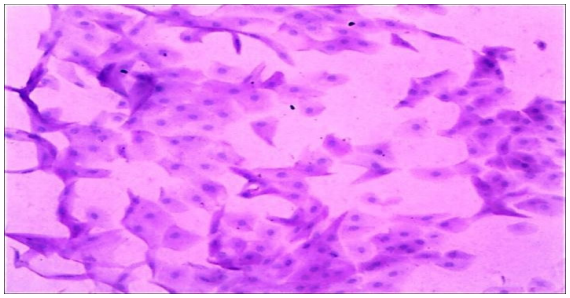


Figure-3: Microscopic picture showing Grade 3: Goblet cells

Statistical analysis: Chi-square test was applied to find significance among qualitative variables. Paired t-test was applied to find significance among quantitative variables and to check preoperative and postoperative results. Descriptive statistics were applied to quantitative variables, Mean and S.D. The Statistical software SPSS 20.0 was used for analyzing the data and Microsoft Word, and Excel 2011 has been used to generate graphs and tables.

Results

All the patients were followed for 3 months postoperatively and assessed for the tear film stability by TBUT, RB staining of the ocular surface and conjunctival goblet cells based on impression cytology. The results of the study were analyzed as below.

In the present study majority (51%) of the study, participants were aged between 51 to 60 years [Figure-4]. Females (59%) outnumbered males (41%).

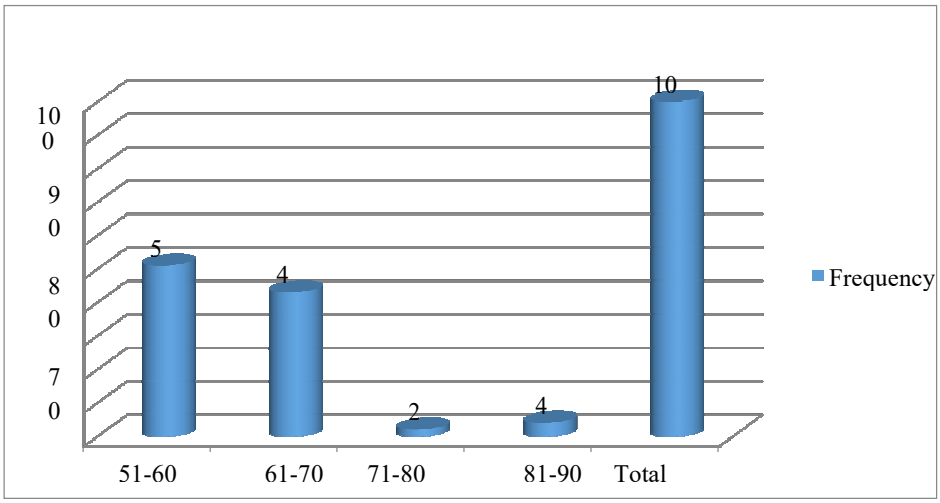


Fig-4: Distribution of study subjects according to age.

The TBUT analysis showed that the preoperative TBUT mean **20.72±5.371** and at postoperative one week, one month and 3 months 6%, 23%, and 8% had low TBUT values respectively. Changes in TBUT were found to be statistically significant through all postoperative periods. In the present study, no patient in the preoperative group had TBUT values in the dry eye range, whereas 6%, 23% and 8% of patients in the postoperative period (1 week, 1 month, and 3 months respectively) had TBUT values in the dry eye range. ($p<0.01$) [Table–1].

Table-1: Comparison of TBUT at Pre-op, Post-op at 1 week, 1 month and 3 months (F: Frequency)

TBUT	Pre-op		Post-op at 1 week		Post-op at 1 month		Post-op at 3 months		t-value	p-value
	F	Mean±SD	F	Mean±SD	F	Mean±SD	F	Mean±SD		
>=10 Normal	100	20.72±5.371	94	17.71±5.028	77	15.15±4.21	92	17.71±4.86	8.33	**P<0.001**
<10 Dry	0	0	6	8±1.09	23	7.30±1.49	8	8±1.85		
Total	**100**		**100**		**100**		**100**			

Ocular surface staining with Rose Bengal stain showed that before surgery, all patients had a rose Bengal stain grading of 0, none of them had abnormal grading. Post-surgerygrading increased to 3 months follow up with statistically significant value at each period [Figure-5].

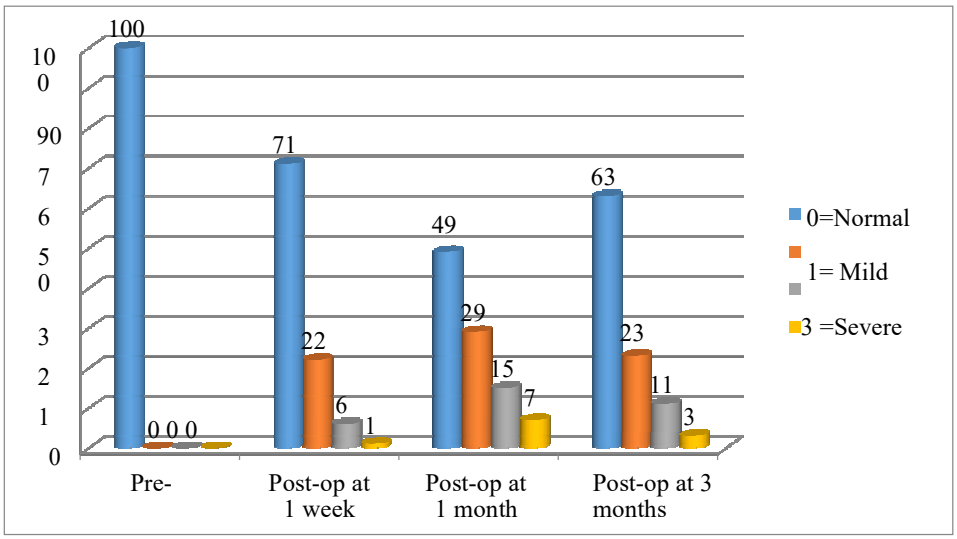


Figure-5: Multiple bar diagram showing RB grades at Pre-op, Post- op at 1 week, 1 month and 3 months

CIC analysis based on Nelson grading system, showed normal grading (grade 0 or 1) preoperatively in all patients, whereas 12%, 49%, 46% of patients showed abnormal grades (grade2 or 3) at post op 1 wk, 1month, and 3 months respectively with a statistically significant value ($P < 0.03$). [Table -2]

Table-2: Comparison of CIC at Pre-op, Post-op at 1 week,1 month and 3 months.

CIC	Pre-op	Post-op at 1 week	Post-op at 1 month	Post-op at 3 months	P - value
0,1=Normal	100	88	51	54	P <0.03
1,2=Abnormal	0	12	49	46	
Total	**100**	**100**	**100**	**100**	

Discussion

A stable and smooth tearfilm is essential for the optimal function of the cornea as a refractive unit of the eye. Dry eye syndrme is a multifactorial disease of the tear film, and ocular surface, which results in visual disturbance, symptoms of discomfort, tear instability with potential damage to the ocular surface. Cataract surgery is known to disrupt the ocular surface and alter the tearfilm quantitatively and qualitatively [3, 4].

The present studyshowed that manual SICS influences the ocular surface changes and thereby tearsfilm instability. The prospective study was conducted on 100 patients who underwent SICS. For these 100 patients, various parameters were used to assess the tear film stability preoperatively and postoperatively at 1 week, 1 month, and 3 months. Out of the 100 patients who underwent SICS, 95% belonged to 51-70 years age group. Females (59%) were more compared to males (41%).

Concerning the tear film break up time (TBUT). In the present study, the TBUT in all the patients preoperatively was in the normal range. During the post-op period, 6% of the patients, 23% of the patients and 8% of the patients at 1wk, 1month and 3 monthsrespectively had TBUT valuesin dry eye range ($p<0.01$). The lowest value of TBUT was noticed at 1 month, and after 3 months there was a slight improvement in value again.

Chandan C et al [8], and Mohana S et al [9], in their study also found a lower value of TBUT at 1month follow up. In a study by Chandan C et al. [8], TBUT values decreased in the postoperative period to statistically significant levels. In a study by Mohana S et al [9], TBUT values significantly decreased at 1 week, 1 month, and reached near normal values at 3 months. In the present study, 92% of the patients showed normal TBUT values at 3 months postoperative period. In a study by Li XM et al [4], Srinivasan R et al [10] Liu Z et al [11], and Ram et al [12], it had shown that significant decreasein TBUT value post operatively after phacoemulsification. In a study by Neda A et al [13], which was done to examine the dry eye after cataract surgery, there was a decrease in TBUT values postoperatively.

Ocular surface staining in the present study by the Rose Bengal staining did not show any abnormality in any of the patients, where as 29%, 51% and 37% of patients in the postoperative 1 week, 1 month, and 3 months respectively had abnormal RB staining. In a study by Oh et al [5], RB staining showed a similar pattern. In a study by Yusuf Rizvi et al [14], Corneal staining studied by fluorescein stain scores differed significantly frombaseline values in the postoperativeperiod of one month. Corneal staining pattern differed in the SICS group but notthe phacoemulsification group at day 60.

However Staining scores were not significantly different from pre-operative levels at day 90, for SICS aswell as phacoemulsification group suggesting aquiescent surface. This is similar to the studies conducted by Li, et al [4] and Ram, et al [12]. However, Liu et al [11], found that fluorescein staining increased in the 1st-week follow-up visits and decreased in the next visits subsequently. In a study by P.K. Sahu et al [15], showed that postoperatively, the lissamine grading increased till 1-month, then found a reversal trend, with statisticallysignificant values at each period.

In the present study, the CIC assessmentshowed significant changes postoperatively. CIC showed abnormality in none of the cases preoperatively, whereas 12%, 49% and 46% of cases showed abnormality at postoperative 1week, 1month, and 3 months, respectively ($p<0.03$). Similar to the present study, Oh T et al [5], had shown that mean goblet cell density reduced significantly at 1 day, 1 month and 3 months postoperatively ($p<0.01$).

In a study by Li et al [4], CIC demonstrated that even 3 months after the cataract surgery, goblet cells were reduced along with squamous metaplasia which suggests that dry eye might have been induced by eye drops. In a study by Mohan S et al, mean number of goblet cells found in CIC was 214.92, and the standard deviation was 54.59 preoperatively in the control group. At the end of 3 months mean a number of goblet cells did not show much change in the control group whereas in the study group number of goblet cells decreased significantly from 223.37±148.61 to 163.79±61.47 at 3 months [9].

The changes in ocular surface and tear film function following cataract surgery causing dry eye to the patient may be due to mechanisms like chronic use of eye drops following the cataract surgery due to the presence of preservatives [16], tear film irregularity at the site of incision which causes tear film to break up faster or the mucin production from conjunctiva may be decreased, exposure to light from operating microscope [3, 17], misuse of eye drops [18, 19], decreased corneal

sensations (a study by Donnenfeld ED et al [20]. disrupting the corneal lacrimal gland loops resulting in decreased tear secretion and the incision might result in severing of the corneal nerves which cause decreased corneal sensation (a study by Kohlhaas M et al [21].

The major limitations of the present study were short-term follow up (3 months), long-term effects were not evaluated., The subjective symptoms of dry eye OSDI scoring were not considered as part of the study. The effect of preservative free eye dropsafter cataract surgery on the ocular surface was not studied.

Conclusion

The present study suggests that manual SICS with Corneo-scleral incision has effects on the ocular surface and tear film stability. Goblet cell study by impression cytology showed abnormal grading postoperatively compared topre-op grading. The decrease in goblet cell density and altered morphology had not recovered at 3 months post op of cataract surgery. Therefore, ocular surface damage during and after cataract surgery appears to be one of the pathological factor causing ocular discomfort and dry eye syndrome after cataract surgery with corneo-scleral incision.

Ocular surface instability is the leading cause of dissatisfaction among cataract patients postoperatively. Dry eye is the disease of the ocular surface and the tear film, which results in symptoms such as ocular discomfort, visual disturbanceandpotential damage to the ocular surface.

Because cataract surgery has been shown to exacerbate orinduce pre-existing ocular surface changes and dry eye, it is of significanceto physicians to be vigilant of the syndrome while evaluating cataract patients, to plan surgery accordingly and treat the condition preoperatively and post operatively.

The improved stability and quality of the tearfilm results in a regular ocular surface and improve refractive outcomes after cataract.

What the study adds to the existing knowledge?

The present study, Conjunctival impression cytology as an assessment of ocular surface changes following manual small incision cataract surgery suggests that CIC is more sensitive for evaluation of ocular surface changes and detect early subtle changes in the ocular surface in post-cataract surgery patients.

Author's contribution

Dr. SreeLakshmi Pallamreddy: Design of the study, Data collection, Data analysis and interpretation, Drafting the article, Revision of the article, Approval of the manuscript to be published.

Dr. C.S. Sandhya: Design of the study, Data analysis and interpretation, Drafting the article, Revision of the article, Approval of the manuscript to be published

Dr. C. Jagannath: Data analysis and interpretation, Revision of the article, Approval of the manuscript to be published

Dr. K. Madhavi: Design of the study, Data collection, Data analysis and interpretation, Approval of the manuscript to be published

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Permission from IRB: Yes

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