Glaucoma Drainage Devices: A Systematic Literature Review and Current Controversies

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Abstract. Glaucoma drainage devices create alternate aqueous pathways by channeling aqueous from the anterior chamber through a long tube to an equatorial plate that promotes bleb formation. Glaucoma drainage devices are being used more frequently in the treatment of glaucoma that does not respond to medications or trabeculectomy operations. In certain conditions, such as neovascular glaucoma, iridio-corneal syndrome, penetrating keratoplasty with glaucoma, glaucoma following retinal detachment surgery, and so on, it is becoming the primary operation. This review provides a systematic review of the literature and outlines the current controversies involving different glaucoma drainage devices and their design, overall surgical success, and complications following glaucoma drainage device insertion. (Surv Ophthalmol 50:48–60, 2005. © 2005 Elsevier Inc. All rights reserved.)

Key words. aqueous shunts • drainage device • glaucoma • implant • valve

Historical Perspective

The earliest attempts to drain fluid out of the anterior chamber into the subconjunctival space at the limbus date back to 1907 when Rollet implanted a horse-hair thread connecting the anterior chamber to the subconjunctival space near the limbus. Numerous attempts have been made since then without much success, until 1969. These include a silk, gold, platinum, tantalum, glass rod, and polythene tube. But all these operations failed because of excessive scar formation near the limbus, seton migration, conjunctival erosion, and so forth.

Molteno, in 1969, introduced the concept of the large surface area needed to disperse the aqueous. He inserted a short acrylic tube attached to a thin acrylic plate and sutured it to the sclera, adjacent to the limbus. Most of the operations failed after the first 3 to 6 months because of plate exposure, tube erosion, and scar tissue formation. In 1973, Molteno introduced the concept of draining the fluid away from the source to increase the success rate. All of the currently available glaucoma drainage devices are based on this concept of the Molteno implant (Molteno Ophthalmic Limited, Dunedin New Zealand).
which has a long silicone tube attached to a large explant placed 9–10 mm posterior to the limbus. The Molteno and similar implants offer no resistance to the outflow resulting in hypotony, flat anterior chambers, and choroidal effusions.

Since then, two major concepts have been introduced to modify glaucoma drainage devices. The first concept was that of a valve to offer resistance to the outflow and thus reduce the incidence of postoperative hypotony. Theodore Krupin, in 1976, introduced the pressure-sensitive, unidirectional valve that provides resistance to the flow of aqueous and prevents early, post-operative hypotony. This slit valve is designed to open at a pressure of 11 mm Hg and close at a pressure of 9 mm Hg. In 1993, Marteen Ahmed introduced the Ahmed Glaucoma Valve (New World Medical, Rancho Cucamonga, CA), a pressure-sensitive, unidirectional valve that is designed to open when the IOP is 8 mm Hg.

The second major modification was the increase in the surface area of the end-plate or the explant, resulting in lower intraocular pressures. Molteno, in 1981, introduced the double-plate implant and George Baerveldt, in 1992, introduced a non-valved silicone tube attached to a large barium-impregnated silicone plate.

**Current Glaucoma Drainage Devices**

Recently, glaucoma drainage devices have been used more frequently in the management of resistant glaucomas as an alternative to trabeculectomy and cyclodestructive procedures. The glaucoma drainage devices in common use at the present time include those which offer no resistance to immediate outflow (single-plate and double-plate Molteno and Baerveldt) and those that offer some resistance, such as the Ahmed glaucoma valve and the Krupin slit valve (Hood Laboratories, Pembroke, MA). The Molteno implant has been in use since the early 1970s. The other devices that followed are essentially modifications of the original Molteno concept of a silicone tube that opens onto a plate which acts as a base for the bleb to form.

Certain devices such as the Shocket, the OptiMed, White shunt pump, the Joseph implants, and the more recently introduced translimbal stainless steel tube, the EXPRESS shunt (Boston Scientific, Inc, Natick, MA), all lack substantial peer-reviewed literature at the present time and were not evaluated in the present article.

The Molteno and similar implants offer no resistance to immediate outflow, resulting in hypotony, flat anterior chambers, and choroidal effusions. In order to overcome these complications, several modifications have been proposed which include intraoperative placement of temporary, absorbable ligature (such as 5-0 or 6-0 polyglactin sutures) around the silicone tube, internal occlusion of the tube with a 3-0 prolene or 4-0 chromic suture that can be removed later, or a combination of 5-0 nylon internal occlusion suture and an external polyglactin ligature. As mentioned earlier, the original Molteno tube-plate design has been modified in two ways: 1) the introduction of aqueous shunts with a unidirectional valve, such as the Krupin and the Ahmed valves, to prevent the early postoperative hypotony; and 2) the increase in the surface area of the end-plate, resulting in lower intraocular pressure (IOP). The double-plate Molteno implant has a surface area of 270 mm² and the Baerveldt glaucoma implant (Advanced Medical Optics, Inc., Santa Ana, CA) has a large barium-impregnated silicone plate with a surface area of 250, 350, or 500 mm² with the 350 mm² being the most commonly used (more recently, the 500 mm² has been replaced by the 425 mm² end-plate). The single-plate Molteno has a surface area of 130 mm², the Ahmed glaucoma valve has a surface area of 185 mm², and the Krupin disk implant has a surface area of 184 mm². These devices are made of different biomaterials: the Molteno and Ahmed valves are made of polypropylene whereas the Krupin and the Baerveldt are made of silicone. The end-plate biomaterial of the Ahmed valve was recently changed to silicone (the Ahmed glaucoma valve-flexible plate).

Thus, it is evident that each of these devices has its own unique design made of different biomaterials with varying sizes of end-plates. With the increasing use of the glaucoma drainage devices, it is important for physicians to be aware of the advantages and disadvantages of the various devices to enable them to select the appropriate device for a given case. At the present time, it is not clear if these devices exhibit similar efficacy or if one device has certain advantages over the others.

**Material and Methods**

We performed a systematic review of the literature to answer the following questions:

1. Do all the glaucoma drainage devices lower the IOP, irrespective of their design?
2. Do larger end-plates result in lower IOP compared to devices with smaller end-plates?
3. Does the design of the glaucoma drainage device influence the incidence of complications, mainly, hypotony and diplopia?

A Medline search of literature published in English or English abstracts from 1966 to 2002 was performed using combinations of relevant key words. Various
search terms, including aqueous shunts, glaucoma seton, implant, valve, drainage device, and the names of specific implants were used. Direct comparison of the published literature was not possible because the majority of the studies are largely restricted to retrospective case series with different definitions of success, different follow-up times, and a lack of homogeneity in the cases included. For example, some of the published reports dealt exclusively with glaucoma drainage devices in patients with neovascular or uveitic glaucoma, a group with a high likelihood for failure. In an attempt to standardize the various studies to produce meaningful comparison, the following exclusion criteria were applied: any study with fewer than 10 eyes or less than 6 months of follow-up period; articles that focused on specific populations, diagnoses, or complications (i.e., reports focused on patients with a specific diagnosis such as neovascular glaucoma or articles that are focused on only the complications such as diplopia); and all review articles were excluded. Articles that may have repeated the same subjects more than once were excluded. For example, in studies that were published as the early, intermediate, and late findings (from the same group or authors and from the same clinic/hospital), only the last article was used. Manuscripts with similar follow-up times and case mixtures were included.

A total of 147 articles were reviewed. After applying the exclusion criteria, 54 articles were included in the final analysis (29 with Molteno, single- and double-plate with some form of intraoperative modification to prevent hypotony, 6 with single-plate Molteno without any form of surgical modification to prevent hypotony, 9 with Baerveldt, 8 with Ahmed glaucoma valve, and 2 with Krupin valves). The published data on the Molteno implant was divided into two categories, with and without the modification to reduce postoperative hypotony, because surgical outcomes were significantly different between the two groups. Furthermore, the Molteno implant data was divided into single-plate vs. double-plate where possible to study the effect of larger end-plates on the percentage reduction in the intraocular pressure. All the Baerveldt implant articles included in this analysis had modification of the silicone tube (vicryl tie with anterior slit) to reduce postoperative hypotony and were of the 350 mm$^2$ size (except for 2 articles comparing the 350 with the 500 mm$^2$ implants).

**SURGICAL SUCCESS**

Surgical success was defined as postoperative IOP greater than 5 mm Hg and less than 22 mm Hg without devastating complications, such as suprachoroidal hemorrhage or endophthalmitis leading to visual loss, or need for re-operation. Early hypotony was defined as intraocular pressure of 5 mm Hg or less in the first postoperative month. Late hypotony was defined as intraocular pressure of 5 mm Hg or less any time after the first postoperative month. Visual loss was defined as loss of visual acuity by two or more lines at the last follow-up (considered by the authors to be related directly to uncontrolled glaucoma and not cataract).

**STATISTICAL ANALYSIS**

Data regarding preoperative and postoperative intraocular pressure, surgical success, postoperative hypotony, suprachoroidal hemorrhage, and diplopia were retrieved from each study. These numbers were compiled and separated for each drainage device. The data from the Molteno device was further divided based on the plate size and if outflow resistance was achieved with surgical modification. Weighted averages for success rates and complications were calculated. The Pearson chi-square test was used to compare the incidence of surgical outcomes and complications among the glaucoma drainage device groups. Analysis of variance (ANOVA) was used to compare differences between groups in IOP controlling for pre-op intraocular pressure as a covariate. Changes in IOP within a device group were assessed by paired $t$-test. A two-tailed $p < 0.05$ was considered statistically significant. Analysis of the data was performed using the SPSS software package (version 11.0, SPSS Inc., Chicago, IL). A power analysis indicated that the number of studies provided 80% power ($\beta = 0.2$, alpha = 0.05) to detect significant group differences in intraocular pressure as well as in complication rates between the five major drainage device groups. All reported p-values are two-tailed with an alpha level of 0.05 used to indicate statistical significance.

**Results**

Table 1 summarizes the results from the systematic literature review among the five devices and Table 2 analyses the differences within the Molteno group. There were no statistically significant differences in the postoperative follow-up time among the five devices ($p = 0.72$) (Table 1) except for the double-plate Molteno group that had a shorter follow-up time of 12 months (Table 2). The overall surgical success rate averaged between 72% and 79% among the five devices with no statistical significant difference at the last follow-up ($p = 0.94$). Within the Molteno group, the double-plate Molteno achieved the highest success rate of 90%, however this success rate was at 12 months whereas the other groups were...
followed for longer duration. All five devices significantly decreased the IOP (p < 0.001). The percentage change in the IOP was similar among the five devices after controlling for preoperative IOP (p = 0.27) and within the Molteno group (p = 0.58) and was between 51% and 62%. There were no statistically significant differences in either the percentage change in intraocular pressure or the overall surgical success rate at the last follow up among the five devices or within the subdivisions of the Molteno group based on the size of the end-plate.

There were no statistically significant differences among the devices in the overall incidence of transient hypotony in the immediate postoperative period (p = 0.17), chronic hypotony (p = 0.51), suprachoroidal hemorrhage (p = 0.47), or in the decrease of visual acuity after the surgery (p = 0.90). The Molteno implant with modified technique had the lowest incidence of transient hypotony (12%) followed by the Ahmed valve (14%) and the Baerveldt (15%). The Molteno without any surgical modification to prevent hypotony had a statistically higher rate of hypotony (26%) compared to the Ahmed valve (p = 0.04) but no statistically significant difference was found compared to the Krupin valve. There were no statistically significant differences in the number of preoperative (p = 0.40) or postoperative medications (p = 0.40) among the devices. All five devices significantly reduced the number of medications in the postoperative period (p ≤ 0.01).

The occurrence of diplopia was significantly higher with the Baerveldt implant (9%) compared to the Ahmed valve (3%), the Molteno implant with ligature (2%) (p < 0.01), or the Krupin implant (p = 0.03). There was no mention of diplopia as a complication in any of the articles with Molteno implantation without the modified technique.

## Discussion

### IOP CONTROL AND GLAUCOMA DRAINAGE DEVICES

The overall success rate among the five glaucoma drainage devices analyzed appears to be very similar in controlling IOP and preserving vision in cases with intractable glaucoma. At last follow-up, all five devices reduced the intraocular pressure by greater than 50% compared to the preoperative intraocular pressure (at last follow-up) (Table 1). All the published data analyzed supported this recommendation. The double-plate Molteno had the highest success rate at 91% (Table 2). However this success rate was at

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### Table 1: Systematic Literature Review of the Glaucoma Drainage Devices

<table>
<thead>
<tr>
<th>Variable</th>
<th>Molteno with no Modification</th>
<th>Molteno with Modification</th>
<th>Baerveldt</th>
<th>Ahmed Glaucoma Valve</th>
<th>Krupin Valve</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of published studies</td>
<td>6</td>
<td>27</td>
<td>9</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total no. of patients (all studies)</td>
<td>234</td>
<td>1297</td>
<td>550</td>
<td>526</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>23.1 ± 10.8</td>
<td>27.1 ± 14.2</td>
<td>18.6 ± 7.8</td>
<td>16.0 ± 7.5</td>
<td>21.3 ± 11.2</td>
<td>0.72</td>
</tr>
<tr>
<td>Pre-op IOP, mm Hg</td>
<td>42.1 ± 2.1</td>
<td>34.1 ± 4.8</td>
<td>30.8 ± 4.2</td>
<td>33.9 ± 4.5</td>
<td>36.3 ± 1.5</td>
<td>0.02a</td>
</tr>
<tr>
<td>Post-op IOP, mm Hg</td>
<td>17.1 ± 1.3</td>
<td>16.6 ± 2.1</td>
<td>14.3 ± 1.8</td>
<td>16.6 ± 1.8</td>
<td>13.8 ± 1.6</td>
<td>0.32</td>
</tr>
<tr>
<td>% change in IOP</td>
<td>59 ± 3</td>
<td>51 ± 6</td>
<td>54 ± 8</td>
<td>51 ± 8</td>
<td>62 ± 5</td>
<td>0.20</td>
</tr>
<tr>
<td>Surgical success, %</td>
<td>75 ± 12</td>
<td>77 ± 13</td>
<td>75 ± 10</td>
<td>79 ± 8</td>
<td>72 ± 11</td>
<td>0.94</td>
</tr>
<tr>
<td>Decrease in visual acuity, %</td>
<td>33 ± 18</td>
<td>30 ± 13</td>
<td>27 ± 10</td>
<td>24 ± 7</td>
<td>28 ± 4</td>
<td>0.90</td>
</tr>
<tr>
<td>Pre-op meds, no.</td>
<td>NR</td>
<td>2.3 ± 0.3</td>
<td>2.2 ± 0.3</td>
<td>2.7 ± 0.3</td>
<td>2.7 ± 0.3</td>
<td>0.40</td>
</tr>
<tr>
<td>Post-op meds, no.</td>
<td>1.5 ± 1.0</td>
<td>1.1 ± 0.6</td>
<td>0.8 ± 0.2</td>
<td>1.0 ± 0.3</td>
<td>1.0 ± 0.2</td>
<td>0.86</td>
</tr>
<tr>
<td>Transient hypotony, %</td>
<td>26 ± 14</td>
<td>12 ± 7</td>
<td>15 ± 8</td>
<td>14 ± 8</td>
<td>17 ± 12</td>
<td>0.17</td>
</tr>
<tr>
<td>Chronic hypotony, %</td>
<td>5 ± 3</td>
<td>6 ± 5</td>
<td>6 ± 3</td>
<td>2 ± 1</td>
<td>2 ± 2</td>
<td>0.51</td>
</tr>
<tr>
<td>Diplopia, %</td>
<td>NR</td>
<td>2 ± 2</td>
<td>9 ± 5</td>
<td>3 ± 1</td>
<td>7 ± 5</td>
<td>0.01b</td>
</tr>
<tr>
<td>Suprachoroidal hemorrhage, %</td>
<td>NR</td>
<td>4 ± 3</td>
<td>5 ± 3</td>
<td>3 ± 3</td>
<td>8 ± 7</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Plus/minus values represent the weighted mean and standard deviation of published studies in the respective aqueous shunt groups.

NR = not reported. ANOVA used to compare IOP, other variables based on Pearson chi-square tests.

a Pre-op IOP was significantly higher in Molteno with no modification group. ANOVA.

b Diplopia rate was significantly higher in Baerveldt group compared to Molteno and Ahmed glaucoma valve groups.
TABLE 2

Breakdown of Molteno Implant Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>SPM with no Modification</th>
<th>SPM with Modification</th>
<th>DPM with Modification</th>
<th>SPM &amp; DPM with Modification</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of published studies</td>
<td>6</td>
<td>12</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Total no. of patients (all studies)</td>
<td>234</td>
<td>571</td>
<td>165</td>
<td>582</td>
<td></td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>23.1 ± 10.8</td>
<td>18.2 ± 11.6</td>
<td>12.0 ± 7.1</td>
<td>41.4 ± 15.6</td>
<td>0.02a</td>
</tr>
<tr>
<td>Pre-op IOP, mm Hg</td>
<td>42.1 ± 2.1</td>
<td>35.8 ± 4.0</td>
<td>33.0 ± 2.9</td>
<td>32.1 ± 5.2</td>
<td>0.38</td>
</tr>
<tr>
<td>Post-op IOP, mm Hg</td>
<td>17.1 ± 1.3</td>
<td>17.1 ± 1.8</td>
<td>14.7 ± 1.3</td>
<td>16.8 ± 2.4</td>
<td>0.09</td>
</tr>
<tr>
<td>% change in IOP</td>
<td>59 ± 3</td>
<td>52 ± 6</td>
<td>56 ± 3</td>
<td>48 ± 8</td>
<td>0.50</td>
</tr>
<tr>
<td>Surgical success, %</td>
<td>75 ± 12</td>
<td>74 ± 11</td>
<td>90 ± 10</td>
<td>69 ± 13</td>
<td>0.07</td>
</tr>
<tr>
<td>Decrease in visual acuity, %</td>
<td>33 ± 18</td>
<td>32 ± 13</td>
<td>28 ± 10</td>
<td>30 ± 10</td>
<td>0.60</td>
</tr>
<tr>
<td>Pre-op meds, no.</td>
<td>NR</td>
<td>2.5 ± 0.3</td>
<td>2.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>0.25</td>
</tr>
<tr>
<td>Post-op meds, no.</td>
<td>1.5 ± 1.0</td>
<td>1.6 ± 0.6</td>
<td>1.0 ± 0.2</td>
<td>0.8 ± 0.5</td>
<td>0.28</td>
</tr>
<tr>
<td>Transient hypotony, %</td>
<td>26 ± 14</td>
<td>11 ± 8</td>
<td>15 ± 12</td>
<td>12 ± 10</td>
<td>0.94</td>
</tr>
<tr>
<td>Chronic hypotony, %</td>
<td>5 ± 3</td>
<td>5 ± 4</td>
<td>1 ± 1</td>
<td>9 ± 4</td>
<td>0.37</td>
</tr>
<tr>
<td>Diplopia, %</td>
<td>NR</td>
<td>6 ± 2</td>
<td>0 ± 0</td>
<td>2 ± 1</td>
<td>0.08</td>
</tr>
<tr>
<td>Suprachoroidal hemorrhage, %</td>
<td>NR</td>
<td>6 ± 3</td>
<td>2 ± 2</td>
<td>5 ± 4</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Plus-minus values represent the weighted mean and standard deviation of published studies in the respective implant groups. SPM = single plate Molteno; DPM = double plate Molteno; NR = not reported. ANOVA used to compare IOP, other variables based on Person chi-square tests.  

*Mean follow-up was significantly shorter in the DPM with modification implant group, ANOVA.*

1 year, whereas the other groups had longer follow-up (22–26 months). The success rate would probably be similar to other devices had the double-plate Molteno cases been followed for longer duration. The life table analysis comparing the double-plate Molteno with the Ahmed glaucoma valve, by Ayala et al in a recent report, demonstrated that the success rate decreases by 10–15% every year in the first 3 years. 

END-PLATE SIZE AND IOP

The percentage reduction in the IOP among the groups in the present study was similar, with no statistically significant differences in either the postoperative IOP, percentage change in the IOP, the number of postoperative medications needed to achieve this pressure, or the overall surgical success rate among the devices at the last follow-up. Specific analysis comparing the device with the smallest surface area, the single-plate Molteno (surface area 130 mm²), to the device with the largest surface area, the Baerveldt (350 mm²), has not shown any statistical difference in any of the parameters tested. These conclusions were supported by recent studies with long-term follow-up. This is in contrast to the results shown by several well-performed studies comparing devices with a smaller surface area to those with a larger surface area. This may be because of the inherent weakness of the systematic review technique (i.e., compiling data from large number of reports that follow different methods of presenting the data). It also may be that these well-designed studies with limited numbers of patients and, in some cases, limited follow-up, do not reflect the true outcome.

In a study comparing the single-plate (surface area 130 mm²) versus the double-plate (surface area 270 mm²) Molteno implantation, Heuer et al concluded that the double-plate implants resulted in a statistically significant lower IOP and higher overall surgical success compared to single-plate implants, both in the early and late (24 months) postoperative follow-up. However, the double-plate Molteno success and final IOP were not twice as great as the results with the single-plate implant. In a prospective study, comparing the 350 mm² vs 500 mm² Baerveldt implant, Lloyd et al found no statistical difference in the overall surgical success rate or intraocular pressure control at 18 months. This finding may indicate that there is a maximum useful end-plate surface area beyond which there is minimal improvement in the IOP control. The 350 mm² Baerveldt implant...
may have surpassed this limit. In another retrospective study, Smith et al compared the 350 mm$^2$ Baerveldt implant in 18 eyes and the double-plate Molteno (270 mm$^2$) in 19 eyes. The mean IOP was similar between the two groups (13 mm Hg) at the end of 11.3 months of follow-up. This may mean that the 270 mm$^2$ surface area may be the optimal area beyond which there is no benefit.

The size of the end-plate appears to influence the level of the IOP to a point, but not the overall success rate of the operation. A recent study by Ayyala et al, comparing the double-plate Molteno and the single-plate Ahmed valve, supports this conclusion. The overall success rate at three years was 50% in both groups, even though the IOP was significantly lower in the double-plate Molteno group at all time points. In a study by Mills et al, the qualified success rate was found to be 57% at 44 months using single- or double-plate Molteno implants. They concluded that these implants fail at the rate of 10% per year leading to a 50% failure rate at 5 years. In another recent study, Broadway et al performed a retrospective 10-year chart review on patients who underwent single- and double-plate Molteno implants. They concluded that despite the overall tendency for the double-plate Molteno to be more effective than the single-plate, there was no statistical difference by survival analysis. Additional pressure lowering with a maximum-sized end-plate will probably depend on other factors such as the resistance of the encapsulation. The ideal size of the end-plate is not known at the present.

GLAUCOMA DRAINAGE DEVICE DESIGN AND POSTOPERATIVE COMPLICATIONS

The literature supports the concept that the design of the glaucoma drainage device influences the incidence of the postoperative complications, especially early postoperative hypotony and diplopia. Both the Ahmed valve and the Krupin valve had lower incidence of early postoperative hypotony compared to the Molteno when inserted without an outflow restricting modification. This demonstrates that the valve design does work to lower the incidence of early postoperative hypotony. However, the incidence of early postoperative hypotony, with the Ahmed valve at 14% and the Krupin valve at 17%, indicates that the valves do not function according to the manufacturers’ stated lower limit of closing pressure (8–9 mm Hg). It could be that other factors such as leakage of aqueous from the insertion site of the silicone tube might contribute to early hypotony.

The non-valved implants such as the double-plate Molteno and the Baerveldt achieved low incidence of hypotony when the operation was modified. In the absence of any surgical modification to regulate the flow, these non-valved implants were associated with a statistically higher incidence of hypotony.

The incidence of diplopia was highest with the Baerveldt implant and is probably related to the insertion of the wings of the end plate underneath the recti muscles, leading to subsequent scar tissue formation and muscle imbalance. Smith et al reported 77% incidence of diplopia following Baerveldt device implantation. These authors were the first to draw attention to diplopia with the Baerveldt implant. Other authors did not report this high incidence. This may be related to an evolving surgical technique. Subsequent studies have documented the incidence of diplopia to be between 6% and 18%. Because of this big difference in the incidence of diplopia between the Smith paper and subsequent articles, we chose to exclude the results from the Smith paper from the systematic review. Even after this exclusion, the incidence of diplopia was found to be significantly higher with the Baerveldt. It has been suggested that diplopia may be related to the height of the bleb or due to the adhesions to the recti muscles as the Baerveldt end-plate is inserted under the muscle belly. It has also been suggested that the incidence of diplopia will be less with modifications in the end-plate (i.e., fenestrating the end-plate). Most of the recent publications reporting on the Baerveldt implant with the modified end-plate did not report the incidence of diplopia; therefore, the true incidence of this complication in the Baerveldt implant is not known at the present time. However, because the height of the bleb is a common phenomenon among all the four devices, the higher incidence of diplopia with the Baerveldt implant probably is related to its unique design and its placement underneath the muscle belly. Diplopia from the other implants appears to be related to the height of the bleb and is significantly less than the Baerveldt implant.

In summary, systematic literature review reveals that all five devices appear to be effective in controlling the IOP and preserving the vision in cases with refractory glaucomas. The design of the implant appears to influence the incidence of the postoperative complications, especially hypotony and diplopia. The percentage reduction of mean postoperative IOP may be influenced by the size of the end-plate, but only to a certain point. Beyond this, other factors such as the degree of encapsulation around the end-plate influence the final intraocular pressure. The long-term success of any glaucoma drainage device appears to be limited by the fibrous reaction around the end-plate.
Factors Contributing to Early and Late Long-Term Failure

Hypertensive Phase with Bleb Encapsulation and Its Management

Following the insertion of a glaucoma drainage device, the bleb goes through two stages prior to becoming stable without any inflammation. The hypotensive phase is the initial stage lasting 1–4 weeks and is associated with an edematous conjunctiva and low IOP. The second stage is the hypertensive phase that begins 3–6 weeks after the operation and can last for 4–6 months. The bleb becomes visibly inflamed and encapsulated and may be associated with an increase in the IOP to greater than 30 mm Hg in some cases. Some authors arbitrarily defined the hypertensive phase as intraocular pressure greater than 21 mm Hg during the first 6 postoperative months in association with bleb encapsulation. This phenomenon is more frequently seen following the Ahmed valve (40–80% incidence in various reports) than the Baerveldt (20–30% incidence) or the double-plate Molteno (20–30%). The reasons for the higher incidence of hypertensive phase following the Ahmed glaucoma valve are not clear at the present time. Some authors speculate that this may be related to the effects of immediate fluid filtration with the Ahmed valves as opposed to delayed filtration with the ligated, non-valved implants. It has been suggested that the aqueous humor contains certain factors that stimulate a fibrotic response in the subconjunctival space. The exact nature of these proinflammatory factor or factors is not known at the present time. It is postulated that in implants inserted with tube ligation, because of the delay in the aqueous outflow into the bleb by 2–4 weeks, less fibrous reaction is elicited leading to lower incidence of bleb encapsulation.

Another explanation for the higher incidence of hypertensive phase among the Ahmed glaucoma valve group may be related to the smaller surface area of the Ahmed glaucoma valve (185 mm²) when compared to the double-plate Molteno (270 mm²) or the Baerveldt (350 mm²). It may also be related to the biomaterial, shape, and consistency of the end-plate. Even though the double-plate Molteno and Ahmed valves are made of the same biomaterial (polypropylene), the consistency and the shape of the end-plates are very different. For example, the Ahmed glaucoma valve end-plate is extremely rigid and hence may exhibit more micro motion in the postoperative period that might result in more inflammation and increasing intraocular pressure. On the other hand, the ridged, disk-shaped end-plates of the double-plate Molteno is more flexible and may be more stable on the scleral surface. Also, the ridge on the Molteno end-plate may prevent the fibrous capsule from growing directly on the implant, unlike the smooth surface of the Ahmed valve end-plate, which seems to attract the growth of white cells and collagen on its surface that can lead to a failed bleb. The Baerveldt implant is made of flexible silicone and in the rabbit model attracted the least amount of inflammation/fibroblasts. Based on these studies, the Ahmed glaucoma valve end-plate has recently been changed to silicone (the flexiplate Ahmed valve). If future studies show lower incidence of the hypertensive phase with the flexiplate Ahmed compared to the old plate made of polypropylene, then it will lend credence to the biomaterial theory. However, it is clear that many other factors may be responsible for this phenomenon and future research should be directed toward identifying these factors.

During the hypertensive phase, antiglaucoma medications along with digital massage are indicated when the IOP is considered to be too high by the treating physician, usually greater than 21 mm Hg. In those cases that do not respond to the above treatment measures, stent removal and/or suturelysis should be considered among the nonvalved implants. Bleb revision with needling of the bleb is an option for both nonvalved and valved implants with encapsulated blebs. Surgical excision of the encapsulated bleb has been recommended in cases that do not respond to needling.

Bleb Fibrosis

The introduction of a biomaterial such as the end-plate of any glaucoma drainage device appears to be associated with a fibrovascular response in the subconjunctival space. The introduction of glaucomatous aqueous humor from patients with elevated IOP into the subconjunctival space in itself can stimulate fibrovascular proliferation in the episcleral tissue, whereas the aqueous of normal rabbit eyes and normotensive, previously glaucomatous human eyes stimulate connective tissue degeneration. Early fibroproliferative changes followed later by a fibrodegenerative response appears to be the common histologic pattern of the blebs following the glaucoma drainage devices implantation into the subconjunctival space. Excessive proliferative changes appears to be associated with bleb failure and elevated intraocular pressure. It has been proposed that the timing of the introduction of the aqueous humor into the bleb might influence the fibroproliferative vs fibrodegenerative response and thus the success rate of the operation.

The histologic changes following the introduction of these implants has been best studied with the...
Moteno implants. The introduction of the Molteno end-plate into the subconjunctival space (in the absence of aqueous humor) appears to result in a uniform layer of avascular and modestly cellular connective tissue 20–60 µm thick and remains unchanged after 4 weeks.

The introduction of the Molteno implant without the vicryl tie (one-stage technique) results in marked vasodilation with edema, fibrin deposition involving the full thickness of Tenon’s connective tissue layer, and a moderate infiltration by polymorphonuclear leukocytes in the first week followed by gradual resolution of all signs of active inflammation over the next 4–6 weeks, leaving behind a thick capsule measuring approximately 400 µm in thickness. The histologic changes following the two-stage insertion of the Molteno implant (or with the vicryl tie technique) were similar except that the resulting fibrous capsules were significantly thinner (200 µm), with the intensity of the inflammation and the amount of collagen tissue laid being much less compared to the one-stage technique.

With either technique, the avascular fibrodegenerative phase appears to begin after the first postoperative month with progressive reduction in the cellularity and fragmentation and delamination of the innermost collagen layers of the bleb cavity. It has been suggested that these changes imply that the fibroproliferative response was stimulated when aqueous drained into vascular Tenon’s tissue, whereas the fibrodegenerative response was dependent on aqueous displacing normal interstitial tissue fluid at intraocular pressure that exceeded the intracapillary pressure in the deeper layers of the capsule.64 Excessive fibrous reaction around the bleb appears to be the major cause of long-term glaucoma drainage device failure. Failure appears to be more common in the first postoperative year than subsequent years.16 This lends support to the concept that bleb fibrosis may be the major cause for glaucoma drainage device failure. Studies have demonstrated the critical importance of the permeability of the bleb lining in determining the long-term control of the intraocular pressure: a thin permeable bleb lining giving good control of the IOP while a thicker, less permeable lining gives poorer results.56,77,97 Usage of anti-inflammatory agents has been shown to be associated with thin-walled blebs and lower IOP in certain patient groups.65 Based on histological analysis of 75 autopsy eyes (wherein the Molteno implant was implanted as a single stage vs. two stages or with vicryl tie technique) it has been suggested that thinner blebs with lower intraocular pressures could be achieved by exposing the preformed blebs (as in the two-stage implantation or with vicryl tie technique) to aqueous at elevated IOP. It has been proposed that this results in greater fibrodegenerative response and hence thinner blebs and lower IOP. However, review of the literature involving different implants inserted with different techniques (single-stage vs. two-stage vs. vicryl tie) has failed to show any difference in the postoperative intraocular level or the surgical success rate in the long term (Tables 1 and 2).

The intensity of the fibrous reaction may vary depending on a number of factors, such as the biomaterial, size, and/or design of the end-plate and the individual patient’s immune reaction to the operation, the glaucoma drainage device itself, and the presence of aqueous in the subconjunctival space and factors that are not well understood at the present time. In case of certain implants like the Ahmed glaucoma valve, holding the implant across the end-plate with a forceps while tucking the end-plate into the sub-Tenon’s space can potentially break the rivets holding the sheet valve.32 This can lead to fibrous tissue growing into the sheet valve causing late failure. Also, holding the end-plate with toothed forceps can indent the smooth surface of the end-plate and, in rabbit studies, the roughened end-plate surface attracted more fibrous tissue adherence to it, leading to late failure.4,6

End-plate Biomaterials/Biocompatibility

Inflammation around the end-plate, resulting in excessive scar tissue formation, is the leading cause of glaucoma drainage device failure.62 The overall success rate of the currently available glaucoma drainage devices may be improved with modified end-plates made of the least inflammatory biomaterial. Currently most of the glaucoma drainage devices are made of silicone or polypropylene. These polymers have a high binding affinity for plasma and interstitial proteins which in turn leads to cellular adhesion and subsequent cytokine release, chronic inflammation and fibrosis.88 Ayyala et al have demonstrated in the rabbit model that polypropylene end-plates are more inflammatory than silicone.4,6 They further concluded that the inflammation appears to be related not only to the biomaterial but also to the rigidity, flexibility, and the shape of the end-plate. These rabbit model study results need to be confirmed in humans. Future studies involving the new Ahmed valve with the flexible silicone plate compared to the old polypropylene one will demonstrate if this conclusion is valid. The end-plate should be made of a biomaterial that is totally inert and should not attract fibroblast or protein deposits that in turn could lead to cytokine release, chronic low-grade inflammation, and bleb failure. Future research...
should also be directed towards minimizing the fibrous reaction around the bleb with new drugs that will target the inflammatory factors.

**End-plate Design**

The end-plate design might influence not only postoperative complications such as diplopia but also the degree of fibrous reaction. The rigid plates of the current glaucoma drainage devices might exhibit low-grade to-and-fro micro motion with ocular movement resulting in chronic low-grade inflammation. Fenestrated end-plates designed to promote fibrous tissue anchoring may reduce micro motion and long-term fibrous encapsulation (Jacob-Labarre JT, McKinnon SJ, Tanji T: Biocompatibilty response to modified Baerveldt glaucoma drains [abstract]. Invest Ophthalmol Vis Sci 37[Suppl]:1164, 1996).

The potential for micromotion may be more pronounced with implants like the Ahmed valve that have an oblong-shaped positioned in an anterio-posterior direction. As has been discussed previously, although the design of the Baerveldt end-plate is responsible for the higher incidence of diplopia (compared to the other glaucoma drainage devices), the shape and size of the Ahmed valve end-plate, when placed too far posteriorly, can potentially compromise the health of the optic nerve. In a rabbit model, Ayyala et al have presented data suggesting early optic nerve degeneration following posterior insertion of the Ahmed valves at the end of 2 months of follow-up. Degeneration of the optic nerve appears to be more pronounced in those rabbit eyes whose plates were found to be impinging on the nerve. Mild degenerative changes were found with the end-plate at 0.5–1.0 mm distance from the nerve. In the human eye, placement of the 16-mm end-plate of the Ahmed valve (the adult model) 10 mm posterior to the limbus can potentially place the end-plate in the vicinity of the optic nerve, especially in the superonasal quadrant. Previous reports suggest that the plate will be within 2 mm of the optic nerve when placed 8–10 mm from the limbus in the superonasal quadrant in the human eye. The findings of the rabbit model experiments and the anatomical correlation of the Ahmed glaucoma valve end-plate to the optic nerve in the human eye may suggest that the end-plate of the Ahmed glaucoma valve may be positioned in such a way as to avoid direct optic nerve impingement. Axial length measurements, at least in patients with shorter eyebrows, may be necessary to determine the ideal insertion site.

**ROLE OF MITOMYCIN AND 5-FU**

Antifibrotic agents such as the mitomycin C and 5-fluorouracil have been used successfully to decrease the fibrous reaction following trabeculectomy operation. However, the advantages of mitomycin C at the time of the glaucoma drainage device implantation remain unclear. In one study, 21 patients with double-plate Moltene and mitomycin C were followed for 2–3 years. Sixty-eight percent of the patients had IOP less than 21 mm Hg at 1 year and 35% at 2 years, which is comparable to the control group. Susanna et al reported 76% success rate (IOP less than 21 mm Hg) at 9.4 months. Cantor et al and Lee et al have concluded that mitomycin C did not demonstrate any advantage in the IOP control, compared to the control group. In fact, all the published studies have shown incidences of hypotony (10–63%), flat anterior chambers (18–43%), and choroidal effusions (>71%) to be higher in the mitomycin C group. In all these studies, the operation was performed using some form of ligature or the ripcord technique to control the rate of flow of the glaucoma drainage device. Ayyala et al have reported conjunctival melts in two of the six patients that had mytomycin C during Ahmed glaucoma valve implantation. Thus, there appears to be no clear advantage in using mitomycin C at the time of the glaucoma drainage device operation. It remains unclear as to why these antifibrotic agents enhance the surgical success following trabeculectomy operation and not following glaucoma drainage device surgery. The fibrosis following glaucoma drainage device surgery is probably instigated by mature fibroblasts as the bleb is formed 7–8 mm from the limbus as opposed to the bleb forming at the limbus following the trabeculectomy operation.

**CORNEAL DECOMPENSATION AND PARS PLANA PLACEMENT OF GLAUCOMA DRAINAGE DEVICES**

Corneal decompensation appears to be one of the main complications following glaucoma drainage device surgery. It has been reported in up to 30% of the patients with long-term follow up. Graft failure from decompensation or rejection in patients with penetrating keratoplasty and glaucoma following glaucoma drainage device surgery has been reported in the range of 10–51% (an average of 36.2%). The etiology of corneal decompensation and graft failure is probably multifactorial. Preoperative factors such as previous surgeries and previous episodes of inflammation together with chronic or episodes of acute elevated intraocular pressure can all contribute to endothelial cell damage and subsequent corneal decompensation in the postoperative period. The degree and duration of elevated IOP has been shown to result in significant endothelial cell loss. Ten percent to 33% endothelial cell loss has been reported following an acute attack
of angle-closure glaucoma and 77% cell loss has been reported in eyes with acute angle-closure glaucoma lasting more than 12 days. Morphological changes in the endothelial cells, such as vacuolization, loosening of cell junctions, blebbing, disruption of the plasma membrane, exkaryocytosis, and the loss of whole cells, have been observed in experimentally induced acute glaucoma. Corneal sensation is also noted to be decreased in cases of angle-closure glaucoma. This, together with postoperative factors, such as the inflammation and possible corneal-tube touch, either directly or during eyelid rubbing or blinking, may explain corneal decompensation and/or graft failure in some patients.

Another factor that could explain this phenomenon is the state of the endothelial cells prior to glaucoma drainage device implantation. If the endothelial cell health is compromised prior to surgery, for any reason, the postoperative corneal decompensation is just a reflection of the natural course of the disease state versus the glaucoma drainage device implantation compromising the endothelial status.

Literature search revealed only one article, by McDermott et al., reporting on the endothelial cell changes following glaucoma drainage device surgery. They reported no clinically significant endothelial cell loss in 19 patients undergoing uncomplicated Molteno implants with an average follow-up period of 1 year.

The timing of glaucoma drainage device surgery is another factor that can contribute to graft failure. In the series published by Beebe et al. and Rapuano et al., there is a trend toward a higher incidence of graft failure when glaucoma drainage device surgery was performed after penetrating keratoplasty. It is possible that glaucoma drainage device surgery-related complications (including inflammation, shallow anterior chamber with iris graft, endothelial touch, tube-endothelial touch) could contribute to graft failure.

Pars plana placement of the glaucoma drainage device after complete vitrectomy has been advocated by some surgeons in patients with very shallow anterior chambers and in patients with penetrating keratoplasty with glaucoma to avoid complications such as tube-corneal touch and mechanical endothelial damage. A recent study by Sidoti et al. has failed to reveal any advantage to this approach in patients with penetrating keratoplasty and glaucoma. A graft rejection rate of 15% and a failure rate of 50% was comparable to the results seen with anterior tube placement. In addition, the article highlights the posterior segment complications associated with pars plana vitrectomy technique, namely, incidence of retinal detachment (6%), vitreal obstruction of the tube tip (9%), development of epiretinal membrane (9%), and cystoid macular edema (3%). In summary, this technique should be reserved for cases with very shallow or no peripheral anterior chamber, glaucoma associated with a retinal pathology for which vitrectomy is being performed primarily for the retinal pathology such as neovascular glaucoma with vitreous hemorrhage secondary to neovascularization of retinal vessels. It is also advocated in patients with tube-related anterior chamber complications, such as recurrent tube erosions that did not respond to scleral patching and shallow anterior chamber secondary to chronic angle-closure glaucoma and corneal decompensation. In these patients, reposition of the tube from its limbal location into parsplana position combined with vitrectomy, without disturbing the end-plate/bleb, appears to work well.

FUTURE RESEARCH

The current generation of glaucoma drainage devices are beset with a number of problems, most of which appear to be related to suboptimal design, less than ideal biomaterial usage, and lack of innovation in the control of fibrous reaction around the endplate leading to poor and often unpredictable success rates and complications. The plate and the tube concept introduced 30 years ago still dominate the market. In the absence of ideal methods of controlling the inevitable fibrosis around the end-plate, new research is focusing on limbal implants. Some researchers are working on a trabecular implant that can bypass the trabecular resistance and let the aqueous flow directly into the Schlemms canal. Apart from changing the design of the implants, future research should take into account newer, biologically more inert biomaterials and innovative drug-delivery systems to minimize postoperative fibrosis.

Current literature review suggests several limitations. Variable definitions of success, using arbitrary numbers such as 21 or 22 mm Hg as the target IOP, different follow-up times, and variable study designs make direct comparisons between different types of operations very challenging. In the future, researchers should strive to standardize the definition of success following a glaucoma surgical procedure. This improvement in comparability of outcome criteria will allow for proper comparison of different glaucoma drainage devices and will lead to greater objectivity in performing systematic reviews and synthesizing the results of separate studies.

With improvements in biomaterials to minimize fibrous reaction, designs to obtain predictable IOP and minimize design-related complications, and the
use of current or newer antifibrotic agents with innovative drug delivery systems, we may be able to achieve the ideal glaucoma drainage device.

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