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The course of dry eye following phacoemulsification and manual-SICS: a prospective study based on Indian scenario

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不同术式治疗白内障患者术后干眼情况比较

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摘要

目的:从主客观方面比较超声乳化术(PKE)和手法小切口白内障手术(SICS)术后致干眼的研究,并对致病因素进行分析。

方法:单中心前瞻性研究。选取2013-07/2014-12接受同一医生治疗白内障手术及人工晶体植入术患者,100例患者100眼分为两组(第一组:50例50眼手法小切口白内障手术患者;第二组:50例50眼超声乳化术患者)。术后所有干眼患者都作表记录,从主客观方面评估其第1、4、12wk术后干眼情况,并分析其致病诱因。

结果:干眼测试(DET)值在主客观方面无显著差异($P>0.05$)。相较于各自术前值,尽管期间无显著变化($P>0.05$),两组在第12wk目标干眼测试值呈持续下降趋势($P<0.05$)。超声乳化术在第12wk结束时干眼测试值更主观。

结论:白内障术后干眼症是不可避免的。在术后12wk前超声乳化术组和手法小切口白内障手术组术后干眼测试值影响相似。进一步研究需要更多样本、更长随访时间的随机多中心临床试验来证实。

关键词:超声乳化术;手法小切口白内障手术;干眼测试;术后干眼

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Abstract

• AIM: To evaluate and compare subjective and objectively, the course of surgically induced dry eye following both phacoemulsification (PKE) and manual-small incision cataract surgery (SICS) procedure, and to analyze the result in terms of causative factors.

• METHODS: This single centre prospective study included 100 eyes of 100 patients randomly divided into two groups (Group 1, SICS-50 patients; Group 2, PKE-50 patients), who underwent cataract surgery with intraocular lens (IOL)-implantation from Jun. 2013 to Dec. 2014 for a period of one and half year by single surgeon. In all patients post operative course of dry eye were tabulated and assessed at 1, 4, 12wk, subjectively and objectively, and thereafter analyzed in terms of possible causative factors. Statistical data were calculated using SPSS 23.0 Windows software.

RESULTS: There was no significant preoperative intergroup difference in subjective and objective dry eye test (DET) values ($P>0.05$). Both the groups showed similar trend of persistently declining objective DET-values till at the end 12wk, as compared to their respective preoperative values ($P<0.05$), although there were no significant intergroup changes seen throughout the postoperative period ($P>0.05$). PKE seems to have better subjective DET-value at the end of 12wk.

• CONCLUSION: Dry eye disease is inevitable following cataract surgery. Both PKE and SICS, can affect the dry eye test values in almost similar manner post operatively till up to 12wk. Randomized multicentre trial with larger cohort and longer follow-up is warranted to substantiate our findings.

• KEYWORDS: phacoemulsification; manual small incision cataract surgery; dry eye test; postoperative dry eye

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INTRODUCTION

In 2007, the International Dry Eye Workshop defined dry eye disease (DED) as "a multifactorial disease of the tears and ocular surface that results in symptoms of

discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolality of the tear film and inflammation of the ocular surface"[1].

DED is especially common in the elderly, occurring in approximately 5-30% of the general elderly population, women more commonly than men, and the symptoms may range from blurred vision, foreign body sensation, pain, injection, reflex lacrimation, and in severe cases loss of vision[2]. There are several reports of aggravation of dry eye status following cataract surgery[3-4].

In the Indian context where high volume cataract surgery is still a priority, cataract operations have substantially increased from 16 lakh in 1992-1993 to 59.1 lakh in 2009-2010 according to the annual report 2010-2011 of National Programme for Control of Blindness (NPCB)[5]. Especially, in those base-camp surgeries governed by NPCB, manual sutureless small incision cataract surgery (SICS) due to its low cost, less instrumentation, faster speed, easier in harder grade cataract, easy learning curve, lesser complications still remain the preferred surgical technique and found to be "equally effective" to phacoemulsification (PKE)[6-7].

Several Meta-analysis concluded, PKE have no edge over SICS in terms of efficacy, safety, cost effectiveness, complications, attainment of best corrected visual acuity (BCVA) in the long term, higher grades of cataract, and total surgical time[8-10]. While the former is still being increasingly practiced especially in the western countries, exclusively because of its advantage of earlier refractive stabilization, reduced astigmatism[11].

Till date, most of the postoperative dry eye or tear film related studies reported in literature are oriented to PKE, related to the corneal sensitivity changes, location or level of incision (grooved or shallow), ultrasound energy consumption or microscope light exposure[3-4,12-13]. But, after extensive search we found only one published single centre Indian cross-sectional study on SICS-induced dry eye, and that too incorporating agriculture-based small cohort who are continually exposed to wind, sunlight and high temperature[6].

Extensive database search reveals only few isolated published data, comparing both the techniques in their course of postoperative dry eyes, which varies grossly in regard nature, duration of study, sample size, criteria of exclusion, material used, or geographical setting[14-16].

The present study had an aim to evaluate and compare subjective and objectively, the course of surgically induced dry eye following both PKE and SICS procedure, and to analyze the result in terms of possible causative factors.

MATERIALSAND METHODS

This study was a single centered prospective comparative study, from Jun. 2013 to Dec. 2014 for a period of one and half year, and has been carried out on patients attending outpatient department (OPD)-clinic in the Medical college associated department of Ophthalmology of North India, which is situated 2 200 feet height from sea level (Latitude-30.3165°N, Longitude-78.0322°E).

This study adhered to the tenets of Declaration of Helsinki. After getting the approval of the Institutional Ethics Committee and written informed consent, 100 eyes of 100 patients with senile cataract of aged between 45-75 years having no prior subjective or objective evidence of dry eye syndrome (DES), and who routinely visited all follow up dates postoperatively, were included in this study and were randomly divided into two groups: 1st group with 50 cases of SICS and 2nd group with 50 cases of PKE. Surgery requiring prolong time and complicated surgeries were excluded from our study.

Demographic information was recorded. Preoperatively, slit lamp biomicroscopy (to rule out lid margin disease or ocular surface disorders), and dry eye tests (DET); DET's [Schirmer's test 1 (ST1); Tear film break-up time (TBUT); Lissamine green stain scoring (LGSS)] were carried out, in all the patients, and postoperatively at 1wk, 4wk, and 12wk, DET were repeated, and patients were subjectively evaluated for dry eye symptoms on the basis of ocular surface index (OSDI) questionnaire.

Technique All the surgeries in both the groups were done by the same surgeon (SDG), having experience of performing at least 5000 SICS and PKE. Moxifloxacin 0.5% and Flubiprofen eye drop were used from 1 day prior to surgery, and pupil was dilated by Tropicamide and phenylephrine 0.5% eye drop from 2h before surgery. All surgeries were done under peribulbar block. In SICS, 6-6.5 mm frown shaped scleral incision was placed superiorly 2 mm behind the limbus extending 2 mm up to the clear cornea , whereas in PKE 3-3.2 mm clear corneal incision was made at superotemporal location. Two 1 mm size paracentesis were made 40 degree apart from main incision in PKE and only one paracentesis of approx 3 mm was made in SICS. In SICS rigid PMMA, whereas in PKE foldable Acrylic IOL, was implanted. Ocular surface was taken care of by intermittent irrigation by assistant throughout the surgery, as par surgeon's demand. Lower fornix Subconjunctival injection of antibiotic and steroid was given at the end of surgery. Postoperatively, all patients had received Moxifloxacin 0.5% eye drop 4 times/day for 15 days, and prednisolone acetate 1% eye drops 8 times/day tapered over 6 weeks. Data were collected, recorded (Table 1), and analyzed using statistical Windows software (SPSS 23.0 Inc., Chicago, IL, USA). Test for significance (P value) was set at <0.05. Values were expressed mean with standard deviation. Paired-t and Fisher's exact test were applied for data interpretation.

a) for (OSDI) questionnaire. The symptoms which were relevant to the dry eyes were analyzed and the severity of dry eye status was inferred; b) for ST1, value less than 10 mm was considered abnormal; c) for TBUT, less than 10 sec was considered abnormal. Average of three such readings were

Table 1 Dry eye severity grading scheme (DEWS-2007)

Dry eye severity level	1	2	3	4[a]
Discomfort, severity & frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
ST1(mm/5min)	Variable	<10 mm	<5 mm	<2 mm
TBUT(sec)	Variable	<10 sec	<5 sec	immediate
LGS	None to mild	Variable	Moderate to marked	Marked

ST1: Schirmer's test 1; TBUT: Tear film break-up time; LGS: Lissamine green staining; [a]must have signs and symptoms.

Table 2 Pre andpostoperative DET-values for SICS

Tests	Pre-op	1wk	4wk	12wk	*P*
ST1	20.92±5.60	11.96±1.93	10.38±1.57	9.66±1.67	<0.05
TBUT	11.46±1.72	7.88±1.89	6.74±1.42	6.22±1.48	<0.05
LGS	1.58±0.92	8.04±1.22	9.66±1.37	10.04±1.85	<0.05

ST1: Schirmer's test 1; TBUT: Tear film break-up time; LGS: Lissamine green staining.

taken to be as final; d) LGSS was evaluated using the Oxford scheme of grading staining, where six areas of the interpalpebral conjunctiva were graded based on a six-point scale, taking maximum combined score of 30 for each area.

Above tests data were graded based on the guidelines of International Dry Eye Workshop (DEWS, 2007)[1].

RESULTS

One hundred eyes of 100 patients that included 47 males and 53 females between age group of 45 - 75y were studied prospectively for post-cataract surgery dry eye changes over a period of 18mo, from Jun. 2013 to Dec. 2014.

Among 50 patients in Group 1, there were 23 (46%) males and 27 (54%) females, and among 50 patients in Group 2, there were 24 (48%) males and 26 (52%) females. Intergroup gender distribution difference was insignificant (P=1.000). The mean age range in Group 1 was 63.10±8.35y and in Group 2, 61.84±8.26y. This difference was insignificant (P=0.4499).

Pre-operative ST1, TBUT, and LGSS were 20.92±5.60, 11.46±1.72, 1.58±0.92 respectively in Group 1, and 20.06±4.64, 11.54±1.58, 1.36±0.72 respectively in Group 2. The corresponding P=0.20, 0.41 and 0.058 respectively, were not significant.

Post-operatively at 1wk, ST1, TBUT and LGSS, in Group 1 were 11.96±1.93, 7.88±1.89, 8.04±1.22 respectively, and in Group 2 were 12.14±1.14, 7.94±2.09, 7.74±1.17 respectively (between group corresponding P=0.28, 0.44, 0.10 respectively, were not significant). At 4wk, in Group 1 the values were 10.38±1.57, 6.74±1.42, 9.66±1.37, and in Group 2 10.64±1.71, 7.02±1.22, 9.36±0.87, respectively (between group corresponding P=0.214, 0.153, 0.076 respectively, were not significant). At 12wk, in Group 1 the values were 9.66±1.67, 6.22±1.48, 10.04±1.85, and 9.72±1.95, 6.56±1.34, 9.80±1.32 in Group 2, respectively (between group corresponding P=0.44, 0.134, 0.22 respectively, were not significant).

Both the groups showed similar trend of persistently declining DET-values till at the end 12wk (Figure 1, 2, 3). Maximum significant changes took place within the first postoperative week (P<0.0001), thereafter at 4wk and 12wk the changes were found significant to a lesser extent (P<0.05; Table 2, 3), as compared to the pre-operative DET-values.

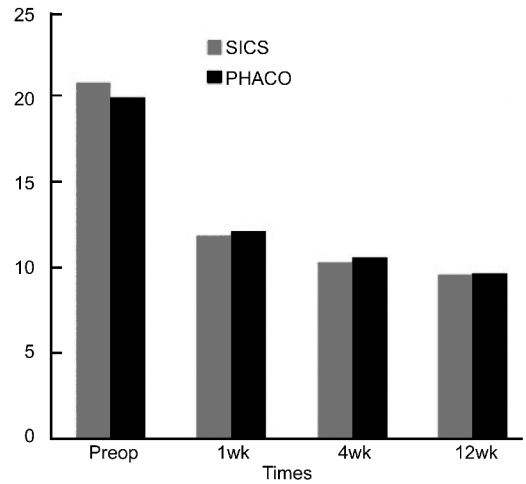

Figure 1 Showing comparison of ST1-value changes in two groups.

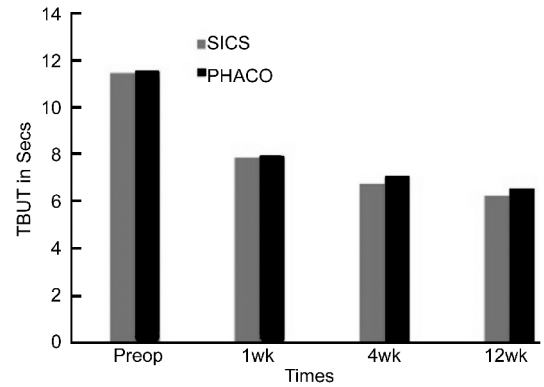

Figure 2 Showing comparison of TBUT-changes in two groups.

While comparing both the groups, there was no statistically significant changes of tear secretion or tear-film stability at any point of time throughout the study (P>0.05; Figure 4, Table 4).

Subjectively, majority of Group 1 patients experienced moderate dry eye (60%) followed by severe dry eye (22%)

Table 3 Pre and Postoperative DET-values for PKE

Tests	Pre-op	1wk	4wk	12wk	*P*
ST1	20.06±4.64	12.14±1.14	10.64±1.71	9.72±1.95	<0.05
TBUT	11.54±1.58	7.94±2.09	7.02±1.22	6.56±1.34	<0.05
LGS	1.36±0.72	7.74±1.17	9.36±0.87	9.80±1.32	<0.05

DET:Dry eye test; PKE: Phacomulsification; ST1: Schirmer's test 1; TBUT: Tear film break-up time; LGS: Lissamine green staining.

Table 4 DET-value comparison between groups at different follow-up periods

Tests	Surg	Pre-op	*P*	1wk	*P*	4wk	*P*	12wk	*P*
ST1	SICS	20.92±5.60	0.20	11.96±1.93	0.28	10.38±1.57	0.21	9.66±1.67	0.44
	PKE	20.06±4.64		12.14±1.14		10.64±1.71		9.72±1.95	
TBUT	SICS	11.46±1.72	0.41	7.88±1.89	0.44	6.74±1.42	0.15	6.22±1.48	0.13
	PKE	11.54±1.58		7.94±2.09		7.02±1.22		6.56±1.34	
LGSS	SICS	1.58±0.92	0.05	8.04±1.22	0.10	9.66±1.37	0.07	10.04±1.85	0.22
	PKE	1.36±0.72		7.74±1.17		9.36±0.87		9.80±1.32	

DET:Dry eye test; ST1: Schirmer's test 1; TBUT: Tear film break-up time; LGS: Lissamine green staining; SICS: Small incision cataract surgery; PKE: Phacoemulsification.

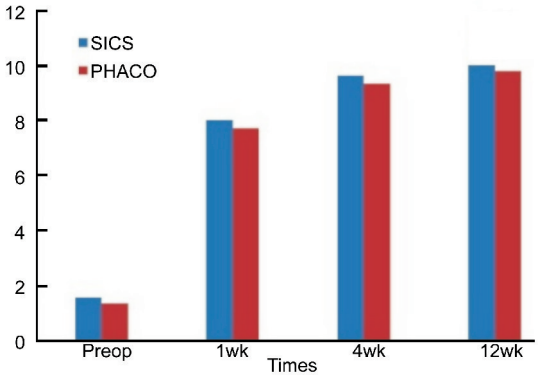

Figure 3 Showing LGS-Score comparison in two groups.

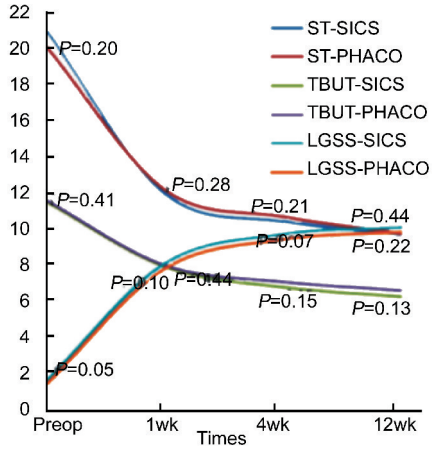

Figure 4 Comparative changes between two groups, at follow-ups.

and mild dry eye (18%), whereas in Group 2 majority (58%) experienced mild dry eye followed by moderate dry eye (28%) and only 9% experienced severe dry eye, at their last visit. In Group 2, 5% patients did not experience any dry eye symptoms at all (Figure 5).

DISCUSSION

The DES is a recognized entity frequently occurs after cataract surgeries. Post cataract surgery quality of vision due to dryness is compromised despite good visual outcome[17].

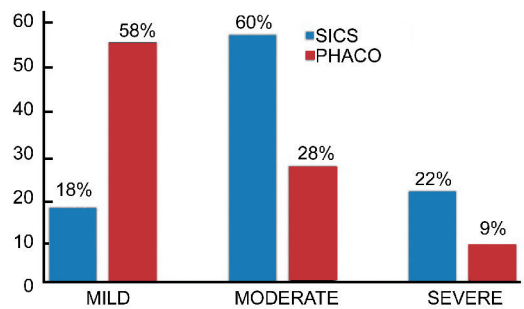

Figure 5 Showing severity of DES, according to OSDI-questionnaire, at 12wk.

There are several mechanisms documented in literature by which post-cataract surgery dry eye develops: 1) as, intact corneal innervation is mandatory for normal tearing reflexes, incision wound from corneal section sever the corneal nerves resulting in decreased corneal sensation, which in turn disrupts the neural circuit up to the Lacrimal gland [Lacrimal functional unit (LFU)] resulting in reduced tear secretion. This is thought to be the major etiopathogenic factor leading to dennervation - induced dry eye[18-19]. Although, incision location has not been found to have any effect but grooved incisions can aggravate DES[4,20]; 2) the tear film instability resulting, either from a surface irregularity at the site of the incision or decrease of mucin production from destruction of conjunctival goblet cells[21]; 3) Benzalkonium chloride, the preservative in eye drops, often destabilizes the lipid layer leading to evaporative dry eye[22]; 4) prolong exposure to light from the operating microscope has also been reported to cause post-operative dry eyes[23]; 5) the use of ultrasound in cataract surgery may further damage corneal structures such as the epithelium, stroma, keratocyte, endothelium, and nerve plexuses[24]; 6) the environmental exposure to excessive wind, sunlight and a high temperature increases the Post-op dry eye status[25].

As, there is no generally agreed "gold standard" diagnostic

test for DES, a pragmatic approach was adopted in all of our patients at each follow-up, by applying standard objective (ST1, TBUT, LGSS) and subjective DET's (OSDI-Questionnaire), as par the subcommittee recommendation laid down by DEWS 2007[1,26] in view of their practicality in general clinic, economy and acceptability.

We preferred Lissamine green over Fluorescein and Rose Bengal, as it stains both conjunctiva as well as cornea effectively, no toxicity reported so far, stains only dead and devitalized cells, and is better tolerated by patient[27].

Although it is advisable by several authors[32] to prescribe artificial tear postoperatively in order to alleviate dry eye symptoms , in our study we did not prescribe artificial tear to any of our patients primarily because they may affect the analysis result, moreover several study reported addition of artificial tear in the postoperative regimen does not necessarily facilitate recovery of tear physiology and corneal sensitivity[4,19].

Irrespective of type of surgery, at 12wk, all of our study population (n = 100) showed statistically significant deterioration of tear secretion and tear stability proven by dry eye test results ($P<0.05$), as compared to their preoperative values. Similar comparative studies by Egyptian author by Saif *et al*[14] and Indian authors Shankar *et al*[16], Mohana *et al*[15] also reported same where all the mean DET-values despite of showing trend of recovery did not return completely to their pre-op values by the end of 3rd month. In contradistinction, meta-analysis on PKE-induced dry eye reported tear film stability (TBUT) did not recover, although tear secretion (ST1) recovered to their pre-op value at the end of 3rd month ($P<0.05$, $P>0.05$ respectively)[28]. Some more studies reported in literature shows varied and confusing results, where authors observed recovery of individual DET values at different time period, even much earlier than the study period[12-13,19,29]. In ours, it is reasonable to speculate that some unknown environmental triggers related to high altitude, might prolong the postoperative dry eye status, as supported by Gupta *et al*[30] where authors observed increased tear film evaporation contributed by high altitude. Role of other contributing factors like, hormonal changes, eyelid laxity, and oxidative stress which are solely prevalent in the geriatric age group, cannot be ruled out, and needs further study by different authors.

Rapid deterioration of all the DET-values were observed in our study in the initial first week postoperatively, in both the groups ($P<0.0001$), which is coexistent with the finding by several authors[14]. The reason can be explained because of the liberation of intense inflammatory mediators desensitizing the corneal sub-epithelial axons with resultant tear-film instability[31]. Thereafter, at 4wk and 12wk the changes were much gradual ($P<0.05$), at par with the healing process where the nerve regenerate slowly due to release of nerve growth factor (NGF).

When compared between groups, changes in DET-values were found to be almost similar at any point of follow-up time, in both the techniques ($P>0.05$) (Table 4; Figure 4). Saif *et al*[14] also observed similar insignificant changes in total 40 patients while comparing between groups, but no explanation was cited for this. Mohana *et al*[15] rather found something different in their study in total 69 patients while comparing between group, and reported PKE marginally better than SICS in objective tests whereas SICS finds an edge over PKE subjectively. Result obtained by Shankar *et al*[16] is still more confusing while comparing between groups in 100 patients, as authors claim that SICS gives better DET-values than PKE, although ocular surface staining was not included in their study. Contrary to our speculation at the beginning of the study, SICS might result significant DET-value changes as compared to PKE because of longer corneal section contributed by conjunctival peritomy and cauterization of bleeders with resultant decrease of corneal sensitivity into higher extent, as observed by Anom-Supradnya *et al*[18] our hypothesis did not work here, which can only be explained by less exposure to operating microscope light because of faster surgical time, and exclusion of ultrasound mediated damage.

Comparative study by Mohana *et al*[15] and Venugopal *et al*[6] reported patients enrolled in SICS-group were symptomatically better than PKE even though in both the groups OSDI-scoring continued to deteriorate, while Saif *et al*[14] reported no one in either group had experience of dry eye symptoms, at the end of 12 weeks . In contrary, at the end of our study, majority of SICS-group patients experienced moderate dry eye (60%) followed by severe (22%) and mild dry eye (18%), whereas majority of PKE-group patients experienced mild dry eye (58%) followed by moderate (28%) and severe dry eye (9%). This may be explained by more number of female cohort (hormonal factors) and aged persons (oxidative stress, tissue laxity) in the former group[32]. Venugopal *et al*[6] observed persistence of mild dry eye symptoms post-SICS in majority (52%) at the end of 12wk, whereas several reports on post-PKE induced symptoms indicates even earlier recovery to pre-op-level[12]. It is a well established fact that OSDI-scoring does not correlate with the traditional objective clinical DET-s, because of lack of sensitivity, but still it has been validated as a tool for measuring the subjective severity of dry eye[33].

Obviously we had some limitations in our study, in that it was a single-center small-group study, further it was not feasible for us to incorporate more DET-variables such as tear osmolality, conjunctival impression-cytology, etc. More multicentre randomized comparative clinical trials are warranted by different authors, especially focusing on the influencing factors like, age, hormonal factor, and different geographic location on post-op dry eye before substantiating our findings.

In conclusion, dry eye disease is inevitable following cataract surgery, irrespective of the type of surgery, which affects both tear quantity and quality. PKE and SICS, both can affect the dry eye test values in almost similar manner in the post operative period till 12wk. PKE may although seems to induce

less post-op dry eye symptoms, randomized multicentre trial with larger cohort and longer follow-up, is warranted to substantiate our findings. Patients must be informed preoperatively about the possible development of dry eye disease and related symptoms, and surgeon should practice intraoperatively allowing minimum light exposure, saline irrigation and ultrasound energy at the cost of minimum operating time and routine use of preservative free artificial tears postopearatively to alleviate symptoms.

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