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Aqueous shunts for glaucoma

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Abstract

Background—Aqueous shunts are employed for intraocular pressure (IOP) control in primary and secondary glaucomas that fail medical, laser, and other surgical therapies.

Objectives—This review compares aqueous shunts for IOP control and safety.

Search strategy—We searched CENTRAL, MEDLINE, PubMed, EMBASE, NRR in January 2006, LILACS to February 2004 and reference lists of included trials.

Selection criteria—We included all randomized and quasi-randomized trials in which one arm of the study involved shunts.

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*Indicates the major publication for the study

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Coordinating the review: DM, SSV, MM

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Data collection and analysis—Two authors independently extracted data for included studies and a third adjudicated discrepancies. We contacted investigators for missing information. We used fixed-effect models and summarized continuous outcomes using mean differences.

Main results—We included fifteen trials with a total of 1153 participants with mixed diagnoses. Five studies reported details sufficient to verify the method of randomization but only two had adequate allocation concealment. Data collection and follow-up times were variable.

Meta-analysis of two trials comparing Ahmed implant with trabeculectomy found trabeculectomy resulted in lower mean IOPs 11 to 13 months later (mean difference 3.81 mm Hg, 95% CI 1.94 to 5.69 mm Hg). Meta-analysis of two trials comparing double-plate Molteno implant with the Schocket shunt was not done due to substantial heterogeneity. One study comparing ridged with standard double-plate Molteno implants found no clinically significant differences in outcome. Two trials investigating the effectiveness of adjunctive mitomycin (MMC) with the Molteno and Ahmed implants found no evidence of benefit with MMC. Two trials that investigated surgical technique variations with the Ahmed found no benefit with partial tube ligation or excision of Tenon's capsule. One study concluded there were outcome advantages with a double versus a single-plate Molteno implant and one trial comparing the 350 mm² and 500 mm² Baerveldt shunts found no clinically significant advantage of the larger device but neither of these trials included all patients randomized. One study suggested improved clinical outcome when MMC was employed with a newly described shunt including ultrasound supporting the conclusion. One small study did not demonstrate an outcome advantage to systemic steroid use postoperatively with single-plate Molteno shunts. One study comparing endocyclophotocoagulation (ECP) with Ahmed implant in complicated glaucomas found no evidence of better IOP control with Ahmed implant over ECP.

Authors' conclusions—Relatively few randomized trials have been published on aqueous shunts and methodology and data quality among them is poor. To date there is no evidence of superiority of one shunt over another.

Medical Subject Headings (MeSH)

*Glaucoma Drainage Implants [adverse effects]; *Intraocular Pressure; Cataract Extraction; Glaucoma [*surgery]; Molteno Implants [adverse effects]; Ocular Hypertension [surgery]; Randomized Controlled Trials as Topic; Trabeculectomy

MeSH check words

Humans

Background

Introduction

Aqueous shunts are employed as surgical interventions to control intraocular pressure (IOP) in primary open-angle or secondary angle-closure glaucomas that have failed medical and laser therapies in addition to one or more surgical procedures such as trabeculectomy. The term aqueous shunt is preferred by the American National Standards Institute (ANSI) as most appropriate for the group of devices referred to in current peer reviewed literature as

glaucoma drainage devices, tube-implants, tube-shunts or inappropriately as setons, a term that should be reserved for non-lumened devices (ANSI Z80 1998; Minckler 1997).

All the aqueous shunts considered in this review are composed of a lumened silicone rubber tube attached to an explant plate. The Molteno implant, the first successful and widely utilized such device, remains the gold standard commercially available example (Molteno 1981; Molteno 2001; Molteno 2003). Newer shunts, including the Ahmed, Baerveldt, and Krupin, have features in common with the Molteno, but vary in size, shape, composition and the presence or absence of flow-restricting components (Prata 1996). Among these four, all but the Krupin are available with different sized explants. The Ahmed and Molteno devices come in one or two-plate versions. The Ahmed is now available in either rigid (polymethylmethacrylate) or flexible (silicone rubber) versions in one or two plate models. The Schocket shunt, assembled intraoperatively, utilizes buckling elements and a segment of silicone rubber tubing. The modified Schocket shunt or anterior chamber tube shunt to an encircling band (ACTSEB) procedure utilizes a previously installed buckle element as the explant to which a segment of tubing is attached. Schocket shunts are essentially equivalent in concept to commercially available devices (Schocket 1982; Sidoti 1994). The surface area of the explant has been demonstrated to correlate with clinical effectiveness in humans (Heuer 1992). No randomized trials utilizing the most recently marketed shunt, the EXPRESS, a translimbal stainless steel tube with an internal diameter of 50µm, have been published (Gandolfi 2002). The OptiMed, White shunt pump, and Joseph implants, are relatively recent in origin, and not in current use. Only sparse details are available regarding the specifications of the Hunan shunt (Duan 2003).

Epidemiology

Based on informal feedback from manufacturers and US Medicare database information (1995 and 1998), approximately 3000 to 4000 aqueous shunts are utilized per year in the US alone. Aqueous shunts are used in infants and children in addition to adults, but no survey has been done allowing breakdown by glaucoma category, sex or specific age ranges, or safety and effectiveness of the variety of different sized devices available. There are no data that track the utilization patterns of aqueous shunts with regard to age, sex, or race, but it seems likely they will be increasingly applied to complex glaucomas at an earlier stage among patients of all ages and races, especially during combined glaucoma and cataract procedures (Hoffman 2002). Commercially available aqueous shunts cost between \$400 and \$600 in the US, not including surgeon fees or other costs associated with surgery.

Indications for use

The majority of adult eyes in which aqueous shunts are currently used in the US are pseudophakic (contain a lens implant after cataract extraction) (Mills 1996; Minckler 1988). Aqueous shunts also have clinical application to neovascular, post-traumatic, inflammatory glaucomas, and congenital glaucomas that fail goniotomy or trabeculotomy (Djodeyre 2001). Aqueous shunts are used to manage glaucoma in complex cases where penetrating keratoplasty and retina-vitreous surgery may be simultaneously or serially performed (Lloyd 1989). They are generally preferred to cyclodestructive procedures in the US (surgery that destroys part of the ciliary body, cyclocryotherapy or trans-scleral laser) when functional

central vision (better than 20/100) is present (Chalam 2002), but not in Europe where cyclodestruction is still preferable. Aqueous shunts may be preferable to trabeculectomy with adjunctive anti-fibrotic agents in people who work in dusty or dirty environments or who require contact lenses for functional vision or in those who are immunocompromised, as the risk of late infection is less.

The flow-restricted devices (Ahmed, Krupin, White shunt pump, Joseph implant, OptiMed) have typically been installed in one stage (complete installation) with immediate function. The nonflow-restricted devices (Molteno, Baerveldt) are typically installed in two stages either in two separate operations or with utilization of a variety of temporary flow-restricting techniques. With all of these devices the anterior edge of the explant plate is generally located 8 to 10 mm posterior to the limbus with the explant centered at the equator (Minckler 1988; Prata 1995a; Prata 1995b). The delay in opening of the non flow-restricted shunts via two-stage operations allows encapsulation to develop over the explant before flow of aqueous humor begins and reduces the risk of hypotony postoperatively. The ExPRESS is currently being marketed as a one-stage device.

Prognosis, complications and alternatives

Aqueous shunts may prevent or delay blindness and visual disability in a large percentage of people in whom they are used. Comorbidities, including optic nerve injury, corneal disease, or other damage related to past trauma or previous surgery are frequently present in eyes in which shunts are employed. Prospectively, aqueous shunts probably increase the risk of endothelial failure and they are widely thought to increase the risk of graft failure after penetrating keratoplasty, especially with the drainage tube installed in the anterior chamber.

The long-term outcome (success and persistence of benefit) for aqueous shunts has not been well studied, but some reports indicate that IOP control benefits may extend for several decades (Molteno 2001; Molteno 2003). In general, the failure rates per year parallel those of trabeculectomy in similar cases (FFSSG 1996). The principal long-term complication of anterior chamber aqueous shunts is corneal endothelial decompensation. Other postoperative problems include transient hypotony, probably due to leak around the tube in limbal tissues or failure of flow-restricting devices to maintain sufficient resistance. Additionally, several reports have described a postoperative hypertensive phase, probably due to inflammation induced by flow of aqueous humor around the explant, necessitating resumption of topical anti-glaucoma medications for many weeks. Clinical failure in many cases is due to excessive fibrosis and relative impermeability of the capsule around the explant.

The current standard initial surgical procedure for glaucoma is trabeculectomy. In some locales, non-penetrating filtering procedures, either viscocanalostomy or deep sclerectomy would be the first alternative before trabeculectomy and before aqueous shunts. Aqueous shunts are currently the standard of care in the US for complicated glaucomas, especially pseudophakic eyes that have failed one or more previous trabeculectomies.

Rationale for systematic review

Recently published retrospective case series have indicated long-term benefit from aqueous shunts in pseudophakic, inflammatory, and traumatic glaucomas (Molteno 2001; Molteno

2003). However, there has been no review of randomized trials as to the effectiveness and safety of aqueous shunts as surgical therapy for glaucomas. Controversy persists regarding when aqueous shunts should be used in the sequence of glaucoma surgeries as well as the effectiveness of different aqueous shunts. Most US surgeons reserve aqueous shunts until one or more standard procedures have failed. The use of aqueous shunts in combined cataract and glaucoma surgeries has received relatively little attention and no randomized trials investigating this issue have been identified (Hoffman 2002). Only two published randomized trials (Wilson 2000; Wilson 2003) have compared a shunt (Ahmed) with trabeculectomy and only the latter included previously un-operated eyes. Virtually all previously published case series have described the utilization of shunts in eyes after previous failed standard filtering surgery. A new study currently in progress, the Tube versus Trabeculectomy Study centered at Bascom Palmer Eye Institute in Miami Florida, is comparing Baerveldt shunts with trabeculectomy in phakic and pseudophakic eyes after previous cataract or filtering surgery, or both (Gedde 2005).

Objectives

The objective of this review was to assess the safety and effectiveness of aqueous shunts for reducing IOP in glaucoma.

Methods

Criteria for considering studies for this review

Types of studies—Only randomized and quasi-randomized trials were included.

Types of participants—We included trials in which the participants were diagnosed with glaucoma irrespective of their lens status. There were no restrictions with regard to patient age, gender, ethnicity, co-morbidities, use of adjunctive medications or the numbers of participants.

Types of interventions—All trials that compared various aqueous shunts with standard surgery or cyclodestruction or to each other were included. We also included trials that compared different surgical techniques and use or non-use of adjunctive mitomycin C or corticosteroids with specific shunts.

Types of outcome measures

Primary outcomes

1. Control of IOP assessed as:
 - a. mean decrease from baseline (immediate pre-operative IOP) on day one, during weeks one to 12, six months, one year and as available throughout follow up and at last follow up, measured using Goldmann tonometry, TonoPen, or other standard devices. Mean decrease from baseline at one year was considered as the main primary outcome of the review;
 - b. dichotomization of data, wherever possible, was attempted using the following definitions for control of IOP:

- success - a decrease of IOP by 15% from baseline at 12 months;
- complete success - IOP $\leq$ 21 mm Hg on no adjunctive medications at 12 months;
- qualified success - IOP $\leq$ 21 mm Hg on medications at 12 months;
- failure - IOP $>$ 21 mm Hg on or off medications at 12 months or complete loss of vision or performance of additional surgery or loss of the eye.

Secondary outcomes

1. Visual acuity was considered stable if unchanged or within one line of letters of baseline measurements (Snellen; ETDTRS; logMAR) at last follow up. Decreased vision was defined as loss of two or more lines or 10 or more letters compared with baseline using the same measuring methods at last follow up.
2. The duration (weeks) of a recognizable postoperative hypertensive phase (more than 5 mm Hg elevation of IOP above baseline levels).
3. The follow-up interval required to reach a 15% reduction from baseline IOP in weeks and the duration of this effect (months-years) attributable to the shunt through last follow up.
4. Visual field as available throughout follow up and at last follow up as measured by any method.
5. Total number of anti-glaucoma medications, both topical and systemic, as adjuncts to surgery at variable lengths of follow up.

Complications—Complications were tabulated as adverse events during the duration of follow up for all trials. Data was too sparse and inconsistently recorded to stratify all complications as intraoperative or by time postoperatively although some ‘late’ complications were reported. Adverse effects of interest included but were not limited to:

- corneal injury (endothelial decompensation/edema);
- suprachoroidal hemorrhage;
- retinal detachment;
- cataract;
- hypotony;
- infection;
- strabismus;
- host-immune response to anterior chamber tubes (keratic precipitates);
- clinical failure;
- late hypotony;

- late wound leaks;
- late failure due to vitreous or fibrin plugging of tubes including pars plana installations in post-vitrectomy eyes.

Quality of life—Data on quality of life available from the included studies were to be summarized.

Follow up: No restrictions were placed on the duration of follow up.

Search methods for identification of studies

Electronic searches—We identified trials from the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) in *The Cochrane Library* (Issue 1, 2006), MEDLINE (1966 to January 2006, week 4), PubMed (31st January 2006, restricted to last 90 days), EMBASE (1980 to 2006, week 4) and Latin American and Caribbean Health Sciences Literature Database (LILACS) (February 2004). The updated searches included the National Research Register (NRR) database (Issue 1, 2006). There were no language or date restrictions in the electronic searches.

See: Appendices for details of search strategies for each database.

Searching other resources—We searched the reference lists of identified trial reports to find additional trials. We used the Science Citation Index to find studies that cited the identified trials. We did not conduct manual searches of conference proceedings or abstracts specifically for this review.

Data collection and analysis

Assessment of search results—Two authors independently assessed the titles and abstracts of all reports identified by the electronic and manual searches as per the ‘Criteria for considering studies for this review’. The abstracts were classified as (a) definitely include, (b) unsure or (c) definitely exclude. Full copies of those classified as (a) definitely include and (b) unsure were obtained and re-assessed. These studies were classified as (1) included, (2) awaiting assessment or (3) excluded. A third author resolved any disagreements. Studies identified as (1) included were assessed for methodological quality. We contacted the primary investigators for clarification of studies classified as (2) awaiting assessment. We excluded studies identified by both authors as (3) excluded. The authors were unmasked to the report authors, institutions and trial results during this assessment.

Assessment of methodological quality—Two authors assessed trials according to methods set out in Section 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2005b). We considered the following parameters: method of allocation and concealment of allocation (selection bias), rates of follow up and intention-to-treat analysis (attrition bias). Allocation concealment was graded as: (A) adequate; or (B) unclear or not reported; or (C) inadequate. Any method which suggested appropriate concealment of allocation such as centralized randomization, use of opaque, sealed

envelopes was considered to be adequate. We contacted the primary investigators when the method of allocation concealment was unclear. A third author resolved any disagreement on assessment of quality of the included studies. Masking of investigators during clinical trials comparing aqueous shunts with other methods of glaucoma surgery would not be possible, as the presence of an anterior chamber or vitreous tube or standard filtering bleb would be obvious to any observer. Hence we did not use masking of care providers, participants and outcome assessors as quality criteria for such comparisons in this review.

Assessment of study characteristics—In addition to the parameters described above, we extracted study characteristics such as details of participants, the interventions, the outcomes, and other relevant information.

Data collection—Two authors independently extracted data for the primary and secondary outcomes onto paper data collection forms developed by the Cochrane Eyes and Vision Group. The forms were pilot tested on two trials and the revised form was used to extract data from the included trials. We resolved discrepancies by discussion. We contacted primary investigators for missing data. Wherever possible, and for included trials for which the investigators were unable to provide us with the data, we extracted the same from figures in the published papers. We extracted the mean IOP values where mean change in IOP was not available. Where success in controlling IOP was analyzed using Kaplan-Meier or life-table analyses, we tried to extract data on log-hazard ratios either through log-rank statistics or through published Kaplan-Meier curves if time points for losses to follow up were mentioned. One author entered data into RevMan 4.2 and this was verified using the double data-entry facility.

Data synthesis—Data analysis followed the guidelines in Section 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2005). For dichotomous outcomes we calculated a summary risk ratio. We calculated mean differences for continuous outcomes including mean postoperative IOP, logMAR visual acuity, and anti-glaucoma medications. We tested for statistical heterogeneity using the chi-square test and by examining the I-square value. If no statistical heterogeneity was detected and if there was no clinical heterogeneity within the trials we combined the results in a meta-analysis. We used a fixed-effect model since there were fewer than three trials in the analyses. In case of statistical or clinical heterogeneity we did not combine study results but presented a narrative summary.

It was not possible to perform subgroup analyses according to the type of glaucoma (primary angle-closure; primary open-angle; secondary including neovascular) and the number of previous surgeries as sufficient numbers specifying these parameters were not available due to marked variability in data reporting.

Sensitivity analysis—There were too few studies to conduct sensitivity analyses to examine the impact of exclusion of studies with lower methodological quality as stated in the protocol. We planned to conduct sensitivity analyses by excluding industry-funded trials but none of the included studies reported being funded by industry.

Results

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search—The original electronic searches yielded 851 titles and abstracts. Searching the Science Citation Index resulted in an additional 204 titles and abstracts. Out of a total of 1055 titles and abstracts 74 were identified to be relevant. On examining the full text, 16 articles were identified to be eligible for inclusion and 47 studies were excluded. Of the 16 trial reports eligible for inclusion in the review two were reports of the same study at different times of follow up. Thus, we found 15 trials eligible for inclusion in this review. Further clarification was required for 10 studies and these are currently listed as ‘Characteristics of studies awaiting classification’. We will update the review with information on these studies as it becomes available.

Included studies—The following is a concise summary of the salient features of the included studies. A detailed description of each trial is presented in the ‘Characteristics of included studies’ table.

Types of participants: The trials enrolled a total of 1153 participants. These were mostly adult patients from both genders over a wide range of ages, and some children. Wilson 2003 included only patients with primary open-angle and closed-angle glaucoma. Susanna 2003 included only patients with neovascular glaucoma. Participants in the remaining 13 trials had varied diagnoses in terms of the type of glaucoma including primary glaucomas, neovascular glaucoma, uveitic glaucoma, and other forms of secondary glaucomas. The trials also varied in lens status of enrolled participants. None of them excluded patients with aphakia or pseudophakia. None of the studies attempted to stratify patients by disease severity. The trials varied in size with the smallest one enrolling only 17 participants (Hwang 2004) and the largest enrolling 154 participants (Duan 2003).

Types of interventions: The included trials varied widely with regard to the interventions they evaluated. Two trials (Smith 1992; Wilson 1992) compared double-plate Molteno implants with a Schocket shunt (ACTSEB). Two trials (Wilson 2000; Wilson 2003) compared the Ahmed implant with trabeculectomy and adjunct MMC. The interventions compared in the remaining trials included 350 mm² and 500 mm² Baerveldt implants; single-plate and double-plate Molteno implants; ridged and standard Molteno implants; use of anti-fibrotic agents such as MMC and corticosteroids; different surgical techniques such as partial resection of Tenon's capsule and partial ligation of the tube with Ahmed implants (Table 1).

Types of outcomes: All but one trial (Kee 2001) considered IOP control as the main outcome. Kee 2001 also compared the incidence of hypotony between experimental and control groups. Eleven trials defined success in IOP control. However, only Wilson 2000 and Wilson 2003 used identical success and failure definitions. None of the trials reviewed used the a priori criteria exactly as stated in the ‘Criteria for considering studies for this

review' section above. Only Wilson 1992 and Valimaki 1999 reported the mean change in IOP from baseline as an outcome. We used final mean IOP values where reported and mean IOP where mean change in IOP was not reported.

Visual fields data were included in only three trials (Duan 2003; Wilson 2000; Wilson 2003). The average number of postoperative medications was reported in all trials except Susanna 2003. Visual acuity measurements were by logMAR charts, the most standardized method, in four trials (Cantor 1998; Lima 2004; Wilson 2000; Wilson 2003). Duan 2003 utilized an internationally standardized visual acuity chart but did not provide further details regarding the chart. Wilson 1992 measured postoperative acuity as decline in number of Snellen lines from baseline, and Heuer 1992 noted postoperative visions as 'stable' within one line of baseline; 'better' improved by at least two lines from baseline; and 'worse' at least two lines less than baseline. Smith 1992 reported Snellen acuities pre and postoperatively.

The postoperative 'hypertensive phase' was acknowledged and specifically reported only in Susanna 2003 but was discussed in Hwang 2004, Lima 2004 and Smith 1992. Only Wilson 2000 and Wilson 2003 included quantitative data on lens changes after shunts in phakic eyes.

Complications were too variably reported to allow comparative tabulation of intraoperative, early (within the first two days) and late (after two days) or postoperatively throughout follow up. Adverse effects of interest included corneal injury (endothelial decompensation with edema); choroidal effusion; suprachoroidal hemorrhage; retinal detachment; cataract; hypotony, infection, strabismus, host-immune response to anterior chamber tubes (keratic precipitates), postoperative hypertensive phase duration, clinical failure, late hypotony and late wound leaks were also variably reported and could not be compared across devices. Important complications reported in the published papers of the included studies are tabulated in Table 2.

Excluded studies—See 'Characteristics of excluded studies' table for further details.

Risk of bias in included studies

Overall, the trials included in this review were of low methodological quality. The results of our quality assessment are described in detail in the 'Characteristics of included studies' table. Below is a concise overall summary of the methodological quality of trials included in this review.

The method of randomization was explicitly stated and methodologically adequate in five trials (Britt 1999; Heuer 1992; Wilson 1992; Wilson 2000; Wilson 2003). The method of randomization was not explicitly stated in eight of the 15 included trials. Two trials adopted a method of quasi-randomization, flipping a coin for the first patient and alternating assignment of the remaining patients (Lima 2004; Susanna 2003). Consequently, allocation concealment was not possible in these two trials. The method of allocation concealment was adequate in two trials (Britt 1999; Heuer 1992) and unclear for the remaining included trials.

Primary investigators whom we were able to contact could not provide us with further information.

Masking of participants and surgeons is not possible with the kind of interventions involved when two different types of aqueous shunts are evaluated. However, masking of surgeons, and sometimes participants, is possible when adjunctive treatments are being evaluated such as adjunctive topical use of MMC with an implant. Of the four trials evaluating adjunctive treatment where masking of the operating surgeon was possible (Cantor 1998, Costa 2004, Duan 2003; Valimaki 1999), Cantor 1998 reported adequate masking of the operating surgeon; masking of the surgeon was not attempted in Costa 2004, Duan 2003 and Valimaki 1999. Masking of investigators measuring the IOP and visual acuity outcomes may be possible but was either not attempted or attempted and not reported in any of the included trials.

There were significant losses to follow up in many of the included trials. We considered a trial to have been analyzed by intention-to-treat only if all patients randomized were included. Only three trials reported an intention-to-treat analysis (Hwang 2004; Lima 2004; Smith 1992).

The unit of randomization in the trials was the patient except for two trials which randomized eyes to the different intervention groups (Gerber 1997; Smith 1992). The unit of randomization was unclear in two trials (Duan 2003; Hwang 2004). The unit of analysis was eyes in all included trials. Four trials randomized both eyes of some of the patients to different intervention groups (Duan 2003; Gerber 1997; Hwang 2004; Smith 1992). Twenty five per cent of participants (2 of 8) in one group and 10% in the other had both eyes included in one trial (Hwang 2004). Such a design is methodologically flawed since we may not consider the treatment effect in both eyes to be independent.

Effects of interventions

All issues evaluated in this review are summarized in Table 1.

Ahmed implant versus trabeculectomy

Mean intraocular pressure (IOP) at 11 to 13 months follow up (Analysis 1.1): Two studies compared Ahmed implant with trabeculectomy (Wilson 2000; Wilson 2003). We extracted data on mean IOP at 11 to 13 months from figures in the published papers since we were unable to procure from the trial investigators, data on mean change of IOP, the primary outcome for this review. Since the participants in both groups in a randomized trial are similar at baseline due to randomization, comparison of the final mean IOP estimates the same treatment effects as comparison of mean change from baseline values. The chi-square test for heterogeneity did not show statistical significance ($P = 0.14$) and the I-square value was 53.5%. Using a fixed-effect model we calculated a pooled mean difference of 3.81 mm Hg in favor of trabeculectomy (95% confidence interval (CI) 1.94 to 5.69). The trial investigators reported findings for only about 73% (Wilson 2000) and 89% (Wilson 2003) of randomized patients at 11 to 13 months follow up.

Ahmed implant versus endocyclophotocoagulation (ECP)

Mean IOP (Analysis 2.1): Seventy nine per cent of participants in Ahmed implant group and 91% in ECP group were analyzed for mean IOP at 12 months follow up in the only trial evaluating this comparison (Lima 2004). Allocation concealment was inadequate and method of allocation was not satisfactory in this trial. In an available-case analysis, the mean difference for mean IOP at 12 months follow up was 1.14 mm Hg (favoring ECP) and confidence intervals were wide and included the null value (95% CI -1.93 to 4.21). At 24 months follow up mean difference was 0.66 mm Hg favoring ECP (95% CI -2.98 to 4.30).

Visual acuity (mean logMAR scores) (Analysis 2.2): Data on visual acuity outcomes were available only as mean logMAR scores at 24 months follow up. The mean difference for visual acuity measured as logMAR scores was 0.24 (95% CI -0.04 to 0.52). Data on visual acuity at 12 months were not available. While the authors describe the proportion of participants with “worsening” and “stable” visual acuity, we were unable to find the definitions used for this study.

Anti-glaucoma medications at 24 months follow up (Analysis 2.3): Mean anti-glaucoma medications at 24 months follow up was greater in the Ahmed implant group but not statistically significant across groups. The mean difference was 0.50 (95% CI -0.17 to 1.17).

Ahmed implant with MMC versus Ahmed implant with balanced salt solution (BSS)

Mean IOP at 12 months follow up (Analysis 3.1): One trial evaluated adjunct use of MMC with Ahmed implants (Costa 2004). The mean difference for mean IOP was -0.20 mm Hg (favoring Ahmed implant with MMC) and 95% CI -2.82 to 2.42.

Anti-glaucoma medications at 12 months follow up (Analysis 3.2): The point estimate for the mean difference for mean anti-glaucoma medication use postoperatively was 0 mm Hg and the 95% confidence interval was very wide and included the null value (95% CI -0.63 to 0.63).

High-pressure Ahmed implant with adjunct MMC and partial Tenon's capsule resection (PTCR) versus Standard Ahmed implant with adjunct MMC alone

Mean IOP at 12 months follow up (Analysis 4.1): One trial comparing mean IOP values with high-pressure Ahmed implant with PTCR and adjunct MMC with standard Ahmed implant with adjunct MMC alone (Susanna 2003) provided data on only 55% and 70% of participants in the two groups respectively. In an available-case analysis, the mean difference in IOP at 12 months follow up was -1.13 mm Hg (in favor of PTCR) but the 95% confidence interval included the null value (95% CI -4.69 to 2.43).

Double-plate Molteno implant versus Schocket (ACTSEB) shunt

Mean IOP at six months follow up (Analysis 5.1): Two studies compared double-plate Molteno implant with the Schocket shunt (Smith 1992; Wilson 1992). Using data extracted from the published papers, with a fixed-effect model, we found a statistically significant chi-square test ($P = 0.03$) and I-square value 79.6%. Hence we do not report a pooled estimate

for the mean difference. The mean difference for IOP at six months was 1.67 mm Hg (95% CI -1.37 to 4.71) in favor of Schocket (ACTSEB) shunt in Smith 1992 and 2.50 mm Hg (95% CI -4.60 to -0.40) in favor of Molteno implant in Wilson 1992.

Single-plate Molteno implant with oral corticosteroids versus single-plate Molteno implant alone

Mean IOP at six months follow up (Analysis 6.1): One trial evaluated the effects of adjunct systemic corticosteroids with single-plate Molteno implant (Valimaki 1999). Mean IOP at 24 weeks (6 months) follow up was not statistically significantly different between the two groups. The point estimate for the mean difference for the mean IOP was 0 mm Hg and the 95% confidence interval was very wide and included the null value (95% CI -4.75 to 4.75).

Visual acuity at six months follow up (Analysis 6.2): Relative risk for stable visual acuity, defined in our protocol as visual acuity within one line from baseline, was 1.22 (95% CI 0.93 to 1.61) in favor of adjunct systemic corticosteroids. However, there were no events in the oral corticosteroid group for the visual acuity outcome, loss of vision. We defined loss of vision as loss of 2 or more lines from baseline, in our protocol.

Anti-glaucoma medications at 6 months follow up (Analysis 6.3): Participants on adjunct oral corticosteroids seemed to require more number of adjunct medications to control IOP postoperatively. The mean difference was 0.80 (95% CI 0.00 to 1.60).

Pressure ridge, double-plate Molteno implant with MMC versus Molteno implant with balanced salt solution (BSS)

Mean IOP (Analysis 7.1): In an available-case analysis, the mean difference for mean IOP at 12 months follow up was 0.30 mm Hg (favoring Molteno implant with BSS) and the confidence interval was wide and included the null value (95% CI -7.75 to 8.35).

Visual acuity (mean logMAR scores) (Analysis 7.2): The mean difference for visual acuity measured as logMAR scores at 12 months follow up was -0.60 (favoring Molteno implant with MMC) and the 95% CI -1.85 to 0.65.

Anti-glaucoma medications at 12 months follow up (Analysis 7.3): There was no statistically significant difference in the mean postoperative anti-glaucoma medications used between the two groups at 12 months follow up. The mean difference was -0.30 (in favor of Molteno implant with MMC) and the 95% CI -1.04 to 0.44.

Single-plate Molteno implant versus double-plate Molteno implant

IOP outcomes at final follow up (Analysis 8.1): One trial (Heuer 1992) compared IOP control in terms of success rates with definitions similar to what we stated in the 'Criteria for considering studies for this review' section above. We used the following definitions:

- success - a decrease of IOP by 15% from baseline at 12 months;
- complete success - IOP $\leq$ 21 mm Hg on no adjunctive medications at 12 months;

- qualified success - IOP $\leq$ 21 mm Hg on medications at 12 months.

Heuer 1992 reported data only at final follow up. Mean (SD) follow up was 14.9 (6.8) months in the single-plate Molteno implant group and 16.4 (6.8) months in the double-plate Molteno implant group. The risk ratio of success as defined above for the double-plate Molteno implant group was 1.41 (95% CI 0.98 to 2.01). Similarly, risk ratio of complete success for the double-plate Molteno implant was 1.18 (95% CI 0.38 to 3.60); for qualified success, risk ratio was 2.18 (95% CI 1.10 to 4.30).

350 mm² Baerveldt implant versus 500 mm² Baerveldt implant

Mean IOP (Analysis 9.1): One trial compared 350 mm² Baerveldt implant versus 500 mm² Baerveldt implant (Britt 1999). The mean difference in IOP at 12 months follow up was 0.50 mm Hg (in favor of 350 mm² Baerveldt implant) and 95% CI -3.15 to 4.15 mm Hg. The mean difference in IOP at longer terms of follow up in mm Hg was -0.90 (95% CI -3.12 to 1.32) at two years, -1.50 (95% CI -3.55 to 0.55) at three years, -1.40 (95% CI -4.55 to 1.75) at four years and -0.60 (95% CI -3.93 to 2.73) at five years follow up.

Lack of adequate data on outcomes precluded us from conducting analyses for several trials (Duan 2003; Gerber 1997; Hwang 2004; Kee 2001). Data available for Duan 2003 suffered from several losses to follow up. Hwang 2004 randomized both eyes in about 18% of all participants in the trial. Participants in Gerber 1997 were followed up only for 12 weeks. While the authors of this study reported mean IOP values at 12 weeks, we were unable to find information on standard deviations for the mean IOP values in the two groups. Similarly, no data on standard deviations were available in Kee 2001, which also adopted a different definition to dichotomize IOP outcomes as success and failure. Gerber 1997, Hwang 2004 and Kee 2001 did not find evidence of benefit of one treatment over the other, for treatments they evaluated, while Duan 2003 concluded adjunct MMC with the Hunan aqueous device was associated with better success rates in terms of IOP control compared with the Hunan aqueous device without MMC even with long-term follow up.

Complications—Though we intended to compare complication rates in different trials according to time of occurrence, we were unable to extract adequate information from the published papers. Our efforts to procure additional information from trial investigators were not fruitful due to unavailability of original data. No meta-Analysis was possible. However, details of important complications reported in the included trials are summarized in Table 2.

Discussion

Summary of main results

A meta-analysis of two trials found that trabeculectomy resulted in a lower mean IOP at 11 to 13 months follow up compared with Ahmed implant (Wilson 2000; Wilson 2003).

Although the I-square statistic of 53.5% suggested the presence of statistical heterogeneity, the two trials were conducted with similar methodology, and the baseline IOP values were similar in both the trials. Further the effect estimates are in the same direction and the 95% confidence intervals for the effect estimate in both trials overlapped each other. However, we conducted an available-case analysis using standard deviations extracted from figures in

the published paper as we were unable to procure data on the same. Additionally, inadequate methodological details warrant consideration such as the method of allocation concealment. One of these studies included previously unoperated eyes. The vast majority of previously published case series have described the utilization of shunts in eyes after previous failed standard filtering surgery.

Two studies compared double-plate Molteno implant with the Schocket shunt (Smith 1992; Wilson 1992). The results could not be pooled due to significant heterogeneity as noted above. One trial (Wilson 1992) found IOP was lower in the Molteno implant group. However, the results in this trial, though statistically significant, must be viewed in light of the methodological inadequacies including allocation concealment and exclusion of participants from the analyses. The second trial (Smith 1992) reported a greater decrease in IOP with the Schocket shunt. However, the 95% confidence interval for the mean difference included the null value and hence was consistent with IOP being lower in either the Molteno implant group or the Schocket shunt group. The duration of follow up differed between the two trials, which could have been one of the sources of heterogeneity observed.

Of the three trials investigating the effectiveness of adjunctive MMC two found no evidence of its benefits in terms of mean postoperative IOP, logMAR visual acuity scores or postoperative anti-glaucoma medications at 12 months followup (Cantor 1998; Costa 2004). Duan 2003 concluded adjunct MMC with the Hunan aqueous device is associated with better success rates. However, these conclusions were influenced by losses to follow up in both treatment groups and while two trials (Cantor 1998; Costa 2004) reported an available-case analysis, details in Duan 2003 are not clear.

Results from one trial (Valimaki 1999) suggest no evidence of benefit with the use of systemic steroids as a method of decreasing bleb fibrosis. However, these conclusions are limited by methodological inadequacies and the small sample size in the trial. No evidence of benefit with excision of Tenon's capsule was found in one quasi-randomized trial (Susanna 2003). One quasi-randomized trial demonstrated no evidence of superiority of Ahmed implant or endocyclophotocoagulation over each other in terms of mean IOP at 12 months follow up, mean logMAR visual acuity, and complications at 24 months follow up (Lima 2004). Where success in controlling IOP was analyzed using Kaplan-Meier or life-table analyses, varied definitions of "success" and lack of adequate information precluded us from conducting analyses based on Kaplan-Meier curves.

Analysis of mean difference in IOP at different times of follow up showed no evidence of benefit of using a Baerveldt implant with a greater surface area. Though the point estimate tended towards the 500 mm² Baerveldt implant, the 95% confidence intervals included the null value. However, life-table analyses reported in the published trial report showed statistically significant differences in cumulative success rates in favor of the 350 mm² Baerveldt implant (Britt 1999). Success in this study was defined as an IOP $\leq$ 6 mm Hg and $\geq$ 21 mm Hg.

In a comparison of single-plate Molteno implant with double-plate Molteno implant, an available case analysis of IOP as a dichotomous outcome, defined as stated earlier in this

review, showed statistically significant differences favoring the double-plate Molteno implant in only two of the three defined categories, “success” (IOP < 21 or at least a 30% reduction from baseline) and “qualified success” (IOP < 21 on medications). Though the relative risks of success and qualified success suggested statistical significance, the confidence interval was close to the null value for the outcome, “success” (0.98 to 2.01), and was quite wide for the outcome, “qualified success” (1.10 to 4.30). However, the authors of this trial (Heuer 1992) report a statistically significant difference in success rates using a life-table analysis (p-value for log-rank test = 0.0035). For this analysis, they defined ‘success’ to mean a final IOP at least 6 mm Hg but not greater than 21 mm Hg without additional glaucoma surgery or devastating complications.

Complications were too variably reported in this series of trials to allow comparative tabulation of intraoperative, early or late complications associated with specific aqueous shunts. Reported adverse effects of interest included corneal injury (endothelial decompensation/edema); suprachoroidal hemorrhage; retinal detachment; cataract; hypotony; infection; strabismus; host-immune response to anterior chamber tubes (keratic precipitates); post-operative hypertensive phase duration; and clinical failure. Late hypotony and late wound leaks were also variably reported and could not be fairly compared across trials employing different or the same devices.

Quality of the evidence

Overall, the trials included in this review were of poor methodological quality. The method of randomization was clearly adequate in only five trials and allocation concealment was clearly adequate in only two trials. Only three trials reported an intention-to-treat analysis. The results of the meta-analysis reported in this review are influenced by methodological limitations as well as the extraction of data on mean IOP from the published figures, although two authors independently extracted the data from the figures in published papers.

Authors' Conclusions

Implications for practice

Meta-analysis of two trials comparing Ahmed implant versus trabeculectomy reinforces the commonly held impression among glaucoma surgeons that trabeculectomy, especially with anti-fibrotic enhancement intraoperatively, will likely produce lower IOP than aqueous shunts. However the differences in IOP outcomes between Ahmed shunts and trabeculectomy were surprisingly small, only 3.81 mm Hg (95% CI 1.94 to 5.69 mm Hg). Based on this review, no specific aqueous shunt stands out as clearly clinically superior with regard to either safety or efficacy. Practitioners should base their choice of device on their own experience and continue to utilize the shunt with which they are most comfortable. Although frequencies of complications among control and experimental groups in a study of Ahmed implants with and without MMC seemed similar, further studies are needed to better evaluate short or long-term risks. However, two trials did not show an IOP outcome advantage with MMC use intraoperatively. There is little or no incentive, based on this review, to recommend adjunctive MMC use with aqueous shunts.

Implications for research

Additional trials should be organized to compare devices with regard to specific issues of safety including the risks of immediate postoperative hypotony and its complications such as choroidal effusion and suprachoroidal hemorrhage in various glaucoma disease groups. Future clinical trials should use standard definitions and terminology for glaucoma types and complications. While IOP is measured as a continuous outcome, it can also be categorized and analyzed as a dichotomous outcome. Categorization of the outcome helps conduct an intention to treat analysis by adopting methods such as Kaplan-Meier analyses. It is very apparent that standardization of definitions for outcomes such as “success”, “failure”, “qualified success”, etc., to allow for comparison between trials, would greatly enhance research synthesis. Data collection and data collection intervals should also be standardized and follow up should be continued for several years. The postoperative hypertensive phase and inflammatory reaction should be better defined and characterized to allow more rational use of anti-glaucoma and anti-inflammatory agents pre and postoperatively.

Neovascular glaucoma in particular is a frequently encountered complex glaucoma in which the use of aqueous shunts has been growing. Planning for future studies of aqueous shunts in neovascular or other complicated glaucomas should include pre-study planning, ideally for multi-center trials, to allow sufficient sample sizes to be recruited in each disease type to answer specific study questions such as:

- Are shunts as effective as trabeculectomy?
- Is one aqueous shunt superior to any other?
- When is the optimal time to employ aqueous shunts in neovascular or other complicated glaucomas?
- Are there any differences in effectiveness or complications rates with anterior chamber compared with pars-plana insertion of shunt tubes?
- Is there an optimum explant size, shape, or material?
- Do intraoperative or postoperative complications differ among available shunts?
- Do all types of aqueous shunts have a hypertensive phase and, if so, what is the most rational management or method of prevention?
- What are the optimal pre and postoperative treatment regimens for use with aqueous shunts for various glaucoma types?
- Which supplemental anti-glaucoma medications are best with aqueous shunts?
- What is the role, if any, for antifibrotic agents as adjuncts to utilizing various aqueous shunts?
- How can surgical techniques be changed to minimize erosions of tubes or explants?
- Are all cyclodestructive interventions just as efficacious and equally complicated as aqueous shunts?

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Characteristics Of Studies

Characteristics of included studies [ordered by study ID]

Britt 1999

Methods	<p>Method of randomization: random numbers table used to generate the allocation sequence. Number randomized: 107 (55 to 350 mm2 Baerveldt implant arm; 52 to 500 mm2 Baerveldt implant arm).</p> <p>Exclusions after randomization (total and per group): none.</p> <p>Losses to follow up: 2 participants in each arm were lost to follow up either because of operative complications or for unknown reasons.</p> <p>Method of allocation concealment: "Operating room personnel read the assignment from the randomization list, to which the surgeons were masked."</p> <p>Outcome assessor masking: not reported.</p> <p>Intention-to-treat analysis: no. Analysis excludes 2 participants in each arm who were lost to follow up. Unusual study design: none.</p>
Participants	<p>Age: mean (SD) 67.5 (18) years in 350 mm2 Baerveldt implant arm; 68.9 (16.7) years in 500 mm2 Baerveldt implant arm.</p> <p>Sex: not reported.</p> <p>Inclusion Criteria: medically uncontrollable glaucoma associated with aphakia, pseudophakia or failed filtering procedures.</p> <p>Exclusion Criteria: age less than 12 years; neovascular glaucoma; uveitis; previous muscle surgery; extensive scarring; existing scleral buckles or glaucoma implants; prior cyclodestructive procedures.</p> <p>Equivalence of baseline characteristics: age; race; types of glaucoma; mean IOP were similar in both treatment arms at baseline.</p> <p>Diagnoses in participants: aphakic; pseudophakic; failed filtering procedures.</p>
Interventions	<p>Treatment: 500 mm2 Baerveldt implant.</p> <p>Control: 350 mm2 Baerveldt implant.</p> <p>Not all implants were placed temporally in both arms.</p> <p>All eyes received scleral patch grafts.</p> <p>Topical atropine sulfate (1%) was instilled after completion of procedure. Subconjunctival injections of 12 mg dexamethasone phosphate and 20 mg gentamicin sulfate were administered separately after all procedures followed by overnight patching.</p> <p>Postoperative regimen included topical tobramycin for 2 weeks, 1% atropine sulfate and 1% prednisolone acetate or phosphate for 4 to 6 weeks.</p>
Outcomes	<p>Primary outcome: IOP control.</p> <p>Complete success: IOP between 6 mm Hg and 21 mm Hg inclusive without additional glaucoma surgery and without devastating complications.</p> <p>Qualified success: IOP between 6 mm Hg and 21 mm Hg inclusive with additional glaucoma surgery and without devastating complications.</p> <p>Qualified failure: IOP > 21mm Hg with medications</p>

	Complete failure: additional glaucoma surgery; hypotony (IOP < 6 mm Hg); devastating complications; loss of light perception. Secondary outcomes: visual acuity; number of anti-glaucoma medications; complications
Notes	Country and period of study: USA. Enrollment period was from March 21, 1991 to April 29, 1993. Follow-up intervals: not reported. Outcomes were analyzed at 1, 2, 3, 4 and 5 years postoperatively. "Data for the current report were collected during the interval between the installation of the implants and the most recent ophthalmic visits on or before September 1, 1997..."

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A-Adequate

Cantor 1998

Methods	Method of randomization: unclear. "participants were randomized to receive either MMC or a control solution (balanced salt solution, BSS) prospectively." Number randomized: 25 (12 to Molteno implant with MMC arm and 13 to Molteno implant with BSS arm). Exclusions after randomization (total and per group): None Losses to follow up: 2 participants in Molteno implant with MMC arm and 1 patient in Molteno implant without MMC arm at 12 months of follow up. Reasons not reported. Method of allocation concealment: not reported. Participant masking: not reported. Provider masking: "The surgeon remained masked to which solution was being used." Balanced salt solution was stained with gentian violet. Outcome assessor masking: Not reported. Intention-to-treat analysis: no. Participants lost to follow up at 12 months were excluded from the analysis. Unusual study design: none.
Participants	Age: mean (SD) 66.4 (14) years in Molteno implant with MMC arm; 67.1 (11.4) years in control arm. Sex: 50% in Molteno implant with MMC arm and 54% in control arm were females. Inclusion criteria: Age 21 years or older; any race; either sex; any lens status; primary open-angle glaucoma; pigment dispersion glaucoma; pseudoexfoliation glaucoma; primary angle-closure glaucoma; neovascular glaucoma; traumatic glaucoma; any secondary open or angle-closure glaucoma; congenital glaucoma; inflammatory glaucoma; any previous ocular surgery other than scleral buckling. Exclusion criteria: previous aqueous implant shunt placement; previous scleral encircling band placement; pregnancy or lactation. Equivalence of baseline characteristics: mean IOP at baseline was 41.54 (17.8) mm Hg in Molteno implant with MMC arm and 34.65 (8.43) mm Hg in control arm at baseline. 3 black participants in control arm, none in Molteno implant with MMC arm. Diagnoses in participants: neovascular glaucoma; chronic angle-closure glaucoma; aphakia; primary open-angle glaucoma; glaucoma secondary to trauma; ruptured globe; inflammation.
Interventions	Treatment: pressure-ridge, double-plate Molteno implant with topical MMC (0.4 mg/ml applied for 2 minutes with a sponge soaked in the solution). Control: pressure-ridge, double-plate Molteno implant with BSS stained with gentian violet. All patients in both arms received scleral patch grafts. Postoperative management included 1% prednisolone acetate and gentamicin four times a day, 1% atropine 2 to 4 times a day and glaucoma medications (except for carbonic anhydrase inhibitors) in the fellow eye as required
Outcomes	IOP control reported as final mean IOP; visual acuity; number of postoperative medications; complications.
Notes	Country and period of study: USA. Study period not reported. Follow-up intervals: Postoperative week 1, months 1, 3, 6 and 12.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Costa 2004

Methods	Method of randomization: not reported - “participants were randomized to receive intraoperative MMC or a placebo.” Number randomized: 60 (34 to Ahmed valve with MMC and 26 to Ahmed valve implant with placebo). Exclusions after randomization (total and per group): None. Losses to follow up: no losses of follow up reported explicitly. Method of allocation concealment: not reported. Participant masking: not reported. Provider masking: not reported. Outcome assessor masking: not reported. Intention-to-treat: unclear Unusual study design: none.	
Participants	Age: mean (SD) 62.7 (16.5) years in Ahmed implant with MMC arm; 61.1 (20.6) years in Ahmed implant with placebo arm. Sex: 32% in Ahmed implant with MMC arm and 50% in Ahmed implant with placebo arm were females. Inclusion criteria: uncontrolled glaucoma requiring glaucoma drainage device implantation. Exclusion criteria: younger than 18 years of age; learning difficulties; mental illness; dementia; unconsciousness or severe illness. Equivalence of baseline characteristics: Age; race; lens status; prior glaucoma surgery status; IOP similar in the two arms at baseline. Diagnoses in participants: primary open-angle glaucoma; chronic angle-closure glaucoma; neovascular glaucoma; aphakic/pseudophakic, congenital, traumatic glaucomas; inflammatory and steroid-induced glaucoma; glaucoma following penetrating keratoplasty.	
Interventions	Treatment: Ahmed valve implant with 0.5 mg/ml solution of MMC placed on the episclera, under the conjunctiva and Tenon's capsule at the site for implant plate for 5 minutes. Control: Ahmed valve implant with topical application of BSS using a soaked sponge on the episclera at site for implant plate for 5 minutes. Postoperative regimen included a topical antibiotic and a cycloplegic for 2 to 4 weeks and topical steroids for approximately 2 months.	
Outcomes	IOP control reported as final mean IOP and surgical success; best-corrected visual acuity; number of anti-glaucoma medications; complications. Surgical success: (1) postoperative IOP between 6 and 21mm Hg with or without anti-glaucoma medications or (2) IOP reduction of at least 30% relative to preoperative values.	
Notes	Country and period of study: Brazil, Scotland, USA, Canada. Study period was not reported. Follow-up intervals: postoperative day 1, weeks 1 and 2, months 1, 3, 6, 12 and 18.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Duan 2003

Methods	Method of randomization: not reported "randomization was used". Number randomized: 159 (4 eyes to HAD without MMC and 65 eyes to HAD with MMC). Exclusions after randomization (total and per group): none reported. Losses to follow up: 23 (5 not accounted for) in HAD without MMC and 20 (5 eyes more than the randomized number included) in HAD with MMC arms at 1 year. 32 (13 not accounted for) in HAD without MMC and 27 (6 not accounted for) in HAD with MMC arms at 24 months of follow up. 43 (15 not accounted for) in HAD without MMC and 37 (9 not accounted for) in HAD with MMC arms at 36 months of follow up. 64 in HAD without MMC and 51 (1 eye more than the number enrolled was included) in HAD with MMC arms at 48 months of follow up. 70 (2 not accounted for) in HAD without MMC and 56 in HAD with MMC arms at 60 months of follow up. 72 (8 not accounted for) in HAD without MMC and all participants in HAD with MMC arms at 72 months of follow up. Reasons were not reported. Method of allocation concealment: not reported. Outcome assessor masking: not reported.
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	Intention-to-treat analysis: no. Participants lost to follow-up were excluded from the analysis. Unusual study design: 5 participants served as their own controls.
Participants	Age: average age reported as 49.71 ± 6.9 years. Group-wise age distributions not reported. Sex: 85 male patients (87 eyes) and 69 female patients (72 eyes). Group-wise gender distribution not reported. Inclusion criteria: refractory glaucoma (IOP > 25 mm Hg on combined pharmacologic therapy). Exclusion criteria: none reported. Equivalence of baseline characteristics: mean IOP at baseline is similar in both intervention groups. However, no information on other baseline characters was reported. HAD without MMC arm had almost twice as many patients with aphakia as in HAD with MMC arm. Diagnoses in participants: aphakia; pseudophakia; neovascular glaucoma; uveitic glaucoma; traumatic glaucoma; primary angle-closure glaucoma; juvenile glaucoma; ICE
Interventions	Treatment: HAD with adjunctive topical application of 0.4 mg/ml MMC with a sponge, applied to the sclera near the equator for 1 to 5 minutes followed by rinsing of extra MMC with balanced salt solution. (Duration of MMC was determined as follows: minimum duration was 1 minute with addition of 1 minute with each of the following characteristics: age of patient less than 40 years; thick connective tissue; rubeosis iris; IOP > 40 mm Hg after combined drug therapy). Control: HAD without MMC.
Outcomes	Visual acuity (including best corrected visual acuity) measured with "international standardized chart"; IOP control with measurements using Goldmann applanation (success: 6 mm Hg < IOP > 21 mm Hg); visual field of those patients with good visual acuity; standardized ocular echography; slit lamp biomicroscope examination.
Notes	Country and period of study: China, July 1995 to July 2001 Follow-up intervals: Every 3 months for the first postoperative year and every 6 months thereafter.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Gerber 1997

Methods	Method of randomization: not clear. "Randomization procedure consisted of a nurse selecting a card from a stack at the time of the patient's entry into the operating room." Number randomized: 30 (15 in each arm). Exclusions after randomization (total and per group): none. Losses to follow up: 1 patient in the Pressure ridge Molteno implant arm had penetrating keratoplasty at 8 weeks and did not have 12 week follow-up data. Method of allocation concealment: not reported. Outcome assessor masking: not reported. Intention-to-treat analysis: no. Patients were excluded from analysis from the point they underwent additional surgical procedures in the postoperative period. Unusual study design: 1 patient had both eyes randomized.
Participants	Age: mean age 61.5 years in Pressure ridge Molteno implant arm; 64.5 years in Standard Molteno implant with suture ligation arm. Standard deviations were not reported. Sex: 67% in Pressure ridge Molteno implant arm and 60% in Standard Molteno implant arm were females. Inclusion criteria: inclusion criteria were not stated explicitly. Exclusion criteria: patients with prior cyclodestructive procedures were excluded. Equivalence of baseline characteristics: age; race; gender and type of glaucoma were similar in the two arms at baseline. Diagnoses in participants: pseudophakic/aphakic glaucoma; primary open-angle glaucoma; neovascular glaucoma; inflammatory glaucoma; chronic angle-closure glaucoma; post-penetrating keratoplasty; ectopia lentis; ICE syndrome.
Interventions	Treatment: Pressure-ridge, double-plate Molteno implant without tube ligature. Control: standard double-plate Molteno implant with 9-0 nylon suture ligation. A donor scleral graft was placed in all patients. Postoperative medications included a combined steroid-antibiotic ointment for night-time use and a separate antibiotic and steroid to be applied four times a day for at least 1 month following surgery. Steroids were phased out after 1 month at the discretion of the surgeon.

Outcomes	IOP control reported as final mean IOP; anterior chamber depth; visual acuity.	
Notes	Country and period of study: USA. Study period not reported. Follow-up intervals: postoperative days 1 and 2, weeks 1, 2, 4, 8 and 12.	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Heuer 1992

Methods	<p>Method of randomization: random number table was used to generate the allocation sequence. Randomization was stratified for 1 stage and 2 stage installations.</p> <p>Number randomized: 132 (66 to Double plate Molteno implant and 66 to Single plate Molteno implant).</p> <p>Exclusions after randomization (total and per group): 31 (15 patients in Double plate Molteno implant arm and 16 in Single plate Molteno implant arm were excluded after the first stage of installation "because either their IOPs were adequately controlled or their visual potentials were subsequently judged to be inadequate to justify further intraocular surgical procedures."</p> <p>Losses to follow up: 1 patient in each arm with less than 6 months of follow up.</p> <p>Method of allocation concealment: surgeons were masked to allocation lists (personal communication).</p> <p>The lists, which were kept in large envelopes in a drawer in one of the operating rooms, were not accessible to the operating surgeons. Treatment assignment was declared by one of the operating room personnel after the surgeon confirmed feasibility of the procedure.</p> <p>Outcome assessor masking: not reported.</p> <p>Intention-to-treat analysis: no. 31 patients excluded after randomization were not included in the analysis.</p> <p>Unusual study design: none.</p>
Participants	<p>Age: mean (SD) 62.1 (20.8) years in Double plate Molteno implant arm; 61.1 (16.2) years in Single plate Molteno implant arm.</p> <p>Sex: not reported.</p> <p>Inclusion criteria: medically uncontrollable non-neovascular glaucoma in patients with aphakia or pseudophakia.</p> <p>Exclusion criteria: concurrent retinal detachment; first stage of Molteno implantation performed during non-glaucoma surgery in eye with marginally functioning filtering bleb; prior cyclodestructive procedures; prior Molteno implantation in eye undergoing surgery; prior scleral buckling procedure; recent corneoscleral or corneal wound.</p> <p>Equivalence of baseline characteristics: the two groups were similar with respect to age, preoperative IOP, and type of glaucoma.</p> <p>Diagnoses in participants: open-angle glaucoma; angle-closure glaucoma; uveitic glaucoma; congenital glaucoma; traumatic glaucoma; glaucoma of uncertain etiology.</p>
Interventions	<p>Treatment: Double-plate Molteno implant.</p> <p>Control: Single-plate Molteno implant.</p> <p>Subconjunctival injections of 12 mg dexamethasone phosphate and 20 mg of gentamicin sulfate were administered separately after most procedures. Postoperative regimen in both arms included topical corticosteroids (1% prednisolone acetate or phosphate) for 2 to 4 months, tapered based on the intraocular and bleb capsule inflammation, topical atropine sulfate (1%) for 4 to 6 weeks and topical antibiotics (0.3% gentamicin or 0.3% tobramycin) for 1 to 4 weeks.</p>
Outcomes	<p>Primary outcome: IOP control.</p> <p>Success: IOP between 6 and 21 mm Hg inclusive with no additional glaucoma surgery (other than surgical tube ligature release) and no devastating complications.</p> <p>Complete success: no additional glaucoma procedures, final IOP > 5 mm Hg and < 22 mm Hg without anti-glaucoma medications.</p> <p>Qualified success: no additional glaucoma procedures; final IOP > 5 mm Hg and < 22 mm Hg with anti-glaucoma medications.</p> <p>Qualified failure: no additional glaucoma procedures; final IOP > 21 mm Hg.</p> <p>Complete failure: additional glaucoma procedures; loss of light perception attributed to glaucoma; final IOP < 6 mm Hg; or devastating complications.</p> <p>Secondary outcomes: visual acuity; complications; number of postoperative anti-glaucoma medications.</p>
Notes	<p>Country and period of study: USA. March 1988 to February 1990</p> <p>Follow-up intervals: intervals at which outcome was assessed was not explicitly reported. However, success at months 6, 12, 18 and 24 were reported in the results.</p>

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A-Adequate

Hwang 2004

Methods	Method of randomization: not clear. "Randomization procedure consisted of a nurse selecting a card from a stack at the time of the patient's entry into the operating room." Number randomized: 30 (15 in each arm). Exclusions after randomization (total and per group): none. Losses to follow up: 1 patient in the Pressure ridge Molteno implant arm had penetrating keratoplasty at 8 weeks and did not have 12 week follow-up data. Method of allocation concealment: not reported. Outcome assessor masking: not reported. Intention-to-treat analysis: no. Participants were excluded from analysis from the point they underwent additional surgical procedures in the postoperative period. Unusual study design: 1 patient had both eyes randomized.
Participants	Age: mean (SD) 44.3 (25.3) years in Ahmed implant group; 42.7 (23) years for the Ahmed implant with pericardial membrane surface expansion group. Participants ranged from 9 to 73 years and 2 to 81 years in the two groups, respectively. Sex: proportion of females in each intervention group is unclear. Inclusion criteria: glaucoma not responsive to medical, laser or previous surgical treatment. Exclusion criteria: none reported. Equivalence of baseline characteristics: mean IOP; age and diagnoses in participants at baseline is similar in both intervention groups. Diagnoses in participants: neovascular glaucoma; secondary glaucoma; pseudophakic glaucoma; failed trabeculectomy.
Interventions	Treatment: Ahmed valve implant with a pericardial membrane surface expansion. Control: Ahmed valve implant. Participants in both treatment groups received subconjunctival injections of 0.3 ml gentamicin (40 mg/ml) and dexamethasone (5 mg/ml) soon after surgery. Postoperative treatment in both groups included topical corticosteroids and antibiotics.
Outcomes	IOP control: Success: IOP < 22 mm Hg and > 5 mm Hg without additional glaucoma surgery and without loss of light perception. Complete success: IOP control as defined above without use of anti-glaucoma medications. Qualified success: IOP control as defined above with adjunctive anti-glaucoma medications. Failure: IOP > 21 mm Hg on maximally tolerated medications or < 6 mm Hg; or additional glaucoma surgery including laser treatment; or loss of light perception; or phthisis bulbi. Hypotony defined as IOP < 6 mm Hg in 2 consecutive visits. Postoperative hypertensive phase defined as IOP > 21 mm Hg in the first 6 postoperative months.
Notes	Country and period of study: Korea; study period was not reported. Follow-up intervals: not explicitly reported. Mean (SD) of total follow up was 14.9 (4.3) months in Ahmed implant group and 11.5 (5.1) months in Ahmed implant with surface expansion group.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Kee 2001

Methods	Method of randomization: not reported "patients were randomly assigned". Number randomized: 32 (16 to each arm). Exclusions after randomization (total and per group): none. Losses to follow up: none reported. Method of allocation concealment: not reported. 1 surgeon performed all surgeries and postoperative examinations. Outcome assessor masking: Outcome assessment was not masked.
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	Intention-to-treat analysis: unclear. Unusual study design: none.
Participants	Age: Mean (SD) 55.3 (12.6) years in Ahmed implant with partial ligation arm; 58.9 (13.1) years in Ahmed implant without ligation arm. Sex: no data provided. Inclusion criteria: high IOP not responding to medical treatment, laser surgery or prior conventional surgery. Exclusion criteria: no exclusion criteria reported. Equivalence of baseline characteristics: mean age and diagnosis in participants were similar at baseline in the 2 arms. Diagnoses in participants: neovascular glaucoma; secondary glaucoma; aphakic glaucoma; previous failed trabeculectomy.
Interventions	Treatment: Ahmed valve implant with partial ligation of the tube. Control: Ahmed valve implant, no ligation of the tube. Postoperative treatment included topical 0.3% ofloxacin and 1% prednisolone acetate eye drops four times a day for 4 weeks.
Outcomes	IOP control; incidence of hypotony defined as IOP $\leq$ 5 mm Hg on any single visit. Complete success: IOP $<$ 22 mm Hg and $>$ 5 mm Hg for the last two visits without additional glaucoma surgery and without anti-glaucoma medications. Qualified success: IOP $<$ 22 mm Hg and $>$ 5 mm Hg with the use of anti-glaucoma medications. Failure: IOP $>$ 22 mm Hg or greater on maximally tolerated anti-glaucoma medications or that requiring additional glaucoma surgery.
Notes	Country and period of study: Korea, January 1999 to March 2000. Follow-up intervals: patients were examined on postoperative day 1 and "regularly thereafter by one doctor". Analysis of data at 6 months of follow up was presented in the paper.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Lima 2004

Methods	Method of randomization: not reported "participants were randomly assigned". Number randomized: 32 (16 to each arm). Exclusions after randomization (total and per group): none. Losses to follow up: none reported. Method of allocation concealment: not reported. One surgeon performed all surgeries and postoperative examinations. Outcome assessor masking: outcome assessment was not masked. Intention-to-treat analysis: unclear. Unusual study design: none.
Participants	Age: mean (SD) 56.64 (11.33) years in Ahmed implant arm; 53.76 (10.4) years in ECP arm. Sex: 44% in Ahmed implant arm and 41% in ECP arm were females. Inclusion criteria: pseudophakic eyes with an IOP $\geq$ 35 mm Hg on maximum tolerated therapy; at least one previous trabeculectomy with antimetabolite; visual acuity better than light perception. Exclusion criteria: previous glaucoma drainage device implantation; prior cyclodestructive procedure; no light perception; retinal or choroidal detachment; failed corneal graft. Equivalence of baseline characteristics: age; race; gender; preoperative IOP; exposure to antimetabolite; type of glaucoma similar in the two arms at baseline. Diagnoses in participants: neovascular glaucoma; pseudophakic glaucoma; glaucoma associated with penetrating keratoplasty; glaucoma associated with vitreoretinal surgery.
Interventions	Treatment: Ahmed valve implant. Control: ECP. All procedures in both arms were followed by subconjunctival injection of tobramycin and dexamethasone. Additionally, 0.1 ml of dexamethasone was injected in the anterior chamber. Topical antibiotics, corticosteroids and atropine were prescribed postoperatively and tapered as the intraocular inflammation decreased.
Outcomes	IOP control reported as final mean IOP and also as success and failure; visual acuity (LogMAR method).

	Success: IOP between 6 and 21 mm Hg at 24 months of follow up with or without maximum tolerated therapy. Failure: IOP > 21 mm Hg during 3 consecutive postoperative visits; IOP below 6 mm Hg for 60 days or more; necessity for another surgical intervention to control IOP.
Notes	Country and period of study: Brazil. January 1998 to April 2000 Follow-up intervals: Postoperative day 7, months 1, 2, 3, 4, 5, 6, 12, 18 and 24

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Smith 1992

Methods	Method of randomization: "randomized" - method of randomization was not reported. Number randomized: 40 eyes (19 to Double plate Molteno implant and 21 to Schocket shunt). Exclusions after randomization (total and per group): none. Losses to follow up: none. Method of allocation concealment: not reported. Outcome assessor masking: not reported. Intention-to-treat analysis: yes. Unusual study design: initially 46 eyes of 40 participants were randomized to the 2 treatment arms. 6 participants who required bilateral surgery were randomized for the first eye and the other eye received the alternate treatment. Since the 2 eyes cannot be considered independent in the analysis, "three participants (three eyes) were assigned to each group using a random digit table."
Participants	Age: not reported. Sex: 84% in Molteno implant arm and 62% in ACTSEB arm were females. Inclusion criteria: eyes with refractory glaucoma requiring surgery irrespective of type of glaucoma except the congenital variety. Exclusion criteria: children with congenital glaucoma; patients undergoing simultaneous penetrating keratoplasty and drainage tube procedure. Equivalence of baseline characteristics: mean IOP; glaucoma medications; types of glaucoma similar at baseline. Diagnoses in participants: aphakia/pseudophakia; prior unsuccessful glaucoma filter surgery; uveitic glaucoma; neovascular glaucoma; glaucoma following penetrating keratoplasty; glaucoma associated with congenital rubella syndrome (aphakic).
Interventions	Treatment: Double-plate Molteno implant. Control: ACTSEB /Schocket procedure. All participants received topical prednisolone acetate (1%) and topical tobramycin in the early postoperative period.
Outcomes	IOP control reported as final mean IOP; mean change in IOP; number of postoperative medications; decrease in visual acuity.
Notes	Country and period of study: USA, 1987 to 1989 Follow-up intervals: day 1, day 2, weeks 1, 2, 3, months 1, 3, 6 and every 3 to 6 months thereafter. Mean (SD) of follow up was 22.89 (9.68) months for Molteno implant arm and 29.10 (13.30) months for ACTSEB/Schocket procedure arm.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Susanna 2003

Methods	Method of randomization: the first patient was assigned to treatment with a coin flip. Rest of participants were alternated consecutively to either treatment arm. Number randomized: 92 (45 to S-2 high pressure Ahmed valve with resection of Tenon's capsule and 47 to Standard Ahmed valve without Tenon's resection). Exclusions after randomization (total and per group): none.
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	Losses to follow up: 20 patients in Ahmed valve with Tenon's capsule resection and 14 patients in control group were lost to follow up at 12 months. Reasons were not reported. Method of allocation concealment: Not possible due to alternating assignment. Outcome assessor masking: not reported. Intention-to-treat analysis: no. Patients lost to follow up were excluded from the analysis. Unusual study design: none.	
Participants	Age: mean (SD) 60.6 (12.1) years in Ahmed valve with resection of Tenon's capsule arm; 60.7 (12.2) years in control arm. Sex: 44.4% in Ahmed valve with resection of Tenon's capsule arm and 46.8% in control arm were females. Inclusion criteria: neovascular glaucoma without previous surgery; visual acuity of light perception or better; neovascular glaucoma associated with CRVO or diabetes. Exclusion criteria: no light perception; neovascular glaucoma with previous surgery; neovascular glaucoma not associated with CRVO or diabetes. Equivalence of baseline characteristics: age; gender; race; etiology of glaucoma; prior PRP and preoperative IOP were similar at baseline in both treatment arms. Diagnoses in participants: neovascular glaucoma.	
Interventions	Treatment: High-pressure Ahmed valve with resection of Tenon's capsule. Control: Standard Ahmed valve. All eyes in both treatment arms were administered topical 1 mg/ml MMC for 3 minutes, placed below the Tenon's capsule at the site of insertion of the polypropylene reservoir. All eyes received a scleral patch graft, subconjunctival injections of steroids and antibiotics.	
Outcomes	IOP control reported as final mean IOP and also as success; occurrence of postoperative hypertensive phase; type of bleb (ischemic or non-ischemic). Success: IOP > 4 mm Hg and < 22 mm Hg and at least 30% reduction from preoperative values.	
Notes	Country and period of study: Brazil, Argentina, Columbia, Peru. January 2000 to December 2000. Follow-up intervals: postoperative days 1 and 10, months 1, 3, 6 and one year.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Valimaki 1999

Methods	<p>Method of randomization: the first patient was assigned to treatment with a coin flip. Rest of participants were alternated consecutively to either treatment arm.</p> <p>Number randomized: 92 (45 to S-2 high pressure Ahmed valve with resection of Tenon's capsule and 47 to Standard Ahmed valve without Tenon's resection).</p> <p>Exclusions after randomization (total and per group): none.</p> <p>Losses to follow up: 20 participants in Ahmed valve with Tenon's capsule resection and 14 participants in control group were lost to follow up at 12 months. Reasons were not reported.</p> <p>Method of allocation concealment: Not possible due to alternating assignment.</p> <p>Outcome assessor masking: not reported.</p> <p>Intention-to-treat analysis: no. Participants lost to follow up were excluded from the analysis.</p> <p>Unusual study design: none.</p>
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Participants	Age: mean (SD) 60 (16) years in Molteno implant with oral corticosteroids arm; 74 (9) years in control arm. Sex: 30% in Molteno implant with oral corticosteroids and 64% in control arm were females. Inclusion criteria: patients older than 25 years of age; no history of any type of corticosteroid treatment within 2 weeks of surgery; high risk of filtration failure (failed conventional glaucoma surgery, neovascular, traumatic, uveitic glaucoma); progressing or likely to progress visual function status at current level of IOP on maximal-tolerated medical and laser treatment. Exclusion criteria: diabetes mellitus; congestive heart failure; gastric or duodenal ulcer disease; history of psychiatric disease or active infection; regular use of NSAIDs; pregnant or nursing women; women on inadequate contraception; patients who underwent argon laser trabeculoplasty or any type of ocular surgery within 6 months prior to enrollment. Equivalence of baseline characteristics: age of participants appears to differ in the 2 treatment arms. Diagnoses in participants: primary open-angle glaucoma; exfoliative glaucoma; neovascular glaucoma; uveitic glaucoma; traumatic and juvenile glaucoma.	
Interventions	Treatment: Single-plate, single-stage Molteno implant with postoperative oral corticosteroids, started on 14th postoperative day. Oral steroids were given for 10 weeks (60 mg on days 1 to 3, 50 mg on days 4 to 6, 40 mg on days 7 to 9, 30 mg on days 10 to 12, 25 mg on days 13 to 14, 15 mg on days 29 to 42, 10 mg on days 43 to 56, 7.5 mg on days 57 to 63 and 5 mg on days 64 to 70). Control: Single plate, single stage, Molteno implant. All participants in both arms were treated with topical chloramphenicol 5 times daily for 12 weeks following surgery.	
Outcomes	Primary outcome: IOP control at 6 months. Success: IOP between 6 and 22 mm Hg inclusive with less than or as much anti-glaucoma medications as at the preoperative visit. Secondary outcomes: serum marker studies for collagen synthesis (PICP and PIIINP).	
Notes	Country and period of study: Finland, August 1995 to February 1997. Follow-up intervals: postoperative day 1, weeks 2, 4, 6, 8, 10, 12, 24.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Wilson 1992

Methods	<p>Method of randomization: random number table was used. Randomization was stratified for the following groups in blocks of 10: phakic, neovascular, aphakic or pseudophakic with intact posterior lens capsule and pseudophakic without an intact posterior lens capsule.</p> <p>Number randomized: 134 in total. Number of participants randomized to each group was not reported.</p> <p>Exclusions after randomization (total and per group): none.</p> <p>Losses to follow up: 6 participants were lost to follow-up. Losses in each group not reported and neither were the reasons for losses to follow-up.</p> <p>Method of allocation concealment: "Type of treatment method selected was sealed in sequentially numbered envelopes until needed."</p> <p>Outcome assessor masking: outcome assessment was not masked as it was performed by the "surgeon involved". However, the follow-up evaluation is reported to be standardized.</p> <p>Intention-to-treat analysis: no. Data for 9 participants who did not yet complete 6 months of follow up, 6 participants lost to follow-up and 1 patient with sympathetic ophthalmia were not included.</p> <p>Unusual study design: none.</p>	
Participants	<p>Age: mean age 58.2 years in Molteno implant arm; 59.1 years in ACTSEB/Schocket procedure arm.</p> <p>Neither standard deviation nor range was reported.</p> <p>Sex: 55% of participants in Molteno arm and 56% in ACTSEB/Schocket procedure arm were females.</p> <p>Inclusion criteria: uncontrolled IOP; prior unsuccessful filtration surgery with an antifibrosis regimen diagnosis that would be expected to have poor response to filtration surgery; private patient status.</p> <p>Exclusion criteria: no explicit exclusion criteria were stated.</p> <p>Equivalence of baseline characteristics: age; gender; diagnosis; and IOP similar at baseline.</p> <p>Diagnoses in participants: aniridia; chronic angle-closure glaucoma (aphakia); chronic open-angle glaucoma (aphakia); combined mechanism (phakic); congenital glaucoma; inflammatory (phakic) glaucoma; ICE syndrome; neovascular glaucoma; primary angle-</p>	

	closure and primary open-angle glaucoma; pseudoexfoliation glaucoma; traumatic glaucoma.	
Interventions	Treatment: Double-plate Molteno implant. Control: ACTSEB/Schocket procedure.	
Outcomes	IOP control reported as final mean IOP; visual acuity; number of anti-glaucoma medications; complications.	
Notes	Country and period of study: USA. Study period not reported Follow-up intervals: postoperative weeks 1, 2, months 1, 3, 6, 9 and 12. The paper reported analysis of data at 6 months only.	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Wilson 2000

Methods	Method of randomization: computer generated list of random numbers was used. Number randomized: 117 (62 to Trabeculectomy and 55 to Ahmed implant). Exclusions after randomization (total and per group): none. Losses to follow up: 16 participants in Trabeculectomy arm and 15 in Ahmed implant arm at 11 to 13 months. Method of allocation concealment: not stated. Outcome assessor masking: not reported. Intention-to-treat analysis: not clear. Handling of participants lost to follow up was not clearly reported. Unusual study design: none.	
Participants	Age: mean (SD) 51.76 (17.16) years for trabeculectomy arm; 52.63 (18.61) years for Ahmed implant arm. Sex: 67% in trabeculectomy arm and 69% in Ahmed implant arm were females. Inclusion criteria: patients requiring glaucoma surgery for control of IOP. Exclusion criteria: patients requiring combined surgery; unable or unwilling to maintain follow up; age less than 4 years; eyes with a visual acuity of no light perception. Equivalence of baseline characteristics: A higher proportion of eyes in trabeculectomy arm were being treated with more than or equal to 4 medications at baseline. Visual acuity and visual field scores were similar at baseline in the 2 arms. Diagnoses in participants: primary open-angle and angle-closure glaucoma, neovascular glaucoma, uveitic glaucoma and traumatic glaucoma.	
Interventions	Treatment: Ahmed valve implant. Control: trabeculectomy with administration of MMC left to the discretion of the surgeon.	
Outcomes	Primary outcome: IOP control reported as final mean IOP Secondary outcomes: Success defined as IOP < 21mm Hg and at least a 15% reduction from baseline, IOP > 5mm Hg and no loss of light perception of visual acuity. Other outcomes: visual acuity; visual field; cataract formation; anterior chamber depth; glaucoma medication requirement; operative and postoperative complications	
Notes	Country and period of study: Saudi Arabia, Colombo, Sri Lanka. Study period not reported. Follow-up intervals: patients were examined on postoperative day 1, days 7 to 14, weeks 6 to 15, months 5 to 7 and months 11 to 13.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Wilson 2003

Methods	Method of randomization: computer-generated list of random numbers was used. Number randomized: 123 (64 to Trabeculectomy and 59 to Ahmed implant). Exclusions after randomization (total and per group): none.	
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	<p>Losses to follow up: 6 participants in Trabeculectomy arm and 7 in Ahmed implant arm were lost to follow up by days 7 to 14. Losses to follow up at 11 to 13 months were not reported.</p> <p>Mean follow up (SD): 31 (10.6) months for Trabeculectomy arm; 31 (7.1) months for Ahmed implant arm.</p> <p>Method of allocation concealment: not reported.</p> <p>Outcome assessor masking: not reported.</p> <p>Intention-to-treat analysis: not clear. Handling of participants lost to follow up was not clearly reported.</p> <p>Unusual study design: none.</p>
Participants	<p>Age: Mean (SD) 51.92 (16.39) years for Trabeculectomy arm; 52.02 (18.85) years for Ahmed implant arm.</p> <p>Sex: 67% in Trabeculectomy arm and 70% in Ahmed implant arm were females.</p> <p>Inclusion criteria: primary open-angle or primary chronic angle-closure glaucoma requiring surgical intervention.</p> <p>Exclusion criteria: causes for glaucoma other than those stated in inclusion criteria; eyes with prior intraocular surgery; eyes with visual acuity of no light perception; requirement for combined surgery; age less than 4 years; inability to maintain follow up for a prolonged period.</p> <p>Equivalence of baseline characteristics: a higher proportion of eyes in trabeculectomy arm were being treated with ≥ 4 medications at baseline. Visual acuity and visual field scores were similar at baseline in the 2 arms.</p> <p>Diagnoses in participants: primary open-angle glaucoma; primary chronic angle-closure glaucoma.</p>
Interventions	<p>Treatment: Single-plate Ahmed valve implant (Model S-2).</p> <p>Control: trabeculectomy with administration of MMC left to the discretion of the surgeon.</p>
Outcomes	<p>Primary outcome: IOP control reported as final mean IOP</p> <p>Secondary outcomes: success defined as IOP < 21 mm Hg and at least a 15% reduction from baseline, IOP > 5 mm Hg; no need for further glaucoma surgery; no loss of light perception of visual acuity.</p> <p>Other outcomes: decrease in visual acuity; progression of visual field; cataract formation; anterior chamber depth; glaucoma medication requirement; operative and postoperative complications.</p>
Notes	<p>Country and period of study: Colombo, Sri Lanka. Study period not reported</p> <p>Follow-up intervals: participants were examined on postoperative day 1, days 7 to 14, weeks 6 to 15, months 5 to 7, months 11 to 13, months 14 to 18, months 20 to 24, months 25 to 30, months 34 to 40, months 41 to 46 and months 50 to 52.</p>

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

ACTSEB: anterior chamber tube shunt to an encircling band (Schocket shunt)

BSS: balanced salt solution

CRVO: central retinal vein occlusion

ECP: endocyclophotocoagulation

HAD: human aqueous device

ICE syndrome: iridocorneal endothelial syndrome

IOP: intraocular pressure

MMC: mitomycin C

NSAIDs: non-steroidal anti-inflammatory drugs

PICP: carboxyterminal propeptide of type I procollagen

PIINP: aminoterminal propeptide of type III procollagen

PRP: pan retinal photocoagulation

SD: standard deviation

Characteristics of excluded studies [ordered by study ID]

Arroyave 2003	Retrospective case series
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Ayyala 1998	Retrospective case series
Ayyala 2002	Retrospective case series with concurrent controls
Beck 2003	Retrospective time series study with comparison group
Benz 2002	Retrospective case series
Budenz 2002	Retrospective case series
Chen 1997	Retrospective case series
Coleman 1995	Prospective case series
Coleman 1997	Prospective case series
Djodeyre 2001	Retrospective case series
Eid 1997	Retrospective case series with matched controls
Francis 2005	Prospective case series
Hill 1991	Consecutive case series
Hill 2003	Retrospective case series
Hong 2005	Review article
Huang 1999	Retrospective case series
Kansal 2002	Prospective cohort study on patient comfort with different types of anesthesia in aqueous shunt surgery
KEVFSSG 1994	Prospective case series
Kim 2003	Retrospective case series
Lee 1997	Retrospective case series with historical controls
Leuenberger 1999	Review article
Lloyd 1992	Prospective case series
Lloyd 1994a	Prospective case series
Luttrull 1995	Retrospective case series
Minckler 2001	Review article
Molteno 1969	Prospective case series
Molteno 2001a	Prospective case series
Molteno 2001b	Prospective case series
Morad 2003	Retrospective case series
Noureddin 1992	Retrospective cohort study
Nouri-Madhavi 2003	Retrospective case series
Pastor 2001	Review article
Paysse 1996	Case control study
Perkins 1995	Prospective case series with historical controls
Perkins 1998	Prospective case series with historical controls
Rapuano 1995	Retrospective case series
Saw 2003	Review article
Sayyad 1995	Retrospective case series with historical controls
Seah 2003	Retrospective cohort study
Shaikh 2002	Prospective case series
Sivak-Callcott 2001	Review article

Strum 1998	Case series
Taglia 1999	Case report
Topouzis 1999	Prospective cohort study
Tsai 2003	Retrospective cohort study
Tuli 2001	Case control study
Whittaker 2003	Retrospective case series

Characteristics of ongoing studies [ordered by study ID]

Gedde 2005

Trial name or title	The Tube versus Trabeculectomy Study
Methods	
Participants	<p>Age: Mean (SD) was 70.9 (11.0) years for 350-mm² Baerveldt implant arm and 71.1 (9.9) years for trabeculectomy arm</p> <p>Sex: 60% in 350 mm² Baerveldt implant arm and 46% in trabeculectomy arm were females</p> <p>Inclusion Criteria: Participants with inadequately controlled glaucoma with IOP greater than or equal to 18 mm Hg but less than or equal to 40 mm Hg on tolerated medical therapy, and who had previous trabeculectomy, cataract extraction with intraocular lens implantation or both</p> <p>Exclusion Criteria: Participants requiring combined surgery, unable or unwilling to give consent, accept randomization and maintain follow-up, pregnant and nursing women, eyes with a visual acuity of no light perception, active iris neovascularization or active proliferative retinopathy, iridocorneal endothelial syndrome, epithelial or fibrous downgrowth, aphakia, chronic or recurrent uveitis, previous history of cyclodestructive procedure, scleral buckling procedure, conjunctival scarring precluding a trabeculectomy superiorly, vitreous in the anterior chamber for which a vitrectomy was anticipated, and severe posterior blepharitis</p> <p>Equivalence of baseline characteristics: Participants in both treatment arms were similar at baseline with respect to mean visual acuity, visual field, mean number of preoperative anti-glaucoma medications, mean IOP, number of previous intraocular surgical procedures, and lens status. A greater number of participants in the Baerveldt implant arm were females, had a diagnosis of pseudoexfoliative glaucoma. A greater number of participants in the trabeculectomy arm had a lower visual acuity due to cataract.</p> <p>Diagnoses in participants: Primary open angle, chronic angle closure glaucoma, pseudoexfoliative glaucoma, and other forms of glaucoma</p>
Interventions	<p>Treatment: 350 mm² Baerveldt implant</p> <p>Control: Trabeculectomy with administration of Mitomycin C (0.4mg/ml for 4 minutes)</p>
Outcomes	<p>Primary outcome: Level of intraocular pressure; rate of complications</p> <p>Secondary outcomes: Failure as defined by the following: IOP > 21 mm Hg or not reduced by 20% below baseline on two consecutive follow-up visits after 3 months, IOP less than or equal to 5 mm Hg on two consecutive follow-up visits after 3 months, additional glaucoma surgery, loss of light perception.</p> <p>Complete success: eyes that have not failed and are not on supplemental medical therapy,</p> <p>Qualified success: eyes that have not failed but require supplemental medical therapy</p> <p>Visual acuity</p> <p>Visual field</p> <p>Quality of life</p>
Starting date	October 1999 to April 2004
Contact information	Steven J. Gedde, MD, Bascom Palmer Eye Institute, 900 NW 17th Street, Miami, Florida 33136
Notes	<p>Country and period of study: USA</p> <p>Study period: October 1999 to April 2004</p> <p>Follow up intervals: Patients were examined on postoperative day 1, week 1, months 3, 6, 12, 18, years 2, 3, 4, and 5</p>

Data and Analyses

Comparison 1. Ahmed implant versus trabeculectomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at 11 to 13 months follow up	2	195	Mean Difference (IV, Fixed, 95% CI)	-3.81 [-5.69, -1.94]

Comparison 2. Ahmed implant versus endocyclophotocoagulation (ECP)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 At 12-months follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.2 At 24-months follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2 Mean logMAR visual acuity at 24 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Anti-glaucoma medications at 24 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 3. Ahmed implant with MMC versus Ahmed implant with balanced salt solution (BSS)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Anti-glaucoma medications at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 4. High-pressure Ahmed implant + MMC + partial Tenon capsule resection versus Standard Ahmed implant + MMC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 5. Double-plate Molteno implant versus Schocket shunt

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at six months follow up	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 6. Single-plate Molteno implant with oral corticosteroids versus single-plate Molteno implant alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at six months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Visual acuity	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Stable vision - visual acuity unchanged or within one line from baseline	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2.2 Loss of vision - loss of 2 or more lines from baseline	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
3 Anti-glaucoma medications	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 7. Double-plate Molteno implant + MMC versus Molteno implant + balanced salt solution (BSS)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Mean logMAR visual acuity at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Anti-glaucoma medications at 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 8. Single-plate Molteno implant versus double-plate Molteno implant

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IOP outcomes at final follow up	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Success (final IOP not greater than 21 mm Hg and at least a 30% reduction from baseline)	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
1.2 Complete success (final IOP not greater than 21 mm Hg without additional anti-glaucoma medications)	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
1.3 Qualified success (final IOP not greater than 21 mm Hg and on adjunctive anti-glaucoma medications)	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

Comparison 9. 350 mm² Baerveldt implant versus 500 mm² Baerveldt implant

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean intraocular pressure	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 At 12 months follow up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.2 At 2 years follow up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.3 At 3 years follow up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.4 At 4 years follow up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.5 At 5 years follow up	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable

Analysis 1.1. Comparison 1 Ahmed implant versus trabeculectomy, Outcome 1 Mean intraocular pressure at 11 to 13 months follow up

Analysis 2.1. Comparison 2 Ahmed implant versus endocyclophotocoagulation (ECP), Outcome 1 Mean intraocular pressure

Analysis 2.2. Comparison 2 Ahmed implant versus endocyclophotocoagulation (ECP), Outcome 2 Mean logMAR visual acuity at 24 months follow up

Analysis 2.3. Comparison 2 Ahmed implant versus endocyclophotocoagulation (ECP), Outcome 3 Anti-glaucoma medications at 24 months follow up

Analysis 3.1. Comparison 3 Ahmed implant with MMC versus Ahmed implant with balanced salt solution (BSS), Outcome 1 Mean intraocular pressure at 12 months follow up

Analysis 3.2. Comparison 3 Ahmed implant with MMC versus Ahmed implant with balanced salt solution (BSS), Outcome 2 Anti-glaucoma medications at 12 months follow up

Analysis 4.1. Comparison 4 High-pressure Ahmed implant + MMC + partial Tenon capsule resection versus Standard Ahmed implant + MMC, Outcome 1 Mean intraocular pressure at 12 months follow up

Analysis 5.1. Comparison 5 Double-plate Molteno implant versus Schocket shunt, Outcome 1 Mean intraocular pressure at six months follow up

Analysis 6.1. Comparison 6 Single-plate Molteno implant with oral corticosteroids versus single-plate Molteno implant alone, Outcome 1 Mean intraocular pressure at six months follow up

Analysis 6.2. Comparison 6 Single-plate Molteno implant with oral corticosteroids versus single-plate Molteno implant alone, Outcome 2 Visual acuity

Analysis 6.3. Comparison 6 Single-plate Molteno implant with oral corticosteroids versus single-plate Molteno implant alone, Outcome 3 Anti-glaucoma medications

Analysis 7.1. Comparison 7 Double-plate Molteno implant + MMC versus Molteno implant + balanced salt solution (BSS), Outcome 1 Mean intraocular pressure at 12 months follow up

Analysis 7.2. Comparison 7 Double-plate Molteno implant + MMC versus Molteno implant + balanced salt solution (BSS), Outcome 2 Mean logMAR visual acuity at 12 months follow up

Analysis 7.3. Comparison 7 Double-plate Molteno implant + MMC versus Molteno implant + balanced salt solution (BSS), Outcome 3 Anti-glaucoma medications at 12 months follow up

Analysis 8.1. Comparison 8 Single-plate Molteno implant versus double-plate Molteno implant, Outcome 1 IOP outcomes at final follow up

Analysis 9.1. Comparison 9 350 mm² Baerveldt implant versus 500 mm² Baerveldt implant, Outcome 1 Mean intraocular pressure

Appendix 1. CENTRAL and NRR search strategies

- #1 GLAUCOMA
- #2 INTRAOCULAR PRESSURE
- #3 CATARACT EXTRACTION
- #4 glaucoma*
- #5 (intraocular near pressur*)
- #6 (intra-ocular near pressur*)
- #7 (extract* or surg* or operat* or remov*)
- #8 cataract*
- #9 (#7 and #8)
- #10 (#1 or #2 or #3 or #4 or #5 or #6 or #9)
- #11 GLAUCOMA DRAINAGE IMPLANTS
- #12 MOLTENO IMPLANTS
- #13 (glaucom* and (molteno or ahmed or baerveldt or krupin or schocket or joseph or optimed or white or express))
- #14 (glaucom* and (tube* or devic* or drain* or shunt* or implant* or seton*))

#15 (#11 or #12 or #13 or #14)

#16 (#10 and #15)

Appendix 2. MEDLINE and PubMed search strategies

#1 explode “Glaucoma-” / all SUBHEADINGS in MIME,MJME

#2 explode “Intraocular-Pressure” / all SUBHEADINGS in MIME,MJME

#3 explode “Cataract-Extraction” / all SUBHEADINGS in MIME,MJME

#4 ((glaucoma* or intra?ocular near pressure)) in AB)or((glaucoma* or intra?ocular near pressure)) in TI)

#5 (((extract* or surg* or operat* or remov*) near cataract*) in AB)or(((extract* or surg* or operat* or remov*) near cataract*) in TI)

#6 #1 or #2 or #3 or #4 or #5

#7 explode “Glaucoma-Drainage-Implants” / all SUBHEADINGS in MIME,MJME

#8 explode “Molteno-Implants” / all SUBHEADINGS in MIME,MJME

#9 ((Molteno or Ahmed or Baerveldt or Krupin or Schocket or Joseph or Optimed or White or Express) in AB)or((Molteno or Ahmed or Baerveldt or Krupin or Schocket or Joseph or Optimed or White or Express) in TI)

#10 (((glaucoma*) near (tube* or devic* or drain* or shunt* or implant* or seton*)) in AB)or(((glaucoma*) near (tube* or devic* or drain* or shunt* or implant* or seton*)) in TI)

#11 #7 or #8 or #9 or #10

#12 #6 and #11

To identify randomized controlled trials, we combined this strategy with the Cochrane Highly Sensitive Search Strategy phases one and two as contained in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2005a).

Appendix 3. EMBASE search strategy

#1 exp GLAUCOMA/

#2 exp Intraocular Pressure/

#3 exp Cataract Extraction/

#4 (glaucom\$ or ((intraocular or intra-ocular) adj3 pressur\$)).mp.

#5 ((extract\$ or surg\$ or operat\$ or remov\$) adj3 cataract\$).mp.

#6 ((extract\$ or surg\$ or operat\$ or remov\$) adj3 cataract\$).ab,ti.

#7 #1 or #2 or #3 or #4 or #5 or #6

#8 exp Glaucoma Drainage Implant/

#9 (Molteno or Ahmed or Baerveldt or Krupin or Schocket or Joseph or Optimed or White or Express).ab,ti.

#10 (glaucom\$ adj5 (tube\$ or devic\$ or drain\$ or shunt\$ or implant\$ or seton)).ab,ti.

#11 #8 or #9 or #10

#12 #7 and #11

To identify randomized controlled trials, we combined this strategy with the following strategy.

#1 Randomized Controlled Trial/

#2 exp Randomization/

#3 Double Blind Procedure/

#4 Single Blind Procedure/

#5 random\$.ab,ti.

#6 #1 or #2 or #3 or #4 or #5

#7 (animal or animal experiment).sh.

#8 human.sh.

#9 #7 and #8

#10 #7 not #9

#11 #6 not #10

#12 Clinical Trial/

#13 (clin\$ adj3 trial\$).ab,ti.

#14 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).ab,ti.

#15 exp PLACEBO/

#16 placebo\$.ab,ti.

#17 random\$.ab,ti.

#18 experimental design/

#19 Crossover Procedure/

#20 exp Control Group/

#21 exp LATIN SQUARE DESIGN/

#22 #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21

#23 #22 not #10

#24 #23 not #11

#25 exp Comparative Study/

#26 exp Evaluation/
 #27 exp Prospective Study/
 #28 (control\$ or prospectiv\$ or volunteer\$).ab,ti.
 #29 #25 or #26 or #27 or #28
 #30 #29 not #10
 #31 #30 not (#11 or #23)
 #32 #11 or #24 or #31

Appendix 4. LILACS search terms

glaucoma\$ combined with the terms Molteno, Ahmed, Baerveldt, Krupin, Schocket, Optimed, ExPRESS, device\$, shunt\$, drainage, White pump shunt, Joseph valve or Joseph device

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Plain Language Summary

Aqueous shunts for glaucoma

Glaucoma is a leading cause of blindness worldwide. Treatments for glaucoma include the use of eye drops, laser treatment, and a variety of surgical operations. Surgery is usually considered only after eye drops and lasers have proven to be ineffective. Among surgical operations, aqueous shunts or glaucoma drainage devices which come in a variety of sizes and shapes are often used in complicated cases when traditional types of surgery such as trabeculectomy (making a cleft in the eye wall) have not worked. The typical aqueous shunt includes a tiny rubber tube (drain) that connects the eye fluid chamber to a plate that is attached to the eye wall. The plate or explant stimulates the formation by the body of a space into which eye fluid can drain. This review summarizes previously published randomized and quasi-randomized controlled trial results for aqueous shunts (studies that compare treatment with no treatment or to alternative treatments including a control group). We included 15 trials involving 1153 participants with varied diagnoses of glaucoma. At present there is insufficient evidence to conclude that clinical outcomes of trabeculectomy differ substantially from those of aqueous shunts in similar patients with complicated glaucomas. There is also insufficient evidence to conclude that any specific aqueous shunt is superior to the others currently in widespread use.

Table 1
Interventions evaluated in trials included in this review

Comparison	Author Year	No. eyes exp/control
Ahmed implant versus trabeculectomy	Wilson 2000	55/62
Ahmed implant versus trabeculectomy	Wilson 2003	59/64
Ahmed implant with and without partial resection of Tenon's capsule	Susanna 2003	45/47
Ahmed implant with and without partial ligation of tube	Kee 2001	16/16
Ahmed implant with Mitomycin C versus Ahmed implant with balanced salt solution	Costa 2004	34/26
Ahmed implant with and without pericardial surface expansion	Hwang 2004	10/10
Ahmed implant versus endocyclophotocoagulation	Lima 2004	34/34
500 mm Baerveldt versus 350 mm Baerveldt	Britt 1999	52/55
Double-plate pressure-ridge Molteno implant with Mitomycin C versus Molteno implant with balanced salt solution	Cantor 1998	12/13
Single-plate Molteno implant versus double-plate Molteno implant	Heuer 1992	66/66
Double-plate Molteno implant versus Schocket shunt	Smith 1992	19/21
Double-plate Molteno implant versus Schocket shunt	Wilson 1992	134 (allocation not reported)
Double-plate pressure-ridge Molteno implant versus standard double-plate Molteno implant with tube ligation	Gerber 1997	15/15
Single-plate Molteno implant with and without postoperative oral corticosteroids	Valimaki 1999	11/11
Hunan aqueous device with and without Mitomycin C	Duan 2003	65/94

Table 2

Table of complications reported in included studies

Intervention	Trial ID (No. in grp)	No light perception	Choroidal hemorrhage	Phthisis	Tube exposure	Retinal detachment	Corneal failure	Strabismus	Infection
Ahmed implant	Costa 2004 (26)	0	0	0	1	1	1	3	0
	Hwang 2004 (10)	0	0	0	0	0	0	0	0
	Kee 2001 (16)	0	0	0	0	0	0	0	0
	Lima 2004 (34)	0	0	0	2	2	4	0	1
	Wilson 2000 (55)	0	0	0	2	0	0	0	0
	Wilson 2003 (59)	0	0	0	3	0	0	0	0
Ahmed implant with Mitomycin-C	Costa 2004 (34)	0	0	0	2	1	3	2	0
	Susanna 2003 (47)	See below	0	0	2	0	0	0	0
High-pressure Ahmed implant with partial Tenon's capsule resection and Mitomycin-C	Susanna 2003 (45)	7 patients in both groups together	0	1	4	1	0	0	1
Ahmed implant with partial ligation of tube	Kee 2001 (16)	0	0	0	0	0	0	0	0
Ahmed implant with pericardial membrane expansion	Hwang 2004 (10)	0	0	0	0	0	0	0	0
Single-plate Molteno implant	Heuer 1992 (50)	0	1	0	1	1	3	0	0
	Valimaki 1999(11)	0	0	0	1	0	1	0	0
Single-plate Molteno implant with oral corticosteroids	Valimaki 1999(11)	0	0	0	0	0	0	5	0
Double-plate Molteno implant	Gerber 1997 (15)	0	0	0	0	0	0	0	0
	Heuer 1992 (51)	0	5	2	2	1	5	0	1
	Smith 1992 (19)	0	0	0	0	1	1	0	0
	Wilson 1992 (65)	0	1	0	0	0	1	0	0
Pressure-ridge double-plate Molteno implant	Cantor 1998 (13)	2	1	2	0	0	2	0	0
	Gerber 1997 (15)	0	3	0	0	0	0	0	0
Pressure-ridge double-plate Molteno implant with Mitomycin-C	Cantor 1998 (12)	0	2	0	0	1	4	0	0

Intervention	Trial ID (No. in grp)	No light perception	Choroidal hemorrhage	Phthisis	Tube exposure	Retinal detachment	Corneal failure	Strabismus	Infection
Schocket shunt	Smith 1992 (21)	0	3	0	0	0	5	0	0
	Wilson 1992 (53)	0	1	0	1	0	1	0	0
350-mm Baerveldt implant	Britt 1999 (55)	0	13*	0	0	2	17**	10	0
500-mm Baerveldt implant	Britt 1999 (52)	0	19*	0	0	5	19**	8	0
Hunan aqueous device with and without Mitomycin-C	Duan 2003 (159)***	0	2	0	18	0	2	1	0

* Reported all choroidal complications together

** Reported all corneal complications together

*** Reported complications in both groups together