LAPORAN AKHIR PROJEK PENYELIDIKAN
R & D JANGKA PENDEK

"A RANDOMIZED COMPARISON ON THE CORNEAL ENDOTHELIAL MORPHOLOGY AFTER THE USE OF 2 DIFFERENT VISCOELASTIC AGENTS DURING PHACOEMULSIFICATION SURGERY"

Investigators:

Dr Shatriah Ismail
Dr Mohtar Ibrahim
Dr Zulkifli Abd Ghani

Grant No: 304/PPSP/6131283

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BAHAGIAN PENYELIDIKAN & PEMBANGUNAN
CANSELORI
UNIVERSITI SAINS MALAYSIA

Laporan Akhir Projek Penyelidikan Jangka Pendek

1) Nama Penyelidik: **Dr Shatriah Ismail**

Nama Penyelidik-Penyelidik
Lain (Jika berkaitan): **Dr Mohtar Ibrahim**
Dr Zulkifli Abdul Ghani

2) Pusat Pengajian/Pusat/Unit: **Pusat Pengajian Sains Perubatan**

3) Tajuk Projek: **A randomized comparison on the corneal endothelial cells after the use of 2 different viscoelastic agents during phacoemulsification surgery.**

4) (a) Penemuan Projek/Abstrak

(Perlu disediakan makluman di antara 100 – 200 perkataan di dalam Bahasa Malaysia dan Bahasa Inggeris. Ini kemudiannya akan dimuatkan ke dalam Laporan Tahunan Bahagian Penyelidikan & Pembangunan sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti).

Sila rujuk lampiran

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(b) Senaraikan Kata Kunci yang digunakan di dalam abstrak:

Bahasa Malaysia	Bahasa Inggeris
Sel-sel endothelium kornea	Cornea endothelial cells
Bahan viskoelastik	Viscoelastic agents
Pembedahan phakoemulsifikasi	Phacoemulsification surgery
Ketumpatan sel-sel	Cells density
Purata saiz sel	Average cell size
Variasi koeffisi saiz sel	Coefficient variation of the cell size
Hexagonaliti sel	Hexagonality
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5) Output Dan Faedah Projek

(a) Penerbitan (termasuk laporan/kertas seminar)
(Sila nyatakan jenis, tajuk, pengarang, tahun terbitan dan di mana telah diterbit/dibentangkan).

Manuskrip bertajuk 'Effect of Healon 5 and Healon GV on corneal endothelial morphology after cataract surgery' telah diterima untuk penerbitan 'International Medical Journal – pending printing'

Persembahan lisan bertajuk 'A randomized comparison on the corneal endothelial cells after the use of two different viscoelastic agents during phacoemulsification surgery' telah dibentangkan di 'The 20th Asia Pacific Academy of Ophthalmology Congress' pada 29 Mac 2005, Sunway Lagoon Convention Centre, Kuala Lumpur.

Persembahan lisan bertajuk 'Effects of Healon 5 and Healon GV on corneal endothelium after phacoemulsification surgery' telah dibentangkan di 'National Conference on Medical Sciences'pada 21 Mei 2005 di Kampus Kesihatan USM.

Penerbitan (abstrak) bertajuk 'Effects of Healon 5 and Healon GV on corneal endothelium after phacoemulsification surgery' dalam Malaysian Journal of Medical Sciences Volume 12 (Supplementary 1) 2005, page 58

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(b) Faedah-Faedah Lain Seperti Perkembangan Produk, Prospek Komersialisasi Dan Pendaftaran Paten.
(Jika ada dan jika perlu, sila guna kertas berasingan)

....Tiada..

(c) Latihan Gunatenaga Manusia

i) Pelajar Siswazah: ....**Tiada**..

ii) Pelajar Prasiswazah:..............**Tiada**.......................................

iii) Lain-Lain :..............**Tiada**...

6. Peralatan Yang Telah Dibeli:

Tiada

UNTUK KEGUNAAN JAWATANKUASA PENYELIDIKAN UNIVERSITI

Beberapa pendapatan sepatutnya dikaitkan

T/TANGAN PENGERUSI
J/K PENYELIDIKAN
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PROFESSOR ABDUL AZIZ BABA
Chairman of Research & Ethics Committee
School of Medical Sciences
Health Campus
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan

UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
PENYATA PERBELANJAAN SEHINGGA 28 FEBRUARI 2005

Jumlah Geran:	RM	19,629.00	Ketua Projek:	DR. SHATRIAH ISMAIL
Peruntukan 2003 (Tahun 1)	RM	0.00	Tajuk Projek:	A Randomized Comparison on the Corneal Endothelial Cells After the Use of 2 Different Viscoelastic Agents During Phacoemulsification Surgery
Peruntukan 2004 (Tahun 2)	RM	0.00		
Peruntukan 2005 (Tahun 3)	RM	0.00	Tempoh:	15 Jun 03- 14 Jun 05 BEKU 12.08.05
			No.Akaun:	304/PPSP/6131283

Kwg	Akaun	PTJ	Projek	Donor	Peruntukan Projek	Perbelanjaan Tkumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6131283		504.00	-	504.00	-	-	-	504.00
304	14000	PPSP	6131283		-	-	-	-	-	-	-
304	15000	PPSP	6131283		-	-	-	-	-	-	-
304	21000	PPSP	6131283		870.00	964.00	(94.00)	-	684.00	684.00	(778.00)
304	22000	PPSP	6131283		-	-	-	-	-	-	-
304	23000	PPSP	6131283		300.00	-	300.00	-	-	-	300.00
304	24000	PPSP	6131283		-	-	-	-	-	-	-
304	25000	PPSP	6131283		-	-	-	-	-	-	-
304	26000	PPSP	6131283		-	-	-	-	-	-	-
304	27000	PPSP	6131283		8,300.00	363.40	7,936.60	300.00	2,615.00	2,915.00	5,021.60
304	28000	PPSP	6131283		-	-	-	-	-	-	-
304	29000	PPSP	6131283		9,655.00	4,555.20	5,099.80	3,950.00	550.00	4,500.00	599.80
304	32000	PPSP	6131283		-	-	-	-	-	-	-
304	35000	PPSP	6131283		-	-	-	-	-	-	-
					19,629.00	5,882.60	13,746.40	4,250.00	3,849.00	8,099.00	5,647.40

Effect of Healon 5 and Healon GV on corneal endothelial morphology after phacoemulsification surgery

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ABSTRACT

Objective: To compare corneal endothelial morphological changes after the use of Healon 5 (sodium hyaluronate 2.3%) and Healon GV (sodium hyaluronate 1.4%) during phacoemulsification surgery, particularly at three months after the surgery.

Settings: Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia, Malaysia and Eye clinic, Hospital Kota Bharu, Kelantan, Malaysia.

Materials and Methods: One hundred and ten patients were randomized, 55 per group, in a prospective randomized clinical trial of phacoemulsification surgery using Healon 5 or Healon GV. Three ophthalmologists performed the surgeries. The corneal endothelial cells density, average cell size, coefficient variation and hexagonality were assessed preoperatively and at three months postoperatively using a non-contact specular microscope Topcon SP2000P. Analysis of the data was performed using SPSS version 10.0, Independent-Samples T Test.

Results: There was statistically significant difference between Healon 5 group and Healon GV group based on endothelial cell density **(p=0.015)** and percentage of cell loss **(p=0.033)**. The cell size was noted significantly smaller in the Healon 5 group compared to the Healon GV group at three months **(p=0.004)**. A similar result was also noted in percentage of changes in cell size **(p=0.033)**. There were no statistically significant differences in changes of coefficient variation of cell size and hexagonality in both groups at three months after the surgery.

Conclusion: Minimal corneal endothelial morphological changes were noted in the Healon 5 group compared to the Healon GV group, particularly in term of less cell loss and less alteration in cell size at three months after the surgery. Thus, indicates that Healon 5 is more effective than Healon GV in minimizing risk of corneal endothelial injury during phacoemulsification surgery.

KEYWORDS

phacoemulsification surgery, endothelial morphology, viscoelastic substances

INTRODUCTION

Phacoemulsification surgery was first introduced by Dr Charles Kelman in 1967 with numerous convincing outcomes; such as small incision surgery, improving astigmatism and leading to a faster recovery period[1]. The evolution of cataract surgery techniques and instrumentations started changing thereafter. Despite this promising outcome, the endothelial cell loss due to phacoemulsification surgery becomes a major concern among the ophthalmologists world wide.

Ophthalmic viscosurgical devices (OVDs) are the most commonly used tool in modern cataract surgery mainly to protect the corneal endothelium from mechanical and surgical trauma[2-3]. Secondly, they also maintain anterior chamber depth during cataract surgery.[2-3] Therefore, they facilitate the surgery, minimize trauma to the corneal endothelium and reduce the amount of endothelial loss in anterior segment surgery, particularly cataract surgery[2-3].

Healon GV (sodium hyaluronate 1.4%, Pharmacia) was introduced into the market in 1993. Its cohesive property made manipulation of anterior and posterior tissues much easier. Healon 5 (sodium hyaluronate 2.3%, Pharmacia) became available 5 years later and claimed to be the first of new generation of more versatile viscoelastic agents designed specifically for phacoemulsification. It actually exhibits both cohesive and dispersive properties. In low flow settings during capsulorhexis and lens implantation, Healon 5 behaves a cohesive property and maintains space better than previously available viscoelastic[4]. While in high flow settings used in modern phacoemulsification, such as chopping, cracking and supercapsular phaco, it displays a dispersive property[4].

Argument and discussion regarding advantages and disadvantages of Healon 5 and Healon GV are very interesting, mainly upon their protective behavior on cornea endothelial cells during the surgery. Endothelial cell density and other morphological changes, i.e. cell size, coefficient variation of cell size and hexagonality are important parameters to reflect the state of endothelial cells.

However to our knowledge, there is no single study yet that evaluates the morphological changes of endothelial cells, particularly regarding changes in cells density, average cell size, coefficient variation and hexagonality pertaining to Healon 5 and Healon GV in phacoemulsification surgery. We believe that there is a need to confirm the overall morphological change of the corneal endothelium after phacoemulsification surgery, particularly using Healon 5 and Healon GV as the viscoelastic substances intraoperatively.

This study aimed to compare corneal endothelial morphological changes (i.e. cell density, cell size, coefficient of variation in cell size and hexagonality) after use of Healon 5 and Healon GV at three months after phacoemulsification surgery.

MATERIALS AND METHODS

This randomized clinical trial was conducted between 1st January 2003 till 28th February 2004 at the Eye Clinic, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan and Eye Clinic, Hospital Kota Bharu, Kelantan, Malaysia. The study protocol was approved by the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia. A minimum of hundred and ten patients were required for this study based on 2 mean formula. 55 patients recruited into Healon 5 group and another 55 patients into Healon GV group using a sealed envelope technique.

Patients of either sex who were 40-75 years old, age related cataract, normal intraocular pressure, axial length of eyeball between 22-26 mm, baseline endothelial count more than 2000 cells/mm^2 and underwent uncomplicated phacoemulsification surgery with posterior chamber intraocular lens implantation were included.

Patients were excluded if they had endothelial cell disease, glaucoma, uveitis, previous ocular trauma/surgery, intraoperative complications e.g. posterior capsule rupture, vitreous loss, anterior chamber lens implantation etc. and post operative complications e.g. raised intraocular pressure, hyphema etc. Patients with systemic illnesses that would compromise endothelial cell function e.g. diabetes mellitus, chronic renal failure and chronic obstructive airway disease were also excluded.

All potential patients underwent a complete ocular and systemic assessment at two weeks before the surgery (pre-op assessment) in both centers. A thorough ocular and systemic history was taken. Visual acuity of both eyes was tested with the standard retroilluminated Snellen Chart. Proper examinations of both anterior segment and posterior segment were performed to look for any apparent ocular abnormalities. Lens density was graded using Emery's Classification based on combination of opalescence and yellowing of nuclear sclerosis[5]. A complete systemic examination and baseline investigations that include electrocardiograph, full blood count, random blood sugar and serum electrolytes were performed to rule out systemic illness.

Selection of patients was made on the admission day by two co-investigators in both centers respectively. Written informed consents were taken from the patients. The baseline central corneal endothelial photomicrograph was performed. Endothelial morphology was measured using a non-contact Topcon SP2000P specular microscope.

All the patients would be randomized using envelope technique. A stack of opaque envelopes was prepared earlier with 55 envelopes containing a piece of paper with the word 'Healon 5' and the remaining 55 envelopes stated 'Healon GV'. These envelopes were shuffled and stored at the randomization room in Hospital Universiti Sains Malaysia. The envelope was drawn for each patient. The ophthalmic viscoelastic device would be assigned during the phacoemulsification surgery based on the printed paper selected for every patient.

All the patients were admitted to the respective centers for elective phacoemulsification and intraocular lens implantation. The surgeries had been performed by experienced phacoemulsification surgeons. There were two surgeons in Hospital Universiti Sains Malaysia and one surgeon in Hospital Kota Bharu, Kelantan involved in this study.

On the operative day, the pupillary dilatation was accomplished with 2.5% phenylepinephrine and 1% tropicamide. This was done at one hour before the surgery. Lid speculum was inserted to separate the eyelids. Subtenon anaesthesia (Lignocaine and Marcaine ratio was 1:1) was administered to every patient. Standard phacoemulsification surgeries were performed in all patients. Limbal scleral- tunnel incision was made at 12 o'clock using a 3.5 mm phaco knife. A side port was established to allow the entry of a nucleus rotator (second instrument) at 2.30 o'clock position. Next, the assigned viscoelastic device was injected into the anterior chamber. A continuous curvilinear capsulorhexis was made. Lens nucleus and cortex were hydrodissected with balanced salt solutions. The nucleus was removed using phacoemulsification technique. After the remaining lens cortex was removed with an irrigation/aspiration (I/A) probe, the anterior chamber and capsular bag were expanded with the remaining viscoelastic device. A foldable acrylic intraocular lens was then implanted in the capsular bag. The viscoelastic material was removed using the irrigation/aspiration (I/A) probe. The incision was left either sutureless (stromal hydration) or sutured with 10/0 nylon to a maximum of three stitches.

As Healon 5 and Healon GV were packed in distinctive syringes and had distinctive handling characteristics (Table 1), it was not possible to mask the surgeons to the device used. Throughout the surgery, the surgeons were allowed to use one vial of viscoelastic material only. Patients who required more than one vial of viscoelastic intraoperatively would be excluded from the study. Pupillary size, type of viscoelastic agent used, ultrasound time, phaco power and duration of the procedure were documented in the study forms.

Postoperatively, all patients in both centers were prescribed oral acetazolamide 250 mg three times daily for a day. After being reviewed on day one postoperatively, they were discharged home with prednisolone acetate 1% ophthalmic solution two hourly for a week, tapered to four hourly for a month and six hourly for another one month. All patients were examined postoperatively at their respective centers; at one week, one month and three months after the surgery and had their cornea endothelial photomicrograph at three months postoperatively.

The endothelial morphology analysis was done by the principal investigator in Hospital Universiti Sains Malaysia using the IMAGEnet 2000, cell analysis software (version 2.11). The endothelial cells density, average cell size, coefficient of variation in cell size and the percentage of hexagonal cells were analyzed using a traced method[6]. To improve accuracy, we standardized to minimum of 100 cells required for a baseline data analysis[7].

All the statistical analysis was done with Statistical Package for Social Sciences (SPSS Inc) software, version 10.0. Normality was tested using Eye-balling (histogram pattern). In a normally distributed data, difference of means between the two groups were tested with an Independent Sample T-test (p=0.05). While in skewed data, difference of means between the two groups were tested with Mann-Whitney U test (p=0.05).

Table 1. Physical and biochemical properties comparing Healon 5 and Healon GV

Physical / Biochemical properties	Healon 5	Healon GV
Storage (C)	2-8	2-8
Ingredients/ ml	23 mg NaHa	14 mg NaHa
Concentration (%)	2.3	1.4
Viscosity (mPas)	7 000 000	2 000 000
Osmolarity (mosm/L)	309	302
Molecular weight (Dalton)	4 000 000	5 000 000
pH value	7.0-7.5	7.0-7.5

RESULTS

There were no statistically significant differences between Healon 5 group and Healon GV group before surgery with regards to age and nucleus density ($p>0.05$). We found there were no statistically significant differences regarding phaco time and phaco power intraoperatively between the two groups ($p>0.05$).

The mean endothelial cell parameters preoperative and postoperatively were illustrated in Table 2. These include endothelial cell density, average cell size, coefficient variation of cell size and hexagonality.

Table 2. Outcome variables.

	Healon 5 (n=55)	Healon GV (n=55)	p value
Endothelial density (cells/mm²)			
Preoperative	2529.73 ± 301.73	2504.09 ± 306.64	0.174
3 months postoperative	2279.58 ± 395.63	2067.86 ± 439.80	**0.015**
Changes (%)	9.8	17.4	**0.033**
Average cell size (µm²)			
Preoperative	385.85 ± 43.05	403.11 ± 54.68	0.069
3 months postoperative	446.29 ± 87.02	511.61 ± 61.67	**0.004**
Changes (%)	15.6	26.9	**0.033**
Coefficient of variation in cell size			
Preoperative	39.84 ± 6.52	38.30 ± 5.83	0.181
3 months postoperative	40.26 ± 4.92	40.22 ± 7.16	0.973
Changes (%)	1.1	5.0	0.261
Hexagonality (%)			
Preoperative	51.39 ± 6.48	50.82 ± 6.71	0.652
3 months postoperative	46.87 ± 7.77	44.25 ± 7.93	0.083
Changes (%)	8.8	12.9	0.120

* p-value < 0.05 (significant)

Independent-Samples T Test

DISCUSSION

Endothelial cell loss is an indicator of permanent injury to the cornea. When endothelial cells die and drop out, adjacent cells expand to fill the gaps created in order to keep the Descemet's membrane remains covered. As a result, the endothelial cells densities decrease and mean cells size increase. Severe degree of trauma will lead to pleomorphism and polymegathism. The resulting changes are secondary indicator of cornea endothelial injury.

We studied the difference of cell density, average cell size, coefficient of variation in cell size and hexagonality at three months postoperative period. The endothelial cells sustain variable degree of injury following phacoemulsification surgery. An adequate time needs to be given for the cells to recover and reorganize. The endothelial cells were reported to stabilize and reorganize at least at three months post operative period[8].

There was a statistically significant difference in cell density and percentage of cell loss between the Healon 5 group and the Healon GV group at three months after the surgery. This finding suggested that Healon 5 was better than Healon GV in preserving endothelial cell density during phacoemulsification surgery.

This result is consistent with a study conducted by Holzer et al in 2001[9]. They randomly assigned eighty one eyes to receive one of five viscoelastic agents which were Healon 5, Healon GV, Viscoat, Ocucoat and Celoftal during phacoemulsification. They found that the Healon 5 group had the lowest mean endothelial cell loss (6.2%), significantly lower that in the other groups. Mean cell loss was 10.9% in the Healon GV group, 12.9% in the Celoftal group, 15.4% in the Viscoat group and 16.7% in the Ocucoat group.

We reported a slightly higher percentage of cell loss as compared to the Holzer et al (2001). In our study, the amount of cell loss in the Healon 5 group was 9.8% and 17.4% in the Healon GV group compared to 6.2% in the Healon 5 group and 10.9% in the Healon GV group as reported by Holzer et al.

Multiple surgeon involvement and differences in their techniques could be the main confounding factor in our study. We agreed that they definitely had some differences in their skills of performing phacoemulsification surgery though they were experienced surgeons. In contrast to Holzer et al (2001), there was only single surgeon involved who performed similar technique in all the patients.

The surgeon's technique was another major contributing factor to the above result. Pirazzoli et al in 1996 reported that there was increased endothelial cell loss with divide and conquer technique (13.8%) compared to phaco and chop technique (4.72%)[10]. In our study, two surgeons performed divide and conquer technique while one surgeon preferred phaco and chop technique. In contrast to Holzer et al (2001), the surgeon performed phaco and chop technique in all studied patients.

We found that the average cell size and the changes of average cell size at three months after the surgery were statistically significant. Again, this observation suggested that Healon 5 was better than Healon GV in preserving the endothelial cell size.

We found no statistical differences between the Healon 5 and Healon GV groups with regards to changes in percentage of coefficient variation and hexagonality of the cells at three months postoperative period. This phenomenon was probably because all the cases included in this study were actually had uncomplicated phacoemulsification surgery for age related cataract only. We had excluded earlier patients with small pupil diameter[11], shorter axial length[12], past history of trauma, compromised endothelial cell function, uveitis[13], glaucoma[14], known systemic disorder[15-16] and with intra or postoperative complications who were at higher risk of developing severe injury to the endothelial cells following phacoemulsification surgery.

We do believe that the viscoadaptive property of Healon 5 will be more beneficial in the difficult cases, as mentioned above. Perhaps the above two variables will display a statistically significant outcome if they are being assessed in complicated cases which require more surgical manipulations. However, another prospective randomized study is needed to prove this theory.

This result also agrees with a study by Koch et al in 1993 as they found no statistically significant differences between the Healon and Viscoat groups with respect to changes in percentage of hexagonality and coefficient variation after posterior chamber phacoemulsification at four months after the surgery. However, they demonstrated significant increased in coefficient of variation and decreased in hexagonality in Viscoat group that underwent iris-plane phacoemulsification compared to Viscoat group, whom had posterior chamber phacoemulsification surgery[17].

This finding suggested that the coefficient variation and hexagonality were actually less sensitive indicators in assessing the degree of endothelial damage. The endothelial cells need to sustain a greater degree of trauma, thus the above two variables will show a significant difference.

There are many other factors predispose to cornea endothelial damage during phacoemulsification surgery. Apart from factors mentioned above, the other confounding factors include age[18], density of the nucleus[11], phacoemulsification time and power[19]. In this study, we found no statistically significant differences of these parameters between both Healon 5 and Healon GV groups. We also standardized steps of cataract surgery including wound size[19], site[20] and method of lens insertion[21] as they might predispose to the endothelial cells injury during phacoemulsification surgery.

Dick et al (1996) reported that wound size influenced the risk of endothelial loss and injury[19]. We performed a 3.5 mm corneoscleral wounds with the aim of minimizing endothelial damage in relation to wound size and site. Beltrame et al (2002) reported that as it was placed more posteriorly, corneoscleral wound caused minimal trauma as compared to clear corneal incision[20]. Levy et al (1988) reported that flat insertion technique caused 7.7% cell loss compared to 14.3% loss with forcep technique and 16.9% loss with syringe-style insertion technique[21]. Choice of local anaesthesia[22], amount of irrigating solutions[23] and sutureless versus few stitches[24] used were reported that did not cause significant influence to the endothelial cells.

As a conclusion, we would like to state that Healon 5 is generally superior to Healon GV during uncomplicated phacoemulsification surgery. It preserves cornea endothelial morphology mainly the cells density and the average cell size. Thus, we would like to suggest usage of Healon 5 in cataract surgery especially in complicated cases, diseased corneas and patients with pre-existing endothelial morphological changes.

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A RANDOMIZED COMPARISON ON THE CORNEAL ENDOTHELIAL MORPHOLOGY AFTER THE USE OF 2 DIFFERENT VISCOELASTIC AGENTS DURING PHACOEMULSIFICATION SURGERY

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I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been dully acknowledged.

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ABSTRAK

Objektif: Untuk membandingkan perbezaan morfologi pada sel-sel endothelium kornea selepas pembedahan phakoemulsifikasi menggunakan 'Healon 5' (2.3% 'sodium hyaluronate') dan 'Healon GV' (1.4% 'sodium hyaluronate'), iaitu pada bulan ketiga selepas pembedahan.

Methodologi: Seratus sepuluh orang pesakit dibahagikan secara rambang kepada dua kumpulan iaitu 55 pesakit setiap kumpulan menggunakan 'Healon 5' atau 'Healon GV' semasa pembedahan phakoemulsifikasi. Tiga pakar oftalmologi telah melakukan pembedahan-pembedahan ini secara berasingan. Kepadatan sel, purata saiz sel, variasi koeffisien dan peratus hexagonal telah dicatatkan sebelum pembedahan dan pada bulan ketiga selepas pembedahan. Prosedur ini dilakukan dengan menggunakan mikroskop spekular tanpa sentuh (Topcon SP2000). Analisis data telah dilakukan menggunakan 'SPSS versi 10.0, Independent-Samples T Test'.

Keputusan: Terdapat perbezaan yang signifikan secara statistik diantara kumpulan 'Healon 5' dan kumpulan 'Healon GV' berdasarkan kepadatan sel **(p=0.015)** dan peratusan kehilangan sel-sel endothelium **(p=0.033)**. Didapati saiz sel endothelium kornea mengalami perbezaan yang signifikan secara statistik diantara kumpulan 'Healon 5' dan kumpulan 'Healon GV' **(p=0.004)** pada bulan ketiga selepas pembedahan. Keputusan yang serupa juga dilihat melibatkan peratusan perubahan saiz sel **(p=0.033)**.

Tidak terdapat sebarang perbezaan yang signifikan secara statistik berdasarkan perubahan variasi koeffisien saiz sel dan peratus hexagonal diantara kedua-dua kumpulan dicatatkan.

Kesimpulan: Terdapat perubahan morfologi sel-sel endothelium kornea yang minimum didalam kumpulan 'Healon 5' berbanding kumpulan 'Healon GV', terutamanya didalam kehilangan sel-sel dan perubahan saiz sel-sel pada bulan ketiga selepas pembedahan. Ini bermakna, 'Healon 5' adalah lebih berkesan berbanding 'Healon GV' bagi mengurangkan risiko kecederaan pada sel-sel endothelium kornea semasa pembedahan katarak secara phakoemulsifikasi.

ABSTRACT

Objective: To compare corneal endothelial morphological changes after the use of Healon 5 (sodium hyaluronate 2.3%) and Healon GV (sodium hyaluronate 1.4%) during phacoemulsification surgery, particularly at three months after the surgery.

Methodology: One hundred and ten patients were randomized, 55 per group, in a prospective randomized clinical trial of phacoemulsification surgery using Healon 5 or Healon GV. Three ophthalmologists performed the surgeries. The corneal endothelial cells density, average cell size, coefficient variation and hexagonality were assessed preoperatively and at three months postoperatively using a non-contact specular microscope Topcon SP2000. Analysis of the data was performed using SPSS version 10.0, Independent-Samples T Test.

Result: There was statistically significant difference between Healon 5 group and Healon GV group based on endothelial cell density **(p=0.015)** and percentage of cell loss **(p=0.033)**. The cell size was noted significantly smaller in the Healon 5 group compared to the Healon GV group at three months **(p=0.004)**. A similar result was also noted in term of percentage of changes in cell size **(p=0.033)** .

There were no statistically significant differences in changes of coefficient variation of cell size and hexagonality in both groups at three months after the surgery.

Conclusion: Minimal corneal endothelial morphological changes were noted in the Healon 5 group compared to the Healon GV group, particularly in term of less cell loss and less alteration in cell size at three months after the surgery. Thus, indicates that Healon 5 is more effective than Healon GV in minimizing risk of corneal endothelial injury during phacoemulsification surgery.

LIST OF TABLES

LIST OF FIGURES

CONTENTS

1. INTRODUCTION

1.1 BACKGROUND

Phacoemulsification surgery was first introduced by Dr Charles Kelman in 1967 with numerous convincing outcomes; such as small incision surgery, improving astigmatism and leading to a faster recovery period. The evolution of cataract surgery techniques and instrumentations started changing thereafter. Despite this promising outcome, the endothelial cell loss due to phacoemulsification surgery becomes a major concern among the ophthalmologists world wide.

Ophthalmic viscosurgical devices (OVDs) are the most commonly used tool in modern cataract surgery mainly to protect the corneal endothelium from mechanical and surgical trauma. Secondly, they also maintain anterior chamber depth during cataract surgery. Therefore, they facilitate the surgery, minimize trauma to the corneal endothelium and reduce the amount of endothelial loss in anterior segment surgery, particularly cataract surgery.

Both Healon 5 and Healon GV were recently introduced into ophthalmic use and has become an important tool in phacoemulsification surgery. However, argument and discussion regarding their advantages and disadvantages are very interesting, mainly upon their protective behavior on cornea endothelial cells during the surgery.

There were few studies evaluating the amount of central endothelial loss after phacoemulsification surgery between Healon 5 with other ophthalmic viscosurgical device(s) or Healon GV with other ophthalmic viscosurgical device(s) had been published.

There was a study conducted by Holzer et al in 2001, comparing the effect of Healon 5 and other four viscoelastic substances (i.e. Ocucoat, Celoftal, Viscoat and Healon GV) on the corneal endothelium after cataract surgery. The variable assessed in this study was mainly the endothelial cell count, which was performed preoperatively and 90 days postoperatively. They did not evaluate other indicators of endothelial damage including cell size, changes in coefficient variation or hexagonality of the cells. Their conclusion was that the Healon 5 group had the lowest mean endothelial cell loss (6.2%) compared to Healon GV group (10.9%). The other groups have a bigger percentage of loss; Celoftal 12.9%, Viscoat 15.4% and Ocucoat 16.7%.

A fairly similar study to ours was conducted by Miller et al in 1999. They compared the protective effect of Healon GV and Viscoat to the corneal endothelium following phacoemulsification surgery. They analyzed average endothelial cell size and density before and at two weeks after phacoemulsification surgery. The power of their study was sufficient (80%) to confirm a statistically significant mean difference between Healon GV and Viscoat. There were no significant differences in endothelial cell size and density between the two groups. Thus, they concluded that both Healon GV and

Viscoat were comparable in their ability to protect the corneal endothelium during phacoemulsification surgery.

The protective effect of Healon 5 had been compared with Healon recently by Oshika et al in 2004. However, the variables assessed were different from our study. They studied the cell count and corneal thickness before and at one day, one week and three months after the phacoemulsification surgery. They found that both Healon 5 and Healon had no statistically significant difference in cell count and thickness, which implied that both had equal rate of protection on the corneal endothelium during phacoemulsification surgery.

However to our knowledge, there is no single study yet that evaluates the morphological changes of endothelial cells, particularly regarding changes in cell size, coefficient variation, cells density and hexagonality pertaining to Healon 5 and Healon GV in phacoemulsification surgery.

We believe that there is a need to confirm the overall morphological change of the corneal endothelium after phacoemulsification surgery, particularly using Healon 5 and Healon GV as the viscoelastic substances intraoperatively. Thus, we conducted a prospective, randomized, patient and observer masked study to evaluate the above changes. We do hope that the outcome of this study will provide a better understanding of their role in future cataract surgery.

1.2 CORNEA

1.2.1 ANATOMY OF THE CORNEA

Cornea is the clear transparent tissue comprising the central one sixth of the globe. It occupies the center of anterior pole of the globe. Since the sclera and conjunctiva overlap the cornea anteriorly, slightly more above and below than medially and laterally, the cornea appear elliptical when viewed from the front. In adult it measures about 12 mm in the horizontal meridian and about 11 mm in the vertical meridian.

Based on the histological criteria, cornea can be divided into five layers; superficial epithelial layer, Bowman's membrane, cornea stroma, Descemet's membrane and the innermost endothelium layer. The epithelium consists of non keratinized stratified squamous epithelium, which is five to seven layers thick at the centre of the cornea. The thickness is approximately 500 to 550 micrometer. Bowman's layer is formed by the condensation of anterior stroma, located just beneath the epithelial basement membrane. The stroma makes up almost 90% of the total cornea thickness. It consists of 78% water, 20% protein and 1% glycosaminoglycan. Descemet's membrane is thin layer that is actually formed by the cornea endothelial basement membrane.

1.2.2 FUNCTION OF THE CORNEA

The cornea is the most important refractive medium in the eye. This refractive power occurs on the anterior surface of the cornea, where the refractive index of the cornea (1.38) is greatly different from that of the air. Tear film is very crucial in maintaining the normal environment for the corneal epithelial cells.

The transparency of the cornea results from uniform spacing of the collagen fibrils in the substantia propria. Any increase in tissue fluid between the fibrils causes cloudiness of the cornea. The endothelial cells play a major role in limiting fluid uptake by the cornea stroma. This mechanism most probably occurs as the result of both its barrier function and most important, its active transport function.

If the above mechanism fails as a result of trauma or disease, the stroma loose its' dehydration state and present clinically as corneal oedema. Thus, this will eliminate the transparency property of the cornea.

1.3 CORNEA ENDOTHELIUM

The cornea endothelium is derived from the embryonic neural crest cells. It is a single layer of predominantly hexagonal cells that completely covers the posterior cornea surface. At birth, the endothelial cell density is approximately 4000 cells/mm^2. The density then rapidly falls over the first two years of life. This is mainly due to the rapid cornea growth and subsequent larger surface area of the posterior cornea. At the age of 20 years, the density is about 3500 cell/mm^2. This reduces further to about 2000 cell/mm^2 in the eighth to ninth decades of life.

The American Academy of Ophthalmology (1991) reported that cornea with an endothelial density between 2000 and 1000 cells/mm^2 are susceptible to decompensation. Those with density of less than 1000 cells/mm2 are more susceptible to surgical trauma.

A minimum level of 400 to 700 cells/mm^2 is required for maintenance of normal corneal function. This was clearly demonstrated by Bourne et al in 1976 who studied corneal endothelial morphology on healthy and diseased corneas of human volunteers soon after the introduction of specular microscopy. If the above critical number was not attained, the pumping and barrier function ceased. This would result in irreversible cloudiness and corneal decompensation with bullous keratopathy.

The absolute cell density is not the only sole determinant of endothelial health and physiological function. Endothelial health is also influenced by cell morphology. Thus, to accurately describe the endothelium health and function, it is useful to look at other variables such as cell size, variation of cell size in term of 'coefficient of variation' (CV) and variation of endothelium shape in terms of 'hexagonality'.

Cell size is determined by measuring the areas between the apical membranes. A population based study by Padilla et al in 2004 among healthy Filipinos revealed that the mean cell size was 363.0 μm. An increased in cell size usually occurs following surgery especially during early postoperative period and this signifies degree of damage to the endothelium.

Coefficient of variation (CV) shows degree of uniformity of the cell size within the whole endothelium population (standard deviation of cell area/ mean cell area). It provides a quantitative measurement of cell variation. Another population based study by Snellingen et al in 2001 suggested a mean coefficient variation of 37.8% among senile cataract patients, aged 40-75 years old in South Asia population. An increase in this value indicates high variability of cell size, known as 'polymegathism'. Increases in coefficient of variation in cell size signify a decrease in uniformity of cell size and indicate certain degree of endothelial injury.

Generally, over 60 % of the cells have a hexagonal shape as documented earlier by Yee at al (1985). However, a slightly difference data was demonstrated in South Asia population by Snellingen et al (2001). Among 1235 patients in this area of the world, aged between 40-75 years old with senile cataract, they found that the mean hexagonality was actually 40%. A decreased in this percentage with concomitant increase in the number of non hexagonal shape cells is known as 'pleomorphism'. Having a low percentage of hexagonality or pleomorphism is also another indicator of endothelial injury.

Both the coefficient of variation in cell size and hexagonality are independent of cell density. Schultz et al (1984) reported that the coefficient of variation in cell size and the hexagonality were inversely related. They noted that there were no significant differences of the endothelial cell density both in type I and type II diabetes mellitus compared to the age-matched non-diabetic populations. They also demonstrated that these patients have a significantly higher coefficient of variation and a decrease in the percentage of hexagonal cells.

1.3.1 CORNEAL ENDOTHELIUM MORPHOLOGICAL CHANGES IN VARIOUS CONDITIONS

The corneal endothelium can be damaged by a variety of insults, including inflammation, increased intraocular pressure, contact lenses, intraocular surgery and intracamerally administered pharmaceuticals, for example epinephrine. Systemic diseases, for example diabetes, chronic renal failure and chronic obstructive airway disease (COAD) are at risk to endothelial cell damage.

Anterior segment inflammation particularly uveitis, causes significant endothelial morphological changes as observed by specular microscopy in various studies. Pillai et al in 2000 studied the morphological changes in corneal endothelium in 13 patients with unilateral uveitis. They noted a significant difference in mean cell size and density in the vicinity of fresh keratic precipitate compared with normal endothelium of the opposite eye. However, this abnormal morphology returned to near normal values on resolution of uveitis.

High intraocular pressure is a known factor to compromise the corneal endothelial function. Glaucoma patients are at risk of having endothelial morphological changes. This was demonstrated by Sihota et al (2003) who studied the endothelial changes in patients with primary angle closure glaucoma. They found a significant decrease in the corneal endothelial cell density in eyes with previous attack of acute angle closure glaucoma and in eyes with chronic primary angle closure glaucoma. However, there was no further difference of cell density in eyes with subacute attack or the fellow eyes in primary angle closure glaucoma as compared to age-matched population.

An interesting change in endothelium morphology occurs during long term contact lens wear. Mac Rae et al (1986) discovered significant degree of pleomorphism and polymegathism without cell loss in patients who wore hard or soft contact lens over six years or more. Only a little recovery occurred after cessation of hard contact lens after four years period.

Keratoconus is another ocular condition that is associated with corneal endothelial morphological changes. Maurice in 1980 found that keratoconus patients had normal endothelial cells density but their coefficient variation was significantly high. Their percentage of hexagonality also dropped to 50% as compared to age matched population.

Matsuda et al (1984) demonstrated significant endothelial morphological changes in the graft following penetrating keratoplasty. Cell density in the graft was often less than $1000/mm^2$. Morphometric analysis showed that the cell loss and increased in polymegathism and pleomorphism continued for six months following keratoplasty, after which the cornea stabilized. A normal restoration of cell shape, coefficient variation and hexagonal pattern were recovered by two years after the surgery.

Diabetes mellitus is a known systemic disorder causing significant endothelial morphological changes. Schultz et al (1984) demonstrated that in type 2 diabetics over ten years or longer duration, their endothelial morphology showed an abnormal pattern of analysis. These patients were found to have normal endothelial density but high tendency of pleomorphism and polymegathism. Similar changes were also seen in type 1 diabetes mellitus. This phenomenon could be explained in relation to changes in cellular metabolism. The osmotic effects of sugars perhaps inhibited the Na/K pumps and caused alteration in the cell volume regulation. Hence, their endothelial cells were less stable and more vulnerable to surgical trauma than in normal populations.

Chronic renal failure is another systemic disease known to have alteration in endothelial morphological changes. Ohguro et al (1999) studied the corneal endothelial morphological changes using a specular microscopy in a 20 patients with chronic renal failure patients undergoing hemodialysis. Despite normal endothelial density, their corneal endothelium also showed increased percentage of pleomorphism and polymegathism. This phenomenon was related to high concentration of urea in the aqueous humor. An abnormally high level of oxidized glutathione (GSSG) was also noted in the aqueous humor. As the endothelium was nourished by the aqueous humor, breakdown in the homeostasis of the aqueous humor resulted in endothelial morphology abnormalities in chronic renal failure patients.

1.3.2 CORNEAL ENDOTHELIAL CHANGES FOLLOWING CATARACT SURGERY

Traditionally, the cataract surgery were performed with intracapsular technique and subsequently followed with extracapsular technique with intraocular lens implantation. In modern surgery, phacoemulsification is currently a preferable technique world wide.

Phacoemulsification with its well-recognized benefits, such as early visual rehabilitation, freedom from sutures and ability to permit controlled nuclear removal and in-the-bag intraocular (IOL) fixation is currently the most frequently utilized technique of cataract removal. However, it is a technique that is highly dependent on the utilization of expensive and sophisticated technology.

Endothelial cell loss is a primary indicator of corneal endothelial injury following cataract surgery regardless the type of surgery; intracapsular extraction, extracapsular technique or even phacoemulsification surgery. When the endothelial cells die and drop out, adjacent cells expand to fill the gaps created, so that the Descemet's membrane remains covered. As a result, the endothelial cell densities decrease and mean cells size increases.

The resulting change in average cell size is a secondary indicator of corneal injury. Apart from the above, endothelial cell hexagonality and coefficient variation are other common indicators of corneal stress. These parameters also change in response to corneal injury.

Matsuda et al in 1984 conducted a study to assess serial alteration in endothelial cell shape and pattern after intraocular surgery. They studied the hexagonality changes in 20 eyes after intracapsular cataract extraction using a computer-assisted digitizer. They discovered that during the first one month, the hexagonality significantly dropped to a lower level (52%) from the baseline value (68%). Between one to four months, the frequency of hexagonality increased gradually to 64%.

Increased in coefficient variation and decreased numbers of hexagonal cells occurred during the first one month as the cells spread to replace the lost cells. This fact was demonstrated earlier by Rao et al in 1978 who studied the morphological changes of corneal endothelial following intracapsular cataract extraction surgery. The above changes were found usually during early postoperative period and restored close to baseline values after a period of time following the surgery.

A long term observation by Dejaco-Ruhswurm et al in 2002 revealed that continuous endothelial cell loss was noted until at four years after posterior chamber lens implantation to correct ametropia in thirty four phakic patients. There was a rapid loss within one year after the surgery, after which the rate of loss was no longer significant thereafter. Despite that, the coefficient of variation and hexagonality remained stable during four year follow-up period.

1.3.3. RISK FACTORS FOR CORNEAL ENDOTHELIAL INJURY DURING PHACOEMULSIFICATION

These factors had been studied extensively by various researchers ever the first introduction of phacoemulsification in the late 1960s. Undoubtedly, the outcome of their studies had a great contribution in the improvement of phacoemulsification skills, techniques and also the instruments.

Converting to phacoemulsification technique from other conventional techniques also causes a significant clinical outcome to the corneal endothelium. Phacoemulsification was claimed to be more traumatized to the endothelium compared to the two previous techniques. Sugar et al in 1978 studied the mean endothelial density using specular microscopy in 86 patients who undergone phacoemulsification and intracapsular cataract extractions. Cataract extraction by the phacoemulsification appeared to be more traumatic (mean cell loss of 33.8%) to the endothelium than intracapsular extraction (mean cell loss of 14.9%).

A contradictory finding however was recently published. Bourne et al in 2004 examined 500 patients, age 40 years and older who had undergone phacoemulsification or extracapsular cataract extraction with posterior chamber lens implantation. They assessed the mean cell loss, coefficient of variation and hexagonality in both groups preoperatively and up to one year postoperatively. They found generally, there was no significant difference in both surgical techniques, though phacoemulsification carried a higher risk of cell loss in patients with hard nucleus and vitreous loss. This changing trend could be explained with regards to improvements in skills, techniques and instruments during phacoemulsification nowadays.

Hayashi et al in 1996 conducted a study to determine the principal risk factors for corneal endothelial injury during phacoemulsification. They investigated 859 eyes of patients who had undergone phacoemulsification surgery. The percentage of corneal endothelial cell loss was quantified using specular microscopy. They found that the firmness of the nucleus was the most significant risk factor compared to other factors including older age group, small pupil diameter, large nucleus, greater infusion volume, type of intraocular lens implanted and ultrasound time.

Shorter eye, especially with shallow anterior chamber is at risk of being traumatized during phacoemulsification. This had been confirmed by Walkow et al (2000) who found significant amount of endothelial loss in eyes with shorter axial length. A possible explanation of this fact could be related to the mean distance from the phaco tip and the cornea. Thus, phaco tip that was nearer to the endothelium would cause more degree of endothelial loss.

Site of wound incision also influence the severity of endothelial loss. Amon et al in 1995 found a difference in endothelial cell loss between a 3.5 mm superior scleral tunnel incision (3.0%) and a 3.5 mm temporal clear corneal incision (8.1%). This was probably because the scleral tunnel incision was placed more posterior and therefore induced less endothelial trauma. Thus, they recommended avoiding clear corneal incisions in eyes with very hard cataracts and pre-existing low cell density.

The wound size is also another confounding factor of endothelial loss during phacoemulsification surgery. Dick et al (1996) studied the percentage of endothelial loss after implanting intraocular lens through 3.5mm and 5.5 mm wound incision. They found that phacoemulsification with 3.5 mm corneal incisions produced slightly less cell loss (6.7%) than phacoemulsification with 5.0 mm incisions (7.9%) at one year after the surgery.

The techniques chosen during phacoemulsification surgery also influence the degree of endothelial cell loss. Kohlaas et al (1998) found that endothelial cell loss was also dependent on the surgical phacoemulsification technique. 10% endothelial cell loss was noted in 'phaco and chop' technique compared to 15% cell loss in 'divide and conquer technique'.

The time and power of the ultrasound are also claimed to be related to endothelial loss during phacoemulsification surgery. Dick et al in 1996 demonstrated a direct linear relationship between endothelial cell loss and ultrasound time and power; endothelial loss increased as the ultrasound time and power increased. They found that after one year, endothelial cell loss was 4.2% with ultrasound time less than 1½ minutes, 6.7% with ultrasound time between 1½ to 2½ minutes and 9.6% with ultrasound time between 2½ and 3½ minutes.

Dick et al (1996) also revealed that the percentage of endothelial cell loss was directly related to the ultrasound power. The endothelial cell loss was 4.1% with ultrasound power less than 10%, 6.7% with ultrasound power between 11-20%, 8.0% with ultrasound power between 21-30% and 9.5% when ultrasound power more than 31% after one year follow-up.

Intraocular lens implantation also causes a significant amount of endothelial loss. This loss of endothelium could be due to mainly contact between the intraocular lens and the endothelium during injection or unfolding. Irvine et al (1978) studied the effect to the corneal endothelium after phacoemulsification with and without intraocular lens implantation. The cell loss was documented as high as 26% with intraocular lens implantation, compared to 18% with phacoemulsification alone.

The other possibility is that, lacking of adhesion between the posterior chamber intraocular lens (plate-haptic) and the lens capsule which was noted in silicone type of intraocular lens. Kraff et al in 1980 demonstrated that the most likely explanation for the above mechanism was 'iris shaving phenomenon' and this, subsequently caused chronic uveitis and further damage the corneal endothelium

Type of intraocular lens is also another subject of debate among the ophthalmologists world wide regarding the amount of cell loss. Kassar et al (1980) studied the effect of contact between silicone and polymethylmethacrylate (PMMA) lenses to the corneal endothelium in the animal models. They found that the silicone intraocular lenses provoked less endothelial loss than PMMA lenses.

With further improvement of surgical skills and instrumentation, Oshika et al in 1994 reported a contradictory result. They demonstrated that both silicone and PMMA lenses had no significant difference of endothelial cell loss. They compared 155 patients who were randomly assigned between silicone intraocular lens implantation through a 3.2 mm incision and polymethylmethacrylate intraocular lens implantation through a 5.5 mm incision phacoemulsification surgery.

Placement of intraocular lens is also another confounding factor in endothelial cell loss. This was demonstrated by Matsuda et al (1988) who studied the endothelial cell loss in different place of intraocular lens implantation after phacoemulsification. They found that 18.1% cell loss in scleral fixated lens, 23.5% cell loss in posterior chamber lens (with intact posterior capsule) and 28.5% cell loss in anterior chamber lens (ruptured posterior capsule) at three years after the surgery.

Regardless all the above risk factors, the surgeons' skills are still the main confounding factor in determining the success of the surgery. This includes their preferred method, how they manipulate the instruments and what phacoemulsification technique they use. These factors are also important parameters that would contribute to the outcome of phacoemulsification surgery.

1.4 QUANTITATIVE MEASUREMENT OF CORNEAL ENDOTHELIUM

Specular microscope is an instrument to examine the endothelial cells. It uses specular reflection from the interface of the endothelial cells and aqueous humor. It enables us to study the changes occurring at different layers of cornea in various anterior segment disorders at much higher magnification.

Since its invention 25 years ago by Maurice in 1968, many technological advances have been made in the design and applications of this technique. Currently with the modern specular microscopes, endothelial images can be digitally captured and automated morphometric analysis of endothelial cells can be done.

Measurement of corneal endothelium can be performed by either contact or non-contact specular microscope. In both cases, the instruments are designed to separate the illumination and viewing light. This allows us to view the very weak reflection from the endothelial cells surface despite reflection from the anterior corneal surface.

Isager et al (2000) compared a contact (Konan Clinical Specular Microscope) and a non-contact specular microscope (Topcon SP-1000) in the determination of endothelial cell density. He showed that the average endothelial cell density and precision of both instruments were similar. Furthermore, the endothelial densities estimated by the two instruments at various values of anterior central corneal refractive power and central corneal thickness were also noted to be similar. Thus, they suggested that the two instruments could be used interchangeably.

There are few advantages of non-contact specular microscopy, for example it is convenient to use, atraumatized, carries less risk of infection and less time consuming as compared to contact specular microscopy. On the other hand, the advantage of using a contact specular microscope was better appreciated when examining a diseased cornea.

This was demonstrated by Hara et al (2003) who compared the clinical efficacy between contact and non-contact specular microscope. They were able to obtain clear images in healthy corneas using both type of specular microscope. However in diseased cornea for example Fuchs's endothelial dystrophy, clear images were obtained only by contact type of specular microscope.

Doughty et al (2000) had assessed the reliability of endothelial cell density estimates using a non-contact specular microscopy. They found that the reliability of the measurement depends greatly on the number of cells being studied. The reliability of cell density estimation was expected within ± 10% if only 25 cells were measured. However, the reliability improved to ± 2% if 75 cells were measured.

1.5 OPHTHALMIC VISCOELASTIC DEVICES

It is a great advantage to maintain anterior chamber depth when performing cataract extraction by phacoemulsification combined with intraocular lens implantation. To achieve this stability, viscous substances are injected into the anterior chamber. The introduction of ophthalmic viscosurgical devices (OVDs) more than 20 years ago substantially improved the efficacy and safety of cataract surgery and intraocular lens implantation.

A variety of ophthalmic viscosurgical devices are now available and each posses specific chemical and physical properties leading to different intraoperative behaviour. The change from extracapsular cataract extraction to phacoemulsification in recent years has placed new demands on the performance of viscoelastic devices.

During phacoemulsification, endothelial injury can result from touch by lens matter or instruments, fluids movement and oxygen free radicals released during ultrasound. Thus, the principal tasks of these viscoelastic devices are mainly to protect the corneal endothelium from the above injuries and maintain depth of the anterior chamber throughout the procedure.

1.5.1 PROPERTIES OF OPHTHALMIC VISCOSURGICAL DEVICES

The contents of currently available viscoelastic devices are based on three main chemical composition; that are hydroxypropyl methylcellulose (HPMC), chondroitin sulfate and sodium hyaluronate. These different materials actually exhibit different properties, in term of shear rate, viscosity, pseudoplasticity, elasticity and cohesion.

Viscosity is a measure of the thickness of a solution. It is actually the property of a solution that resists the displacement of two adjacent layers between which it is sandwiched. This resistance to the displacement is however not constant. Thus, a needed force will vary depending on the speed at which the two surfaces move relative to each other. This velocity is called shear rate.

Viscosity at zero shear rate means the viscosity at rest. It depicts the ability of a viscoelastic device to create anterior chamber depth, which ensures that the intraocular tissues are protected from trauma during surgery.

High shear rates are usually reached during initial injection of viscoelastic device. The initial resistance is therefore perceptibly high because of high zero shear rate. Once the plunger starts to move, viscosity of the viscoelastic device decreases as a result of higher shear rate. This will allow the viscoelastic device to be injected with little energy expenditure.

Pseudoplasticity is defined as a quotient of two different viscosities at two different shear rates. Pseudoplasticity of a solution describes the decrease in viscosity with increasing shear rate, similar to high-flow situations. This property allows easier viscoelastic device injection through a cannula.

Elasticity is the tendency of a material to return to its original shape after stretching, compression or deformation. Cohesion refers to the tendency of a viscoelastic device to resist breaking up and to flow as a unit.