Comparison of Different Biomaterials for Glaucoma Drainage Devices

Ramesh S. Ayyala, MD, FRCS, FRCOphth; Lynn E. Harman, MD; B. Michelini-Norris, PhD; Leo E. Ondrovic, MSES; Edward Haller; Curtis E. Margo, MD, MPH; Scott X. Stevens, MD

**Objectives:** To compare the inflammatory reaction associated with the insertion of silicone and polypropylene endplates and endplates made of a new biocompatible polymer, Vivathane, in the rabbit subconjunctival space.

**Methods:** Similar-sized endplates made of 3 different biomaterials were sutured to the sclera in the superotemporal quadrant of the rabbit eye. Thirty eyes of 15 albino New Zealand rabbits were randomly assigned to the 3 groups. Conjunctival vascular hyperemia was graded in a masked fashion among groups. At the end of 3 weeks, the enucleated eyes were examined histologically and using scanning electron microscopy.

**Results:** Polypropylene and Vivathane were associated with significantly more inflammation in clinical observations and based on histological grading. Silicone was associated with the least amount of inflammation. Three polypropylene and 1 Vivathane plate were extruded between the second and third week.

**Conclusions:** Silicone is the most inert of the 3 materials tested. Inflammation associated with biomaterials may contribute to the failure of the glaucoma drainage devices.

**Clinical Relevance:** Bleb inflammation may be related to the biomaterial being used as the endplate. Endplates should be handled carefully during surgery to avoid creating rough spots.


Changes that the bleb undergoes following the insertion of a single-plate Molteno glaucoma drainage device (GDD) have been described by Molteno and Dempster\(^1\) as hypotensive, hypertensive (HP), and stable phases, according to the behavior of the intraocular pressure (IOP) at the time. The hypotensive phase, which lasts for 7 to 10 days after the operation, is characterized by a low IOP with diffuse edema and congestion of blood vessels in the tissues covering the episcleral plate of the implant. This is followed by the HP, a period of steadily rising IOP accompanied by the formation of a circumscribed bleb. During this phase, the edema disappears, and a definite layer of fibrous tissue appears in the deepest layers of the bleb. The bleb itself becomes raised and distended with aqueous. During the first 1 to 4 weeks of this stage, intense bleb wall congestion is noticed with steadily increasing IOP to 30 to 50 mm Hg in untreated cases. The bleb wall congestion and inflammation gradually subsides with stabilization of the IOP during the next 3 to 6 months.

In a study involving 85 patients, Ayyala et al\(^2\) found the incidence of the HP to be 82% following implantation of the Ahmed glaucoma valve. The HP peaked at 1 month after the operation, followed by a slow stabilization during a 6-month period. One third of these patients required 5-fluorouracil injections with needling of the bleb, while another third required a secondary surgical procedure (such as bleb revision) and/or a second implant to control the IOP during the HP. Siegner et al\(^3\) did not demonstrate an HP following the insertion of the Baerveldt glaucoma implant in 103 eyes. It is possible that the incidence of an HP following implantation of GDDs with larger surface explants such as the double-plate Molteno and the 350- and 500-mm\(^2\) Baerveldt implants may be less than that following implants with smaller endplates, such as the Ahmed glaucoma valve, because of the difference in the surface area. The presence of the HP and the inflammatory-fibrous reaction in the bleb could also be due to differences in the local immune response specific for individual biomaterials. Molteno\(^4\) described bilateral uveitis with sympathetic ophthalmia following the insertion of implants made of Stellon dental and neurosurgical acrylic. Later, he described unilateral uveitis with implants made of a transpex 1 intraocular lens material (Perspex; Rayner Optical Co, London, England). He concluded that the implant material must be inert and impervious with surface characteristics such that cells do not

©1999 American Medical Association. All rights reserved.
MATERIALS AND METHODS

We compared 3 different biomaterials. Polypropylene endplates of the Ahmed glaucoma valve implant supplied by New World Medical (Rancho Cucamonga, Calif) were compared with the silicone endplates of the Baerveldt implants supplied by Pharmacia Iovision Inc (Irvine, Calif). We further chose to study a new biomaterial, Vivathane, which is biocompatible polymer with an extremely smooth surface developed for the University of South Florida Magnetically Actuated Left Ventricular Assist Device project.\(^6\) The hemocompatibility, lack of bacterial adherence, lack of cytotoxicity, chemical stability, and noncancerogenicity of Vivathane have been demonstrated in previous studies.\(^7,8\)

This part of the study was performed to test the suitability of Vivathane as a potential endplate material. The study protocol was approved by the Institutional Animal Care and Use Committee at the University of South Florida, Tampa. Institutional guidelines regarding animal experimentation were followed.

Blocks of sterilized Vivathane, silicone, and polypropylene measuring 10 × 8 × 2 mm were used in the experiment to simulate the endplate of the existing GDDs. Care was taken to ensure that the edges of all the blocks were smooth and that the samples were of uniform size and shape. Fifteen healthy albino rabbits with no preexisting ocular inflammation were used. Both eyes of the 15 rabbits were used for a total of 30 eyes. Five rabbits were randomly assigned to 1 of 3 groups. The test material was sutured to the sclera, 8 to 9 mm from the limbus in the superotemporal subconjunctival quadrant of the right or left eye.

SURGICAL PROCEDURE

After adequate general anesthesia (ketamine hydrochloride [35 mg/kg] and xylazine hydrochloride [5 mg/kg] administered intramuscularly), the rabbit eyes were prepared and draped with sterile towels, and the lids were secured with a lid speculum. Topical 0.5% tetracaine hydrochloride was instilled to prevent any discomfort. The Westcott scissors were used to perform a superior limbal peritomy from the 11- to 2-o’clock meridian. The conjunctival dissection was performed posteriorly in the superotemporal subconjunctival quadrant. Hemostasis was achieved with the help of handheld cautery. A block of the test material was placed on the sclera, 8 to 9 mm from the limbus, and sutured to the sclera with 2 interrupted 9-0 nylon sutures. The conjunctiva was sutured to the limbus with a running 9-0 nylon suture.

POSTOPERATIVE CARE

Postoperative care included 1% atropine sulfate once daily and a combination of tobramycin sulfate and dexamethasone ointment (Tobradex) twice daily for 1 week. General health, presence of conjunctival hyperemia, subconjunctival hemorrhage, biomaterial extrusion, suture exposure, discharge, infection, corneal edema, corneal epithelial defects, anterior chamber reaction, quality of red reflex, and any complications were assessed and recorded at each postoperative examination on days 1, 3, 7, 14, and 21. Slitlamp biomicroscopy was performed on postoperative days 3, 7, and 21. Conjunctival hyperemia was rated by intensity and location in each of the eyes. The examination and grading of the conjunctival hyperemia was performed by one of us (R.S.A.) unaware of the biomaterial. The grading was performed as follows: grade 0 indicated no hyperemia; grade 1, mild hyperemia; grade 2, moderate hyperemia; and grade 3, severe hyperemia. The animals were killed at the end of 3 weeks (sedation with a large dose of ketamine followed by a lethal dose of intracardiac, intravenous pentobarbital sodium [100 mg/kg]). The eyes were enucleated, with care taken not to disturb the conjunctiva in the quadrant containing the implant.

SCANNING ELECTRON MICROSCOPY

Twelve eyes (4 specimens of each test material) were subjected to scanning electron microscopy for detection of inflammatory cells attached to the material surface. The specimens were submitted in isotonic sodium chloride solution. Before fixation, the implants and encasing capsules were carefully dissected from the enucleated eyes. The implants were removed from the fibrous capsules surrounding them and rinsed in isotonic sodium chloride solution to remove adherent blood from the surface of the implants and capsules. The implants and fibrous capsules were placed in 2% buffered paraformaldehyde for 24 hours at 4°C. Following fixation, the implants and capsules were rinsed for 1 hour in physiological saline solution at 4°C, then in distilled water for 30 minutes to ensure removal of erythrocytes from the implants and luminal surfaces of the fibrous capsules that had accumulated in the capsules as a result of manipulation during surgical removal of the eyes from the rabbits.

Following water rinse of the capsule tissue and implants, all samples were dehydrated through a graded series of ethyl alcohol, which was replaced with hexamethyldisilazane, a drying and hardening agent. The samples were air dried at 70°C overnight after removal from the hexamethyldisilazane.\(^9\) Following drying, the samples were mounted on conductive carbon tape so that portions of both sides of the implant and portions of both halves of the fibrous capsule’s inner surface could be evaluated. This generated 4 surfaces to be evaluated per sample. Following mounting, the samples were coated with metal in a sputter coater (Hummer VI; Anatcch Ltd, Alexandria, Va) and subsequently examined in a scanning electron microscope (Phillips Electronic Instruments, Eindhoven, the Netherlands) at 10-kV accelerating voltage.

LIGHT MICROSCOPY

Eighteen of the enucleated eyes (6 specimens of each test material) were fixed immediately in 10% buffered formalin. Semithin sections were cut and stained with hematoxylin-eosin. Light microscopic analysis of the specimens was performed. Attention was directed toward the degree of fibrosis and inflammatory response in the immediate vicinity of the explant material. The relative density of the inflammatory cells (macrophages, lymphocytes, plasma cells, and mast cells) and the amount of fibrosis in the conjunctival substantia propia was graded from 0 to 4. Comparisons were made among the 3 groups by one of us (C.E.M.) who was unaware of the biomaterial.
promptly removed for comfort of the animals. Of infection occurred. Extruded and exposed implants were all animals. Mild mucoid discharge occurred in association with suture exposure and extrusion, but no frank case of infection occurred. Extruded and exposed implants were promptly removed for comfort of the animals.

The Table shows the degree of conjunctival hyperemia on postoperative days 1, 3, 7, 14, and 21. Although the degree of conjunctival hyperemia was similar in all 3 groups on day 1, on all subsequent examinations, hyperemia was least for silicone implants.

Light microscopy revealed mild to moderate fibrosis with the silicone implants, moderate fibrosis with Vivathane implants, and marked fibrosis with polypropylene implants. The inflammatory reaction consisted of polymorphonuclear leukocytes predominantly followed by macrophages, lymphocytes, and giant cells. After exclusion of the eyes with extrusion of the biomaterial, the mean ± SD grade of inflammation (on a scale of 0-4) was 1.6 ± 0.41 with silicone implants, 2.4 ± 1.32 with Vivathane implants, and 2.2 ± 0.7 with polypropylene implants. Three of the 5 Vivathane capsules and 2 of the 3 polypropylene capsules demonstrated marked inflammation. None of the silicone implants had more than moderate (grade 2) inflammation.

Extrusion of the material occurred in 4 eyes, involving 3 polypropylene implants (postoperative days 14, 17, and 19) and 1 Vivathane implant (postoperative day 21). None of the silicone implants was extruded. Before the extrusion, intense conjunctival inflammation was noticed. The inflammation decreased clinically after the material was extruded. The degree of conjunctival hyperemia soon after the extrusion in all 4 eyes was 3. Following the removal of the extruded material, the degree of conjunctival hyperemia decreased to 0 to 1 in all cases. Histological grading for the eye with the extruded Vivathane implant was 3+, with intense inflammatory reaction and moderate fibrosis; for 2 of the eyes with the extruded polypropylene implants, 2+ and 1+. In the third eye with extrusion of the polypropylene implant, there was no cleft with only mild fibrosis. Histological examination of eyes with extruded implants was performed at the end of the study (not as soon as the material was extruded). The reason for delay was because the study protocol did not allow for enucleation before the completion of the 3 weeks.

**RESULTS**

There was no occurrence of anterior chamber reaction, corneal epithelial defects or ulcers, endophthalmitis, or untimely death of the animals. Red reflex remained good in all animals. Mild mucoid discharge occurred in association with suture exposure and extrusion, but no frank case of infection occurred. Extruded and exposed implants were promptly removed for comfort of the animals.

The Table shows the degree of conjunctival hyperemia on postoperative days 1, 3, 7, 14, and 21. Although the degree of conjunctival hyperemia was similar in all 3 groups on day 1, on all subsequent examinations, hyperemia was least for silicone implants.

Light microscopy revealed mild to moderate fibrosis with the silicone implants, moderate fibrosis with Vivathane implants, and marked fibrosis with polypropylene implants. The inflammatory reaction consisted of polymorphonuclear leukocytes predominantly followed by macrophages, lymphocytes, and giant cells. After exclusion of the eyes with extrusion of the biomaterial, the mean ± SD grade of inflammation (on a scale of 0-4) was 1.6 ± 0.41 with silicone implants, 2.4 ± 1.32 with Vivathane implants, and 2.2 ± 0.7 with polypropylene implants. Three of the 5 Vivathane capsules and 2 of the 3 polypropylene capsules demonstrated marked inflammation. None of the silicone implants had more than moderate (grade 2) inflammation.

Extrusion of the material occurred in 4 eyes, involving 3 polypropylene implants (postoperative days 14, 17, and 19) and 1 Vivathane implant (postoperative day 21). None of the silicone implants was extruded. Before the extrusion, intense conjunctival inflammation was noticed. The inflammation decreased clinically after the material was extruded. The degree of conjunctival hyperemia soon after the extrusion in all 4 eyes was 3. Following the removal of the extruded material, the degree of conjunctival hyperemia decreased to 0 to 1 in all cases. Histological grading for the eye with the extruded Vivathane implant was 3+, with intense inflammatory reaction and moderate fibrosis; for 2 of the eyes with the extruded polypropylene implants, 2+ and 1+. In the third eye with extrusion of the polypropylene implant, there was no cleft with only mild fibrosis. Histological examination of eyes with extruded implants was performed at the end of the study (not as soon as the material was extruded). The reason for delay was because the study protocol did not allow for enucleation before the completion of the 3 weeks.

**COMMENT**

The amount of inflammation at 3 weeks may not reflect the true degree of inflammation at the time of the examination. As was noted with the conjunctival hyperemia, the degree of inflammation probably decreased substantially between the day of extrusion and the end of the study, when these eyes were subjected to histological examination.

Scanning electron microscopy demonstrated a cell-lined fibrous capsule formation around all 3 biomaterials. Inflammatory cells were found in the fibrous capsule in all 3 groups. Vivathane and polypropylene implants supported cell growth on the surface of the implants (Figure, A and B). Cells grew more on Vivathane implants, and they appeared to form a more complete cell matrix. The surface of the silicone implants was free of cells and debris (Figure, C), except in areas with rough spots, which appear to attract cells to adhere to the implant surface.

The overall success of the currently available GDDs is 78% at 1 year. In the immediate postoperative phase, hypotony is the major problem. The Ahmed glaucoma valve has a 9.4% incidence of hypotony, which has decreased this complication considerably. The next major hurdle in the management of the GDD is to reduce the HP. The bleb becomes visibly inflamed, associated with an increase in the IOP to greater than 30 mm Hg in many cases. This phase begins 3 to 6 weeks after surgery and lasts for 4 to 6 months. The incidence of HP appears to be higher with the Ahmed glaucoma valve than with the Baervaldt implant. This could be explained on the basis of larger surface area of the Baervaldt implant or because of the different biomaterials used to make the endplates.

Our laboratory studies have demonstrated that the polypropylene in the Ahmed glaucoma valve is more inflammatory than the silicone in the Baervaldt implant in the rabbit subconjunctival space. This response was confirmed clinically and histologically and may account for the high incidence of HP demonstrated with certain glaucoma valve implants. Changing the endplate material from polypropylene to silicone may decrease the incidence of the HP and enhance the success rate of the GDD. The double-plate Molteno endplate and Krupin disc implant endplate were not tested in our study. Also, we do not know if the polypropylene in the Molteno implant is the same medical grade as that of the Ahmed glaucoma valve (the
texture, flexibility, and finish are different). Similarly, although the Baerveldt and the Krupin disc implants are made of medical-grade silicone, they differ in their texture, flexibility, and consistency. Thus, our results cannot be generalized to these implants.

Bleb failure secondary to scar formation is the main reason for GDD failure. Part of the bleb-related inflammation may be due to the biomaterial being used as the endplate. One way of decreasing the inflammatory response in the bleb is to use a biomaterial that has the least inflammatory response. In this regard, the new biomaterial, Vivathane, appears to be more inflammatory than silicone in the rabbit subconjunctival space. Future studies are needed to identify a more inert material. Scanning electron microscopic studies demonstrated that the inflammatory cells appear to adhere to rough spots on the silicone plates. These rough areas may have been surgically induced with the forceps. Thus, the implant endplates must be handled carefully during surgery to avoid creating rough spots on their surface.

In summary, we demonstrated that polypropylene endplate from the Ahmed glaucoma valve induces greater amount of inflammation than the silicone endplate of the Baerveldt implant in the rabbit subconjunctival space. Inflammation caused by biomaterials may contribute to GDD failure and transient periods of elevated IOP. The ideal GDD would be made of an absolutely inert biomaterial. Until such a material is found, the least inflammatory material should be used.

Accepted for publication October 14, 1998.

This work was supported in part by the Dorothy Benjamin Ophthalmology Research Endowment and by Research to Prevent Blindness Inc, New York, NY.

We thank New World Medical (Rancho Cucamonga, Calif), Pharmacia Iovision Inc (Irvine, Calif), and Magnetically Actuated Left Ventricular Assist Device project at the University of South Florida (Tampa), for providing the biomaterials that were used in the laboratory studies; the Pathology Core Facility at the University of South Florida; and the H. Lee Moffitt Cancer Research Institute (Tampa).

Corresponding author: Ramesh S. Ayyala, MD, FRCS, FRCOphth, 12901 Bruce B. Downs Blvd, MDC 21, Tampa, FL 33612-4799 (e-mail: rsayyala@hotmail.com).

REFERENCES