ORIGINAL ARTICLES

Comparison between the Effect of Viscoat and Ocucoat on the Anterior Lens Capsule

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ABSTRACT

Purpose: To compare the morphological effects of Viscoat (Healon or sodium hyaluronate 3.0% chondroitin sulphate 4.0%) and Ocucoat (methylcellulose 2.0%) on the anterior lens capsule. Methods: Our study included a clinical part and an experimental part. Human lens epithelial cells (LECs) were collected via Capsulorhexis in 40 eyes of 40 patients, 10 of which had their Capsulorhexis under air and served as control. The other 30 eyes were divided between Viscoat and Ocucoat, in which 15 cases of each material were performed by them. Experimental part included 15 rabbits. Eyes in which Capsulorhexis was performed in 5 of which under air and served as control. The other 10 eyes had their Capsulorhexis performed under Viscoat and Ocucoat, by 5 eyes in each group. Results: The gathered anterior capsules of Human and rabbit eyes were examined using both light and electron transmission microscope. Human lens capsule collected via Capsulorhexis under Viscoat and examined by light microscopic examination revealed significant changes in the form of thickening of the lens capsule, cytoplasmic degenerative changes and loss of cellular polarity. By electron microscopic examination, the capsules had amorphous appearances and the cells showed degenerative changes in organelles. On the other hand changes in lens capsules under Ocucoat showed slight thickening with less degenerative changes in cellular organelles by both light and transmission electron microscope examination. Light microscopic examination of rabbit anterior lens capsules under Viscoat confirmed nearly the changes showed in human anterior capsules. Where in the group of rabbit lens capsules performed under Ocucoat, the lens capsule appeared less thickened and may appear more or less normal. Conclusion: It is clear from this study that Viscoat and Ocucoat have produced significant changes on human and rabbit lens capsules. These changes aid the surgeon in performing Capsulorhexis and in prevention of posterior capsule opacification afterwards.

Key words:

Introduction

As modern cataract surgery evolved, phacoemulsification techniques were developed. These required less ultrasound energy than the use of mechanical techniques to dissemble the nucleus as well as high vacuum and flow the challenges associated with modern phacoemulsification surgery have led to a shift in surgeons thinking about viscoelastic materials. Although there have been numerous studies reporting the effectiveness of viscoelastic substances in intraocular surgeries, many reports are subjective and based on results with small number of cases (Hidashide and Sugiyama, 2008). The term ophthalmic viscosurgical device (OVD) has become accepted because it more adequately describes the use of viscoelastic agents in cataract surgery. Ophthalmic Viscosurgical Devices (OVDs) have played a key role in the surgery of phacoemulsification.

An ideal OVD is one which is able to maintain the anterior chamber during the procedure particularly capsulorhexis, phaco probe entry and initial phacoemulsification, intraocular lens implantation, maintain mydriasis and media clarity, protect the phaco energy and also prevent postoperative rise in intraocular pressure (Glasser et al., 1989; Arshinoff, 1992 and Holzer et al., 2001). The development of the continuous circular capsulorhexis (CCC) technique has contributed significantly to the safety and effectiveness of cataract extraction and intraocular lens implantation. This technique facilitates every size of smooth, circular, capsular opening, and it produces a strong capsular rim that resists tearing even when stretched during lens material removal or lens implantation. Maintaining the general integrity of the eye and facilitating such procedures as hydrodissection, endolenticular phacoemulsification, capsule polishing, and safe lens implantation in both adults and children are some advantages of CCC (Gimbel and Neuhan, 1990). Viscoat (sodium chondroitin sulphate-sodium hyaluronate) and Ocucoat (hydroxypropyl methyl cellulose) are dispersive viscoelastic agents with low viscosity at zero shear rate. The dispersive nature causes better adherence of the viscoelastic agent to the corneal endothelium, possibly resulting in better protection of the corneal endothelium against fluid turbulence and lens
fragments during phacoemulsification. This had led to frequent use of such dispersive viscoelastic agents in routine small incision cataract surgery. In the USA, among ASCRS members, Viscoat is used as viscoelastic agent in 30% and in Europe, among German language surgeons, Ocucoat preparation are used in about 45% of cataract surgeries (Georg et al., 2001).

As performing anterior continuous circular Capsulorhexis (CCC) is a crucial step in phacoemulsification technique, our aim in this study is to evaluate and compare the effect of the two most popular viscoelastic agents in the form of Ocucoat (hydroxypropyl methylcellulose 2%) and viscoat (sodium chondroitin) sulphate 4% sodium hyaluronate 3%) on the anterior lens capsule.

**Materials And Methods**

Our study included a clinical part and an experimental part.

**Clinical Part:**

Forty eyes of 40 patients were included, all undergoing removal of their cataracts by phacoemulsification technique. They had undergone full medical and ophthalmologic examination, where any patient suffering from any chronic disease such as diabetes mellitus or under treatment from any chronic disease was excluded from the study.

The ophthalmologic examination included uncorrected visual acuity (U.C.V.A), best corrected visual acuity (B.C.V.A). Fundus biomicroscopy and intraocular pressure (IOP) monitoring by Goldmann applanation tonometer. No medical contraindications were presents or any presence of inflammation or ocular disease that can influence the success of surgery or affect the results of our study.

The clinical part of this study was divided into 3 groups:

**Group A:** Included 10 eyes of 10 patients performing capsulorhexis under air and served as control.

**Group B:** Included another 15 eyes of 15 patients, in which we performed capsulorhexis under Viscoat (sodium chondroitin sulphate, 4% - sodium hyaluronate, 3%).

**Group C:** Included another 15 eyes of 15 patients, in which we performed capsulorhexis using Ocucoat (hydroxypropyl methylcellulose).

Human lens capsules including lens epithelial cells (LECs) were gathered from capsulorhexis tissue during cataract surgery. The phacoemulsification has been performed using peribulbar block of 0.75% Marcaine and 2% lidocaine in a 50: 50 mixture. The clear corneal incision was done using a 3.2 mm keratome. Viscoat or Ocucoat were injected followed by a 30-second exposure period. A 5mm capsulorhexis was then made. As the capsulorhexis procedure required about 30 seconds, the total exposure time of lens capsule including lens epithelial cells (LECs) to Viscoat or Ocucoat was approximately 60 seconds. The nucleus was removed by the phacomachine using a phacoemulsifier (Infiniti, Alcon) with a fixed flow rate of 35 ml/min and a linear vacuum level of 300 mm Hg at maximum. A 20 guage straight phaco needle with a 30 degree angulated tip without a by pass hole was used at 30% power. Bottle height was 85cm above the eye. Then the capsular bag was filled with either Viscoat or Ocucoat and a soft acrylate IOC was implanted in the bag.

**Experimental part:**

Because previous studies indicate a significant variation in human LEC morphology during cataract surgery, an animal model was developed to investigate the effect of Viscoat (Healon or sodium hyaluronate, 3.0% - chondroitin salphate, 4.0%) and Ocucoat (hydroxypropyl methylcellulose) on the lens epithelium. Fifteen adult rabbits (average weight 1.5 – 2.25 kg) with apparently healthy eyes were used. All rabbits were housed at room temperature allowed free water and fed ad libitum.

This study included 3 groups:

**Group A:** Control group consisted of 5 eyes, in which the anterior lens capsule containing LECs were gathered via capsulorhexis under air.

**Group B:** Consisted of another 5 eyes of 5 rabbits in which the capsulorhexis was performed under Viscoat (Healon).

**Group C:** Consisted of another 5 eyes of 5 rabbits in which the capsulorhexis was performed under Ocucoat. We used the same technique in performing the capsulorhexis as in the clinical part of the study.

Rabbits were anaesthetized with an intramuscular injection of xylazine and ketamine, and then sacrificed. Using an over dose of phenobarbital immediately before procedures were performed. For histological examination, the anterior lens capsule was extracted, and cut into small pieces. These pieces processed for light and transmission electron microscopic examination.

The specimens (human and rabbit lens capsules including lens epithelial cells (LECs) were immediately fixed in 4% glutaraldehyde, buffered for 6 hours, then were transferred to phosphate buffer solution over night.

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The specimens were then post fixed in buffered osmium tetroxide and dehydrated in graded alcohol then embedded in araldite. Semi-thin sections were cut with glass knives and stained with toluidine blue then examined by the light microscope. For transmission electron microscopy (TEM) specimens were cut with a diamond knife and contrasted with uranyl acetate and lead citrate then examined by the electron microscope.

Results:

The obtained results, all changes occurring in the anterior lens capsule with special stress on the changes occurring on the lens epithelial cells (LECs) will be discussed.

Clinical Part:

Group A: (Capsulorhexis under air):

By light and electron microscopic examination, no significant changes occurred in the control lens capsules (Figs. 1&2). Light microscopy showed that the anterior part of the lens is composed of three components (Fig 1):
- Anterior lens capsule appeared as a thick acellular basement membrane that enclosed the lens
- Epithelium appeared as a single layer of cubical cells.
- Cortical lens fibers appeared as mature lens fibers lacking their nuclei.

By electron microscopic examination, the acellular basement membrane was seen. The epithelial cells contained large rounded and slightly indented nuclei, rough endoplasmic reticulum, Golgi bodies and mitochondria. Vacuoles were occasionally also observed (Fig. 2).

Group B: Viscoat (capsulorhexis under (sodium chondroitin sulphate-sodium hyaluronate):)

Light microscopic examination of the treated patients in this group, revealed significant changes in the form of thickening of the lens capsule. Cytoplasmic degenerative changes in the form of vacuolation and loss of cellular polarity were obvious in most specimens (Fig. 3). By electron microscopic examination, the capsule appeared to have a relatively amorphous appearance. The epithelial cells appeared highly edematous and some of their nuclei appeared more electrons dense with irregular contour and dilated nuclear envelope. The cytoplasm contained degenerated mitochondria and numerous cisternae of endoplasmic reticulum as well as it was occupied by variable size and shape of electron lucent vacuoles. In addition, many membranous structures (organelles) appeared ruptured and fused together to form very large space. Lamellar bodies were also observed (Fig. 4).

Group C: Ocucoat (Capsulorhexis under methyl cellulose):

In comparison to changes that occurred in the human lens capsules under Viscoat, the changes that occurred in this group were less than that observed under Viscoat.

The patient lenses, their epithelium appeared also thickened and vacuolated. The lens capsule as a whole is still thickened but less than in the previous group (Fig. 5).

Experimental part:

Group A: control group (Capsulorhexis under air) as described before in Figs. (1&2).

Group B: Viscoat (Capsulorhexis under sodium chondroitin sulphate-sodium hyaluronate).

Light microscopic examination of anterior lens capsules of treated rabbits confirmed the changes were observed in patient lenses, but less sever, where it showed vacuolation of epithelial cells and the capsule (Fig. 6). By electron microscopic examination, some nuclei became flattened with irregular contour and dilated nuclear envelope. Large number of intercellular vacuoles nearly occupied the cytoplasm; some of them represented degenerated mitochondria, numerous cisternae of endoplasmic reticulum and some healthy mitochondria (Fig. 7).

Group C: Ocucoat (Capsulorhexis under methyl cellulose):

The obtained observations were similar with those of human anterior capsules, where the lens capsule was thickened and epithelium contained tiny vacuoles with variability in shape and size of nuclei while in another cases the lenses appeared more or less normal (Fig. 8).
**Discussion:**

The anterior Capsulorhexis is one of the prerequisites for successful and uncomplicated phacoemulsification. The anterior Capsulorhexis has several intra and postoperative advantages over can opener or endocapsular capsulotomies and has become the standard capsulotomy technique for phacoemulsification (Georg et al., 2001; Harinder et al., 2005 and Zamini et al., 2003. The major aim for the application of viscoelastic substances in cataract surgery is prevention of corneal endothelial cell loss. This aim is fulfilled by deepening the anterior chamber, mechanical endothelial protection against surgical trauma, absorption of ultrasound energy, and coating of intraocular lens (Neuhan, 2004 and Augustin & Dick, 2004).

The main aim of this study is to investigate the morphological effects of Viscoat (sodium hyaluronate 3.0% chondroitin sulphate 4.0%) and Ocucoat (hydroxypropyl methyl cellulose 2%) on the anterior lens capsule particularly the lens epithelial cells (LECs). Viscoat and Ocucoat are dispersive viscoelastic agents with low viscosity at zero rate.

**Table 1:** Biophysical properties of the viscoelastic agents (Ray et al., 2006).

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<thead>
<tr>
<th>Content</th>
<th>Viscoat</th>
<th>Ocucoat</th>
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<tbody>
<tr>
<td>Sodium chondroitin sulphate</td>
<td>4%-sodium hyaluronate 3%</td>
<td>Hydroxypropyl methylcellulose 2%</td>
</tr>
<tr>
<td>Molecular weight (dacltons)</td>
<td>600000</td>
<td>90000</td>
</tr>
<tr>
<td>Viscosity at zero shear rate (CPS)</td>
<td>40000</td>
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This study, comparing the effect of these two different materials Viscoat and Ocucoat having different molecular weights and viscosities on the anterior lens capsule regarding the thickness and the effect on lens epithelial cells (LECs) it was found many different changes. By observing the control group of human lens capsules performed under air we noticed that the capsule appeared by light microscopy as a transparent structureless brittle membrane where its anterior surface is covered by a layer of columnar nucleated epithelium. By comparing the effect of Viscoat (sodium hyaluronate, 3% - sodium chondroitin sulphate, 4%) on the anterior capsule after one minute of exposure, light microscopy a significant revealed thickening of the capsule, with cytoplasmic degenerative changes in the form of vacuolation, and loss of cellular polarity which concludes mainly that cells of the capsular epithelium will no more be viable and this may lead afterward to decrease the probability of operative post capsule opacification.

Electron microscopy confirming these changes where the epithelial cells appeared highly edematous, more electrons dense with diluted nuclear envelop and the cell organelles appeared ruptured with the observation of lamellar bodies. These changes of thickening of the anterior capsule and the degenerative changes of the nuclei and cellular organelles may be in the favor of the surgeon who can perform the capsulorhexis easier with decreasing the probability of posterior capsule opacification after wards. Similar changes were noticed in the rabbit lens capsules. Light microscopy and electron microscopy (TEM) examination revealed thickening of the capsule. In addition, the changes in the nuclei and the cytoplasmic organelles in the form of vacuolation of epithelial cells, flattening of the nucleolus and the degeneration of mitochondria, endoplasmic reticulum and intercellular vacuoles. By comparing our study with that done by C Budo et al., in which the same material Viscoat was used to perform Capsulorhexis, we found nearly the same changes concerning the cells, which grew thinner, nuclear condensations and intercellular vacuolization. The same study, also confirmed the clinical part with an experimental part which confirmed also the same changes (Camille et al., 2003).

In this study, Ocucoat was used also to compare the changes found in human and rabbit capsules with those found using Viscoat. The changes were more or less than that found by using Viscoat. The capsule slightly thickened, with slightly thickened vacuolated epithelium. In comparing the clinical part with the experimental part using Ocucoat, the same changes were observed with tiny vacuoles and variability in shape and size of nuclei. Also in some cases, the effect of Ocucoat may be nearly negligible where the lens capsules appeared more or less normal. As the changes seen in cases using Ocucoat are less than that observed by using Viscoat, it is clearly seen that performing Capsulorhexis by the surgeon is less comfortable as the general thickness of the capsule is thinner than that using Viscoat. Also, the probability of decreasing the posterior capsule opacification is also less as the changes in the nuclei and cellular organelles are less and some lens capsules even appeared by light and transmission electron microscope more or less normal.

It is known from literature that different factors affect the degree of posterior capsule opacification (PCO) (Gibran et al., 2006 and Apple et al., 1992). Posterior capsule opacification is caused when remaining lens epithelial cells (LECs) from the anterior lens capsule and equator migrate to the posterior capsule. The cells proliferate and change morphology, which can cause capsular wrinkling, elsching's pearls and visual loss (Marcantonio and Vrensen 1999). It has been argued that the equatorial lens epithelial cells produce most of the PCO (posterior capsule opacification) and that large Capsulorhexis would then lessen the PCO through fusion of the anterior capsular flap to the posterior capsule (Hollick et al., 1998 and Gisela et al., 2004). It is clear from this study that Viscoat (sodium hyaluronate, 3.0% - chondroitin sulphate, 4.0%) and Ocucoat (methylcellulose,
2% have produced significant morphological changes on human and rabbit lens capsules. These changes aid the surgeon in performing capsulorhexis easier and may aid in the prevention of posterior capsule opacification afterwards. Further research may be needed to assess the probability of prevention of posterior capsule opacification (PCO) afterwards.

Fig. 1: Photomicrograph of the control lens groups (1a from patient and 1b from rabbits) showing, anterior lens capsule (C) invested by a layer of cuboidal subcapsular cells (ep). Toluidine blue X 500) (bottom right sector X1250).

Fig. 2: Electron micrograph of the lens capsule and subcapsular epithelium of the control group. The capsule appears homogenous (C) and the epithelium contains large nucleus (N), rough endoplasmic reticulum (rer), mitochondria and Golgi bodies (arrow head) (X 10000). Note also some vacuoles (arrow).
**Fig. 3:** Photomicrograph of the specimen taken from Viscoat treated patients showing markedly thickened homogenous capsule (C) and vacuolated cytoplasm (V). Note, marked irregularity of the basement membrane (arrow). (Toluidine blue X 1250).

**Fig. 4:** Electron micrograph taken from the Viscoat treated patients revealing condensed nucleus (N) with irregular contour and dilated nuclear envelope (e), Degenerated mitochondria (m) and dilated cisternae of endoplasmic reticulum (R). Note, many vacuoles are variable in shape and size are noticed (V) (X 10000).
Fig. 5: Photomicrograph of specimen taken from Ocucoat treated patient exhibited thick capsule (C) and vacuolated epithelium (E) (Toluidine blue X 1250) Note, the capsule epithelium interface lost its sharp delineation.

Fig. 6: Photomicrograph of the lens from Viscoat treated rabbits group showing normal thickness of the lens capsule (C) and vacuolation of subcapsular epithelium (e) (Toluidine blue X 1250).

Fig. 7: Electron micrograph from the Viscoat treated rabbits group showing irregular contour of the epithelial cells nucleus (N) with dilated nuclear envelop (e) and highly vacuolated cytoplasm (V). Note, degenerated mitochondria (m) and myelin figures (mf) (X 10000).
Fig. 8: Photomicrograph of the specimen taken from Ocucoat animals exhibited slightly thickened lens capsule (C) and tiny vacuoles in the epithelium (V). Note, nuclei appear variable in shape and size (toluidine blue x1250).

References

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