Flaremetric evaluation of blood-aqueous barrier breakdown in diabetic patients after phacoemulsification and intraocular lenses with or without heparin-coated surface implantation

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ABSTRACT

Background: This study compared the intensity of blood-aqueous barrier breakdown in diabetic patients after phacoemulsification with heparin surface-modified and non-modified intraocular lens (IOL) implantation.

Material and methods: In this prospective trial, 68 diabetic patients were enrolled and divided into two groups: 33 patients with heparin surface-modified IOL implants (group 1) and 35 patients with standard hydrophobic IOL implants (group 2). Blood-aqueous barrier breakdown was assessed using a Laser Flare Meter 1 day, 7 days, 14 days, 1 month, and 3 months postoperatively.

Results: On postoperative days 1 and 7, the mean flare value was significantly higher in group 2 compared with group 1. On day 14, the mean flare value in both groups was similar and then higher in group 2.

Conclusions: The implantation of foldable heparin-coated IOLs led to a lower intensity and faster recovery of blood-aqueous barrier breakdown postoperatively.

Keywords: blood-aqueous barrier, flare, heparin surface modified IOL
INTRODUCTION
One of the most important steps of cataract surgery is the replacement of crystalline lens with the best refractive fit-
tted and biocompatible artificial IOL. Choosing the ade-
quate materials as well as modification of its surface makes IOL safer and much more biocompatible leading to lower
inflammatory response after surgery. It is especially advis-
able in patients with high risk of inflammatory reaction
i.e. in patients with diabetes and uveitis. In this context
covering the IOL surface by heparin can lead to sufficient
prevention of bacteria, protein and lens epithelial cells at-
tachment into its surface, in which consequence minimizes
the BAB breakdown [1–4]. This phenomenon is featured
by influx of serum proteins and inflammatory cells into
the aqueous humour of anterior and posterior chamber as
a consequence of BAB breakdown. In the aqueous of ante-
rior chamber these elements can be detected quantitatively
using laser flare photometry [5].

The aim of the study was to assess the flare photometric
measures in patients who underwent phacoemulsification
with implantation of heparin surface modified (HSM) hy-
drophobic acrylic intraocular lens and to compare those
measurements with the ones achieved after standard hy-
drophobic IOLs (AcrySof® IQ) implantation.

MATERIAL AND METHODS
The study was conducted at the Department of Ophthal-
mology and Visual Rehabilitation, Medical University of
Lodz. The approval of a relevant Bioethics Committee
was obtained (number RNN/414/14/KB). This study was
designed as a prospective trial to assess degree of damage
and the time of BAB stabilization in patients who under-
went phacoemulsification and implantation of heparin sur-
face modified (HSM) IOL and standard hydrophobic IOLs
(AcrySof® IQ) implantation. The range of preoperative ex-
amination included best-corrected visual acuity (BCVA),
slit lamp of anterior segment and fundus examination. The
international classification of clinical symptoms was used
for grading the stage of diabetic retinopathy. The non-pro-
liferative retinopathy was exclusively included in the study.
Goldmann applanation tonometry was used to measure the
IOP. Laser Flare Meter (LFM) FM-600, Kowa Co. Ltd. (To-
kyo, Japan) was performed to quantify anterior chamber
protein (flare). In brief, the device uses a diode laser beam
to scan a measurement window that is projected inside the
anterior chamber of the eye.
Measurements were obtained after pupil dilation with
tropicamide eye drop 1% in a dark room condition. The
values of laser flare were expressed in photons per milli-
seconds (ph/ms). All surgeries were performed under topical
anaesthesia using standard phaco chop or divide-and-con-
quar technique. Either the HSM IOL or AcrySof® IQ were
implanted into the capsular bag. In both groups, the post-
surgical medication consisted of: corticosteroid drug four
times a day with dose tapering for up to 4 weeks, topical
nonsteroidal anti-inflammatory drugs given four times
a day for up to 4 weeks, and the fluoroquinolone antibiotic
drug four times a day for 1 week. The follow-up examina-
tions were performed 1, 7, 30 and 90 days postoperatively.

RESULTS
Sixty-eight eyes of 68 patients, including 41 women and
27 men, were enrolled in the study. The mean age was
74 years (range 55–91). In 33 patients heparin surface IOLs
(HSM IOLs – Polytech Polylens, Roßdorf, Germany) were
implanted (group 1). In 35 patients standard hydrophobic
IOLs (Alcon IQ AcrySof®) were implanted (group 2). There
was no significant difference between groups (p > 0.05) in
age, gender, duration of diabetes, type of diabetes treat-
ment, preoperative intraocular pressure (IOP) and preop-
ervative BCVA. Patient data at baseline are summarized in
table 1.

| Table 1 |
|---|---|---|
| Patient data at baseline. | | |
| Characteristic | Group 1 | Group 2 |
| Number of the eyes | 33 (48.53%) | 35 (51.47%) |
| Age | 55–86 | 64–91 |
| Gender | | |
| Female | 22 (66.67%) | 19 (54.29%) |
| Male | 11 (33.33%) | 16 (45.71%) |
| Type of the IOL | Heparin Surface Modified Hydrophobic IOL | Hydrophobic IOL |
| Mean IOP preop | 15.3 mmHg | 16.34 mmHg |

There was no significant difference of flare value between
groups preoperatively (p = 0.246) (tab. 2). In postoperative
day 1st and 7th mean flare value was significantly higher in
group 2 as compared to group 1. Fourteen days postopera-
tively, there was no significant difference (p = 0.921) in flare
measures between groups. The mean flare value measured at
1 and 3 months after surgery was again lower in group 1 as
compared with group 2 (fig. 1).
There was no statistically significant difference in BCVA preoperatively between the two analysed groups (p = 0.317) (fig. 2). Patients in both groups achieved statistically significant visual improvement in every single day of measure in the follow-up. However, there was no statistically significant difference in BCVA between group 1 and group 2 over the 3 months of follow-up.

### Table 2
Mean flare in both groups at specific postoperative time points.

<table>
<thead>
<tr>
<th>Time</th>
<th>Group 1 Mean flare (photons units/100 ms ± SD)</th>
<th>Group 2 Mean flare (photons units ± SD)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.19 ± 6.21</td>
<td>11.97 ± 6.54</td>
<td>0.246</td>
</tr>
<tr>
<td>Day 1st</td>
<td>21.74 ± 13.63</td>
<td>34.31 ± 30.31</td>
<td>0.027</td>
</tr>
<tr>
<td>Day 7th</td>
<td>13.7 ± 8.40</td>
<td>24.16 ± 19.02</td>
<td>0.019</td>
</tr>
<tr>
<td>Day 14th</td>
<td>11.97 ± 8.73</td>
<td>12.15 ± 8.24</td>
<td>0.921</td>
</tr>
<tr>
<td>Month 1st</td>
<td>10.22 ± 5.61</td>
<td>16.86 ± 10.95</td>
<td>0.034</td>
</tr>
<tr>
<td>Month 3rd</td>
<td>10.28 ± 5.56</td>
<td>15.32 ± 7.81</td>
<td>0.003</td>
</tr>
</tbody>
</table>

### Figure 1
Means flare values over the 3-month follow-up.

### Figure 2
Best corrected visual acuity (logMAR).
DISCUSSION

Blood-aqueous barrier belongs to the physiological barriers within the human eye. It is located at the non-pigmented epithelium of the ciliary body as well as in the endothelium of the iris blood vessels. Due to the fact that BAB is physiologically leaky there is a small amount of plasma proteins identified in aqueous humour of the eye. However, there is no agreement how the blood-aqueous barrier (BAB) is susceptible to some factors. Cataract surgery can induce dysregulation of the BAB function resulting in huge leakage of serum protein and blood cells into the aqueous humour. This protein in anterior chamber may be objectively quantified using Laser Flare Meter in a safe, non-invasive and efficient manner [6].

It is well-documented that postoperative BAB breakdown is connected up to many factors along with cataract surgical technique [7, 8], including the duration of surgery as well as the type of implanted IOL [9]. The reason for the observed phenomenon is not clearly known. It is also suggested that cataract surgery and the implantation of IOL may cause some changes in the nitric oxide (NO) level [10–12]. As a consequence, NO production may contribute to pathological developments in the anterior chamber such as vessel dilation, changes in perfusion, increased vessel permeability, and BAB breakdown. In patients with diabetes, the microcirculation per se is impaired and intraocular surgery can aggravate this impairment [13]. It is also suggested that the IOL material may be an important factor of BAB destabilisation.

Technology of IOL surface modification comprised ion beam, plasma, layer-by-layer self-assembly, ultraviolet radiation, and ozone. In those techniques such molecules as: poly(ethylene glycol), polyhedral oligomeric silsesquioxane, 2-methacryloyloxyethyl phosphorylcholine, TiO2, heparin, F-heparin, titanium, titanium nitride, vinyl pyrrolidone, and inhibitors of cytokines are introduced into IOLs surface [3]. It is advocated that coating the surface with heparin has a potential of reducing BAB breakdown. Heparin is a well-known anticoagulant commonly used in medicine without any serious side effects. Studies have shown that heparin can suppress proliferation of lens epithelial cell and fibroblast and reduce adhesion as well as deposition of platelets, fibroblasts and macrophage on posterior capsular surface [14, 15]. Importantly, heparinization can attenuate the foreign body response and reduce in some extent breakdown of BAB. It is suggested that it is the effect of the same charges on the IOL surface and bacteria cell wall [16]. Additionally, the IOL surface is relatively non-adherent to inflammatory active particles, which potentially reduces the postoperative inflammatory reaction [17].

The technology of heparin surface modification of IOL has a long history. This process was originally used in polymethyl methacrylate (PMMA) lenses in the early 1990s. The investigators of this modification showed advantages in diminishing the postoperative inflammatory reaction [18]. Based on several studies, heparin-coated PMMA IOLs have been recommended for use in cataract surgery as treatment of choice, especially for high-risk populations such as those with uveitis or diabetes [19]. Studies strongly suggested that initial increase in anterior chamber flare is mainly the result of the trauma caused during surgery, especially in diabetic patients [20]. Heparin surface modified (HSM) foldable IOL in contrast to PMMA IOL requires a significantly smaller self-sealing incision resulting in much lower surgical trauma.

Krall et al. compared the flare value in patients who underwent phacoemulsification with HSM implantation in one eye and hydrophobic acrylic IOL in the contralateral eye [21]. In the HSM group lower laser flare values in the early postoperative period was observed with a significantly faster decrease in cells level than in the group in which the uncoated IOL was used. According to these researchers anti-inflammatory effect of heparin can be confirmed [21]. In this study the laser flare measures were used to determine aqueous flare in the anterior chamber. Patients with HSM IOL in this study showed lower flare values in the early postoperative period. What was especially surprising, in patients with implanted uncoated IOL changes of flare value were more variable, in 14 days the mean flare value achieved again higher level in contrast to those having HSM IOL. The mean flare value at 3 months was still higher than at baseline by 27.98% in the uncoated IOL group in contrast to patients with HSM IOL for whom the flare value decreased to nearly baseline levels at this time. It is commonly reported that BAB stabilization occurs usually after 3 months. Taking this into account it can be shown that BAB stabilization is much faster in patients with HSM IOL.

CONCLUSIONS

The modification of artificial IOL seems to be a reasonable method of stabilizing BAB and making postoperative rehabilitation much faster, especially in diabetic patients.
References