Original Article

Comparison of corneal endothelial cell loss during manual small-incision cataract surgery using viscoelastic-assisted nucleus removal versus continuous balanced salt solution plus technique - Randomized controlled trial

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Purpose: The purpose of this study was to compare and analyze the endothelial cell loss during manual small-incision cataract surgery (MSICS) using the viscoelastic-assisted nucleus removal versus basal salt solution plus technique. **Methods:** This was a prospective randomized trial of 204 patients who underwent MSICS using viscoelastic-assisted nucleus removal (Group 1- OVD) versus basal salt solution plus technique (Group 2- BSS) at a tertiary eye care hospital in North India from January 2018 to 2021. Of these 204 patients, 103 (50.5%) and 101 (49.5%) were allocated to Group 1 and 2, respectively. The parameters assessed were detailed history, demographics, and anterior and posterior segment details. Visual acuity, intraocular pressure (IOP), keratometry, pachymetry, and endothelial cell density were evaluated preoperatively and postoperatively on day 1 and 30. **Results:** The mean age of the patients was 64.5 ± 8.2 years (range 48–82 years). There were 129 (63.2%) males and 75 (36.8%) females. The mean LogMAR visual acuity for both groups on day 1 (Group 1- 0.3 ± 0.1, Group 2- 0.5 ± 0.2) and day 30 (Group 1- 0.1 ± 0.2, Group 2- 0.1 ± 0.1) was statistically significant ($P < 0.001$), and the mean IO*P* value showed a statistically significant value ($P < 0.009$) on day 1 in Group 2 (15.0 ± 2.4 mmHg) and on day 30 ($P < 0.001$) in both the groups (Group 1- 13.6 ± 1.8 mmHg, Group 2- 13.5 ± 2 mmHg). The horizontal and vertical k values also showed a statistically significant difference on day 1 and day 30 ($P < 0.001$). The mean percentage change of central corneal thickness (CCT) in Group 1 was 17.7% and in Group 2 was 17.4% on day 1, and it was 1.1% on day 30 in both the groups, which was statistically significant ($P < 0.001$) compared to preoperative values. The percentage change in endothelial cell density on day 1 was 9% in Group 1 and 4.6% in Group 2, which was statistically significant ($P < 0.001$). On day 30, it was 9.7% and 4.8%, respectively, which was statistically significant ($P < 0.001$). **Conclusion:** Our study highlights statistically significant endothelial cell loss with viscoelastic-assisted nuclear delivery compared to BSS-assisted nuclear delivery during MSICS in a short follow-up of 1 month. The CCT values showed a slight increase, and the keratometry and IOP were unaffected compared to the preoperative parameters in both the groups.

Key words: Balanced salt solution, endothelial cell count, manual small-incision cataract surgery (MSICS), nucleus extraction, viscoelastic

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Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1871_22

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Age-related cataract is the major cause of vision loss in developing countries and across the globe.[1] It accounts for approximately 50% of blindness worldwide. Cataract surgery is the most common ophthalmic procedure performed nowadays.[2] Continued research, advances in surgical techniques, development and modification of instruments, and newer pharmacological advancements have revolutionized cataract surgical management.[3] The surgery has evolved from extracapsular cataract extraction (ECCE) to manual small-incision cataract surgery (MSICS) and phacoemulsification.[4] Phacoemulsification became popular in early 1990, and MSICS took a stride forward in early 2000. The recent innovations are femtosecond laser-assisted cataract surgery and robotic cataract surgery.[5] Every surgical procedure has a nominal complication rate, and the goal and challenge for ophthalmic surgeons are to minimize the complication rate.[6,7] Elective cataract surgery is

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Received: 30-Jul-2022 Revision: 30-Aug-2022
Accepted: 07-Sep-2022 Published: 25-Oct-2022

Cite this article as: Morya AK, Gurnani B, Mishra D, Kaur K, Porwal A, Sisodia P, *et al*. Comparison of corneal endothelial cell loss during manual small-incision cataract surgery using viscoelastic-assisted nucleus removal versus continuous balanced salt solution plus technique - Randomized controlled trial. Indian J Ophthalmol 2022;70:3960-6.

associated with some endothelial cell loss, which is well proven in the literature. This is of particular concern as endothelial cells cannot regenerate, and cellular decline below an acceptable limit of 1000 cells/mm^2 can lead to corneal decompensation.[8] Earlier studies have reported 16%–67% of endothelial cell loss during phacoemulsification, and this majorly happens when bursts of ultrasonic energy are used to emulsify the nucleus.[9] The plane of phacoemulsification also governs the degree of trauma to the endothelium.[10] MSICS is also associated with endothelial cell loss, and the reported incidence is 4%–17% in various studies.[11] Less viscoelastic cover to the endothelium, nucleus prolapse, nucleus delivery, and continued jet of irrigation and aspiration are the significant factors causing endothelial cell loss during MSICS.[11] Nayak and Jain,[12] in their analysis, compared the endothelial cell loss during phacoemulsification using continuous anterior chamber (AC) infusion versus the endothelial cell loss on using an ophthalmic viscosurgical device and found that there is not much difference in endothelial cell loss during the two techniques. Gogate *et al*.[13] studied endothelial cell loss in 200 patients using phacoemulsification and small-incision cataract surgery (SICS). They concluded that there was no clinically or statistically significant difference in endothelial cell loss or visual acuity (VA) between the two techniques. Still, there was a small difference in the astigmatic shift. Many studies have been performed on a similar concept, but as per the best of literature review, none has compared endothelial cell loss during different steps of MSICS. Considering this as our research question, we, in this randomized controlled trial, compared the endothelial cell loss during MSICS by using viscoelastic-assisted nucleus removal versus continuous basal salt solution plus nucleus removal.

Methods

This was a prospective randomized controlled trial conducted at a tertiary eye care hospital in North India from January 2018 to 2021. A total of 204 patients were randomized into two groups by the computer-generated binary randomization method. The study adhered to the tenets of the Declaration of Helsinki, and institutional review board approval was obtained from the institutional ethics committee of the hospital. Informed consent was obtained from all the study participants. The inclusion criteria were patients aged between 40 and 80 years, with nuclear sclerosis from grades 1 to 5 with or without pseudoexfoliation, controlled diabetes mellitus (DM), hypertension (HTN), and intraocular pressure (IOP). The exclusion criteria were subluxated, dislocated nucleus, hard mature cataract, any other preexisting ocular pathology, previous ocular surgery including refractive surgery, corneal pachymetry greater than 630 μm, preoperative endothelial cell count less than 1500 cells/mm^2, pupillary dilatation less than 6 mm, AC depth less than 2.5 mm, and systemic comorbidities apart from controlled glaucoma and HTN. A detailed history was obtained from all the patients, and all patients underwent a thorough slit-lamp anterior segment examination, dilated fundus examination, Snellen's best-corrected VA, IOP by noncontact tonometry, A-scan (Axis II, Quantel Medical, Rue Newton, France) using immersion technique, keratometry (Nidek KM 500, Washington Drive Fermont, CA 94539, USA), central corneal thickness (CCT), and noncontact specular endothelial cell count (SP-2000P; Topcon, 111 Bauer Drive Oakland NJ 07436, USA). The grading of nuclear sclerosis was done in accordance with Emery and Little nuclear hardness classification. The IOL power was calculated using Sanders, Retzlaff, Kraff (SRK-T) formula for all patients. The patients were divided into two groups by the computer-generated binary randomization method as follows:

Group 1 (Ophthalmic Viscosurgical Devices, *n* = 103): The patients underwent cataract surgery by MSICS technique, and nucleus removal was performed by using BSS (BSS plus) (Alcon Laboratories, Inc, Fort Worth, Texas, 76134, USA) [Fig. 1].

Group 2 (basal salt solution [BSS], *n* = 101): The patients underwent cataract surgery by MSICS technique, and nucleus removal was performed by using BSS (BSS plus) (Alcon Surgical, USA) [Fig. 1].

Postoperatively, in both the groups, the VA, IOP, central corneal pachymetry, and endothelial cell count were assessed on days 1 and 30. All the surgeries were performed by a single surgeon (AKM) who was informed about the patient group by the assisting mid-level ophthalmic personnel (MLOP) on the operation table before starting the surgery. All the doctors who performed the postoperative examination were masked about the patient group.

Surgical technique

Preop 0.5% moxifloxacin eye drop was instilled 6 h for 3 days before surgery in the eye to be operated. Topical tropicamide 0.8% and phenylephrine 5% eye drops were used preoperatively for pupillary dilatation. All surgeries were performed under peribulbar anesthesia using 4 ml 2% lignocaine mixed with 150 IU of hyaluronidase. The MSICS technique was used for cataract surgery and IOL implantation. After superior conjunctival peritomy from 10-1 o clock, cauterization of conjunctival vessels was performed to get a smooth scleral bed for scleral incision. This was followed by a 7-mm horizontal scleral incision with a blade, triplanar sclerocorneal tunnel formation, and a crescent with approximately 1 mm corneal entry. Next, a side port incision was made with a 15° side port at 8 o clock to facilitate side port steps. Through the side port, diluted adrenaline, 0.06% trypan blue, and viscoelastic were injected in sequence to stain the anterior capsule and form the AC. This was followed by an AC entry with a 3.2-mm keratome. Further, after viscoelastic injection, 7–8 mm continuous curvilinear capsulorhexis (CCC) was performed with a bent 26-G needle or Utrata's forceps, and

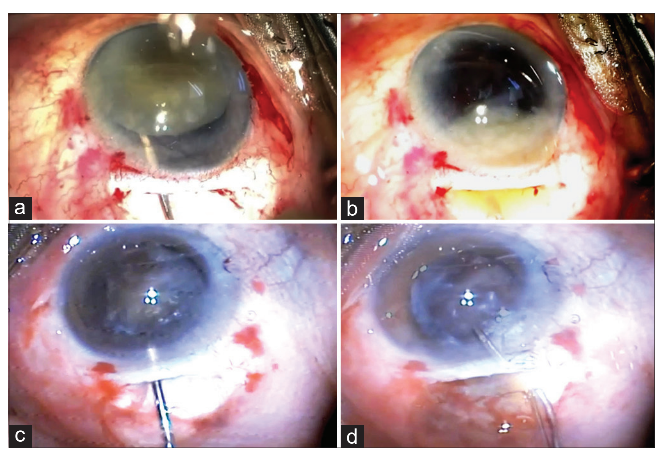

Figure 1: (a, b) Digital image depicting nucleus removal with the help of basal salt solution plus during manual small-incision cataract surgery. (c, d) Digital image depicting nucleus removal with the help of viscoelastic during manual small-incision cataract surgery

hydrodissection was performed with a 5-ml syringe attached to a 30-G cannula. Nucleus prolapse in the AC was performed with hydrodissection or using a sinskey hook. In Group 1, the nucleus delivery was facilitated by using 2% HPMC (2% Occugel, Ophtechnics Ltd). In Group B, nucleus delivery was reduced by using BSS plus (Intasol Plus 500 ml Intravenous (IV) fluid; Intas Pharmaceuticals Ltd, India). Cortical aspiration was done with the help of a bimanual irrigation and aspiration Simcoe cannula attached to a 5-ml syringe. Lastly, rigid single-piece PMMA IOL implantation was performed under viscoelastic cover. After IOL implantation, the viscoelastic was thoroughly washed with BSS, and AC reformation was done through side port hydration. The tunnel was covered with conjunctiva, and cautery was performed to close the tunnel. In the end, intracameral 0.1 ml moxifloxacin was injected. Postoperatively, all patients were started on 0.5% moxifloxacin eye drops four times, 0.5% Carboxymethylcellulose (CMC) three times, and 0.05% difluprednate six times in tapering doses for 6 weeks. The pachymeter readings were taken when the cell borders appeared well defined on the monitor. The endothelial cell density was assessed by manually counting 70 cells after freezing the screen. A total of three readings were taken, and the mean was taken into account [Fig. 1 and Video 1].[14]

Statistical analyses

Descriptive statistics were presented with frequency and percentage for categorical parameters. Mean and standard deviations (SDs) were used for continuous parametric data, while median and interquartile ranges (IQRs) were used for nonparametric data. The normality of the data was checked using the Shapiro–Wilk test. Student's *t*-test/Mann–Whitney U test was used to determine the significant difference in continuous factors between the two techniques. Wilcoxon signed rank test was used to determine the difference between pre- and postoperative values. Chi-square/Fisher's exact test was used to find the association between the factors and techniques. *P* value < 0.05 was considered as statistically significant. All statistical analyses were carried out using STATA 17.0 (StataCorp LLC, College Station, TX, USA).

Results

The mean ± SD age was 64.5 ± 8.2 years, and the range was 48–82 years. A total of 129 patients (63.2%) were male, and 75 (36.8%) were female. The mean ± SD IOP was 15.2 ± 4.1 mmHg, ranging from 10 to 38 mmHg for the patients in Group 1, and for the patients in Group 2, it was 14.9 ± 3.4 mmHg and ranged from 10 to 30 mmHg. There was no significant difference in various preoperative parameters in the two groups, except the axial length and uncorrected distant VA, which showed a significant *P* values of 0.027 and 0.006, respectively [Table 1]. The preoperative to postoperative percentage change in VA in both the groups was approximately 40% and the *P* value was significant (*P* < 0.001) [Table 2]. The percentage change in IOP from preoperative to postoperative day 1 and day 30 in Group 1 was 0.7% and 8.7%, respectively, and in Group 2 was 2.7% and 7.5%, respectively. The *P* value of change in IOP was significant in Group 2 on day 1 (*P*-0.009) and day 30 (*P* < 0.001); but in Group 2, it was significant on day 30 (*P* < 0.001) [Table 3]. The preoperative mean ± SD (μm) CCT was 470.4 ± 12.2 in group 1 and 470.9 ± 17.7 in Group 2. On postoperative day 1 and day 30, the mean ± SD (μm) CCT in Group 1 was 553.8 ± 24.1 and 475.4 ± 12.4, respectively, and in Group 2 was 552.8 ± 27.2 and 476.1 ± 1.9, respectively. The percentage change on postoperative day 1 was 17.7% in Group 1 and 17.4% in Group 2 and at 1 month was 1.1% in the groups [Table 4a]. The preoperative mean ± SD (μm) horizontal k value was 43.3 ± 1.8 in Group 1 and 43.5 ± 1.7 in Group 2. The postoperative day 1 and day 30 mean ± SD (μm) horizontal k values were 42.8 ± 1.9 and 42.9 ± 1.8, respectively, in Group 1 and 43.2 ± 1.8 and 43.1 ± 1.7, respectively, in Group 2. The percentage change of horizontal k value on postoperative day 1 was 1.2% in Group 1 and 0.7% in Group 2, and at 1 month, it was 0.9% in both groups [Table 4b]. The preoperative mean ± SD (μm) vertical k value was 43.2 ± 1.5 in Group 1 and 43.1 ± 1.7 in Group 2. The postoperative day 1 and day 30 mean ± SD (μm) vertical k values were 43.7 ± 1.6 and 43.0 ± 1.5, respectively, in Group 1 and 43.2 ± 1.7 and 43.6 ± 1.6, respectively, in Group 2. The percentage change on postoperative day 1 was 1.2% in Group 1 and 0.2% in Group 2; at 1 month, it was 0.5% and 1.2% in Group 1 and Group 2, respectively. The *P* value was significant on postoperative day 1 and day 30 (*P* < 0.001) [Fig. 2a and Table 5a]. The preoperative mean ± SD (μm) endothelial cell density value was 2307.2 ± 215.1 in Group 1 and 2491.1 ± 203.5 in Group 2. The postoperative day 1 and day 30 mean ± SD (μm) endothelial cell density values in Group 1 were 2099.2 ± 210.9 and 2083.8 ± 228.9, respectively, and in Group 2 were 2376.7 ± 191.3 and 2371.8 ± 190.8, respectively. The percentage change on postoperative day 1 was 9% in Group 1 and 4.6% in Group 2; at 1 month, it was 9.7% and 4.8% in Group 1 and Group 2, respectively. When the two groups were compared, the *P* value was significant on postoperative day 1 and day 30 (*P* < 0.001) [Fig. 2b and Table 5b].

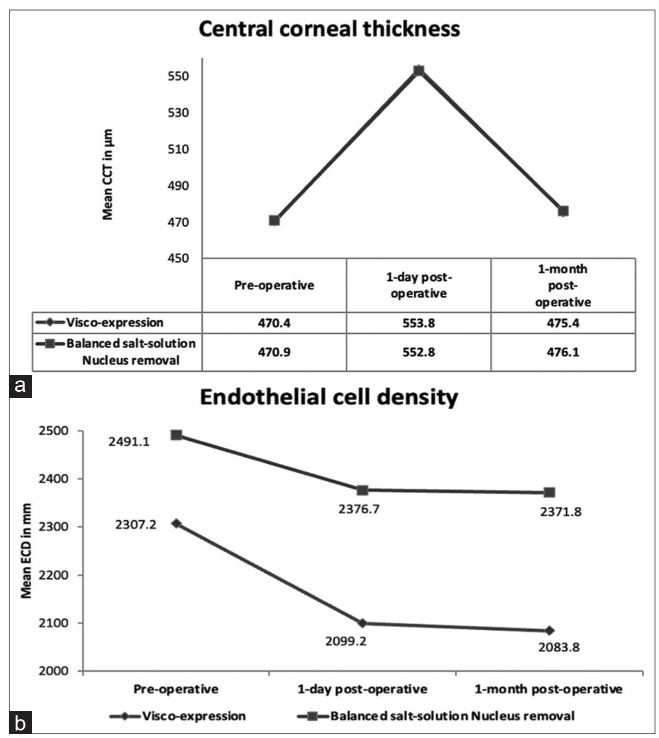

Figure 2: (a) Digital line graph depicting the changes in central corneal thickness on day 1 and day 30 postoperatively compared to preoperative values during the two techniques of nucleus removal while performing manual small-incision cataract surgery. (b) Digital line graph depicting the changes in endothelial cell density on day 1 and day 30 postoperatively compared to preoperative values during the two techniques of nucleus removal while performing manual small-incision cataract surgery

Table 1: Demographic data and clinical parameters of Group 1 and Group 2

Parameters	Group		Overall (*n*=204)	*P*
	Group 1 (*n*=103) (OVD)	Group 2 (*n*=101) (BSS plus)		
Cataract grading				
Nuclear sclerosis 1	1 (1.0)	2 (2.0)	3 (1.5)	0.3351
Nuclear sclerosis 2	50 (48.5)	44 (43.6)	94 (46.1)	
Nuclear sclerosis 3	37 (35.9)	30 (29.7)	67 (32.8)	
Nuclear sclerosis 4	12 (11.6)	17 (16.8)	29 (14.2)	
Nuclear sclerosis 5	3 (2.9)	8 (7.9)	11 (5.4)	
Pseudoexfoliation				
Absent	96 (93.2)	93 (92.1)	189 (92.6)	0.7581
Present	7 (6.8)	8 (7.9)	15 (7.4)	
Diabetic mellitus				
No	79 (76.7)	88 (87.1)	167 (81.9)	0.0531
Yes	24 (23.3)	13 (12.9)	37 (18.1)	
Hypertension				
No	84 (81.6)	89 (88.1)	173 (84.8)	0.1921
Yes	19 (18.4)	12 (11.9)	31 (15.2)	
Anterior chamber depth				
Mean±SD	3.1±0.6	3.1±0.6	3.1±0.6	0.5882
Min.-Max.	2.1-4.1	2.1-4.1	2.1-4.1	
Axial length				
Mean±SD	23.3±1.9	22.8±1.0	23.0±1.6	0.0272
Min.-Max.	20.6-32.8	20.6-25.4	20.6-32.8	
Uncorrected distant visual acuity				
LogMAR median (Snellen's VA)	0.6 (6/24)	0.78 (6/36)	0.6 (6/24)	0.0062
IQR	0.3-0.78	0.48-1	0.48-0.78	
Fundus				
No abnormality	25 (24.3)	29 (28.7)	54 (26.5)	0.5981
Media-hazy	12 (11.6)	18 (17.8)	30 (14.7)	
Foveal reflex-dull	15 (14.6)	14 (13.9)	29 (14.2)	
Hazy view	8 (7.8)	11 (10.9)	19 (9.3)	
Tessellated fundus	10 (9.7)	8 (7.9)	18 (8.8)	
Pathological myopia	6 (5.8)	6 (5.9)	12 (5.9)	
Drusen along vessel	2 (1.9)	2 (2.0)	4 (2.0)	
Vitreous degeneration	2 (1.9)	2 (2.0)	4 (2.0)	

BSS=Basal salt solution, IQR=Interquartile range, SD=Standard deviation, VA=Visual acuity. 1- Chi-square test/Fisher's exact test; 2- Student's *t*-test/Mann-Whitney U test

Table 2: Preoperative, postoperative day 1 and day 30 changes in visual acuity in Group 1 and Group 2

Visual acuity	Preoperative		Postoperative			
			1 day		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (LogMAR)	0.5±0.2	0.8±0.4	0.3±0.1	0.5±0.2	0.1±0.2	0.1±0.1
Mean difference (LogMAR)	-	-	0.3	0.4	0.5	0.6
SD (LogMAR)	-	-	0.2	0.3	0.2	0.4
% of change	-	-	40.0%	37.5%	80%	87.5%
*P**	-	-	**<0.001**	**<0.001**	**<0.001**	**<0.001**
*P***	-	-	**<0.001**		**<0.001**	

LogMAR=Logarithm of the Minimum Angle of Resolution, BSS=basal salt solution, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and 1 month postoperative changes between Group 1 and Group 2. Boldface indicates statistical significance

Discussion

The endothelial cell monolayer is vital as it is responsible for maintaining a dehydrated state of the cornea through the Na+/K+-ATPase pump and active bicarbonate gradient, thus maintaining corneal transparency.[15] The endothelial cell loss during cataract surgery is of significant concern for any operating surgeon.[16] The average endothelial cell density in

Table 3: Preoperative, postoperative day 1 and day 30 changes in IOP in Group 1 and Group 2

IOP	Preoperative		Postoperative			
			1 day		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (mmHg)	14.9±2.7	14.6±2.7	15.0±2.3	15.0±2.4	13.6±1.8	13.5±2.0
Mean difference (mmHg)	-	-	1.3	1.6	1.8	1.3
SD (difference)	-	-	0.6	1.0	1.2	1.1
% of change	-	-	0.7%	2.7%	8.7%	7.5%
*P**	-	-	0.341	**0.009**	**<0.001**	**<0.001**
*P***	-	-	0.893		0.594	

BSS=basal salt solution, IOP=intraocular pressure, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and day 30 postoperative values between Group 1 and Group 2. Boldface indicates statistical significance

Table 4a: Preoperative, postoperative day 1 and day 30 changes in horizontal keratometry value (k) in Group 1 and Group 2

Horizontal keratometry	Preoperative		Postoperative			
			Day 1		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (D)	43.3±1.8	43.5±1.7	42.8±1.9	43.2±1.8	42.9±1.8	43.1±1.7
Mean difference (D)	-	-	0.6	0.6	0.4	0.5
SD (difference)	-	-	0.2	0.4	0.2	0.4
% of change	-	-	1.2%	0.7%	0.9%	0.9%
*P**	-	-	**<0.001**	**<0.001**	**<0.001**	**<0.001**
*P***	-	-	0.148		0.449	

BSS=basal salt solution, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and 1 month postoperative values between Group 1 and Group 2. Boldface indicates statistical significance

Table 4b: Preoperative, postoperative day 1 and day 30 changes in vertical keratometry value (k) in Group 1 and Group 2

Vertical keratometry	Preoperative		Postoperative			
			1 day		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (D)	43.2±1.5	43.1±1.7	43.7±1.6	43.2±1.7	43.0±1.5	43.6±1.6
Mean difference (D)	-	-	0.5	0.4	0.3	0.5
SD (difference)	-	-	0.04	0.1	0.5	0.3
% of change	-	-	1.2%	0.2%	0.5%	1.2%
*P**	-	-	**<0.001**	**<0.001**	**<0.001**	**<0.001**
*P***	-	-	0.072		0.006	

BSS=basal salt solution, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and 1 month postoperative values between Group 1 and Group 2. Boldface indicates statistical significance

the Indian population is approximately 2527 ± 337 cells/mm^2.[17] During surgery, iatrogenic trauma to the endothelium may result in pseudophakic bullous keratopathy and may cause a gross reduction in VA.[18] The other disadvantage is that once lost, endothelial cells do not replicate *in vivo*.[10] The various factors which are known to cause a reduction in endothelial cell count are senile degeneration of cornea, small pupillary diameter, advanced cataract grade, large nuclear size, air bubbles, a greater volume of irrigation during irrigation and aspiration (I/A), longer duration of surgery, nucleus rubbing the endothelium, less or no viscoelastic cover to the endothelium, free-floating lens fragments in the AC, and higher ultrasound energy during phacoemulsification.[19] In this randomized trial, we kept most of the comparative parameters in two groups nearly similar to reduce any potential bias. Although higher grades of cataract are implicated to cause more endothelial cell loss, we excluded hard mature cataracts. We had only a few patients with nuclear sclerosis grade 5 in the two groups. Maggon *et al*.,[20] in their analysis, concluded that phacoemulsification in eyes with small pupillary diameter (<5 mm) results in more endothelial cell loss, compared to eyes with more than 5 mm pupillary diameter.

Table 5a: Preoperative, postoperative day 1 and day 30 changes in CCT in Group 1 and Group 2

CCT	Preoperative		Postoperative			
			1 day		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (μm)	470.4±12.2	470.9±17.7	553.8±24.1	552.8±27.2	475.4±12.4	476.1±17.9
Mean difference (μm)	-	-	83.5	81.9	5.0	5.1
SD (difference)	-	-	22.2	26.2	1.2	1.4
% of change	-	-	17.7%	17.4%	1.1%	1.1%
*P**	-	-	**<0.001**	**<0.001**	**<0.001**	**<0.001**
*P***	-	-	0.735		0.801	

BSS=basal salt solution, CCT=central corneal thickness, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and 1 month postoperative values between Group 1 and Group 2. Boldface indicates statistical significance

Table 5b: Preoperative, postoperative day 1 and day 30 changes in ECD in Group 1 and Group 2

ECD	Preoperative		Postoperative			
			1 day		1 month	
	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)	Group 1 (OVD)	Group 2 (BSS plus)
Mean±SD (μm)	2307.2±215.1	2491.1±203.5	2099.2±210.9	2376.7±191.3	2083.8±228.9	2371.8±190.8
Mean difference (μm)	-	-	208.0	114.4	223.4	124.9
SD (difference)	-	-	51.6	41.6	86.0	47.2
% of change	-	-	9.0%	4.6%	9.7%	4.8%
*P**	-	-	**<0.001**	**<0.001**	**<0.001**	**<0.001**
*P***	-	-	**<0.001**		**<0.001**	

BSS=basal salt solution, ECD=endothelial cell density, SD=standard deviation. *Wilcoxon signed rank test to compare the paired observation within the group. **Mann-Whitney U test to compare the day 1 and 1 month postoperative values between Group 1 and Group 2. Boldface indicates statistical significance

Similarly, Perez *et al*.[21] also documented that the smaller the pupillary size, the more the endothelial cell loss.

Most of the previous studies have focused on endothelial cell loss in various steps during phacoemulsification or compared endothelial cell loss during phacoemulsification with SICS.[13,16] We studied the endothelial cell loss during nucleus removal using two techniques in MSICS, which is less well explored. The technique of viscoexpression of the nucleus during MSICS is well studied and documented, and in Group 2, we used BSS plus as it has been known to cause less postoperative corneal edema after intraocular surgery.

In the current study, we had 101 patients in Group 1 and 103 patients in Group 2, which was comparatively higher than in previous studies to get better insights about endothelial cell loss post-MSICS. The patient population and demographics were compared in the two groups, and also, age, nuclear grade, and systemic parameters were comparable with previous studies. The mean postoperative VA values were 0.1 ± 0.2 and 0.1 ± 0.1 in Group 1 and 2, respectively, which were comparable with a *P* value of < 0.001. This shows that VA is not affected much by different cataract surgery techniques. Similarly, the IOP in the two groups was also nearly similar at the end of 1 month, with values of 13.6 ± 1.8 and 13.5 ± 2 mmHg in Group 1 and Group 2, respectively, and the *P* value (<0.001) was significant compared to preoperative values. This signifies that there was no to minimal corneal edema postoperatively in the two groups, which could impact the IOP. We also assessed the impact of two techniques on keratometry values in our study. The horizontal K values at the end of 1 month were 42.9 ± 1.8 and 43.1 ± 1.7 in Group 1 and Group 2, respectively, which were nearly similar to the preoperative values. The vertical K values at the end of 1 month in Group 1 was 43.0 ± 1.5 and 43.6 ± 1.6 and was nearly identical to preoperative values. This shows that modification of any step of MSICS does not affect the keratometry values. The CCT at 1 month was slightly higher compared to the preoperative values, and there was no significant difference between the two groups. This is in accordance with the results of Nayak and Jain.[12] They also showed that the CCT returned close to preoperative values at the end of 1 month in both the groups, and there were no significant differences between groups. Similarly, in the analysis by Maggon *et al*.,[20] the CCT values in Group A (523.44 ± 20.31), Group B (512.56 ± 35.65), and Group C (515.78 ± 19.9) at the end of 1 month were nearly similar to the preoperative values (515.98 ± 19.99, 506.9 ± 35.15, and 513.54 ± 19.77, respectively). Ganekal and Nagarajappa,[22] in their study, also showed that CCT values are unaffected at 6 weeks from baseline with a value of 574.04 ± 21.29 versus 574.04 ± 23.96 in Group 1 and 559.76 ± 32.05 versus 560.76 ± 33.68 in Group 2. We found an endothelial cell loss of 9.7% and 4.8% at 1 month in Group 1 and Group 2, respectively, with a *P* value of 0.001, which was significant. Nayak and Jain[12] reported an endothelial cell loss of 7.38% and 7.47% at 1 month in Groups A and B, respectively, during phacoemulsification using OVD in Group A and BSS plus in Group B. This proves that OVD may not be necessary, and the endothelial cell protection can be better with BSS plus in experienced hands. Similarly, Jagani *et al*.[23] reported a mean endothelial cell loss (cells/mm^2) of 307.80 (12.33%), 397.79 (15.93%), and 421.69 (16.89%) at 1 week, 6 weeks, and 3 months postoperatively, respectively, in Group A undergoing phacoemulsification and 270.86 (10.63%), 385.22 (15.12%), and 413.68 (16.24%) at 1 week, 6 weeks, and 3 months postoperatively, respectively, in Group B undergoing MSICS. There was no clinical and statistically significant difference (P >0.05) between the two groups. In our analysis, the endothelial cells were comparatively lesser, probably due to single surgeon's expertise and the technique of nucleus delivery. Still, large-scale studies are needed to get better insights.

The major limitation of our study was the follow-up period was 1 month. The other morphological endothelial parameters, like the coefficient of variation and SD, were not compared. The strengths of our study were the prospective nature of the study, large sample size, and computer-based randomization to avoid selection bias. A study from the USA reported that the rate of endothelial cell decreases with time.[24] In contrast, a short-term follow-up usually highlights a more significant endothelial loss, as reported in the literature. Hence short-term follow-up is enough to denote the long-term consequences. A short-term follow-up will also prevent loss to follow-up of patients. A recent article reported acute shortage of OVD in the European market, and it is likely to affect the whole world due to scarcity of raw materials. Hence, we have to look for alternatives of OVD and also minimize its usage in various steps of surgery.[25] As per our knowledge, this is the first large-scale analysis highlighting the pachymetric and endothelial cell changes during nucleus removal by two different techniques of MSICS.

Conclusion

Our study highlights statistically significant endothelial cell loss with viscoelastic-assisted nuclear delivery compared to BSS-assisted nuclear delivery during MSICS in a short follow-up of 1 month. The CCT values showed a slight increase, and the keratometry and IO*P* values were unaffected compared to preoperative parameters in both the groups.

Compliance with ethical standards

The article has not been submitted elsewhere for consideration of publication. The article complies with the ethical standards by the Declaration of Helsinki.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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