Aqueous shunt versus trabeculectomy for treatment of glaucoma

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Key words aqueous shunt, trabeculectomy, Epistemonikos, GRADE

Abstract

Introduction

Aqueous shunt has emerged as an alternative technique to trabeculectomy, which is considered the standard treatment for glaucoma surgery. Currently, it is mainly indicated after failure of trabeculectomy or in some types of glaucoma with high risk of failure. However, there is still controversy regarding its effectiveness compared to trabeculectomy.

Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

Results and conclusions

We identified five systematic reviews including nine studies overall, of which four were randomized trials. We concluded that aqueous shunt might increase the qualified success compared to trabeculectomy, but it is not clear whether it has any effect on the rest of the critical outcomes for decision-making because the certainty of the evidence is very low.

Problem

According to the World Health Organization, glaucoma is the second cause of blindness worldwide. Among the risk factors for its development, intraocular pressure (IOP) is the only one that can be modified.

Since the end of the last century, the introduction of aqueous shunt has emerged as an alternative surgery to trabeculectomy. The aqueous shunt can be defined as a silicone tube with a lumen attached to an explant plate. Currently, its main indication is for glaucoma with failed trabeculectomy or in some types of glaucoma with a high risk of failure (for example, neovascular or uveitic glaucoma). Over the years, the use of aqueous shunt has spread, being currently chosen as primary surgery by many specialists. However, there is controversy about this last scenario.

Key messages

- Aqueous shunt might achieve greater qualified success than trabeculectomy, but the certainty of the evidence is low.
- It is not clear whether aqueous shunt compared to trabeculectomy, has any effect on intraocular pressure or whether it decreases complete success, increases visual impairment or decreases the need for reoperation, because the certainty of the evidence is very low.
- Similarly, regarding the safety profile, it is not clear whether aqueous shunt increases the anterior narrow chamber, the persistent corneal edema or the choroidal effusion, because the certainty of the evidence is very low.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found five systematic reviews[1-5] including nine primary studies reported in 16 references[6-21], of which four correspond to randomized controlled trials, reported in 11 references[7-21]. However, one trial[16] was performed in pediatric population with aphakic glaucoma, which is not considered comparable with the rest of patients, so it was excluded from this analysis. This table and the summary in general are based on three randomized trials[10,20,21], since the inclusion of the observational studies did not increase the certainty of the evidence or added additional information.
What types of patients were included*	All trials included patients with glaucoma, with an average age of 53.9 years, of both genders, with average IOP of 25.96 mmHg (25.46 mmHg in the aqueous shunt arm, and 26.45 mmHg in the trabeculectomy arm). Regarding the type of glaucoma, one trial included patients with primary open-angle glaucoma, chronic angle-closure glaucoma, pseudoexfoliative glaucoma, pigmentary glaucoma[10], one trial included patients with primary open-angle glaucoma, primary angle-closure glaucoma, neovascular glaucoma, uveitic glaucoma and traumatic glaucoma[20] and one trial included primary open-angle glaucoma and angle-closure glaucoma[21]. In terms of the severity of glaucoma, all trials included patients with indication for surgical treatment[10,20,21]. One trial included patients both refractory to medical management and to surgical management (previous trabeculectomy, cataract extraction surgery, or both)[10]. One trial included patients refractory to medical management, and a proportion of patients refractory to surgical management (29.0% in the aqueous shunt arm, 43.6% in the trabeculectomy arm, without specifying the type of previous surgical intervention)[20]. One trial included only patients refractory to medical treatment, excluding patients with previous intraocular surgery[21].

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

What types of interventions were included*	All trials compared aqueous shunt with trabeculectomy[10,20,21]. As aqueous shunt, two trials used the Ahmed valve[20,21] and one trial used the Baerveldt implant[10]. Regarding the use of mitomycin C (MMC), in two trials its use was at the discretion of the surgeon (both arms)[20,21] and in one trial a 0.4 mg/ml solution was used for 4 minutes in the trabeculectomy arm[10].
What types of outcomes were measured	The trials evaluated multiple outcomes, which were grouped by the systematic reviews as follows: • Average IOP at the end of follow-up. • Percentage reduction of postsurgical IOP. • Absolute reduction of postsurgical IOP. • Qualified success (objective IOP independent of the use of medical treatment). • Complete success (objective IOP without the need of medical treatment). • Complications (narrow anterior chamber, choroidal effusion, hyphema, persistent corneal edema, cystic macular edema, bleb filtration, encapsulated bleb, endophthalmitis, corneal ulcer, dysesthesia, persistent diplopia, hypotony, hypotonic maculopathy, implant exposition, tube deviation, retinal detachment and suprachoroidal hemorrhage). • Need of reintervention. • Number of drugs used in the postoperative period. • Decrease in visual acuity. • Decrease in visual field. The average follow-up of the trials was 40 months, with a range between 12 and 60 months.

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Summary of Findings

The information about the effects of the use of aqueous shunts compared to trabeculectomy is based on three randomized trials involving 452 eyes[10,20,21]

All trials reported the mean intraocular pressure at the end of follow-up (320 eyes), change in visual acuity at one year (360 eyes), need of reintervention (452 eyes) and narrow anterior chamber (452 eyes)[10,20,21]. Two trials evaluated choroidal effusion (329 eyes)[10,20]. Only one trial evaluated complete success at the end of follow-up (157 eyes), qualified success at the end of follow-up (157 eyes) and persistent corneal edema (212 eyes)[10].The summary of findings is as follows:

- It is not clear the effect of aqueous shunt on intraocular pressure, compared to trabeculectomy, because the certainty of the evidence is very low.
- It is not clear whether the aqueous shunt decreases complete success compared to trabeculectomy, because the certainty of the evidence is very low.
- Aqueous shunt might achieve greater qualified success compared to trabeculectomy, but the certainty of the evidence is low.
- It is not clear whether the aqueous shunt leads to a greater deterioration in visual acuity compared to trabeculectomy, because the certainty of the evidence is very low.
- It is not clear whether aqueous shunt decreases the need of reintervention compared to trabeculectomy, because the certainty of the evidence is very low.
- It is not clear whether aqueous shunt increases the risk of narrow anterior chamber compared to trabeculectomy, because the certainty of the evidence is very low.
- It is not clear whether aqueous shunt increases the risk of persistent corneal edema compared to trabeculectomy, because the certainty of the evidence is very low.
- It is not clear whether aqueous shunt increases the risk of choroidal effusion compared to trabeculectomy, because the certainty of the evidence is very low.

Aqueous shunt versus trabeculectomy in glaucoma

Patients Patients with glaucoma with indication for surgical treatment
Intervention Aqueous shunt
Comparison Trabeculectomy

Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITH trabeculectomy	WITH aqueous shunt		
	Difference: eyes per 1000			
IOP (mmHg)	12.8 mmHg	16.1 mmHg	--	⨁◯◯◯[1,2] Very Low
	MD: 3.3 mmHg more (Margin of error: 1.76 to 4.64 more)			
Complete success	286 per 1000	246 per 1000	RR 0.86 (0.51 to 1.46)	⨁◯◯◯[1,3] Very Low
	Difference: 40 less (Margin of error: 140 less to 131 more)			
Qualified success	500 per 1000	670 per 1000	RR 1.34 (1.03 to 1.75)	⨁⨁◯◯[1] Low
	Difference: 170 more (Margin of error: 15 to 375 more)			
Visual acuity change (logMAR)	2.74 units	2.86 units	--	⨁◯◯◯[1,3] Very Low
	MD: 0.12 units more (Margin of error: 0.07 less to 0.31 more)			
Reintervention	91 per 1000	54 per 1000	RR 0.59 (0.3 to 1.14)	⨁◯◯◯[1,2,3] Very Low
	Difference: 37 less (Margin of error: 64 less to 13 more)			
Narrow anterior chamber	134 per 1000	148 per 1000	RR 1.1 (0.69 to 1.73)	⨁◯◯◯[1,3] Very Low
	Difference: 14 more (Margin of error: 41 less to 98 more)			
Persistent corneal edema	86 per 1000	159 per 1000	RR 1.85 (0.87 to 3.97)	⨁◯◯◯[1,3] Very Low
	Difference: 73 more (Margin of error: 11 less to 254 more)			
Choroidal effusion	132 per 1000	140 per 1000	RR 1.06 (0.62 to 1.81)	⨁◯◯◯[1,3] Very Low
	Difference: 8 more (Margin of error: 50 less to 106 more)			

Margin of error: 95% confidence interval (CI).
RR: Risk ratio.
MD: Mean difference.
GRADE: Evidence grades of the GRADE Working Group (see later).

*The risk **WITH trabeculectomy** is based on the risk in the control group of the trials. The risk **WITH aqueous shunt** (and its margin of error) is calculated from relative effect (and its margin of error).

[1] The certainty of the evidence was downgraded in two levels due to very serious risk of bias.
[2] The certainty of the evidence was downgraded in one level due to inconsistency of the results.
[3] The certainty of the evidence was downgraded in one level due to imprecision of the results.

Follow the link to access the interactive version of this table (Interactive Summary of Findings – iSoF)

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision

Other considerations for decision-making

To whom this evidence does and does not apply

The evidence presented in this summary applies to patients with glaucoma with indication for surgical treatment.

The patients included in the trials were adults. Because of this, the results should be extrapolated cautiously to the pediatric population, in the absence of direct evidence.

About the outcomes included in this summary

The outcomes of intraocular pressure, complete success, qualified success, visual acuity change and reintervention were chosen because they are considered critical for surgery success. In addition, outcomes related to complications of surgery were chosen as safety parameters of the intervention. This selection is based on the opinion of the authors of the summary, but in general coincide with the outcomes reported in the systematic reviews identified.

Balance between benefits and risks, and certainty of the evidence

Aqueous shunt might achieve greater qualified success than trabeculectomy. However, it is not possible to conclude about other outcomes, both from the point of view of efficacy and safety profile, due to a very low certainty of the evidence.

Therefore, it is not possible to make an adequate balance between benefits and risks due to the limitations of the existing evidence.

Resource considerations

None of the systematic reviews considered an economic analysis within its outcomes. However, even if this information were available, the certainty of the evidence on its effects does not currently allow us to make any conclusions regarding the cost-benefit of the intervention.

What would patients and their doctors think about this intervention

Aqueous shunt is used by most of the clinicians in patients whom trabeculectomy has failed or have some types of glaucoma with a high risk of failure. However, this technique is used by a minority of the clinicians as primary surgery for the treatment of glaucoma.

It is unlikely that the limited certainty of the existing evidence could be a determining factor that leads to variations in the decision-making.

Differences between this summary and other sources

The systematic reviews reach similar conclusions to those presented here. Among the systematic reviews evaluated, it is important to highlight three systematic reviews[1,4,5], since these evaluated all three randomized trials used in this analysis.

The main clinical guidelines recommend the use of aqueous shunt in patients who are refractory to trabeculectomy, in those at high risk of it[22,24] or in patients with moderate or advanced glaucoma as a primary alternative to trabeculectomy[23,24]. However, this guidelines do not make a comparison regarding the effectiveness or safety profile between both surgical techniques.

Could this evidence change in the future?

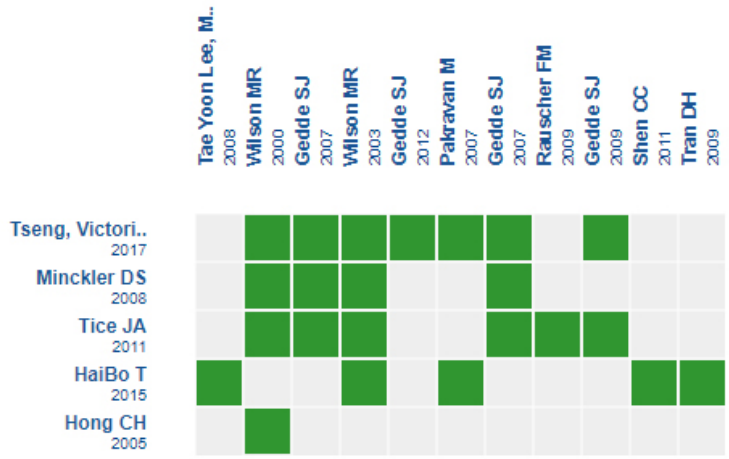
There is a high probability that future research changes the conclusions of this summary due to the existing uncertainty of the evidence.

We found one randomized trial[25] that is not included in any systematic review, that compares the efficacy and safety of aqueous shunt (Baerveldt implant) against trabeculectomy (trabeculectomy with mitomycin C). In addition, there are at least three ongoing trials in the International Clinical Trials Registry Platform of the World Health Organization[26,27,28].

Systematic reviews that include this new evidence could shed new light on this question. However, we did not identify any in progress in the International Prospective Register of Systematic Reviews (PROSPERO) of the National Institute for Health Research.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question.
Rows represent systematic reviews, and columns show primary studies.
The boxes in green correspond to studies included in the respective revisions.
The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version:** Aqueous shunt versus trabeculectomy for glaucoma

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (http://dx.doi.org/10.5867/medwave.2014.06.5997)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database

www.epistemonikos.org.

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