Effects on the Surrounding Tissues and Morphological Changes of Components after Implantation of PMMA and Heparin Surface Modified PMMA Intraocular Lens in Rabbit Eyes

Man Soo Kim, M.D. and Sang Wook Rhee, M.D.

Department of Ophthalmology, Catholic University Medical College, Seoul, Korea

The aim of this study was to evaluate the cellular response and morphological changes of cells on the intraocular lens (IOL) implanted over a course of time and to identify the basic mechanism of IOL adaptation to tissue reaction in the implanted eye by comparing polymethylmethacrylate (PMMA) IOL with heparin surface modified PMMA IOL.

ECCE using Healon® was done in 36 eyes of 36 rabbits. A heparin surface modified IOL was implanted in 18 eyes (Group I), while PMMA IOL was implanted into another 18 eyes (Group II). Corneal thickness and endothelial cell density were measured for 3 months. Postoperatively, the eyes were enucleated, and a cytopathologic examination of the cells on the surface of the IOL and their ultrastructural changes were observed with light and scanning microscope at various points of time.

The findings of this present study suggested that heparin surface modified PMMA IOL reduced the degree of endothelial cell damage, postoperative tissue reaction, and pigment deposits on the surface of the IOL. These were statistically significant. The most important cell was considered to be the macrophage for the adaptation of IOL in the eye which gradually changed into a fibroblast-like cell, giant cell and finally disappeared after forming an acellular membrane on the IOL.

Key words: PMMA IOL, heparin surface modified PMMA IOL, inflammation, endothelial cell, macrophages.

INTRODUCTION

Intraocular lens implantation after cataract operation has already become widespread practice while its clinical results are generally satisfying. Despite this development, however, there still exist various problems in the design, materials and operative methods.

The PMMA intraocular lens, which is the most widely used among a variety of materials, is excellent in optical resolving power and can easily be made into any desired form, while at the same time being economically advantageous.1 But the intraocular lens is hydrophobic and hard, and it is known that it causes much damage to the corneal endothelial cells when in close contact, giving rise to bullous corneal keratopathy.2

Ohara3 could easily find the deposition of a variety of inflammatory cells and pigment epithelial cells by slit lamp biomicroscopically observing deposits on the surface of an intraocular lens. Wolter4 also observed inflammatory cells and proteinic membranes in the cytopathological...
observation of the surface of extracted intraocular lenses. Research designed to solve the problems of intraocular lenses are also diversified.

Therefore, the aim of this study was to evaluated the cellular response and morphological changes of the cells on the intraocular lens (IOL) implanted over a period of time and to identify the basic mechanism of IOL adaptation to tissue reaction in the implanted eye by comparing polymethylmethacrylate (PMMA) IOL with heparin surface modified PMMA IOL.

**MATERIALS AND METHODS**

The intraocular lenses used were one-piece posterior chamber intraocular lenses. They were divided into PMMA material (model No. G107B, IOL-AB, U. S. A.) and heparin surface modified PMMA intraocular lenses (model No. 725C, Pharmacia, Sweden).

In the experiments, 36 mature and healthy rabbits, ranging from 2.0kg to 2.5kg in weight with no abnormal corneal symptoms in slit lamp biomicroscopic observation, were used regardless of sex. They were divided into two groups of 18 each, one group implanted with heparin surface modified PMMA intraocular lenses (Group I) and the other group implanted with PMMA intraocular lenses (Group II).

Each experimental animal was anesthetized by injecting 10mg of ketamine hydrochloride per kg of its weight, and an operation was aseptically performed under an operative microscope. To eliminate any technical differences, all operations were performed by one operator.

Observation methods are as follows: 1) Slit lamp biomicroscopic observation, 2) Measurement of corneal thickness, 3) Measuring the number of corneal endothelial cells, 4) Light microscopic observation, 5) Scanning electron microscopic observation.

**RESULTS**

**Slit lamp biomicroscopic observation**

There was an inflammatory reaction above degree II on the 1st postoperative day, whereas an inflammatory reaction of degree I appeared on the 7th postoperative day, with practically little inflammatory reaction observed on the 14th postoperative day and thereafter (Table 1). There was no significant difference in the inflammatory reaction between the two groups.

**Changes in corneal thickness**

In comparison to free operative data prior to the operation, both groups had significant differences on the 1st, 3rd, and 7th postoperative days \( (P < 0.05) \), but there were no significant differences between the two groups (Table 2).

**Number of corneal endothelial cells**

The average number of corneal endothelial

---

**Table 1. Inflammatory severity in anterior chamber after postoperative periods**

<table>
<thead>
<tr>
<th>Group</th>
<th>Severity (Grade)</th>
<th>Postoperative</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1st day ( N=18 )</td>
<td>3rd day ( N=14 )</td>
</tr>
<tr>
<td>Group I</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Group II</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

\( N \): Number of experimental rabbit eyes,

Group I: Heparin surface modified PMMA IOL,

Group II: PMMA IOL
Table 2. Postoperative changes of corneal thickness, \( \mu m \)

<table>
<thead>
<tr>
<th>Group</th>
<th>Preoperative Thickness</th>
<th>1st day</th>
<th>3rd day</th>
<th>7th day</th>
<th>14th day</th>
<th>1st month</th>
<th>3rd month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>368 ± 23</td>
<td>451 ± 34*</td>
<td>498 ± 25*</td>
<td>437 ± 40*</td>
<td>385 ± 19</td>
<td>369 ± 12</td>
<td>370 ± 13</td>
</tr>
<tr>
<td>Group II</td>
<td>367 ± 19</td>
<td>469 ± 41*</td>
<td>503 ± 27*</td>
<td>462 ± 27*</td>
<td>373 ± 19</td>
<td>370 ± 28</td>
<td>377 ± 29</td>
</tr>
</tbody>
</table>

N: number of experimental rabbit eyes.

*\( p < 0.05 \) between preoperative and postoperative data.

Group I: Heparin surface modified PMMA IOL.
Group II: PMMA IOL

Table 3. Changes of endothelial cell density, cell/mm\(^2\)

<table>
<thead>
<tr>
<th>Group</th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>4th day</td>
</tr>
<tr>
<td>Group I</td>
<td>2580 ± 13</td>
<td>2293 ± 19(11.12**)</td>
</tr>
<tr>
<td>Group II</td>
<td>2726 ± 78</td>
<td>1949 ± 18(28.52**)</td>
</tr>
</tbody>
</table>

N: number of experimental rabbit eyes.

*\( p < 0.05 \) between preoperative and postoperative 4th day.

\(^*\): percent decrease of endothelial cell density.

\(^*\): \( p < 0.05 \) between Group I and Group II at postoperative 4th day.

Group I: Heparin surface modified PMMA IOL.
Group II: PMMA IOL

The number of inflammatory cells was 79 ± 16 per MPF in Group I and 120 ± 25 per MPF in Group II.

The number of inflammatory cells on the 3rd postoperative day was 58 ± 17 per MPF in Group I and 109 ± 22 per MPF in Group II. On the 1st and 3rd postoperative days, there were significant differences (\( p < 0.05 \)), between the two groups in the number of inflammatory cells (Table 4)(Fig. 1,2).

**Light microscopic findings**

In the early stage, there were the loss of iris epithelial cells, the erosion of ciliary body, bleed-
Table 4. Inflammatory cells on the surface of IOLs, cells/MPF

<table>
<thead>
<tr>
<th>Group</th>
<th>Postoperative</th>
<th>1st day</th>
<th>3rd day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>79±16*</td>
<td>58±17**</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>120±25*</td>
<td>109±22**</td>
<td></td>
</tr>
</tbody>
</table>

Results are expressed as M±S.D.,  
N: Number of experimental eyes,  
*: P = 0.013,  
**: P = 0.011,  
Group I: Heparin surface modified PMMA IOL,  
Group II: PMMA IOL,  
IOL: Intraocular lens,  
MPF: Medium power field (×100)

ing in the ciliary body, and the deposition of acute inflammatory cells, along with partial atrophy of the iris(Fig. 3). Macrophages and fibroblast-like cells were observed in the fibrous exudate of the anterior chamber (Fig. 4), while fibroblast-like cells and macrophages also began appearing around the expanded blood vessels of the iris and the ciliary body (Fig. 5). Such changes were more remarkable in the PMMA intraocular lens implantation group than in the heparin surface modified PMMA group.

The deposition of plasma cells, known as a chronic inflammatory reaction, and granulomatous inflammatory reaction were observed one month after the operation (Fig. 6).

Scanning electron microscopic findings

As in their light microscopic findings, both the PMMA intraocular lens and heparin surface modified PMMA intraocular lens implantation groups had the largest distribution of macrophages on the 1st postoperative day, with lymphocytes and leucocytes also having been found (Fig. 7).

Among the macrophages were active macrophages with ruffles on the surface and sessile macrophages with extensive bases on the surface (Fig. 7-a). On the 7th postoperative day, fibroblast-like cells produced cytoplasmic protrusions, while villi in the macrophages extended and fused together to form giant cells (Fig. 8, 9). On the 14th postoperative day, upheaved nuclei flattened gradually, while the cytoplasm also formed many lamellipodia (Fig. 10, 11).

DISCUSSION

The most important complication that follows the implantation of intraocular lens is bullous keratopathy. As a means of preventing direct contact with an intraocular lens, air 5 or a viscoelastic substance 6 is currently used. Kaufman 7 also reports that the hydrophobic surface of PMMA intraocular lens causes more damage to corneal endothelial cells than that of the hydrophilic surface when corneal endothelial cells and intraocular lens are in direct contact. King 8 reports that the heparin surface modification of the intraocular lens decreases surface tension on the boundary surface of solids and water to make it hydrophilic, while Reich 9 also reports a decrease in contact power between the intraocular lens and corneal endothelial cells.

In the inflammatory reaction of the anterior chamber after being operated on, the release of free radical superoxide from the leucocytes is known to be important. According to Dahinden 10, the measurement of free radical superoxide shows that the activation of leucocytes is much smaller in the heparin-modified intraocular lens than in the PMMA intraocular lens.

Uenoyama 11 also reports that the cells mainly observed in the study of cells on the surface of the intraocular lens following the implantation of PMMA posterior chamber intraocular lenses in the eyes of a rabbit, and also in the abdominal cavity of a mouse are macrophages, lymphocytes, fibroblast-like cells, and foreign-body giant cells at various stages of change. Of these cells, the most important were the macrophages, and the cells morphologically changed into active, inactive, and flat epithelium-like cells with the passage of time.

In the cytopathological observation of precipitates on the surface of intraocular lens, inflammatory cells were found in greater numbers in the peripheral section than in the central optical section. The number of inflammatory cells based on the author’s method of observation on the 1st and 3rd postoperative days significantly decreased in the heparin modification group.
rather than in PMMA lens group.

It is considered to be able to hold down the appearance of macrophages not only because the heparin-modified intraocular lens can possibly reduce the cohesive force for anterior chamber inflammatory cells, but also because it decreases the fusion of thrombocytes.

In the light microscopic findings in this experiment, the expanded blood vessels of the iris and ciliary body were occasionally observed in the initial stage of operation. Particularly in view of the emergence of macrophages and fibroblast-like cells around the blood vessels and the fact that many of the inflammatory cells in the anterior chamber were macrophages, it is very possible that the macrophages on the surface of the intraocular lens may have been derived mainly from the blood vessels of the iris and ciliary body.

**SUMMARY**

The heparin surface modified PMMA intraocular lens damaged the corneal endothelial cells to a lesser extent and had less deposition of inflammatory cells on the surface of the intraocular lens than the PMMA intraocular lenses.

Macrophages played an important role in the adaptation process of intraocular lens implanted eyes. They changed into thin membranes after forming giant cells as a morphological change. In such a process, there was no difference between the heparin surface modification of the intraocular lens and the PMMA IOL.

**REFERENCES**


**LEGENDS FOR FIGURES**

**Fig. 1a & 1b.** A portion of IOL surface on the 1st postoperative day after implantation of PMMA IOL(1a) and heparin surface modified PMMA IOL(1b) show sheet of many macrophages revealing an epitheloid appearance. Some of them are out of focus due to the surface of the convex lens (H-E stain, 1a X100, 1b X250).

**Fig. 2a & 2b.** Fibroblast-like cells with abundant cytoplasm and elongated cytoplasmic processes at the 7th postoperative day after implantation of PMMA IOL(2a) and a multinucleated giant cell at the 14th postoperative day after implantation of PMMA IOL(2b) are seen (H-E stain, X250).

**Fig. 3.** The iris after implantation of PMMA IOL shows diffuse atrophy of the epithelial lining. The epithelial lining of the ciliary processes are unremarkable, but telangiectasia and a few inflammatory infiltrates are seen in the stroma. The posterior chamber between the iris and ciliary processes is filled with fibrinous exudate (H-E stain, X100).

**Fig. 4.** High-power view of Fig. 3 shows fibrinous exudate in which macrophages(arrows) with vacuolated cytoplasm are scattered (H-E stain, X250).

**Fig. 5.** Macrophages(dark arrow) and fibroblast-like cells(arrow) after implantation of PMMA IOL are seen in the loose connective tissue and around the capillaries of the iris stroma (H-E stain, X500).

**Fig. 6.** The iris after implantation of heparin surface modified PMMA IOL shows infiltration of connective tissue by plasma cells(arrow). A few lymphocytes are also present (H-E stain, X250).

**Fig. 7.** Scanning electron microphotograph of cells on the PMMA IOL surface removed one day after surgery. The cells consist mostly of macrophages, lymphocytes, and fibroblast-like cells (original magnification X400). Fig. 7a is a scanning electron microphotograph of a side view of broad-based(sessile) macrophages attached to the IOL surface removed one day after surgery. Marked ruffles of the cells are noted (original magnification X5,400).

**Fig. 8.** Scanning electron micrograph of a few fibroblast-like cells extending its cytoplasmic lamellipodia to the substratum surface and being surrounded by a group of macrophages one week after implantation of PMMA IOL (original magnification X1,000).

**Fig. 9.** Scanning electron micrograph shows two macrophages extending cytoplasmic processes, which are observed on PMMA IOL surface removed seven days after surgery (original magnification X3,500).

**Fig. 10.** Scanning electron micrograph shows many flat-type giant cells with central irregular elevations which appear to contain several nuclei two weeks after implantation of heparin surface modified PMMA IOL (original magnification X400).

**Fig. 11.** Scanning electron micrograph of high power view of Fig. 10 shows a giant cell with an extending cytoplasm-like membrane formation (original magnification X3,500).