Effect Of Irrigating Solutions On The Corneal Endothelium Following Phacoemulsification: Balanced Salt Solution Versus Ringer Lactate

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Abstract

Introduction: Phacoemulsification surgery results in endothelial damage, which is permanent. Several studies have shown that Balanced Salt Solution (BSS) helps to preserve endothelium better than Ringer Lactate (RL) due to its superior composition.

Aims & Objectives: To compare the effects of RL and BSS on the corneal endothelium following phacoemulsification cataract surgery.

Methodology: 60 patients were randomly allocated into groups using an envelope system, to RL (n=29) and BSS (n=31). Following phacoemulsification, each patient underwent Central Corneal Thickness (CCT) evaluation by pachymetry at post-op day 1, week 1 and week 6. Endothelial Cell Density (ECD), Co-efficient of variation of cells (COV), and Hexagonality of cells (HEX) were studied using specular microscopy at the post-op 6 week period.

Results: There was no significant difference in the change in CCT between the RL and BSS groups at post-op day 1, week 1 and week 6 periods respectively (p>0.05).

The mean decrease in endothelial cell density was 394.72 cells/mm² (±189.04) and 337.96 cells/mm² (±165.30) in the RL and BSS groups respectively (p=0.220).

The change in COV was 0.21% (±.03.5) and 1.49 (±3.75) % in the RL and BSS groups ((p=0.081)and the change in hexagonality of cells was -2.62 % (±8.77) and -2.61% (±7.59) in the RL and BSS groups respectively. (p=0.997).

There was no significant correlation between the change in ECD/COV/HEX/CCT with respect to effective phaco time/phacoemulsification volume in either group.

Conclusion: Both Ringer Lactate and Balanced salt solution were similar in their ability to protect the endothelium following phacoemulsification surgery.

Keywords: Phacoemulsification; Irrigation Solutions; Corneal Endothelium.

Introduction

Phacoemulsification is now considered the gold standard in cataract surgery. It provides several advantages over its counterpart SICS. Visual recovery is faster, there is minimal post-operative astigmatism and there is better overall patient satisfaction.

However, the major drawback of phacoemulsification is the damage to the endothelium. The extent of damage is substantially higher than in Small Incision cataract surgery. It is also irreversible. Those patients with an already compromised endothelium like in Fuch’s Endothelial dystrophy are poor candidates for the procedure. Another complication to be wary of is the occurrence of pseudophakic bullous keratopathy.

The causes for damage to the endothelium during phacoemulsification are many-including increased age and hardness of cataract. One hypothesis emphasizes the production of free radicals generated as a result of ultrasound energy [1, 2]. In particular, cavitation energy is said to cause splitting of the water to cause hydroxyl ion production, which is the most potent of the free radicals [3]. Several studies have elucidated the harmful effects of hydroxyl ion on the corneal endothelium [4-6].

So how does one protect the corneal endothelium during phaco-
emulsification? One method is to use irrigating solutions that resemble the aqueous as closely as possible in terms of pH and ionic composition. Previously, Normal saline, lactated Ringer's, and Plasma-Lyte 148 were used. These solutions did not "replace" the lost aqueous effectively due to their varied composition and pH. As a result, corneal edema and increased endothelial cell loss were seen postoperatively.

Standard BSS contains magnesium, which is a component of the Mg-ATPase pump, and an acetate-citrate buffer. It is also hypotonic, having an alkaline pH [7]. In vitro studies have shown that BSS is more effective in reducing corneal swelling and maintaining corneal morphology than Ringer Lactate [8].

Balanced Salt Solution PLUS (BSS PLUS) is the most effective irrigating solution available at present. The distinguishing feature is that it contains glutathione, an effective antioxidant. Ascorbic acid and GSSG are naturally found antioxidants in the aqueous humor. When added to the irrigation solution, the endothelium appeared healthier, and that too, for a longer period [9, 10]. In addition to glutathione, BSS PLUS also has glucose, which behaves as an energy source for the Na/K ATPase pump and a bicarbonate buffer which is also found naturally in the aqueous [8, 11].

Our study, we chose to compare standard BSS with Ringer Lactate for the reasons being that there are very few studies comparing these two solutions in the clinical scenario [12]. Ringer Lactate remains the most commonly used irrigating solution at present. Also, it is 50 times less costly than standard BSS and is also more easily available.

The objectives of the study were:

1. To compare the effect of irrigating solutions, BSS and Ringer Lactate on the corneal endothelium following phacoemulsification.
2. To compare the change in CCT/Endothelial cell density/COV/HEX with Effective phacoemulsification time and Phacoemulsification volume in both the groups.

**Methodology**

This was a prospective study conducted at the Department of Ophthalmology, JSS Hospital, Mysore, between November 2017 and March 2019. The source of data included all patients attending the ophthalmology OPD during this time period.

**Sample Size:** On applying the formula $N=Z^2PQ/D^2$, a sample size of 60 is obtained. (This formulation was based on the incidence of nuclear cataract in South India)

**Sampling technique and study population:** The subjects are recruited based on purposeful sampling. All patients with age-related cataract between 50-75 years of age were recruited for the study.

Those patients who were excluded from the study included those with secondary cataract, congenital cataract, with pre-existing corneal pathologies, an endothelial cell density of less than 1500 cells/mm², glaucoma, uveitis, trauma and patients on systemic or topical steroids.

For those patients who met the inclusion criteria, written informed consent was obtained, citing the risks associated with the procedure. The consent was obtained in the patient’s language. The clearance by the institutional ethics committee was obtained. The study followed the tenets of Helsinki.

Pre-operative evaluation included a slit lamp examination followed by a detailed fundus examination. Cataract grading was performed by a single examiner using the Emery Little classification system. Pachymetry was performed using the Anterior Segment OCT (CIRRUS™ HD-OCT 500 Germany). The patient is seated at the machine and is made to focus at an internal ‘light beam’, which behaves as the fixation point with the concerned eye. The image is sharply focused and clicked. An average of three readings are taken.

Specular microscopy was performed with a non-contact specular microscope (TOPCON SP-1P, Japan). Three readings were obtained by a single examiner. The parameters evaluated were Endothelial Cell Density, Co-efficient of variation and Hexagonality of cells.

The endothelial cell Density is the number of cells per mm square and the co-efficient of variation is the ratio of variation of cell size to mean cell size, expressed in percentage. It is indicative of cell polymegathism. Hexagonality of cells is the percentage of the number of endothelial cells maintaining their hexagonal shape. It is a marker of cell pleomorphism. All of these parameters are computed automatically by the specular microscope and displayed on screen.

The patients were randomized into two groups using an envelope system. Group 1 would receive Ringer Lactate as the irrigating solution and Group 2 would receive standard BSS as the irrigating solution.

The surgical procedure was performed by a single surgeon. Under strict aseptic precautions. The main incision is a clear corneal incision, 2.8 mm in size, placed at the superotemporal quadrant. Two side ports are created, each 3 clock hours away from the main incision.

Continuous curvilinear capsulorrhexis is made, about 5.6 mm in size. Hydrodissection is done and it is ensured that the nucleus is freely mobile in the bag. The phacoemulsification procedure is performed using the following settings:

**PHACO 1 - Vacuum of 60mmhg**
- Power of 60%
- Irrigation rate of 24cc/hr

**PHACO 2 - Vacuum of 260-300mmhg**
- Power of 45%
- Irrigation rate of 28cc/hr

Using the ‘Stop-Chop’ technique, the nucleus is emulsified.

**The stop-chop technique:**

Using the chopper, a deep groove is made at the center of the nucleus, such that it is deeper at the center than at the periphery. The groove is made deep enough to identify the posterior plate.
Taking the chopper, on the other hand, cracking of the nucleus is done to separate it into halves. The technique used is cross cracking, where both hands move in opposite directions to separate the two halves of the nucleus. The hemisections are rotated such that one half lies at 12° clock and the other half at 6 o clock positions.

Now each hemisection is grasped using the handpiece, made into two more sections and then aspirated. The other hemisection is rotated inferiorly and a similar procedure is performed.

Next, using the Irrigation-Aspiration system, the cortical matter is removed. A foldable IOL is placed into the bag using an injector. Excess viscoelastic substance is then removed. Sideport incisions are then hydrated.

The Estimated Phaco time and phacoemulsification volume are carefully noted during the procedure.

The Phacoemulsification volume is the amount of irrigating solution used from the beginning of groove formation to end of viscoelastic substance removal.

Effective Phaco time: average ultrasound (u/s) power x average u/s time/100. It is generated automatically by the phaco machine.

Every patient was followed up at post-op day1, post-op week 1 and post-op week 6 periods. The CCT was measured using the ASOCT device at post-op day 1, post-op week 1 and post-op week 6 periods. The endothelial cell density and parameters indicating endothelial morphology (Co-efficient of variation and Hexagonality of cells) were assessed using the specular microscope at the post-op week 6 period.

Statistical Analysis

The following statistical tests will be applied:-

Observed data was described in terms of mean, standard deviation, frequency, and percentage. Chi-Square Test was used to compare the percentage, proportions, and fractions in paired data, before and after an intervention. The t-tests were used to compare means between both the groups. Pearson correlation coefficient was used to measure the linear correlation between any two variables.

P value < 0.05 is considered statistically significant.

Statistical were carried out using the SPSS for Windows (version 20).

Results

Descriptive Analysis

At the end of the study period, there were and 29 patients in the Ringer Lactate group and 31 patients in the BSS group. The two groups were comparable in terms of age, sex, cataract grading, baseline visual acuity, effective phacoemulsification time and phacoemulsification volume (Table 1).

Change in Central Corneal Thickness

The mean baseline central corneal thickness was 499 micron (±30.71) and 495 micron (±36.97) in the RL and BSS groups respectively. The central corneal thickness increased significantly in both the groups at post-op day 1, week 1 and week 6 periods (p<0.05). It returned to baseline at the end of 6 weeks. However, the change in Central corneal thickness was not statistically significant between the two groups at any period (Table 2, Figure 1). In either group, there was no statistically significant correlation between Effective phacoemulsification time with CCT /phacoemulsification volume with CCT.

Change in Endothelial cell density (ECD)

The mean pre-op endothelial cell density was 2512.81 (±395.76) cells/mm² in the Ringer lactate group and 2675.07 (±326.14) cell/mm² in the BSS group. There was a significant decrease in endothelial cell density at the 6 weeks follow up period in both the groups. However, the decrease was not statistically significant between both groups (p=0.220) (Table 2, Figure 2). In either group, there was no statistically significant correlation between Effective phaco time with ECD/phacoemulsification volume with ECD.

Change in Co-efficient of Variation (COV)

The mean pre-op coefficient of variation was 35% (±3.70) in
Table 2. Shows the change in various corneal and endothelial parameters between both the groups following phacoemulsification.

| Change in parameters:       | RL                     | BSS                     |
|-----------------------------|------------------------|-------------------------|
| Change in CCT at post-op day 1 (micron) p=0.17 | 26.48 (±8.41)          | 23.38 (±8.68)           |
| Change in CCT at post-op week 1 (micron) p=0.79 | 16.97 (±8.99)          | 16.28 (±10.50)          |
| Change in CCT at post-op week 6 (micron) p=0.52 | 4.22 (±5.63)           | 4.97 (±2.82)            |
| Change in ECD at post-op week 6 (cells/mm²) p=0.22 | 337.97 (±165.30)       | 394.72 (±189.04)        |
| Change in COV at post-op week 6 (%) p=0.08 | 1.48 (±3.75)           | 0.21% (±3.6)            |
| Change in HEX at post-op week 6 (%) p=0.997 | -2.62 (±8.77)          | -2.61 (±68)             |

Figure 1. Change in Central Corneal thickness.

Figure 2. Change in endothelial cell density.

Figure 3. Change in Co-efficient of variation.

Figure 4. Shows the change in Hexagonality between the groups.

the Ringer Lactate group and 32.06% (±5.04) in the BSS group. There was an increase in COV of 0.21% (±3.6) at the end of six weeks in the RL group and a decrease of 1.48 (±3.75) % in the BSS group. No statistical significance was observed (p=0.081) (Table 2, Figure 3). There was no statistically significant correlation between Effective phaco time and phacoemulsification volume with change in COV throughout the 6 weeks in either group.

Change in Hexagonality of cells (HEX)

The mean pre-op HEX was 51.61% (±8.12) in the RL group and 54.03% (±7.74) in the BSS group. The hexagonality of cells decreased by -2.62 % (±8.77) in the Ringer Lactate group, and by -2.61% (±6.83) in the BSS group. No statistical significance
was observed (p=0.997) (Table 2, Figure 4). There was no statistically significant correlation between Effective phaco time and phacoemulsification volume with change in HEX throughout the 6 weeks in either group.

**Discussion**

In this study, we aimed to evaluate the preservation of the corneal endothelium, comparing two irrigating solutions, ie, Balanced salt solution and Ringer Lactate. Balanced salt solution was chosen in place of BSS PLUS as there are already several clinical studies [13-15] that have effectively proven the efficacy of BSS PLUS over other irrigating solutions. Also, BSS is more economical to use.

Several *in vitro* studies have shown that irrigating solutions closely resembling the aqueous better preserve the corneal endothelium after any traumatic event like phacoemulsification [16-18]. BSS PLUS is ideal, and BSS is more effective than RL in maintaining the corneal endothelium.

As mentioned before, many factors are contributory to endothelial damage during phacoemulsification. Such confounding factors were removed by matching patients in each group in terms of age, cataract grade, phacoemulsification time and volume. Also, individuals with compromised endothelium were excluded from the study.

There was no significant difference in the change in CCT between the groups at any time interval. The change in the CCT is not correlated with the decrease in the Endothelial cell density in the long term. This is evidenced by the fact that the CCT returned to normal values despite the decrease in endothelial cells. Although the endothelial density is reduced, the functional reserve is quickly restored. The compensatory mechanisms to repair damage include a proportional increase in cell size and the return of pachymetry values to pre-op levels. Similar results were also noted by Chang et al [20] Glasser et al [18].

The endothelial cell density decreased significantly in both groups. However, the decrease was not significant between the two groups. There was a decrease of 14% in the BSS group and 15% in the Ringer Lactate group. Lucena et al [14] reported a decrease of 9.2% and 13.1% endothelial cells in the BSS and RL groups respectively.

Endothelial cell area is one of the most sensitive and earliest indicators of cell injury; especially the percentage of hexagonal cells. When there is a loss of even a single endothelial cell, six other surrounding cells lose their hexagonality and increase in size. At the end of six weeks, there was no significant change in the coefficient of variation or in the hexagonality of cells suggesting that the repair mechanism had been well established by that time.

The use of viscoelastic may have played a role in protecting the endothelium from the harmful effects of phaco ultrasound. The exclusion of viscoelastic may have shown a greater difference in the endothelial parameters. However, considering the crucial role viscoelastic play in today’s routine cataract surgeries, such a suggestion would be impractical.

Some authors have claimed that phacoemulsification time and the volume of irrigation solution used, play a role in the changes produced in the endothelium.

Although the two groups were comparable in terms of phacoemulsification time and volume, a linear regression analysis was done to prove any significant change between endothelial parameters, with respect to phacoemulsification time/volume. No such association was found. In contrast, however, Lucena et al found a significant decrease in the endothelial count with respect to phacoemulsification time in the RL group. Hence, concluding that the use of BSS PLUS would be more beneficial for cataracts requiring prolonged operating time like hard cataracts [14].

One reason we did not find any improvement in endothelial integrity while using BSS could be explained by the fact that standard BSS lacks glutathione, which is proven to have antioxidant properties and helps to protect against free radical production as a result of phacoemulsification.

Other studies by Kiss et al [15], Puckett et al [19], and Lucena et al [14] comparing the use of BSS PLUS and RL showed no significant change in the endothelial parameters either in the acute phase or on a long term basis. A similar study by Vasavada et al [12] comparing standard BSS and RL showed a significant rise in central corneal thickness in the RL group at post-op day 1. Joussen et al also reported an acute increase in central corneal thickness in the Ringer Lactate group. But this study used BSS PLUS [18]. There was no significant change in endothelial cell density or Co-efficient of variation between the two groups as per the above mentioned studies.

In our study, both BSS and RL showed similar effects on the corneal endothelium integrity. BSS did not seem more advantageous to Ringer Lactate in protecting the endothelium despite its composition resembling the aqueous closely. Both solutions result in a similar loss of endothelial cells per unit phacoemulsification time.

We recommend performing a prospective study taking into account the effect of all three irrigating solutions ie Balanced salt solution, Ringer Lactate and Balanced salt solution PLUS on the effect on corneal endothelium to accurately delineate the protective capacity of each solution.

**Conclusion**

Although BSS resembles aqueous more closely in terms of composition compared to RL, in the clinical scenario, it does not prove to be more advantageous in the preservation of corneal endothelium. Also considering the high cost of BSS, Ringer Lactate seems a more economical choice for use as an irrigating solution.

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