EXTENDED REPORT

Long-term results of sealed capsule irrigation using distilled water to prevent posterior capsule opacification: a prospective clinical randomised trial

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Background: We investigated long-term safety and efficacy of sealed capsule irrigation (SCI) during cataract surgery to prevent posterior capsule opacification (PCO).

Methods: One eye of each of 17 patients (mean age: 70.1 ± 9.7 years) who presented with bilateral cataracts was randomly chosen for SCI treatment. After phacoemulsification, the capsular bag was vacuum sealed with the PerfectCapsule device (Milvella) followed by SCI using distilled water for two minutes. No vacuum loss occurred during irrigation. Each patient's fellow eye served as a control. One hydrophilic acrylic intraocular lens model was implanted in all eyes. Five patients had to be excluded due to deep anterior chamber, small pupil or unilateral surgery. Follow-up examinations took place one day and one, three, six, 12 and 24 months after surgery. We evaluated safety parameters, anterior capsule (AC) overlapping and PCO.

Results: Postoperatively, mean best corrected visual acuity, pachymetry, endothelial cell count, intraocular pressure, AC overlapping and PCO showed no statistically significant difference between SCI and the control group ($p > 0.05$, Wilcoxon test).

Conclusion: SCI is a safe procedure and enables the specific pharmacological targeting of lens epithelial cells inside the capsular bag. Using distilled water, however, it is not possible to reduce PCO development significantly. Thus, alternative substances should be evaluated.

Secondary cataract is still the most frequent long-term complication of modern cataract surgery.^{1–8} Prevention of posterior capsule opacification (PCO) is especially important for pediatric patients with high PCO rates, in whom a delay in diagnosis can cause amblyopia, or for patients living in developing countries where successful restoration of lasting sight depends on eradication of secondary cataract. When implanting special modern IOL-types such as accommodative or multifocal lens implants, secondary cataract might interfere with their functional performance.^{2–8}

The *in vitro* application of pharmacological substances to prevent lens epithelial cells (LECs) from proliferating and migrating has been investigated over decades.^{9–15} However, clinical use has been critical since serious damage to the surrounding tissue had to be considered.¹⁶

Recently, the PerfectCapsule (Milvella Pty Ltd, Sydney, Australia) system was introduced by Anthony J Maloof.^{17–20} It is a sterile, single-use silicone device and consists of a foldable suction ring with an overall diameter of 7.0 mm and an inner diameter of 5.0 mm. Two separate lines are incorporated. One is used for vacuum application and the other for irrigation, respectively (fig 1).²⁰ The device allows the temporary seal of the capsulorhexis (less than 5 mm) after cataract removal. Using pharmacological agents, the selective irrigation of the internal capsular bag is possible, thus targeting remaining lens epithelial cells without damage to surrounding tissues. The Food and Drug Administration (FDA) and the "Communauté Européenne" (CE) approved the application which is also known as sealed capsule irrigation (SCI).

In a prospective clinical setting, we investigated the safety and efficacy of SCI during cataract surgery. The main outcome measures were best corrected distance visual acuity, surrounding tissue stability (corneal pachymetry and endothelial cell loss, as well as iris and retina), intraocular pressure,

anterior capsule (AC) overlapping and secondary cataract development.

PATIENTS AND METHODS

This prospective, randomised controlled clinical trial was conducted at the Department of Ophthalmology, University of Heidelberg, Germany. The study design obtained ethics committee approval in advance. Seventeen patients who presented with bilateral cataracts were enrolled. The mean age of the 11 women and six men was 70.1 ± 9.7 years, ranging from 47 to 78 years. All patients signed an informed consent prior to surgery, which was performed under general or topical anaesthesia by a single surgeon (GUA). Clear cornea incision was followed by injection of a cohesive ophthalmic viscoelastic device (OVD) (Healon GV, Advanced Medical Optics, Inc., Santa Ana, CA, USA) to deepen the anterior chamber. A sclerocorneal tunnel was not advisable since introduction of the PerfectCapsule device can be difficult. Capsulorhexis was performed using forceps. After phacoemulsification, a sealed envelope was opened containing a letter randomising the eye either to the control or to the sealed capsule irrigation group.

In case the eye served as a control, the capsular bag was then filled with Healon GV and a single-piece, hydrophilic acrylic intraocular lens (IOL) (Centerflex 570H, Rayner Intraocular Lenses Ltd, Hove, East Sussex, England) was implanted. This IOL has an overall diameter of 12.0 mm and an optic diameter of 5.75 mm. The surgery was finished by OVD removal and wound closure.

In case of SCI treatment, the PerfectCapsule device was folded and, using forceps, inserted through the slightly enlarged clear cornea incision (3 to 3.5 mm size) into the anterior chamber. The device was then placed onto the anterior capsule completely covering the capsulorhexis. A second person is needed to apply the vacuum via the lockable syringe (fig 1).

Figure 1 Perfect Capsule device for sealed capsule irrigation.

Figure 2 Development of best corrected visual acuity of sealed capsule irrigation (SCI) and control eyes (mo = months).

The seal was first tested by injection of fluorescein-stained balanced salt solution (BSS) and carefully observed for any leakage. Afterwards, distilled water irrigation was performed for two minutes. The infusion bottle was 110 cm above patient height and the tube connected to a cannula inserted into the PerfectCapsule irrigation channel. At the same time, seal and capsular bag stability was examined by the surgeon using the operating microscope. Finally, the capsular bag was rinsed with BSS to wash out distilled water completely. The vacuum was then released and the device was easily removed from the eye by pulling the irrigation line. After the treatment, the final surgical steps were equivalent to those performed in control eyes (Centerflex IOL implantation, OVD removal, wound closure).

According to the study protocol, both eyes were operated on within one month. Unfortunately, two patients had to be withdrawn from the study because it was impossible to perform the second eye operation within the given time period. Furthermore, in three eyes SCI was not possible because of deep anterior chamber ($n=2$) and a small pupil ($n=1$).

However, once the vacuum was achieved, SCI could be completed without any complications. No capsular bag damage was noted during vacuum application, irrigation or removal of the device from the eye.²⁰

Postoperative, follow-up examinations took place after one day and one, three, six, 12 and 24 months. At each visit, we evaluated functional results (refraction, best corrected visual acuity) and intraocular pressure, and performed slit-lamp biomicroscopy of the anterior and posterior segment. Further safety parameters were investigated preoperatively and three months postoperatively, including corneal endothelial cell count measurement using Tomey Specular Microscope EM-1200 (Tomey GmbH, Erlangen, Germany) and corneal pachymetry evaluation using Orbscan II Topography System (Bausch and Lomb, Rochester, NY, USA).

AC overlapping and PCO were quantified three, six, 12 and 24 months after surgery by importing retroilluminated slit-lamp photos into the EPCO 2000 analysis software (EPCO score 0 to 4). Secondary cataract evaluation was performed for the total IOL-optic, within the central 3 mm zone and within the capsulorhexis.

Statistical analysis was performed using Wilcoxon test and a p -value less than 0.05 was considered statistically significant.

Results

As far as safety is concerned, no surrounding tissue damage was noted clinically. Over a period of two years, slit-lamp biomicroscopy of anterior and posterior eye segments revealed no corneal, iris or retinal changes in the irrigated eyes. Mean best corrected distance visual acuity increased from 20/50 (logMAR 0.37) to 20/25 (logMAR 0.09) in both groups six months after surgery. Slightly decreasing values were noted 12 and 24 months postoperatively (fig 2) due to secondary cataract formation in control as well as treated eyes. No statistically significant difference between the control and SCI group

Table 1 Intraocular pressure (IOP) measured at different follow-up times.

	Preoperative	Postoperative					
IOP [mm Hg]	1 day*	1 day*	1 month*	3 months*	6 months*	12 months*	24 months*
SCI	14.7±2.3	11.9±3.0	11.9±2.5	11.4±2.6	11.1±3.0	12.7±2.0	12.4±2.2
Control	14.8±2.9	11.1±2.3	11.8±2.9	11.1±2.8	11.7±2.2	12.1±1.6	12.3±1.9

*No statistically significant difference between control and SCI group ($p>0.05$, Wilcoxon test)

Table 2 Endothelial cell count (ECC) comparison: sealed capsule irrigation (SCI) vs control group.

	Preoperative*	3 months postoperative*	Difference*
ECC SCI [cells/mm ²]	2438.9±306.0	2244.4±365.2	194.4 (7.95%)
ECC control [cells/mm ²]	2558.3±208.4	2325.0±315.8	233.3 (9.11%)

*No statistically significant difference between control and SCI group ($p>0.05$, Wilcoxon test)

Figure 3 Mean overlapping (OL) between anterior capsule and intraocular lens optic of sealed capsule irrigation (SCI) and control eyes.

($p > 0.05$, Wilcoxon test) was noted. Pachymetry (mean change: SCI 5.4% vs control eyes 7.9%) as well as intraocular pressure measurements (table 1) also did not show a significant difference between the groups ($p > 0.05$, Wilcoxon test).

Three months after surgery, mean endothelial cell loss was 194 cells/mm² (7.95%) in the SCI, compared to 233 cells/mm² in the control group (9.11%) (table 2).

There was also no statistically significant difference in anterior capsule overlapping in the two study groups ($p > 0.05$, Wilcoxon Test). However, mean overlapping seemed to be slightly more stable in the SCI group. During two years of follow-up, the overlapping area ranged within 2% in the SCI group, compared to 5% in the control eyes (fig 3).

With regard to the efficacy of SCI using distilled water, secondary cataract development is shown in table 3. Even though SCI eyes showed a slightly higher EPCO score 3 months after surgery, where the total IOL optic was concerned there was a tendency towards less PCO formation in the SCI group 12 and 24 months postoperatively (table 3). Similar developments were noted within the central 3 mm area and within the capsulorhexis (table 3). However, there was no statistically significant difference for any evaluated IOL area (p Value > 0.05 , Wilcoxon test) when comparing both study groups. Figure 4 illustrates retroilluminated pictures of SCI and corresponding control eyes 24 months after surgery.

After 24 months, three irrigated eyes needed Neodymium:YAG (Nd:YAG) laser capsulotomy, compared to two eyes in the control group. Mean postoperative treatment time was 7.5 ± 2.8 months (control) compared to 16.3 ± 2.5 months (SCI).

Interestingly, the Nd:YAG rate as well as PCO formation increased, particularly in the SCI group, between the first and second postoperative year, indicating the importance of long-term follow-up of modern IOLs and new methods in order to assess secondary cataract development.

Discussion

Several surgical and intraocular lens related factors for secondary cataract prevention have been reported and have led to a significant reduction of PCO development.¹⁻⁸ However, the problem is still present and PCO prevention becomes even more important with the introduction of new intraocular lens

implants. Research concerning the application of pharmacological agents after cataract removal to target remaining lens epithelial cells directly has been conducted for a long time. Most of the studies were performed in cell cultures or in animal models since selective targeting of LECs was not possible and serious damage to surrounding tissues had to be considered. Tested agents were cytostatic drugs, steroids, nonsteroidal antiphlogistics, adhesion inhibitors, heparin, lidocaine, immunotoxins and osmotic effective solutions.^{9-15 21-25} Drug delivery systems were also investigated in order to provide a longer and more effective impact on LECs.^{16 26 27}

Since the advantage of a closed capsular bag model was obvious in order to protect surrounding tissues, different application principles have been developed and evaluated. At the end of the 1980s, Greite and co-authors presented the implantation of a capsular diaphragma made of silicone material which was introduced into the capsular bag through the capsulorhexis followed by injection of an OVD on top.²⁸ Other application principles included a double-lavage system and a combination with a form of stable gel as support medium.²⁸ Fernandez *et al.*²⁹ injected a mixture of an OVD and a drug into the empty capsular bag; however, a complete and safe separation of the capsular bag from other ocular tissues and segments could not be ensured.

The development of the PerfectCapsule device for vacuum-sealed capsule irrigation allows the selective targeting of LECs inside the capsular bag, preventing collateral damage to surrounding intraocular structures.¹⁷⁻¹⁹ Even in case of capsular bag irrigation using extremely toxic agents, histological evaluation showed no damage of corneal endothelium, iris, retina or capsular bag.¹⁹ However, few reports have been published so far regarding the clinical use of the PerfectCapsule system,^{8 18 20} which can be limited in cases of deep anterior chambers or small pupils.²⁰

For a first clinical application of sealed capsule irrigation, distilled water was chosen as the irrigation solution for the following reasons. Greite and co-authors were able to demonstrate that the *in vitro* application of distilled water, a hypotonic solution, led to a 50% reduction of cell proteins, with the advantage of rapid neutralization compared to cytostatic drugs.²⁸ In the very unlikely event of vacuum loss during SCI, it would be sufficient to irrigate with a physiological solution (e.g. BSS) immediately and aspirate with the irrigation/aspiration hand-piece.²⁰ Maloof and Crowston used anterior capsulotomy specimens to evaluate the effect of distilled-deionized water in capsule culture. Within 60 seconds of exposure, lens epithelial cells were markedly swollen and by 120 seconds no intact cells were visible.^{30 31} Fernandez and co-authors compared the efficacy of various drugs in the prevention of PCO, including cytostatic agents (e.g. 5-fluorouracil and mitomycin-C), in an animal model.²⁹ Distilled water and 10 mM EDTA treatments were the most successful in retarding the appearance of secondary cataract.

Regarding clinical results of sealed capsule irrigation using distilled water, another study group evaluated silicone levels and noted significantly less anterior capsule opacification and phimosis evaluating silicone lenses.⁸ In terms of PCO development, we could not find a statistical significant

Table 3 EPCO values (scale 0 to 4) control vs SCI eyes.

	total IOL-optic control	total IOL-optic SCI	3 mm control	3 mm SCI	CR control	CR SCI
3 months*	0.14 ± 0.23	0.19 ± 0.23	0.10 ± 0.15	0.16 ± 0.19	0.15 ± 0.25	0.16 ± 0.21
6 months*	0.26 ± 0.32	0.27 ± 0.28	0.16 ± 0.21	0.22 ± 0.25	0.24 ± 0.27	0.28 ± 0.30
12 months*	0.36 ± 0.36	0.28 ± 0.32	0.27 ± 0.35	0.25 ± 0.34	0.37 ± 0.41	0.33 ± 0.38
24 months*	0.78 ± 0.69	0.68 ± 0.72	0.65 ± 0.75	0.55 ± 0.70	0.73 ± 0.71	0.63 ± 0.73

(IOL, intraocular lens; SCI, sealed capsule irrigation; CR = capsulorhexis)

*No statistically significant difference between control and SCI group ($p > 0.05$, Wilcoxon test)

Figure 4 Control (a) and fellow SCI (b) eyes of three patients (1–3) two years after surgery.

reduction in our trial, even though the anterior capsule overlapping seemed to be slightly more stable in treated eyes.

In summary, application of the PerfectCapsule device is very easy to learn; however, it extends the operation time by approximately four minutes. The procedure can also be performed under topical anaesthesia without complications. Once the vacuum is achieved, sealed capsule irrigation seems to be a safe procedure in terms of intraoperative vacuum stability, postoperative best corrected distance visual acuity, surrounding tissue and capsular bag integrity, and intraocular pressure. Distilled water alone, however, did not reduce secondary cataract formation significantly. Thus, additional studies are necessary to investigate whether alternative pharmacological substances are more effective in terms of PCO inhibition.

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