CLINICAL STUDY

Long-term disorders of the blood–aqueous barrier after small-incision cataract surgery

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Abstract

Purpose **To determine the long-term function of the blood–aqueous barrier after small-incision cataract surgery with implantation of a foldable intraocular lens.**

Methods **The blood–aqueous barrier function in 74 eyes of 62 patients who underwent cataract surgery was examined using a laser flare-cell meter. The measurements were performed pre-operatively and post-operatively between 12 and 35 months after surgery. For statistical analysis a linear regression was used. The study was designed as a single cohort study, with comparison of pre- and post-operative values.**

Results **Highly statistically significant differences ($p < 0.0001$) were found between pre-operative flare values and those measured at the final visit. The linear regression model showed significantly higher flare values post-operatively compared with those measured pre-operatively. Other variables such as incision technique, sex, operation time, phaco time and systemic disease had no influence on this outcome.**

Conclusion **The results suggest that there is persistent blood–aqueous barrier dysregulation even several years after cataract surgery.**

Key words Aqueous humour, metabolism; Blood–aqueous barrier; Inflammation, aetiology; Lasers, diagnostic-use; Lens implantation, intraocular; Phacoemulsification, adverse effects

Many papers concerning the re-establishment of the blood–aqueous barrier (BAB) after cataract surgery have been published during the last decade. Using anterior chamber fluorophotometry, Sanders *et al.*[1] observed re-establishment of the BAB within 3 months after extracapsular cataract surgery with intraocular lens implantation. Ferguson *et al.*,[2] also described recovery within the same time in about 80% of their patients; the rest (~20%) showed persistent BAB damage which was found to be correlated with an abnormal pupil shape or posterior synechiae. Several studies published at this time report persistent BAB dysfunction for more than 6 months after cataract surgery. Kaff *et al.*[3] and Majima[4] observed significant differences in the anterior chamber fluorescein concentration ratios between the operated and normal eye, or the fellow eye, up to 6 months post-operatively. Kaiya[5] and Kimata and co-authors[6] found these differences even up to 4 years after the operation.

At the beginning of the 1990s scientists started to use the laser flare-cell meter to examine BAB disorders by measuring aqueous flare and cells. Shah *et al.*[7] as well as Alio and co-authors[8] examined cataract patients with otherwise normal eyes, and found no significant difference between pre-operative and post-operative (3 months) aqueous flare values. To our knowledge there are no recent publications concerning the long-term effects (up to 1 year and more) of small-incision cataract operation on the BAB, using the laser flare-cell meter. The aim of this study was to examine the integrity of the BAB 1–3 years after small-incision cataract surgery.

Materials and methods

Seventy-four eyes of 62 patients who underwent cataract surgery were examined pre-operatively and post-operatively at their final visit between 12 and 35 months after surgery. All eyes were free of ocular diseases other than cataract, and operated on by our standard cataract procedure (Table 1). None of these patients had any systemic or local anti-inflammatory medication for 1 month before operation.

Standard cataract procedure

All surgery was performed by one experienced surgeon after peribulbar anaesthesia with 2.5 ml of lidocaine 2% plus 2.5 ml of bupivacaine 0.5%. The surgical procedure consisted of a clear cornea incision or sclerocorneal tunnel preparation, using a 3.5 mm steel blade, followed by continuous curvilinear capsulorhexis (CCC) performed under sodium

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Table 1. *Patient characteristics*

Age (mean)	74.1 years
Age (range)	46–89 years
No. of women	55
No. of men	19
Sclerocorneal incision	27
Clear cornea incision	47
No. of patients with hypertension	31
No. of patients with diabetes mellitus (without retinopathy)	10
No. of patients with asthma bronchiale	5
Phaco time (mean)	42.2 s
Operation time (mean)	15 min

hyaluronate (Healon). After hydrodissection and hydrodelineation with fortified balanced salt solution (BSS Plus), phacoemulsification was performed using the bimanual 'divide and conquer' technique. Cortical remnants were removed by irrigation–aspiration. The capsular bag was refilled with sodium hyaluronate (Healon) and a foldable posterior chamber lenses was implanted into the bag. For implantation we used one-piece plate-haptic silicone lenses (n = 64), three-piece acrylic lenses (n = 7) and three-piece MMA-HEMA lenses (n = 3). The viscoelastic was then meticulously removed.

All patients in this group received the same post-operative therapy (topical diclofenac sodium and combined betamethasone-neomycin sulphate eye drops four times daily) for 1 month. No operative or post-operative complications occurred during the time of observation.

Measurement of blood–aqueous barrier function

Aqueous flare and cells were measured using the laser flare-cell meter (Kowa FC-1000, Kowa Europe, Dusseldorf, Germany). All patients had undilated pupils during measurement. Five sequential scans were averaged; the background scatter on each scan was less than 8%. Calibration of the laser flare-cell meter was conducted periodically according to the manufacturer's instructions.

The study was designed as a single cohort study, with comparison of pre- and post-operative values. For statistical analysis of these differences in flare values a linear regression model was used. The time of post-operative measurement, centred at 2 years, was used as independent variable. For the analysis of other

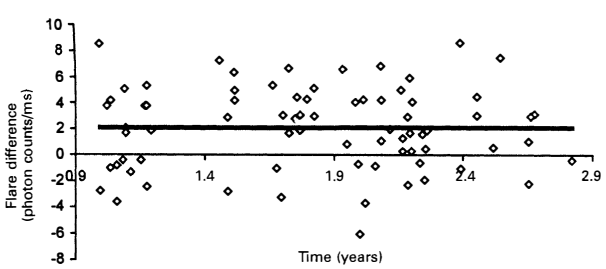

Fig. 1. *Scatter-plot of the flare difference over time for the 74 eyes. The continuous line represents the linear regression. Each point represents the difference in aqueous flare between the pre- and post-operative measurement for one eye.*

Table 2. *Influence of other variables on the flare difference*

Variable	p value
Eye (left/right)	0.52
Incision (CCI/SCI)	0.69
Sex (male/female)	0.41
Phaco time	0.19
Operation time	0.22
Diabetes mellitus	0.72
Hypertension	0.42
Anticoagulative drugs	0.52
Age	0.0489

independent variables a stepwise linear regression was performed. The variables needed a p value lower than 0.05 to be included and to remain in the model.

Results

All 74 eyes had a mean pre-operative flare intensity of 7.62 photon counts/ms (SD ± 2.70). The mean flare value of the final visit was 9.74 photon counts/ms (SD ± 3.29). The mean difference (ΔF) between pre- and post-operative values at 2 years postoperatively was 2.12 photon counts/ms ($p < 0.0001$). The time of the post-operative measurement had no influence on these results, because no difference was seen in ΔF determined between 1 and 3 years after surgery ($p = 0.96$) (Fig. 1). Of the variables eye (left/right), incision (SCI/CCI), sex, phaco time, operating time, diabetes mellitus, hypertension and use of anticoagulative drugs centred at 2 years, only age entered the stepwise regression model ($p = 0.0489$); however, this p value explains only 6.75% of the variability. All other variables had p values > 0.19 (Table 2). There was no noticeable change when comparing the results including those patients with only the first operated eye with those results of both eyes.

Discussion

Any trauma in the eye, whether due to injury or surgery, results in a greater or lesser disturbance of the BAB. In the past, this functional disturbance was studied with special interest in patients after cataract surgery, as advances in surgical technique as well as materials and measuring procedures necessitate continuous, repeated evaluation of this phenomenon. While extracapsular cataract extraction with manual expression of the nucleus of the lens was considered a standard procedure in cataract surgery world-wide until recently, it has now been replaced by small-incision surgery with phacoemulsification. The latter is associated with much less trauma to the operated eye.[9]

At the same time, advances were made in post-operative therapy. The application of highly effective steroid- and non-steroid-based antiphlogistic drugs has markedly reduced post-operative inflammation and subsequent disturbance of the BAB.[10,11] The same effect was achieved by the development of new lens material and design, which reduced the post-operative immunological defence reaction.[12,13] Sophisticated

measuring devices for measuring BAB disturbances (the current standard device being the laser flare-cell meter) permit a much more accurate evaluation of post-operative trauma than was achieved by previous methods (e.g. fluorophotometry).[14] Moreover, as a result of these numerous developments, conflicting reports are found in the literature concerning whether and at which time point re-establishment of the BAB is achieved. This study highlights one aspect of this subject which has been given relatively less attention in the recent past, namely long-term observation of aqueous flare after cataract surgery. The results of our measurements showed significantly higher flare values 1–3 years after cataract surgery compared with those measured pre-operatively.

Apart from the fact that these findings had no clinical significance, the results of our observation are surprising, as the majority of studies performed in a similar setting (healthy eyes, phacoemulsification, in-the-bag implantation) report re-establishment of the BAB within 3 months after surgery.[7,8]

This raises the question as to why persistent disturbance after cataract surgery is reported in spite of minimally invasive surgical techniques, modern medication and modern intraocular lens material. Analysis of our data led to the following conclusions: In our patients, systemic diseases and intra- or post-operative complications may be excluded as causes of persistent BAB disorders. One cause could be age-related changes in barrier function. Oshika *et al*.[15] demonstrated a correlation between aqueous flare and age, which correlates with former observations[16] of increased protein concentrations in older age groups. In contrast, our data show a markedly stronger increase in intracameral flare, especially in consideration of the relatively short time span of 1–3 years.

The assumption that this age-related barrier disorder is precipitated by surgery is also not true for the eyes we examined, In fact, we registered persistently increased flare values over 2 years of observation. Worthy of mention in this context is Kaiya's study,[5] which reports constant BAB dysregulation over a period of 4 years (comparable with our observations). Some additional factors examined by us, such as operating time and phaco time, were also not correlated with the persistently increased flare values. Once these factors are excluded, it appears very likely that the sustained BAB dysregulation we found is an expression of a persistent post-operative immunological reaction, probably a persistent foreign body reaction against the implanted lens. A few publications concerning this subject[17–19] attribute a post-operative inflammatory reaction persisting 1 month postoperatively to this foreign body reaction. However, as yet this hypothesis is supported only by indirect data concerning post-operative cellular colonisation of the intraocular lens. The question concerning immunological processes and whether there are additional factors that favour this persistent BAB dysregulation must be investigated in further studies.

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