·Review·

Liquefaction for cataract extraction

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Received: 2015-07-13 Accepted: 2015-09-16

Abstract

• A systematic review of the recent literature regarding the implementation of the liquefaction in cataract surgery and its short–term and long–term outcomes in various parameters that affect the quality of patients´ life, including visual rehabilitation and possible complications was performed based on the PubMed, Medline, Nature and the American Academy of Ophthalmology databases in November 2013 and data from 14 comparative studies were included in this narrative review. Liquefaction is an innovative technology for cataract extraction that uses micropulses of balanced salt solution to liquefy the lens nucleus. Most studies reported that liquefaction is a reliable technology for mild to moderate cataracts, while fragmentation difficulties may be encountered with harder nuclei.

• **KEYWORDS:** Aqualase; liquefaction; cataract extraction; endothelium; corneal thermal injury
DOI:10.18240/ijo.2016.02.24

Labiris G, Toli A, Polychroni D, Gkika M, Angelonias D, Kozobolis VP. Liquefaction for cataract extraction. *Int J Ophthalmol* 2016;9(2):306–311

INTRODUCTION

Cataract is one of the most common causes of blindness worldwide. However, cataract is preventable and treatable by cataract extraction. Kelman [1] first introduced phacoemulsification in 1967, as a cataract removal technique. Since then, there has been a great progress in cataract surgery and many techniques, ultrasound [torsional and torsional intelligent phaco (IP) phacoemulsification] and non-ultrasound technology based (laser, sonic energy and fluid-based systems), have been used.

Aqualase liquefaction is a fluid-based system, recently introduced and available for lens extraction in the Infinity Vision System (Alcon Laboratories, Fort Worth, TX, USA). Aqualase works by propelling micropulses (maximum rate of 50 per second) of 4 mL of warmed (at 57℃) balanced saline solution (BSS), in order to strain and liquefy the lens material. Depression of a foot-pedal can control the magnitude of the pulses. The pulses are generated by electrodes in the titanium handpiece, then travel into the tip of the instrument and end into the eye. The fluid pulses pass through the outer circumferential sleeve and then exit through a small opening located in the lumen of the polymer tip near its distal end. Then, the liquefied lens material is aspirated through the central or inner lumen of the tip. The tip of the standard Aqualase needle is flared, with an inner diameter of 1.1 mm and an outer diameter of 1.32 mm. Its soft polymer nature makes the instrument capsule-friendly. Nowadays, the techniques of Aqualase are under constant improvement and it is considered to be one of the most up-and-coming technologies of the cataract surgery. One of the most significant advantages[2-10] of this fluid-based system is the reduced risk of thermal injury to the intraocular tissues, since the fluid pulses are quickly dampened in the eye's fluid environment. Using Aqualase, the risk of thermal incisional injury, even at full energy, is negligible. As the water-jet pulse, whose temperature is 57℃, gets mixed with irrigation fluids, the final temperature is stabilized at 32℃. Moreover, Aqualase is related to a reduced incidence of posterior capsule rupture and corneal edema and great visual outcomes. On the other hand, a strong limitation of Aqualase is the fact that it is not as effective as conventional phacoemulsification in cases of dense nuclei.

The purpose of this study is to review the recent literature regarding the implementation of the Aqualase in cataract surgery and its short-term and long-term outcomes in various parameters that affect the quality of patients' life, including visual rehabilitation and possible complications.

MATERIALS AND METHODS

The systematic search for relevant studies was performed based on the PubMed, MEDLINE, Nature and the American Academy of Ophthalmology databases using the following search terms: Aqualase, liquefaction, cataract extraction, visual acuity AND Aqualase, endothelial cell count AND Aqualase, corneal edema AND Aqualase, corneal sensitivity

Table 1 Comparative studies

Authors	Cataract extraction technique	Prospective / retrospective	Clinical outcome	Comments
Mackool and Brint [2]	Aqualase liquefaction *vs* conventional US phacoemulsification & Aqualase *vs* laser phacoemulsification	Retrospective	Aqualase was considered to cause less thermal injury than US Phacoemulsification.	Aqualase could extract easily cataracts up to grade 2 as quickly as conventional phacoemulsification and more quickly than laser and was also able to remove many 3+ cataracts.
von Sonnleithner *et al* [4]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	Aqualase showed significant cell loss in cataracts with density 3 and 4. Only in nuclear grade 4 there was significant difference between the two techniques.	Aqualase was unsuitable for hard nuclei due to very high endothelial cell loss.
Sandoval *et al* [6]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	No significant difference in any of the paremeters	Aqualase seemed to provide equal safety to conventional ultrasound regarding corneal endothelium damage.
Nekolova *et al* [11]	Aqualase liquefaction *vs* Neosonix	Prospective	There was no significant difference with EPCO software, but there was statistically significant difference (worse in neosonix) with OSCA software.	The correlation between EPCO 2000 and OSCA results was very poor.
Jiraskova *et al* [12-13]	Aqualase liquefaction *vs* NeoSonix	Prospective	Aqualase induced significantly better result than NeoSoniX in pachymetry and slightly significantly better results in endothelial cell density[12]. Aqualase induced significantly better endothelial cell count and pachymetry results for older patients than NeoSoniX[13].	Aqualase minimized intraoperative damage to occular structures and maximize the level and rapidity of visual rehabilitation, but it was not as effective as NeoSoniX for cataracts harder than 4 grades.
Barsam *et al* [7]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	Aqualase may carry less risk for the development of postoperative cystoid macular edema, especially in diabetic patients.	In the Aqualase group, 1 patient had a posterior capsule rupture without vitreous loss, not related to Aqualase liquefaction.
Tsorbatzoglou *et al* [5]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	Non significant difference in any of the parameters evaluated.	Hard nuclei cataracts needed longer surgery time and more applied energy with the Aqualase.
Ryu *et al* [16]	Aqualase liquefaction *vs* Microflow System US Phacoemulsification	Prospective	In mild to moderate cataracts Aqualase induced better results than the MicroFlow system only in surgically induced astigmatism.	Improvements in surgical skills (*e.g.* pre-chop method, high vacuum) might enable a wider use of Aqualase in hard cataracts.
Hu *et al* [8]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	Non significant differences in endothelial cell loss and visual recovery.	Aqualase was considered to be as safe as phacoemulsification with regard to corneal trauma, providing less risk to posterior capsular integrity.
Nekolova *et al* [14]	Aqualase liquefaction *vs* NeoSoniX	Prospective	Posterior capsule opacification: There was not significant difference with EPCO software, but there was significantly better OSCA software outcomes for Aqualase at 1y postoperatively.	-
Richard *et al* [9]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	Significantly less endothelial cell loss after Aqualase surgery compared to US phacoemulsification outcomes.	The Aqualase was safer than conventional US in cataracts graded up to 4.9 (LOCSIII). It was not as effective as conventional US in hard nuclei.
Labiris *et al* [15]	Aqualase liquefaction *vs* Torsional phacoemulsification	Prospective	There was no significant difference in any of the parameters (uncorrected visual acuity, central corneal thickness, endothelial cell count, central corneal sensitivity) evaluated.	Aqualase operation was converted to torsional in two eyes, due to inability to fragment the nucleus.
Nakano *et al* [10]	Aqualase liquefaction *vs* conventional US phacoemulsification	Prospective	There was no significant difference in any of the parameters (visual acuity, pachymetry) evaluated.	Both techniques induced minimal cornea edema, with slightly lower edema for the conventional phacoemulsification group and they proved to be equally effective for cataract surgery grade 1 and 2 (LOCSII).

AND Aqualase. Search filters and language restrictions were not used in this initial search. The results of this search were checked and only articles with a relative to the subject title were selected. Afterwards, the abstracts and full texts of these selected articles were reviewed thoroughly and the following data were extracted and assessed: randomization of the study, inclusion/exclusion criteria, number of cases, patients' age, nuclear density, cataract surgery techniques, settings of the Aqualase, type of anesthesia, type of incision, type of intraocular lens used, follow-up examinations results, clinical outcomes and referred complications. Only comparative prospective or retrospective clinical trials in adult patients were included in this review. Articles with no Aqualase clinical outcomes, concerning only other cataract surgery techniques, referring to human cadaver eyes or not available in English or German language were excluded.

RESULTS

Studies Design In the 14 comparative studies included in this review (Table 1), liquefaction was compared to other cataract extraction methods, such as conventional ultrasound phacoemulsification [2,4-10], NeoSoniX system [11-14], torsional ultrasound phacoemulsification[15], laser phacoemulsification[2] and phacoemulsification using MicroFlow System [16]. Conversion from liquefaction to other cataract removal techniques was stated in two studies[12,15]. Eyes that underwent conversion were finally excluded in one of these studies [15]. All of the studies were prospective, with the exception of one retrospective study [2].

Patients´ Selection Criteria Among the exclusion criteria were intraocular inflammation, glaucoma, corneal scars and other ocular pathology potentially affecting visual acuity outcomes, such as history of ocular surgery or trauma[5-9,11-15]. The cataract density was classified according to either Lens Opacities Classification System (LOCSII and LOCSIII)[17] or the Buratto Scale Systems [18] and consisted one of the most important inclusion criteria for ten of the studies. Cataract density was restricted from mild to moderate in most of the cases, but six of the studies included nuclei up to 4.9 grades on LOCSIII system [8-9] and less than 5 on the Buratto System [11-14]. Regarding the participants' age, data were not available in four studies [2,4,12,14]. The mean age was over 70 years old in three studies[7-8,15], while it varied from 44[11] to 93[13] years old in the rest of the studies [5-6, 9-11,13,16]. The age of patients was considered as an exclusion criterion in four studies. For example, Barsam *et al* [7] included patients 45 years old or older, while patients younger than 50 years old were excluded from three studies [4-6]. The number of endothelial cells was also a criterion for the patients selection in three trials [5,12,16], with cases of low endothelial cells not to be selected.

Surgical Data and Outcomes Aqualase settings were described in nine studies [5-7,9-10,12-13,15-16]. Linear magnitude varied from 40% to 100%, while pulses/second varied from 40 to 10770. Fluidics varied from 85 to 120 cm with fixed flow from 12 to 45 mL/min. Also, several ophthalmic viscoelastic devices were used[5-6,9-10,13,15]. All cataract surgeries were conducted under topical anesthesia through an incision of 2.75, 3.0 or 3.2 mm and followed by intraocular lens implantation. Primary outcome criteria, such as best corrected visual acuity, corneal pachymetry, endothelial cell count, posterior capsule opacification (PCO) and corneal edema during the postoperative follow-up, were assessed in all of the studies.

Comparative Studies In most comparative studies, liquefaction was compared to conventional ultrasound phacoemulsification [4-10]. In five of these studies [4-6,8-9] the endothelial cell changes (cell density, cell loss) after Aqualase cataract surgery were assessed in comparison to those after conventional ultrasound phacoemulsification. According to three of these studies [5-6,8], there were no statistically significant differences in endothelial cell changes and it is crucial to mention that the endothelial cell changes were similar after both techniques, even in patients with nuclear sclerosis of grade up to 6 on LOCSIII scale [5]. Richard *et al* [9] showed that Aqualase induced significantly lower endothelial cell loss than conventional ultrasound phacoemulsification, in a sample of cataracts with density up to grade 4.9 on LOCSIII scale. On the other hand, von Sonnleithner *et al* [4] demonstrated that Aqualase was associated with significant endothelial cell loss in cataracts of grade 3 and 4 on LOCSIII scale, while conventional ultrasound phacoemulsification provoked significant cell loss in cataracts of grade 3 on LOCSIII scale. Also, corneal edema after cataract surgery with Aqualase or conventional ultrasound phacoemulsification, based on central corneal thickness, was evaluated in four trials[5-6,9-10]. According to two of these studies [5,9] there was not any significant difference in this parameter between the two cataract surgery techniques. Nakano *et al* [10] pointed out that conventional ultrasound phacoemulsification induced slightly lower corneal edema, probably due to the fact that the total surgery time was smaller and the turbulent flow of fluids and lenticular particles within the anterior chamber was more limited. Sandoval *et al* [6] noticed a significant difference in corneal pachymetry on the first postoperative day compared to the preoperative status in all patients, no matter what cataract removal technique was used, Aqualase or conventional ultrasound phacoemulsification. However, there was no significant difference between these two groups during the whole follow-up period. Regarding the visual outcome, there were not any statistically significant differences between Aqualase and conventional ultrasound phacoemulsification in any of the trials [6,8,10]. In addition, Barsam *et al* [7] compared the effect of Aqualase and conventional ultrasound phacoemulsification on the macula using the optical coherence tomography (OCT) technology. As a result, Aqualase was considered to be equally safe to the conventional ultrasound phacoemulsification and there is possibly less risk of cystoid macular oedema development after surgery, mainly in diabetic patients. Finally, a possible correlation of the Aqualase effectiveness to the cataract density grades was examined in many studies [4-5,8-10]. According to these trials, Aqualase was proved to be equally safe and effective to conventional ultrasound phacoemulsification, with potentially less risk of posterior capsular integrity [19]. However, Aqualase appeared to be not as efficient as conventional ultrasound phacoemulsification in cases of hard nuclei, due to the longer surgery time needed, the more applied energy required [9] and the high endothelial cell loss induced[4].

Ryu *et al* [16] compared Aqualase to phachoemulsification using MicroFlow System, evaluating the mean surgically induced astigmatism (SIA), the corneal endothelial cell loss, the visual acuity and the corneal pachymetry. The only statistically significant difference between the two techniques was noticed in mean SIA at two months follow-up time with Aqualase showing better results.

The Aqualase was compared to the NeoSoniX in four studies [11-14]. Nekolová *et al* [11,14] conducted two studies, in which Aqualase and NeoSoniX techniques were compared as

for the induced PCO, one-year and three-years postoperatively. Both studies, included patients with cataract grade less than five (Buratto classification). Evaluation of the induced PCO using the EPCO software did not detect any significant difference between the two techniques, while the OSCA software outcomes showed that Aqualase had significantly better results at one-year follow-up confirmed in both studies. Eyes with preceding Nd:YAG laser capsulotomy were fewer when Aqualase method was used and were excluded from the PCO assessments. Regarding best-corrected visual acuity, there was not any significant difference between the two methods at any follow-up time. Also, Jirásková *et al*[12-13] conducted two studies, in order to compare the Aqualase with NeoSonix technique as for the visual acuity outcomes, the corneal thickness and the endothelial cell loss, in cases of nuclear sclerosis of 1-5 Buratto grades. In one of the studies[13], patients were divided into two groups according to their age. Patients over 80 years old appeared to have significant differences in endothelial cell density and in pachymetry postoperatively, with the Aqualase having better results. In the second study [12], Aqualase seemed to have a significantly better result in pachymetry compared to the NeoSoniX at 1mo postoperatively but not significantly better results in endothelial cell density. Both studies suggested that Aqualase removed efficiently cataracts of up to grade 3-4 (Buratto scale), but it was not as effective as the NeoSonix in more dense nuclei.

Labiris *et al* [15] assessed the impact of the Aqualase and of the torsional ip phacoemulsification on the endothelial cells, the postoperative corneal oedema and the corneal sensitivity in patients with senile cataract grade 2 on the LOCSIII scale. Regarding the clinical outcomes, both technologies showed similar results, without significant differences in all parameters evaluated, including visual acuity recovery, corneal cell thickness, central corneal sensitivity and endothelial cell count. Aqualase seemed to induce less corneal oedema. In two cases there was a conversion to the torsional phacoemulsification, due to Aqualase inability to fragment the nuclei. Despite these difficulties in nuclei fragmentation, both techniques were considered to be equally efficient with great refractive outcomes, even in grade 2 cataracts.

Finally, Mackool and Brint [2] compared Aqualase with both conventional ultrasound and laser phacoemulsification. They concluded that Aqualase removes with ease cataracts up to grade 2, as quickly as conventional ultrasound phacoemulsification and more quickly than laser phacoemulsification and is able to remove many nuclei of grade 3+. According to their personal experience, Aqualase could also prevent PCO.

DISCUSSION

Aqualase is a fluid-based cataract extraction system that does not use ultrasound energy. To our knowledge, this is the first review assessing clinical trials of Aqualase liquefaction technology for cataract extraction. After a thorough research of the current literature, 14 comparative studies were selected for the review, in which Aqualase technique was compared to other methods of cataract removal, such as conventional ultrasound, torsional and laser phacoemulsification, phacoemulsification using Microflow System and the NeoSonix technology.

One of the most important features of liquefaction is the lack of temperature rise at the wound site and as a result, there is no corneal burn, even at full power. Besides that, the soft polymer tip used during the cataract surgery is safe on the posterior capsule, reducing subsequently the incidence of posterior capsule rupture. Liquefaction seemed to be, at least, equally efficient as conventional ultrasound phacoemulsification in mild to moderate cataracts with excellent refractive results[15]. It could easily extract lens with nuclear sclerosis of grade up to 2 (LOCSIII scale), and efficiently cataracts of grade 3 and many of grade 4 using the nucleus pre-chopping technique [12]. Jirásková *et al*[12] suggested that the effectiveness of Aqualase was partly affiliated with the impressive fluidics of the Infiniti Vision System. However, application of the Aqualase in removal of hard nuclei was associated with increased risk of posterior capsular integrity[8] and significant cell loss[4]. As a result, in most of these cases it was not possible the lens matter to be removed and another cataract extraction technique was used, to prevent from any ocular tissue damage. Regarding patients age, Jirásková *et al*[13] suggested that there were statistically significant differences in endothelial cell count and pachymetry between Aqualase and NeoSonix in a group of patients aged over 80y, with Aqualase having better results. Also, in another study Aqualase seemed to have a significantly less endothelial cell loss compared to the conventional ultrasound phacoemulsification in patients up to 70y, although it was supposed that the cataract density was possibly responsible for the above-mentioned correlation [20]. On the other hand, Hu *et al* [8] showed that there was no significant difference in endothelial cell count depending on the patients age of patients between Aqualase and conventional ultrasound phacoemulsification and there were similar results between the two methods, even in older patients. Anyway, in the majority of the studies that examined the influence of Aqualase on the endothelial cell loss, Aqualase induced minimal cell loss and the differences between Aqualase and other cataract extraction techniques were not statistically important[5-6,8,12,15]. It is worth pointing out that it was safe for patients with nuclear grade up to six

(LOCSIII) [5] and showed better results than conventional ultrasound phacoemulsification in cataract grades up to 4.9 (LOCSIII)[9]. Regarding postoperative corneal thickness, there were not any statistically significant difference between Aqualase and others techniques [5-6,9-10,15-16]. Only Jirásková *et al* [12] showed that Aqualase had better results at the first postoperative month and they demonstrated that there was less corneal oedema incidence in patients older than 80 years old [13]. Regarding visual rehabilitation, Aqualase had very good visual acuity outcomes, comparable to the outcomes of other cataract extraction techniques [6,8,10,15-16]. Mackool and Brint [2] suggested that Aqualase technique was associated with reduced incidence of postoperative PCO. Also, evaluation of PCO OSCA software showed significantly better results for Aqualase at one-year follow-up in two studies [11,14], without having the ability to prevent a natural progression of PCO. However, this incidence was considered as indirect, of questionable validity and able to be influenced by co-existent patient symptoms, surgeons' preferences and opinions, and even by economic considerations[21]. It is worth mentioning that individual surgeon technique was associated with reduction of bias [5], while surgeon technique was considered to be one of the factors influencing PCO formation[21] and inducing corneal astigmatism[16]. In addition, Toyos [20] described one case of bilateral pediatric cataract surgery using Aqualase and pressure washing for the one eye and conventional ultrasound phacoemulsification for the fellow eye. Although the eye where conventional ultrasound phacoemulsification was used required a Nd:YAG laser capsulotomy soon postoperatively, in the eye where the Aqualase was used, the posterior capsule was not opacified even two years after surgery. Finally, Aqualase was considered to have less risk of postoperative cystoid macular oedema development, most evidently in diabetic patients[7].

Although no formal studies have been published, international experience suggests that liquefaction could be used as the cataract-extraction technique in pseudophakic monovision approaches [22-23], multifocal [24-25], and accomodative [26-27] lenses implantation when combined with the proper viscoelastic device[28].

In conclusion, this review evaluated the application of liquefaction in cataract removal concerning its effect on different clinical parameters and in comparison to other cataract extraction techniques. It was indicated that Aqualase is a safe technique and very efficient in soft to moderate nuclei removal, but it is not as effective as conventional ultrasound phacoemulsification in dense nuclei. Our review suggests that liquefaction is a useful and possibly more compatible alternative to conventional ultrasound in selected cases, and should be kept into consideration by the modern cataract surgeon.

ACKNOWLEDGEMENTS

Conflicts of Interest: Labiris G, None; **Toli A,** None; **Polychroni D,** None; **Gkika M,** None; **Angelonias D,** None; **Kozobolis VP,** None.

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