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EVALUATION OF THE ROLE OF 1% CARBOXYMETHYLCELLULOSE AFTER PHACOEMULSIFICATION AMONG NORTH INDIAN POPULATION: A PROSPECTIVE, RANDOMIZED, PLACEBO CONTROLLED STUDY

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Abstract:
Patients undergoing phacoemulsification with intraocular lens implantation present with dry eye symptoms postoperatively. The present study was done to evaluate the role of carboxymethylcellulose 1% added to conventional therapy to treat ocular discomfort and tear film instability in patients after cataract surgery.
Methods: A prospective, placebo controlled study of 150 patients with age-related cataract after undergoing phacoemulsification with intraocular lens implantation were postoperatively randomized to treatment with conventional therapy plus CMC 1% (study group, n = 75) or to conventional therapy plus 0.9% NaCl
(Control group, n = 75). Tear film breakup time (TBUT), schirmer test without anesthesia, lissamine green staining and ocular surface disease index (OSDI) scoring were done preoperatively (baseline) and postoperatively at 7 and 30 days.
Results: A significant increase in TBUT in the study group as compared to the control group on both day 7 and day 30 was seen ($p<0.0001$). The OSDI score on day 30 decreased in study group but increased in control group. Schirmer test showed an increase in both the groups on day 7. Day 30 recorded a significant increase in the study group and a decrease in the control group ($p<0.0001$).
Conclusion: The present study thus concludes that dry eye can develop immediately after phacoemulsification with a peak on day 7. However, use of 1% carboxymethylcellulose stabilizes the tear film and thus prevents development of dry eye.
Keywords: 1%carboxymethylcellulose, phacoemulsification, dry eye, TBUT, OSDI.

Introduction:

For centuries cataract surgery has been practiced and has evolved significantly over the course of time. With the advancement of medical technology, phacoemulsification with intraocular lens implantation has become a routine procedure, reducing the period of hospitalization and hastening visual rehabilitation with less postoperative astigmatism and early stabilization of refraction compared to manual extracapsular cataract extraction.[1]

Though cataract surgery has given innumerable patients a good visual acuity, many patients present with foreign body sensation, fatigue, red or watery eyes postoperatively. These are the symptoms of dry eye disease which affect the daily activities such as reading, driving and working with computer, thereby decreasing the quality of life.[2] The incidence of dry eye after phacoemulsification is about 9.8%.[3]

Dry eye is 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 etiological roles.[4]

Many factors associated with cataract surgery adversely affect the ocular surface environment such as use of preservative containing eye drops, corneal incision causing disruption in corneal innervations, prolonged exposure to intense light from the operating microscope and thermal energy generated from phacoemulsification devices disease.[5] This contributes to tear film instability after cataract surgery which can lead the tear film into a vicious cycle of tear/cell hyperosmolarity, inflammation and apoptosis of conjunctival and corneal cells.[6] Postoperative reduction in goblet cell density has been shown in some studies. There is still debate as to how this happens. Some attribute it to misuse of

eye drops as this was more marked in the regions covered by lower lid[7], whereas many others believe inflammation to be the most likely culprit. The phototoxic effect of the light of operating microscope causes production of reactive oxygen species, leading to devitalization of conjunctival cells and decrease in conjunctival goblet cell density.[8]

Conventional topical therapy following cataract surgery includes topical corticosteroids (to manage inflammation) and antibiotics.[2] Topical corticosteroids commonly used postoperatively are dexamethasone and betamethasone in the form of drops and bed time ointment. They are used in combination form with fourth generation fluoroquinolone like moxifloxacin and gatifloxacin.

Carboxymethylcellulose (CMC) is a high-molecular-weight polysaccharide composed of glucopyranose subunits with anionic charge and is one of the most common viscous polymers used in artificial tears. It has lubricating and mucoadhesive properties that contribute to its prolonged retention time on the ocular surface. It has been seen to remain bound to human corneal epithelial cells for 2 hours through interaction between glucopyranose subunits and glucose transporters. Its efficacy has been shown in managing aqueous tear-deficient dry eye symptoms. This is a dose dependent effect with greater improvement seen with 1% CMC (mid-viscosity) as compared to 0.5% CMC.[9] The mid-viscosity artificial tear is rated well in terms of comfort, duration of effect and general acceptability.[10] Besides, CMC has been found to facilitate corneal epithelial wound healing.[9]

Normal saline 0.9% can be used as an adequate vehicle for dry eye study. The osmolarity of tears is 302 ± 6.2 mOsm/L which is isotonic with that of 0.9% normal saline (308 mOsm/L). Therefore, normal saline 0.9% does not interfere with the ocular surface environment and acts just to lubricate the eye.[11] Because of this property it can be used as a control for our study without interfering with the results.

The effectiveness of corticosteroids in managing dry eye after cataract surgery has also been evaluated. They decrease the symptom of ocular irritation, decrease corneal fluorescein staining, and improve goblet cell number and filamentary keratitis.[12] Literature research shows that only a few studies have been carried out to assess the addition of artificial tears to conventional therapy for treatment of dry eye after cataract surgery.[2] The present study was undertaken to evaluate the role of carboxymethylcellulose 1% added to conventional therapy to treat ocular discomfort and tear film instability in patients after cataract surgery.

METHOD

It was a prospective, randomized, placebo controlled study of 150 patients with age related cataract, above 50 years of age and of either sex, who underwent phacoemulsification surgery with posterior chamber intraocular lens implantation in a tertiary hospital. The Institutional Ethical Committee clearance was obtained for the study in reference.

Patients with a history of any ocular surgery within 3 months prior to enrolment, allergy to any of the study mediations, infectious disease, Contact lens use, history of any ocular chemical or thermal burn, Stevens-Johnson syndrome, ocular pemphigoid, glaucoma or ocular hypertension, eyelid or lacrimal disease and history of any serious systemic disease were excluded from the study. Patients were withdrawn from the study if they experienced complications during surgery or postoperatively.

After obtaining an informed written consent from all the patients enrolled in the study, they were equally divided by block randomization into two groups-study and control group, by the observer. A detailed history of all the patients, their general physical examination and a detailed ocular examination (diffuse examination under torch light and slit lamp examination) was done. Preoperatively tear film break up time (TBUT), Schirmer test without anesthesia, Ocular Surface Disease Index (OSDI) scoring and lissamine green staining were done. All the patients underwent phacoemulsification surgery by 2.8mm clear corneal incision with posterior chamber intraocular lens implantation. Postoperatively, all the patients were started on dexamethasone sodium phosphate 0.1% in combination with moxifloxacin hydrochloride 0.5%, 6 times a day. The study group (group 1) in addition received 1% carboxymethylcellulose to be instilled four times a day. The control group (group 2) was given placebo (normal saline solution 0.9%) four times a day. Patients were evaluated on day 7 and 30. All the above mentioned tests were repeated. A cut-off value of 10 seconds for TBUT was taken as normal. For schirmer test, a value between 10mm to 30mm was taken normal and <5mm as hyposecretion. For lissamine staining, grading was done according to oxford scheme. Patients were

diagnosed as having dry eye if Tear film break up time was <10 sec or, Schirmer test value was <10mm or, Ocular surface disease index score was >25.

After obtaining the data, a comparison in the test values was done between two groups and within two groups. In order to detect differences between subjects the t-test (normal distribution) and the Wilcoxon rank sum test (non-normal distribution) was used for continuous variables while, for categorical variables, the chi-square (χ^2 test) was used. A p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 16.0 (SPSS Inc., Chicago, Illinois) and MedCalcStatistical Software, version 18.10.2. A flow algorithm of the study is shown in fig 1.

RESULTS

The demographics of both the groups in the study are shown in table 1.

Table 1: Demographics of patients in both the groups

Groups	Age of patients (years) (Mean ± Standard Deviation)	Sex distribution		Eye operated	
		Male	Female	Right	Left
Study	61.04 ± 8.19	35 (46.67%)	40 (53.33%)	42 (56%)	33 (44%)
Control	61.39 ± 7.77	42 (56%)	33 (44%)	40 (53.33%)	35 (46.67%)
p-value	0.791	0.191		0.622	

On comparing schirmer test values, a significant increase (p<0.0001), from the baseline was seen in both the groups on day 7 (table 2).

Table 2: Group comparison for Schirmer test and tear film break-up time preoperatively and after cataract surgery.

	SCHIRMER TEST			TEAR FILM BREAK UP TIME		
Clinical assessment	Mean ± Standard Deviation (mm)		p-value (comparison between two groups)	Mean ± Standard Deviation (mm)		p-value (comparison between two groups)
	Treatment group	Control group		Treatment group	Control group	
Pre-operative	14.75 ± 1.95	14.23 ± 1.42	0.064	12.08 ± 1.41	12.20 ± 1.49	0.613
1st visit	21.31 ± 2.49	20.47 ± 1.72	0.018	13.92 ± 1.29	9.57 ± 1.39	<0.0001
2nd visit	16.20 ± 2.07	13.77 ± 1.31	<0.0001	14.73 ± 1.45	10.73 ± 1.41	<0.0001
Change from pre-operative at 1st visit	**7.50 ± 1.17 (<0.0001)**	**7.00 ± 0.98 (<0.0001)**	0.071	**4.50 ± 0.70 (<0.0001)**	-2.00 ± 1.14 (0.078)	<0.0001
Change from pre-operative at 2nd visit	**1.00 ± 0.55 (0.002)**	0.00 ± 0.87 (0.421)	<0.0001	**2.00 ± 1.10 (<0.0001)**	**-1.00 ± 0.64 (0.001)**	<0.0001

On day 30, the values were still significantly raised in the study group from the baseline (p=0.002) but were reduced in control group (p=0.421). The intergroup comparison for change in schirmer test values from baseline showed no significant result on day 7 (p=0.071). Statistically significant change in the test value between two groups was observed only on day 30 (p<0.0001).

The TBUT increased significantly from the baseline in the study group on both the follow-up visits (p<0.0001), but decreased from the baseline on both the visits in control group (table 2). This decrease was insignificant (p=0.078) on day 7 but significant on day 30 (p=0.001). A statistically significant (p<0.0001) change in the test value was observed between the two groups on all the postoperative visits.

Lissamine green staining score showed a decrease from the baseline on day 7, which was statistically significant (p=0.045) in both the groups (table 3). The second follow up (day30) showed a further reduction in the score from the baseline was not statistically significant in both study group (p=0.080) and control group (p=0.099). There was an insignificant change in the lissamine green staining scores between the groups in any of the follow-up visits.

The OSDI score increased significantly on day 7 in both study group (p<0.0001) and control group (p<0.0001) (table 3).

Table 3: Group comparison for lissamine green staining test and OSDI score preoperatively and after cataract surgery.

Clinical assessment	LISSAMINE GREEN STAINING			OSDI SCORE		
	Mean ± Standard Deviation (mm)		p-value (comparison between two groups)	Mean ± Standard Deviation (mm)		p-value (comparison between two groups)
	Treatment group	Control group		Treatment group	Control group	
Pre-operative	0.13 ± 0.41	0.15 ± 0.46	0.851	12.75 ± 3.50	12.76 ± 3.11	0.980
1st visit	0.08 ± 0.32	0.09 ± 0.34	0.803	19.97 ± 3.97	21.45 ± 3.57	0.017
2nd visit	0.05 ± 0.23	0.05 ± 0.23	1.000	8.35 ± 2.67	12.96 ± 2.85	<0.0001
Change from pre-operative at 1st visit	**0.04 ± 0.23 (0.045)**	**0.04 ± 0.23 (0.045)**	1.000	**8.00 ± 1.81 (<0.0001)**	**9.00 ± 1.75 (<0.0001)**	<0.0001
Change from pre-operative at 2nd visit	0.00 ± 0.27 (0.080)	0.00 ± 0.34 (0.099)	0.790	**-3.00 ± 2.07 (<0.0001)**	0.00 ± 1.08 (0.231)	<0.0001

The second follow up visit showed a significant reduction in score in the study group (p<0.0001) which on the contrary was insignificant in control group (p=0.231). A statistically significant difference between two groups was seen on day 7 (p=0.017) and day 30 (p<0.0001).
Preoperatively, none of patients had dry eye in both the groups (table 4).

Table 4: Patients falling under Dry Eye

Follow up visit	Patients falling under the dry eye criteria			
	Treatment group		Control group	
	No. of patients	Percentage	No. of patients	Percentage
Preoperatively	0	0	0	0
First follow up visit	10	13.33	34	45.33
P-value		<0.0001		
Second follow up visit	0	0	16	21.33
P-value		<0.0001		

In the study group, dry eye was seen in 10 patients (13.33%) on day 7 and in none on day 30. In control group dry eye was seen in 34 patients (45.33%) on day 7 and in 16 patients (21.33%) on day 30. This difference in between both the groups was significant on both the follow up visits (p<0.0001).

DISCUSSION

In our study, increase in TBUT was significant in the study group on both day 7 (p<0.0001) and day 30 (p<0.0001), which corroborated with the study of Yao K et al.[2] Also, our study showed a decrease in TBUT values in control group on day 7 and 30, similar to study conducted by Saif MYS et al. [1]

Gupta M et al. in his study reported significant compromise in the TBUT values on day 7 (p<0.05) and day 30 (p<0.05) without the use of carboxymethylcellulose drops.[13]This decrease in the value from the baseline on day 7 was statistically significant in their study but not in our study. This difference was attributed, by them, to the use of topical eye drops with preservatives in their study. Whereas, no preservative containing eye drop was used in our study postoperatively.

Schirmer test values in our study showed a decrease on day 30 in the control group which was in accordance with the study carried out by Chao PMG et al.[14] In the study conducted by Yao K et al. schirmer test without anesthesia was done and values on day 7 showed a reduction in both the groups, this change was not statistically significant (p=0.6620) which was contrary to our study.[2] This can be due to the fact that our study included schirmer test without anesthesia, thus measuring reflex tear secretion as well. In their study, the study group showed an increase of 0.0±5.4mm from the baseline but control group showed reduction of 0.1±5.6mm in values on day 30, which was in agreement with the results of our study.

No significant difference in the lissamine staining score between two groups on day 7 (p= 0.803) and day 30 (p=1.000) was observed in our study comparable to study conducted by Yao K et al.[2]

Our study showed statistically significant increase in OSDI score from baseline in the control group on day 7 (p<0.0001) but not on day 30 (p=0.231). Similar results were obtained in study by Kasetsuwan N et

al.[3] The study conducted by Kohli P et al also showed an increase in values postoperatively, similar to our study.[8]

When compared to the previous studies in the literature, patients falling under dry eye criteria postoperatively were less in our study. This could be because of the difference in the size and site of incision. In our study we used a 2.8mm superior clear corneal incision. In the study conducted by Cho YK et al. 3.2 mm size corneal incision was made in the temporal or superior location.[15]The size of incision was comparatively more, which may be responsible for greater transection of nerves. In another study conducted by Kasetsuwan N et al.2.75mm temporal incision was made.[3]The temporal incision causes transection of large corneal nerve bundles which enter at 9 o'clock position. Thus, a higher reduction in the test values was seen in their study. The mean TBUT value reduced from 12.15sec to 4.59sec on day 7 and to 5.11 on day 30. Similarly OSDI score increased from a mean of 12.57 to 33.87 on day 7 and then decreased to 17.34 on day 30. Our results were comparatively better than their study.

There were certain limitations in our study. First schirmer test without anesthesia was done. So reflex tearing was included. Secondly, the patients in the study and control groups were not divided into subgroups according to their degree of dry eye severity. They were evaluated as one group statistically. This might mask the subgroups which might behave differently from the group as a whole. Third limitation was a short follow up period.

CONCLUSION

The present study thus concludes that dry eye symptoms can develop immediately after phacoemulsification with a peak on day 7. However, use of 1% carboxymethylcellulose stabilizes the tear film and thus prevents development of dry eye. Artificial tears should be used in addition to the conventional antibiotic-steroid therapy, after cataract surgery to prevent ocular surface damage as well as to provide symptomatic relief to the patients from dry eye and improve patient satisfaction. We further recommend increased sample size, increased follow-up time and the study to be carried out in a different geographical location to find the generalisability of the study results.

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