MILESTONES IN CATARACT SURGERY? PHACOEMULSIFICATION USING THE KINETIC ENERGY OF THE FLUID AND RESTORE THE ACCOMMODATION IN PSEUDOPHAKIC PATIENTS

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DEBRECEN, 2006
1. Introduction

Cataract surgery has changed fundamentally by the introduction of phacoemulsification, which has become nowadays the standard method to remove cataract. The self-sealing wound is smaller, postoperative astigmatism is less, and the optical rehabilitation is significantly quicker during the procedure compared to manual extracapsular cataract extraction. Most lens nuclei must be divided first, after which they can be safely removed during surgery. Many complications can occur during standard phacoemulsification using traditional ultrasound. One of the most important complications is damaging the endothelium, which can lead to corneal decompensation if the deterioration is serious.

As a result of progress in ophthalmology, the kinetic energy of the fluid has become usable in cataract surgery. In recent years, one of the most meaningful technical innovations was the introduction of Aqualase. During this procedure, short pulses of warmed balanced salt solution liquefy the lens material. Advantages of the method are that there is no ultrasound and heating effect during the procedure, the Aqualase handpiece is more capsule-friendly than the ultrasound handpiece, and polishing the posterior capsule is possible with the pulses. The only reported limitation of fluid-based system is that it is not as effective in hard cataracts as conventional ultrasound technique. The in vivo effect of Aqualase on the corneal endothelium was unknown in the beginning of our study.

After removing nucleus and cortex, foldable posterior chamber intraocular lens (IOL) is implanted to secure optical rehabilitation to the patient. In recent years, monofocal IOLs are commonly used all over the world, which usually provide perfect uncorrected distance visual acuity for the patients, but near vision is rarely sufficient without correction. Compensating this lack of accommodation is one of the most important challenges in ophthalmologic research. Despite extensive investigations, the problem has not been fully solved. To restore
the missing accommodation we can implant multifocal IOLs, but these lenses can cause reduction in contrast sensitivity and higher incidence of photic phenomena such as halos, flare and glare. Further possibilities to alleviate presbyopia are the accommodating IOLs that move along the visual axis of the eye, but their accommodating ability is sometimes small and temporary. In subjects with bilateral cataracts, we can select one IOL for distance and the fellow IOL for near vision, which is called monovision. However, this strategy does not allow the advantages of binocularity. Besides the above-mentioned options, experimental techniques, such as capsular refilling with different types of materials have been used, but only in animals and not in human eyes. In recent years, one of the most meaningful IOL innovations is the single-piece AcrySof ReSTOR IOL, which has 6.0 mm optic diameter with a 3.6 mm apodized diffractive central zone.

It is known that some pseudophakic patients with monofocal IOLs have good near visual acuity with their distance correction. This phenomenon is called pseudoaccommodation or apparent accommodation, which occurs as a consequence of pseudophakic pseudoaccommodation and pseudophakic accommodation. Distinguishing pseudophakic accommodation from pseudoaccommodation is difficult because of superposing of the two mechanisms. To separate them, a static objective method such as measuring the anterior chamber depth (ACD) shift is indispensable. ACD shift can be measured with various techniques such as ultrasound biometry, high-resolution magnetic resonance imaging, ultrasound biomicroscopy, Scheimpflug imaging, anterior segment optical coherence tomography and partial coherence interferometry (PCI). PCI proved to be much more precise in ocular biometry than the usually used standard ultrasound. The system enables measuring the ACD shift using physiological stimulus. Moreover, other advantages of this method are that in contrast with ultrasound technique, the eye being measured accommodates during the
procedure, off-axis measurement is impossible, and there is no corneal applanation caused by direct contact, which is very important source of error.

Previous studies have investigated ACD changes in different types of standard monofocal and accommodating IOLs. These studies have mainly examined IOL movements after pharmacologic stimulation or relaxation of the ciliary muscle, which can provide only limited information about the physiologic conditions. Therefore, we have to choose an instrument which can determine IOL movements using physiological stimulus.

The aims were the following during our investigations:

1. To compare traditional ultrasound and Aqualase methods regarding surgical parameters and postoperative visual results.
2. To assess corneal endothelial changes caused by newly-developed Aqualase system compared to conventional ultrasound technique.
3. To determine whether applied energy and surgery time decrease using phaco-chop nucleus fragmentation method compared to divide and conquer technique using the Aqualase system.
4. To distinguish pseudophakic accommodation from pseudoaccommodation under physiological conditions with two traditional monofocal intraocular lenses;
5. To compare the traditional monofocal and the AcrySof ReSTOR intraocular lenses regarding visual functions.
6. To determine whether our good clinical experiences with the AcrySof ReSTOR IOL can be explained at least partially by the anterior shift of the IOL.

Regarding the timeliness of our choice of subject and the intensity of clinical investigations, it should be pointed out that at the beginning of our studies only one article could be found in the literature dealing with Aqualase method, and there was no study
regarding the AcrySof ReSTOR IOL. However, currently four articles regarding Aqualase and nine papers dealing with AcrySof ReSTOR IOL are available.

2. Patients and methods

Four prospective, comparative studies were performed at the Department of Ophthalmology, University of Debrecen. A routine ophthalmological examination (corneal astigmatism determination, evaluating best corrected distance visual acuity, slit lamp examination, binocular fundus examination and intraocular pressure measurement) was performed on each patient before surgery or examinations. Exclusion criteria were any eye pathology other than cataract or pseudophakic condition, age less than 50 years, high refractive errors (>4D), more than 1.0D of corneal astigmatism, intra- or postoperative complications, and history of any ocular surgery or trauma or laser. In addition to the above-mentioned, pupillary dilation problem and low endothelial cell count (<1500 cell/mm²) were also exclusion criteria from the Aqualase studies.

2.1. Aqualase studies

Nuclear hardness was graded by the surgeon using the LOCS III system. All operations were performed by the same surgeon, who was experienced in both traditional ultrasound and fluid-based techniques. The phacoemulsifications and the examinations were performed under standardized conditions to reduce bias.

Our first study included 17 patients with bilateral cataract. One eye of each patient was operated on with the traditional ultrasound method and the fellow eye with the Aqualase system using divide and conquer or Nagahara phaco-chop techniques depending on nucleus hardness.
In our next study thirty eyes of 30 patients were operated on with the Aqualase method and 30 eyes of 30 patients with the ultrasound technique using divide and conquer nuclear fragmentation maneuver in all eyes.

In our third study all eyes were operated on with Aqualase method using divide and conquer technique (25 eyes of 25 patients – Group 1) or Nagahara phaco-chop nucleofractis method (25 eyes of 25 patients – Group 2).

At the end of the surgery the following variables were recorded: phaco time, average ultrasound power, effective phaco time, aspiration time and surgery time in case of ultrasound, and Aqualase (AqL) time, number of pulses, average AqL magnitude, effective AqL time, aspiration time and surgery time in case of Aqualase. Effective phaco and Aqualase time is the time that theoretically would be necessary for the same surgery had 100% ultrasound or AqL power been used throughout (effective phaco time = phaco time x mean phaco power / 100, effective AqL time = fluid-based time x mean AqL magnitude / 100).

Routine ophthalmological examination (corneal astigmatism determination, evaluating best corrected distance visual acuity, slit lamp examination and intraocular pressure measurement) was performed in the postoperative period. In addition to the above mentioned, ultrasound pachymetry and endothelial cell analysis (endothelial cell density - ECD, mean endothelial cell area and coefficient of variation in cell size) were performed preoperatively and 10 days, 1 and 3 months and 1 year after surgery during our study investigating surgical effects to the corneal endothelium. Endothelial cell loss (ECL) was defined 1 year postoperatively using the following equation

\[
ECL = \frac{(ECD \text{ preoperative} - ECD \text{ 1 year})}{ECD \text{ preoperative}} \times 100.
\]

Statistical analyses were performed using Mann-Whitney and two-way repeated measure ANOVA tests. The effect of time was calculated with simple and repeated contrast.
2.2. Intraocular lens examinations

100 pseudophakic eyes of 79 patients were enrolled in the study. The following intraocular lenses (IOLs) were implanted: AcrySol® MA60AC (Group 1, N=40), SA60AT (Group 2, N=50), and SA60D3 (ReSTOR®) (Group 3, N=10). Examinations were performed 10.2 ± 9.2 months after surgery.

Best corrected distance and near visual acuities and distance corrected near visual acuity were evaluated. Distance visual acuity was determined using ETDRS chart. Near visual functions were evaluated using Jaeger chart. Special care was taken to keep light conditions constant during evaluation of visual functions.

Total pseudoaccommodative amplitude was measured with defocusing technique. The patients were asked to look with the observed eye at a standard illuminated, distant visual acuity chart at 5 m, with the contralateral eye occluded. After evaluating best corrected distance visual acuity, concave lenses were added in front of the distance correction in 0.25 D steps. Amplitude of pseudoaccommodation was defined as the minus lens power added over the distance correction with which the patient attained a visual acuity of 20/50 (Snellen equivalent).

To distinguish pseudophakic accommodation from pseudoaccommodation, anterior chamber depth measurements were performed using physiological and pharmacological stimuli. The ACD was measured with the AC Master using partial coherence interferometry method. All patients were seated and the investigated eye was fixated on a defined target, with the fellow eye occluded. To correct spherical equivalent of refractive errors, corrective spherical lenses were positioned in the optical path, providing essentially emmetropic conditions for the procedure. The ACD was measured first with target position at infinity followed by internal minus lenses added for near fixating. Ten measurements were taken for distance and near target and the ACD shift was calculated subtracting the two mean values.
After physiologically induced accommodation, some patients were recruited to measure the ACD after pharmacologically induced maximal ciliary relaxation using 1% cyclopentolate hydrochloride administered 3 times at 15-minute intervals (N = 20 in Group 1, N = 20 in Group 2, N = 10 in Group 3). ACD shift was calculated by subtracting ACD measured during near fixation from ACD with maximal ciliary relaxation.

Statistical analyses were performed using Mann-Whitney, Kruskal-Wallis, Wilcoxon and chi square tests.

3. Results

3.1. Aqualase studies

Significant differences between groups were not found regarding age, nucleus hardness, pre- and postoperative visual results in our studies (p>0.05).

Aqualase time was significantly less and average Aqualase magnitude was significantly more using the fluid-based system than phaco time and average ultrasound power using the ultrasound system (UH / AqL time: 21.1 ± 15.6 and 2.6 ± 2.2 sec, p<0.001, UH energy / AqL magnitude: 9.1 ± 4.4 and 44.9 ± 18.8 %, p<0.001). However, effective Aqualase / phaco time, which takes both parameters into consideration, did not differ significantly (UH: 2.1 ± 2.2, AqL: 1.5 ± 1.6 sec, p=0.3). Significant differences between groups were not found regarding surgical and aspiration times.

In our study comparing two different nuclear fragmentation techniques, we found that Aqualase time, mean AqL magnitude, effective AqL time, and the number of 4 µl pulses used during surgery were significantly less using phaco-chop technique compared to divide and conquer method (AqL time: 2.65 ± 1.86 and 1.08 ± 0.89 sec, p<0.001, average AqL magnitude: 57.2 ± 10.7 and 27.7 ± 11.7%, p<0.001, effective AqL time: 1.58 ± 1.28 and 0.37
± 0.41 sec, p<0.001, number of pulses: 3698 ± 2339 and 1842 ± 1535, p=0.001). However, surgery and aspiration times were not shortened using phaco-chop technique in comparison to divide and conquer procedure (aspiration time: 6.2 ± 1.5 and 6.5 ± 2 minutes, p=0.34, surgery time: 15.5 ± 3.1 and 15.7 ± 3.9 minutes, p=0.97).

In our study investigating surgical effect on corneal endothelium, alterations of all evaluated parameters were similar in the Aqualase and in the ultrasound groups during the postoperative period. Significant changes were detected during the study in the central corneal thickness (CCT) (p<0.001, F=20.6, df=4 and 42), in the endothelial cell density (ECD) (p<0.001, F=10.7, df=4 and 41), and in the mean cell size (p<0.001, F=9.2, df=4 and 41), but no significant alteration was found in the coefficient of variation in cell size (p=0.08, F=2.3, df=4 and 41). The “group” had no significant effect within the investigated parameters.

Investigating each parameter separately, an acute increase of central corneal thickness was found in both groups, which was reversible after 1 month (“simple contrast”, p<0.001, p=0.02, p=0.43, p=0.06). The changes of the CCT were similar in both groups (p=0.35).

Endothelial cell density decreased immediately after surgery in both groups. Additional reduction of ECD was not found after the first postoperative visit; however, a slight increase was observed at the 1-year visit (“repeated contrast”, p<0.001, p=0.4, p=0.28, p=0.01). The amount of ECD decrease was similar in both groups (p=0.99).

Mean cell size increased significantly at once after surgery in both groups; 10 days to 3 months it stabilized; after which a slight decrease was detected (“repeated contrast”, p<0.001, p=0.66, p=0.53, p=0.01). The changes of mean cell size were similar in both groups (p=0.85).

The coefficient of variation in cell size remained stable after surgery (p=0.08). Significant difference was not found between groups (p=0.99).
Endothelial cell loss was 6.5 ± 8.4 % in the Aqualase group, and 6.5 ± 11.7 % in the ultrasound group one year after surgery (p=0.69).

3.2. Intraocular lens examinations

Significant differences were not detected between intraocular lenses regarding best corrected distance and near visual acuities (p=0.75, p=0.08). However, distance corrected near visual acuity was significantly better with the ReSTOR IOL than the other two monofocal IOLs (percent of eyes Jaeger 1 or better: MA60AC – 3%, SA60AT – 8%, ReSTOR – 100%, p<0.001).

Mean subjective accommodation measured with defocusing technique was -0.82 ± 0.18 D in MA60AC group, and -1.0 ± 0.35 D in SA60AT group (p=0.3). In the ReSTOR group an accommodation curve with two peaks was observed: -0.25 D added in front of the distance correction caused immediately defocusing, but reaching approximately -3.0 D added over the distance correction the focus resharpened in all patients.

The anterior chamber depth (ACD) with target position at infinity was similar with the three IOLs (p=0.14). Using physiological stimulus, IOL movement differences between groups were not significant (p=0.07) and significant ACD changes from baseline were not detected (p=0.14). Mean ACD changes were 0.016 ± 0.06 mm in MA60AC group, 0.051 ± 0.05 in SA60AT group, and 0.02 ± 0.016 mm in ReSTOR group.

After pharmacological ciliary muscle relaxation statistically significant ACD shift differences between groups were not found (p=0.46) and significant IOL movements were not observed (p=0.1). Mean amplitude of ACD shifts were -0.001 ± 0.07 mm in Group 1, -0.019 ± 0.07 mm in Group 2, and 0.017 ± 0.16 mm in Group 3.

Statistically significant correlations were not detected between ACD shifts and patient age (r = -0.08, p=0.43), accommodative amplitude evaluated with defocusing technique (r = -
0.22, \( p=0.13 \), baseline ACD (\( r = -0.14, \ p=0.18 \)), IOL power (\( r= -0.03, \ p=0.8 \)), or white-to-white distance (\( r = 0.17, \ p=0.16 \)).

4. Discussion

Our studies showed that phacoemulsification can be performed effectively with the Aqualase system. The learning curve is short for a surgeon, who is experienced in the ultrasound technique. Surgery time and postoperative visual results did not differ compared to the ultrasound method. One interesting observation is that Aqualase time proved to be significantly less and average Aqualase magnitude significantly more using the Aqualase technique comparing phaco time and average ultrasound power using the ultrasound method. However, effective Aqualase / phaco time, which takes both parameters into consideration, did not differ significantly. Great caution should be taken with direct comparison of these parameters because of the totally different mechanisms of the two methods.

We were the first to apply Nagahara phaco-chop technique using the Aqualase system. We were also the first to investigate the effect of this maneuver on the surgical parameters compared to divide and conquer nucleofractis technique using the fluid-based method. We demonstrated that the Aqualase energy is reduced by chop maneuver, but that surgery time is not shortened. The latter was caused by the difficulties of reaching the full occlusion necessary to hold the nucleus during the chop maneuver using the Aqualase handpience. Our experiences support previous data from the literature that Aqualase is less effective in cases of harder nuclei than ultrasound. Therefore, we do not recommend the fluid-based system in harder cataracts even when using phaco-chop nucleofractis method.

Endothelial cell loss has to be calculated after all phacoemulsification using the ultrasound system. The results on mean ECL vary from 0.4% to 27.7% in the literature.
However, the *in vivo* ECL was unknown previously using the Aqualase method. We were the first to evaluate the effect of fluid-based phacoemulsification on corneal endothelium compared to traditional ultrasound. In our study significant differences between ultrasound and Aqualase systems were not found regarding endothelial function changes. We found an acute reversible increase of central corneal thickness after both methods. Endothelial cell density decreased, while mean cell size increased significantly after surgery in both groups. Additional worsening did not occur after 1 month. The coefficient of variation in cell size did not change during the investigating period. We found a 6.5% endothelial cell loss one year after surgery using both methods. We were the first to demonstrate that the Aqualase method as safe as conventional ultrasound in cataract surgery.

Besides the surgical technique of cataract removal, preventing the posterior capsule opacification and restoring the missing accommodation are the principally investigated areas in cataract research. To restore the missing accommodation, we can implant multifocal and accommodating IOLs and we can use the monovision strategy. However, because of the side-effects of these techniques, traditional monofocal lenses are the commonly used types of IOLs all over the world. Breakthrough and considerable change of attitude may occur with the appearance of the AcrySof ReSTOR, which is one of the most promising multifocal IOL innovations in recent years. This hydrophobic acrylic IOL has similar haptic as the AcrySof SA60AT IOL (plate haptic configuration and modified L loop), but its optic widely differs, because it has 6.0 mm optic diameter with a 3.6 mm apodized diffractive central zone. The diffractive power of the IOL for near vision is +4.0 diopters of add power at the lens plane, equal to approximately +3.2 diopters at the spectacle plane, which assures the possibility of uncorrected near vision to the patient. In our study, besides perfect distance vision, near visual acuity proved to be excellent under photopic conditions, which is not warrantable with monofocal IOLs. We were the first to investigate the possible movement of the ReSTOR IOL.
With this type of IOL, significant anterior chamber depth shift was not observed during near fixation and after pharmacologically induced ciliary muscle relaxation. Our findings verified first that the pseudoaccommodative ability of this lens is absolutely independent of the IOL movement.

It is known that some pseudophakic patients with monofocal IOLs have good near visual acuity with their distance correction. This phenomenon is called pseudoaccommodation, which occurs as a consequence of pseudophakic pseudoaccommodation and pseudophakic accommodation. The former is independent of the ciliary muscle function and caused by static optical features of the pseudophakic eye such as corneal multifocality, mild against-the-rule myopic astigmatism, and increased depth of field induced by small pupil. In contrast, pseudophakic accommodation is a dynamic change in the refractive state of the eye caused by anterior shift of the IOL during ciliary muscle contraction. Distinguishing pseudophakic accommodation from pseudoaccommodation is difficult because of superposing of the two mechanisms. To separate them, a static objective method such as measuring the ACD shift should be used. Partial coherence interferometry is the most precise method currently to measure the ACD shift.

Many studies in the literature deduce pseudophakic accommodative amplitude from ACD shift with pharmacologically constricted or relaxed ciliary muscle. However, it is known that pharmacologically stimulated accommodation with pilocarpine may overestimate the accommodative effect of an IOL. We can quantify only the maximal potential of the accommodation, and this method cannot provide us exact information about accommodative amplitude under physiological conditions. On the other hand, measuring ACD shift after cyclopentolate evaluates only the difference between IOL position during accommodation and IOL position with maximally relaxed ciliary muscle, which does not necessarily coincide with the position of the IOL under physiological relaxed condition. In accordance with other
authors, we believe that ACD shift measured using physiological stimulus is the most accurate method to evaluate pseudophakic accommodation amplitude.

In our study no significant ACD changes were detected using physiological stimulus and after pharmacological relaxation of the ciliary muscle with the investigated two monofocal IOLs, which have different haptic. It means that the ciliary muscle was maximally relaxed during distance fixation and/or the zonules were permanently relaxed independently of ciliary muscle status and/or the ciliary muscle was unable to contract during near fixation in our patients. Pseudoaccommodative amplitudes of -0.82 D and -1.0 D (means) were detected with these types of IOLs measured with defocusing technique. Statistically significant correlation between this amplitude and ACD shifts was not found. Moreover, it was previously demonstrated that in eyes with normal axial length and with average IOL power approximately 0.5 mm anterior shift is necessary for 0.8 D accommodation, which is in the opposite direction and orders of magnitude higher than we found in this study. Our data suggest that these usable pseudoaccommodative amplitudes with the investigated monofocal IOLs are independent of ciliary muscle function and occur in consequence of other factors such as corneal multifocality, against-the-rule myopic astigmatism, small pupil and patient motivation. We were the first to investigate these types of IOLs under physiological conditions.

In conclusion, we can establish that the newly-developed Aqualase system is a safe procedure to remove soft and moderate cataracts, and the AcrySof ReSTOR IOL is a promising choice of restoring accommodation in pseudophakic patients.
5. **Summary of new results**

1. We were the first to compare traditional ultrasound and newly-developed Aqualase phacoemulsification techniques regarding surgical parameters and postoperative visual functions. We conclude that Aqualase proved to be an effective method in cataract removal, with surgery time, effective Aqualase / phaco time, and postoperative visual acuities being similar to those of the ultrasound technique.

2. We were the first to demonstrate that postoperative endothelial functions are similar using the Aqualase system compared to the traditional ultrasound technique. The Aqualase method proved to be as safe as conventional ultrasound in cataract surgery.

3. We were the first to apply phaco-chop nuclear fragmentation technique during Aqualase phacoemulsification, and we proved that Aqualase energy used in surgery is significantly lessened by this maneuver.

4. We were the first to prove that the usable pseudoaccommodative amplitude of the investigated monofocal lenses is independent of intraocular lens movement under physiological conditions.

5. We demonstrated that in addition to excellent best corrected distance visual acuity, distance corrected near visual acuity is significantly better with the AcrySof ReSTOR intraocular lens than with standard monofocal lenses.

6. We were the first to prove that anterior shift does not play a role in good near visual functions experienced with the AcrySof ReSTOR intraocular lens.
6. Publications

6.1. Publications used in the dissertation


2. Tsorbatzoglou A, Kertész K, Módis L, Németh G, Máth J, Berta A: Corneal endothelial function after phacoemulsification using the fluid-based system compared to conventional ultrasound technique. Eye (advance online publication) /doi:10.1038/sj.eye.6702314/ (March 3, 2006) (IF: 1,867 – SCI05)


6.2. Other publications


6.3. Chapter of a book

1. Tsorbatzoglou A: Diagnostic criteria of keratoconjunctivitis sicca and primary Sjögren syndrome (Modern diagnosis and therapy of dry eye.) In: Módis L, Berta A. (Ed.) Educational CD (ISBN 9632186257)
6.4. Presentations related to the subject of the dissertation


6.5. Citable abstracts related to the subject of the dissertation


6.6. Other citable abstracts

