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Literature Review

The New Era and the Novel Glaucoma Procedures: A Literature Review on Glaucoma Surgical Procedures

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Received: September 19, 2021; **Published:** November 18, 2021

Abstract

Trabeculectomy is still considered the commonest surgical procedure for intraocular pressure (IOP) reduction and management of glaucoma.

This surgical procedure has been in clinical use for more than forty years. However, despite good results, the procedure is still hampered with some significant complications. In the last decade, glaucoma experts have therefore, embarked into other surgical procedures with the aim to control IOP and reduce the postoperative complications. The reviewers hereby described the various glaucoma surgical interventions and assessed whether trabeculectomy would be surviving in the face of the evolving new techniques.

The researchers underwent a literature review of trabeculectomy outcomes and other novel glaucoma procedures. The reviewers compared trabeculectomy outcomes with the newer surgical procedures.

A literature review of all published reviews, HTA reports between January 1985 and January 2019 of all glaucoma surgical procedures published in English language was conducted. The searched databases were Ovid Medline and other non-indexed citations as well as The Cochrane Database of Systematic Reviews.

The search strategy identified 562 abstracts. Fifty-one full articles were retrieved and included in the review for analysis. Currently there are no published randomised studies comparing these novel procedures with trabeculectomy or with other novel procedures.

This work provided the clinicians and other academic researchers and reviewers with insight on glaucoma surgery, comparing the standard trabeculectomy procedure with the new armamentarium in glaucoma surgery. The current literature suggests that well-designed studies providing evidence-based comparisons of the trabeculectomy and the novel glaucoma procedures are lacking.

Keywords: *Glaucoma; Trabeculectomy; MIGS, IOP; Tubes*

Introduction

Trabeculectomy is still considered the commonest surgical procedure for intraocular pressure (IOP) reduction and management of glaucoma.

This surgical procedure has been in practice for more than forty years.

Albeit, satisfactory surgical outcome, the procedure can be hindered with potential complications, involving late-onset bleb leaks, blebitis/endophthalmitis, hypotony, as well as choroidal effusions.

Therefore in the last decade, glaucoma surgeons have embarked into other surgical procedures for controlling IOP and reducing the rate of postoperative complications [1].

Glaucoma surgery for lowering IOP can be classified into two main groups: outflow surgeries aimed to increase the egress of aqueous humour from the eye and inflow surgeries designed to decrease the production of aqueous in the eye. The first category, outflow procedures, comprises the most frequently performed procedures, e.g. trabeculectomy and aqueous shunts with their variations. This category can be further subdivided into other procedures designed to: (1) increase outflow facility by creating a new outflow channel (e.g. Ex-PRESS implant); (2) improve the conventional (trabecular) outflow pathway (e.g. Fugo blade goniotomy, Trabectome, canaloplasty, excimer laser trabeculoplasty (ELT), and trabecular micro-bypass stent); or (3) increase uveoscleral outflow (e.g. SOLX Gold Shunt, Cypass) [2].

The novel glaucoma techniques seek to avoid bleb formation with its complications and rely on augmentation of the physiologic outflow by enhancing aqueous outflow through the trabecular meshwork (TM), Schlemm's canal, and outflow channels. Examples of procedures in this category are Fugo blade goniotomy, excimer laser trabeculoplasty (ELT), canaloplasty, trabeculotomy by internal approach (Trabectome), and trabecular bypass stent (iStent) [2].

The therapeutic goal of the first subgroup should be equal to or exceed the efficacy and safety of the current standard trabeculectomy with antifibrotic agents. The second and third subgroups include procedures designed to increase aqueous outflow without the formation of an external filtering bleb.

The aim in these last 2 surgical classifications is to decrease IOP and reduce need of glaucoma medications while eliminating complications associated with standard filtration as hypotony and other bleb-related problems as blebitis, endophthalmitis [3].

This review is comparing the standard glaucoma surgery with the novel glaucoma surgical techniques. The reviewer assessed whether the standard trabeculectomy would survive in the face of the new surgical glaucoma techniques.

Methods

The reviewer conducted a literature review of studies in glaucoma between January 1985 and January 2019. The researcher (RI) explored all reviews, meta-analyses and HTA reports in glaucoma published in English language without restrictions on the population studied, applied interventions, or glaucoma subtypes. The databases, which were searched, were: Ovid MEDLINE (R) In-Process and Other Non-Indexed Citations and Ovid MEDLINE (R) from January 1984 to first week of January 2019 and the Cochrane Database of Systematic Reviews. A search strategy with both controlled subject headings as well as text terms relevant to glaucoma and glaucoma surgery was conducted.

Inclusion and exclusion criteria

The inclusion criteria were all adult glaucoma population with age ranging between 17 and 100 years old. Congenital glaucoma was excluded from analysis.

Results

The search strategy identified 562 abstracts. Fifty-one full publications were retrieved and included in the manuscript for analysis.

Trabeculectomy: Updates on techniques

Intraoperative antimetabolite use is still considered a principal step during trabeculectomy to avert postoperative fibrosis. The standard options include Mitomycin-C (MMC) and 5-fluoruracil (5-FU). Yet, there are reports reporting complications related to the antimetabolite use [3]. Antimetabolite use has increased the incidence of thin, cystic blebs, which are prone to leak, infection and hypotony.

The Moorfield's safer surgery system was hence implemented to lower the risks associated with trabeculectomy while preserving its efficacy in IOP control. This system encourages two main points: first is to advocate a fornix-based conjunctival incision and second

a larger antimetabolite treatment area. This will eradicate the risks that may induce small, avascular, cystic blebs, which are more prone to leak (e.g. limbus-based incisions) [4].

Recently, alternative methods of drug delivery have been explored to reduce complication risks. However, these are still under trial. Hydrogels have been tested in animal models to assess their ability to provide, sustained release of wound healing modulators and reducing toxicity to the to the filtration site and surrounding tissues. They have been tested by placing in discs and attaching to Ahmed glaucoma valves; MMC was released *In vitro* for 2 weeks and subsequently reduced bleb inflammation and fibrosis in rabbits [5].

Ologen is a Food and Drug Administration-approved collagen matrix implant now used in trabeculectomy surgery. The implant is designed to inhibit scar formation before dissolving by placing directly over the scleral flap. Ologen has been applied in both trabeculectomy surgeries and procedures utilising Ex-Press shunts When used with MMC, Ologen implants reduced the possibility of bleb avascularity and induced more physiologic bleb morphology [3].

He M and coworkers conducted a systematic review, which indicated that trabeculectomy with Ologen is a safe and effective procedure in patients with glaucoma, but it does not seem to offer any significant advantages compared with trabeculectomy plus MMC. Nevertheless, relevant literature is still lacking. Thus, larger studies with longer follow-up durations are needed to endorse this evidence [6]. There is reducing trend of performing trabeculectomy surgery in spite of improvement of surgical technique. Arora and coworkers from 1994 to 2012 recently published an updated rate of trabeculectomy. In 1996 a total of 73 200 glaucoma filtering surgeries were performed, yet have steadily decreased through 2012 when only 23 877 surgeries were performed (including Ex-Press) [7]. This reduction in number is multifactorial including improvement in medications, more tube implantation, and development of less surgically invasive procedures.

Aqueous shunt implantation

Glaucoma surgeons had witnessed in the past decade an increase in shunt procedures. These techniques attempt to save the natural aqueous outflow channels, in addition reducing complications associated with traditional filtering surgery.

The Tube versus Trabeculectomy (TVT) Study [8] is a multicenter randomised controlled trial (RCT) designed to compare the safety and efficacy of aqueous shunt implantation to trabeculectomy with mitomycin C in patients who had undergone previous ocular surgery.

There were 212 participants in this trial who had previous cataract extraction with intraocular lens implantation and/or failed filtering surgery. They were then randomised to receive either glaucoma shunt (350 mm^2 Baerveldt glaucoma implant) or augmented trabeculectomy with MMC (0.4 mg/mL for 4 min).

The 5 years follow up period showed that the postoperative mean IOP was comparable between the two procedures (12.6 ± 5.9 mm Hg for trabeculectomy group) versus (14.4 ± 6.9 mm Hg) in the tube group (P = 0.12).

Failure rate was notably higher in the trabeculectomy group (46.9%) as opposed to the tube group (29.8%) at 5 years of follow up (P = 0.002).

Failure was defined as: IOP more than 21 mm Hg or less than 20% reduction below baseline, reoperation for glaucoma, or loss of light perception vision).

The efficacy results from the TVT Study supported an increase in the use of aqueous shunts beyond only refractory glaucoma's [8].

Early postoperative complications were more reported in the trabeculectomy group (37%) vs the tube group (21%; P = 0.012). Nevertheless, there were comparable results in the rates of late postoperative complications - 34% in the tube group vs 36% in the trabeculectomy group.

Complications resulting from glaucoma drainage devices (GDD) implantation include hypotony, postoperative elevated intraocular pressure, tube erosion, diplopia, motility disturbances, and corneal decompensation [8]. There may be several reasons for these results. In the trabeculectomy group, many patients did not meet success criteria, as their IOP was too low, yet the authors indicate, hypotony may be an acceptable outcome if visual acuity is not affected. Furthermore, the MMC protocol used in the study was for a longer duration and/or concentration than many surgeons use in their practice suggesting that rates of hypotony may be less in reality.

The Primary Tube Versus Trabeculectomy (PTVT) study is multicenter randomized Clinical Trial Comparing Tube Shunt Surgery and trabeculectomy with Mitomycin C in patients without previous ocular surgery [9]. Trabeculectomy with MMC had a higher surgical success rate than tube shunt implantation during the first year of follow-up in the PTVT Study. One year preliminary results showed that trabeculectomy with MMC have lower IOP and adjunctive glaucoma medications compared with tube surgery (12.4 ± 4.6 vs. 14.1 ± 4.2 mm Hg and 0.9 ± 1. vs. 2.0 ± 1.4 medications, respectively). The likelihood of surgical failure during the first year of follow-up was 17.3% in the tube group and 7.9% in the trabeculectomy group (p = 0.013) [9]. There was no significant difference in the rate of surgical failure between the 2 surgical procedures at 3 years. The rate of surgical failure was comparable between the 2 groups at 3 years of follow up. Participants who underwent trabeculectomy with MMC had lower IOP with use of fewer glaucoma medications. Serious complications were equal between the 2 surgical groups.

Micro-invasive glaucoma surgery (MIGS)

The current definition of MIGS comprises three anatomical classifications. The first category includes Schlemm's canal, by improving trabecular outflow. The second category is the suprachoroidal space, and it works by improving the uveoscleral outflow by creating a connection between the anterior chamber and the suprachoroid. The third classification is the subconjunctival space- it creates an alternative outflow pathway for aqueous humour [10].

The Ex-PRESS miniature

The Ex-PRESS miniature glaucoma implant is a biocompatible, valveless stainless steel tube. Originally, it was designed for subconjunctival suprachoroid implantation to drain aqueous into the subconjunctival space [11]. The implants are now implanted under a partial-thickness scleral flap, as advised by Dahan and Carmichael [12]. The technique is analogous to standard trabeculectomy and includes formation of a scleral flap and a conjunctival filtration bleb, without peripheral iridectomy when inserting the Ex-PRESS [2]. There was no difference reported between the Ex-PRESS shunts and standard trabeculectomy as regards occurrence of other complications or long-term safety.

Further, there was no difference noted in the bleb morphology between the two surgical procedures [13].

Elad Moisseiev and colleagues concluded from their results and literature review, that using the Ex-PRESS is not associated with any improvement in efficacy or safety but reduced rate of early postoperative hypotony [14].

This instant difference was certainly not shown to convey into a clinically significant better outcome.

Nonetheless, a retrospective study comparing ExPRESS to standard trabeculectomy in primary open angle glaucoma (POAG), pseudoexfoliative glaucoma (PXFG) and ''complex'' glaucomas did not find a difference between the two procedures as regards surgical success, need for postoperative glaucoma medications, or complications between the different glaucoma subtypes [14].

Shaarawy and coworkers [15] analysed existing data considering the safety and efficacy of the EX-PRESS implant, in contrast with trabeculectomy.

Only one RCT (out of the four prospective RCTs) comparing IOP-lowering efficacy showed longer-term lower IOP control with the EX-PRESS than trabeculectomy.

There was a substantial difference in mean IOP between the groups during the 3 years of follow-up; though this difference was not maintained at longer duration of the study.

Their report showed that neither of the published data showed a significant difference in IOP between groups, though one report showed higher IOP in the device group at one year of follow-up and at last follow-up period.

Shaarawy and coworkers thus concluded that surgery with the EX-PRESS implant is comparable to that of trabeculectomy. Nevertheless, It is still uncertain whether there is clinically long-term, better IOP control with either technique [15].

Wang and colleagues performed a large comprehensive meta-analysis comparing the Express shunt to trabeculectomy in 605 eyes and found no significant difference in IOP lowering potential. However, the Express shunt had lower rates of early postoperative complications as hypotony and hyphemia. The hypothesis is that the small 5-mm diameter of the shunt prevents over filtration and subsequent hypotony. The Ex-Press procedure also does not require an iridectomy, which likely results in less inflammation and a lower risk of hyphemia [9].

The ongoing prospective, randomized clinical trial, XVT (Ex-PRESS vs. trabeculectomy), will elucidate additional information comparing this latest modification to the standard trabeculectomy [16].

Techniques that increase outflow via the trabecular meshwork

Trabectome

Ab interno trabeculotomy or Trabectome is a newer procedure in which ablation of 60 to 120 degrees of trabecular meshwork is performed using focused electrosurgical pulses with simultaneous continuous irrigation to remove debris [17]. The technique can be completed using a comparatively new device, the Trabectome. This procedure is beneficial in patients requiring IOP lowering surgery, but do not need very low IOP. The surgery can be performed in phakic or pseudophakic eyes, and can be combined with cataract surgery. Transient hyphemas are the commonest complication, yet, quickly clearing.

Other reported complications as iridodialysis, cyclodialysis, and IOP spike have been reported.

Complications as sustained hyphema, wound leak, choroidal effusion, and haemorrhage are not common after this procedure.

One of the advantages of this surgery is that it does not avert additional glaucoma surgery involving conjunctiva, e.g. trabeculectomy or drainage implant [18].

Minckler and colleagues, described 101 patients with OAG undergoing Trabectome. The mean preoperative IOP was 27.6 ± 7.2 mm Hg and postoperative IOP at 30 months was 16.3 ± 3.3 mmHg. They reported an overall success of the operation at 84%, defined as an IOP < / 21 mm Hg with or without topical medications and no subsequent surgery [18].

Promising response to Trabectome has likewise been noted in different types of glaucoma.

In 2012, Ting and colleagues compared patients with pseudoexfoliation (PXF) glaucoma and POAG after trabectome with and without cataract surgery. The mean preoperative IOP was 29.0 ± 7.5 mm Hg (PXF glaucoma) and 25.5 ± 7.9 mm Hg (POAG), among the trabectome-alone group. At 1-year postop, the IOP decreased - 12.3 ± 8.0 (PXF glaucoma) and – 7.5 ± 7.4 mm Hg (POAG), respectively. In the combined trabectome-cataract surgery group, the preoperative IOP was 21.7 ± 8.4 and 19.9 ± 5.4 mm Hg, respectively. At 1 year, this decreased IOP was - 7.2 ± 7.7 and - 4.1 ± 4.6, respectively. Jordan and colleagues reported similar results in 2013. These results suggest that trabectome is equally, if not, more effective in reducing IOP in patients with PXF versus POAG [9].

More than 15,000 surgical procedures have been completed since 2004 either alone or in combination with cataract surgery.

Some retrospective studies reported a reduction of both IOP (35%) and the number of glaucoma medications needed (50%). Nearly 1 in 10 patients subsequently required further glaucoma surgery, typically within the first 6 months after a Trabectome. Yet, the literature is lacking as regards prospective trials comparing trabectome and trabeculectomy [19].

Glaukos iStent

A Glaukos iStent procedure is performed through a small temporal clear corneal incision. A titanium (heparin-coated) L-shaped implant is applied to shunt aqueous directly into Schlemm's canal. More than one stent can be inserted into the nasal angle through a temporal clear corneal incision under direct gonioscopic imagining.

The iStent is currently approved only in combination with cataract surgery.

It has comparable advantages to other ab interno procedures with the natural outflow system is not diverted but is supplemented to allow better IOP control with lower or almost no medications.

The results of one-year data of a prospective, randomised, multi-centre trial showed that combined cataract surgery with i Stent implantation achieved better IOP control with less medications and without considerably adverse reactions as compared to cataract surgery alone [19].

In 2012, Craven and colleagues reported similar findings by conducting a 2-year follow-up study. However, they reported that the total number of medications in the iStent group was no long statistically significant at 2 years compared with patients who had cataract surgery alone [9].

The Hydrus microstent is similar to iStent in that it bypasses the trabecular meshwork and shunts fluid from the anterior chamber to the collector channels, and increases outflow by dilating the canal but spans a larger portion of the canal. The Hydrus II study is a multicentre, randomised, controlled trial, which enrolled 100 eyes with OAG and cataract surgery with and without the microstent. At 2 years, patients who underwent combined procedure experienced more reduction of IOP (16.9 ± 3.3 vs. 19.2 ± 4.7 mm Hg) and were more likely to be without IOP-lowering medications (73% vs. 38%). peripheral anterior synechiae was the major device-related adverse event reported in the Hydrus II study. Other complications included iris trauma and hyphema that resolved within a week. In early 2015, the Hydrus IV trial completed patient enrollment of 550 patients and was conducted at over 30 centers worldwide. This was the largest randomised-controlled MIGS study to be ever conducted. The 2-year follow-up outcome was completed by 2017 at which time it underwent FDA review [9].

Canaloplasty

Canaloplasty is a non-penetrating procedure utilising microcatheter technology. The procedure is performed in a similar fashion to a viscocanalostomy where an incision is made to gain access to Schlemm's canal. A microcatheter revolves the Schlemm's canal around the iris, to enlarge the main drainage channel and the smaller collector channels through injection of viscoelastic.

The catheter is later removed and a suture is positioned within the canal. A 3-year report on this procedure (n = 157 eyes), showed a mean IOP drop of 36.1% with an average reduction of medication from 1.8 to 0.9. No ocular serious complications were published during the follow-up of the study; 2.5% of eyes had persistent blebs at three years of follow up and no bleb-related complications [19].

However, this procedure is not favourable as expected because of its steep learning Curve [9].

Trabeculotomy ab externo (non-penetrating trabeculectomy) (NPT)

It is an ab externo (i.e. from the outside), in which the Schlemm's canal is surgically exposed by creating a large and deep scleral flap then the inner wall is stripped off.

More than 1500 procedures have been completed around the world.

Best candidates for trabeculotomy are patients with mild-to-moderate disc damage, especially if they are not a good candidate for trabeculectomy and do not need-marked reduction in IOP.

Patients who have both cataract and glaucoma are judicious candidates for phacotrabeculotomy. Intriguingly, trabeculotomy works better in the older population. The advantage of the procedure is reasonable IOP control without bleb formation but augmenting aqueous outflow through the natural drainage system.

However, side effects of the surgery are the IOP spike on the first postoperative day associated with hyphema, a probable need for postoperative glaucoma medications to further reduce IOP. Moreover, this procedure requires surgical skill to perform angle surgery [20].

Viscocanalostomy

Viscocanalostomy is another technique developed to avoid the risks associated with filtering surgery and aimed to facilitate aqueous egress without completely penetrating the eye wall. In a prospective study comparing viscocanalostomy to trabeculectomy in 50 patients with POAG or PXFG, success rates (IOP < 21 mm Hg with no additional medications and at least a 20% reduction in IOP) were 76% and 80% 2 years after surgery, respectively (P = 0.60) [21]. However, when the IOP level defining success was lowered to 16 mm Hg, success rates decreased to 56% and 72%, respectively (P = 0.17). Of note, the surgical technique described for trabeculectomy did not include the use of antifibrotics agents intraoperatively, although subconjunctival injections of 5-FU were allowed postoperatively. At the final follow-up visit, IOP reductions were similar between the viscocanalostomy group and the trabeculectomy group [21].

A Cochrane review of RCTs and quasi-RCTs comparing trabeculectomy for POAG and non-penetrating surgery (particularly viscocanalostomy or deep sclerectomy), found that the odds of surgical success in viscocanalostomy population was lesser than in trabeculectomy participants (OR = 0.33, 95% CI).

This review also determined that the methodological quality of studies were lacking, with majority of studies were at high risk of bias in as a minimum 1 domain. Further, there was a lack of certainty due to inappropriate reporting. The results of this review emphasize the need for high-quality RCTs to better assess the safety and efficacy of glaucoma procedures [22].

Techniques that increase outflow via suprachoroidal pathways

Cypass

The supraciliary device is a 6.35 - mm tube that is inserted into the potential space between the iris and scleral spur. Hoeh and colleagues conducted a multicenter study on 142 patients with OAG who underwent cataract surgery with Cypass microstent placement. The participants were divided into 2 cohorts based on an IOP greater or lower than 21mmHg. At approximately 1 year, patients with IOP > 21 mm hg had a 35% decrease in IOP and 49% reduction in topical medication. Patients with a pressure < 21 mm Hg maintained that pressure, while having a 75% reduction in topical medication.

The COMPASS a randomised, multicenter study comparing the use of the Cypass microstent with cataract surgery versus cataract surgery alone was recently completed. It followed over 500 patients for 2 years and reported that, 73% of patients achieved an IOP reduction greater than 20% without additional medications. Consequently, it received FDA approval in July 2016 when performed with phacoemulsification [9].

However, in August 2018 - Alcon has released a universal recall of the CyPass microstent, to be inhibited from use.

The statement came when researchers recognised an intense increase in endothelial cell loss (ECL) among population who had the CyPass microstent during cataract surgery 5 years prior, compared to patients who underwent cataract surgery alone.

This result was not obvious immediately two years after the surgery, when the COMPASS safety study found comparable ECL in the CyPass and cataract surgery-only groups.

Depending on those early results, the FDA permitted the device use for long-term IOP control in those patients with mild-to-moderate POAG.

Yet the completed COMPASS-XT study, which reviewed the patients for an additional further three years, found a concerning increase in ECL in the CyPass group.

In a letter to physicians dated August 29th 2018, the company's chief medical officer, Stephen Lane, MD, declared that the damage probably arises from the device's location within the angle.

He noticed that the ECL associated with the number of retention rings seen on gonioscopy, particularly when 2 or more retention rings were observed [23].

SOLX gold shunt

The function of the SOLX Gold Shunt is to shunt aqueous humour from the anterior chamber to the suprachoroidal space. This shunt comprises a thin, 24-karat gold implant measuring about 3 × 6 mm. The head of the implant is placed into the anterior chamber while the tail is introduced into the suprachoroidal space and the incision is closed in a way (watertight fashion), which allows uveoscleral outflow but not producing a filtration bleb. One-year follow-up showed a 30% reduction of IOP in a pilot study, with medications reduced nearly one-half. Complications include transient hyphema and transient hypotony (10%) [19].

Techniques that create a new subconjunctival pathway

Xen

The XEN gel stent created by Aquesys (Viejo, CA) and acquired by Allergan in October 2015, is the first MIGS device to take an ab interno subconjunctival approach for lowering IOP. This procedure is dependent on the conjunctiva; so patients who have failed traditional trabeculectomies and have conjunctival scarring may be at a higher risk of complications. In November 2016, the XEN gel stent was approved by FDA in patients with refractory glaucoma.

In 2015, Sheybani and coworkers evaluated the effectiveness of the gel stent without MMC in OAG patients (n = 37) and who were undergoing cataract surgery. At 1 year postop, the IOP decreased from 22.4 ± 4.2 to 15.4 ± 3.0 mm Hg, and 47.1% of participants were off all medications [9].

Another study was conducted by Khan and colleagues; in which they compared the gel stent to ab interno trabeculotomy in OAG patients performing cataract surgery. Success was defined as: IOP < 18 mm Hg, no glaucoma medications or secondary glaucoma procedures at 1 year postop. They reported that the stent group had a lower IOP (14.3 ± 3.1 vs. 17.3 ± 6.5 mm Hg), higher overall success (39% vs. 14%) as well as lower incidence of hyphema compared with the trabeculotomy group [9].

The Inn focus microshunt (InnFocus, Miami, CA)

A new approach that can be considered a modified trabeculectomy or a non-traditional MIGS procedure (not conjunctival sparing), requiring an ab externo approach. A conjunctival peritomy is created and the Inn Focus microshunt is inserted into the anterior chamber by a scleral tunnel allowing aqueous fluid to flow into the subconjunctival space. MMC is used to prevent early scarring. Batlle and colleagues looked at 23 eyes that failed maximum tolerated medical treatment. They conducted a 3-year non-randomised prospective trial. At 3 years, 95% of the patients had an < /IOP14 mmHg and an IOP reduction > / 20%. Mean IOP was decreased from 23.8 ± 5.3 to 10.7 ±

3.5 mm Hg and number of topical medications was reduced from 2.4 ± 0.9 to 0.7 ± 1.1.50. This procedure results in a bleb with similar risk factors to standard trabeculectomy. Nevertheless, the procedure supposedly has less inflammation because of its new non-inflammatory material [poly (styrene-block-isobutylene-block-styrene) or SIBS] and because no surgical iridectomy is required. In the former study, 13% of patients had transient hypotony and 8.7% had transient choroidal effusion that resolved spontaneously. There was no reported occurrence of infections, leaks or erosions. Dr Palmberg and his colleagues lately presented their 4-year safety and efficacy data at the 2017 American Glaucoma Society meeting in Coronado. At 4 years, 79 patients who had the Inn Focus microshunt (31 phakic, 30 pseudophakic, 18 shunt-phaco) had lower IOP (24.8 ± 6.1 vs. 11.7 ± 4.1 mm Hg) and were on less medications (2.3 ± 1.2 vs. 0.9 ± 1.3). Sixty-five percent of patients were off all medications [9].

New options for combined cataract and glaucoma surgery

Surgical options for both cataract and glaucoma have increased in recent years. These include endoscopic cyclophotocoagulation, trabecular micro-bypass stent, ab interno trabeculectomy, and canaloplasty; these could be undertaken in combination with cataract extraction to provide further IOP reduction. The studies that evaluated these new surgical glaucoma procedures combined with phacoemulsification were retrospective case series with no comparison group [24].

Cataract surgery with istents

Two prospective RCTs confirmed the safety and effectiveness of iStent in conjunction with cataract surgery to reduce IOP to less than 18 mm Hg and medication burden compared with cataract surgery alone for up to 5 years [25,26]. Belovay and coworkers found that implantation of multiple stents during cataract surgery provided a mean reduction in IOP of less than 15 mm Hg with reduction in medications through 1 year [27].

Phacoviscocanalostomy

Kobayashi and Kobayaski [28] compared phacoviscocanalostomy with phacotrabeculectomy (with MMC) in patients with POAG and cataract by conducting an RCT (n=40 eyes) and following them up for 1 year. There were no statistically meaningful differences between the 2 groups as regards IOP control, best-corrected VA, or visual field testing. Complications associated with the phacoviscocanalostomy group were perforation of Descemet membrane (15%), bleb formation (30%), peripheral anterior synechiae (16%) and IOP spike (15%). The complications reported with the phacotrabeculectomy group were hypotony (20%), choroidal detachment (20%), peripheral anterior synechiae (20%), failed bleb (10%) and hyphaema (5%). This study proposed that phacoviscocanalostomy could be alternative to augmented phacotrabeculectomy and could offer the advantage of fewer serious complications with similar IOP control. Of note, the follow-up duration for this study was somewhat short, and longer follow-up trials may revise recommended practice patterns [28].

Wishart and Dagres reported that phacoviscocanalostomy was safe and effective procedure in the elderly white population with uncontrolled glaucoma in a larger prospective case series of 165 eyes. They reported a 33.2% decrease in IOP from baseline. They have not reported complications as bleb leaks, hypotony, blebitis, or endophthalmitis [28].

Cataract surgery with non-penetrating deep sclerectomy

These include insertion of a collagen or other type of implant in the scleral bed. In a prospective RCT, Cillino and coworkers compared non-penetrating deep sclerectomy with punch trabeculectomy (without antimetabolite), with and without phacoemulsification (n = 65 patients) for POAG or PXF glaucoma.

While the authors initially found early comparable IOP reductions among all patient groups (without differences between non-penetrating deep sclerectomy alone, punch trabeculectomy alone, combined phacoemulsification with deep sclerectomy, and combined phacoemulsification with punch trabeculectomy), they later found a tendency for better long-term IOP control in the punch trabeculectomy group as opposed to the deep sclerectomy group.

However, postoperative complications were more common in the trabeculectomy group and these include hypotony, shallow anterior chambers, and choroidal detachments [29].

Cataract surgery with canaloplasty

Shingleton and colleagues looked at multicenter prospective case series of 54 patients with POAG and cataracts. They performed circumferential viscodilation and tensioning of the inner wall of Schlemm canal combined with phacoemulsification. They found that IOP decreased from 24.4mm Hg preoperatively to 13.7 mm Hg at 1 year of follow-up, with a reduction in number of medications from 1.5 preoperatively to 0.2 at year one. Complications reported were hyphema (5.6%), Descemet tear (1.9%), iris prolapse (1.9%), as well as transient elevations in IOP > 30mm Hg (7.3%) [30].

Cataract surgery with ab interno trabeculectomy

Ab interno trabeculectomy was combined with phacoemulsification in a small prospective case series of (9 patients (11 eyes) with medically uncontrolled POAG or PXF glaucoma (n = 2) and previously failed filtering surgery.

One of the 11 patients ''failed'' and needed additional surgery for control of IOP. IOP measurements were reduced by 39%. Postop medications were reduced from 2.4 to 0.8 at the last follow-up appointment [28].

Cataract surgery with trabectome

Francis and colleagues described combined phacoemulsification with Trabectome surgery on 304 eyes with OAG and cataract. IOP was reduced from 20.0mm Hg to15.5mm Hg at year one, besides medications were reduced from 2.65 to 1.44 at 1 year. Complications were blood reflux in most patients (78.4%) [28].

Cataract surgery with ex-press shunt

Rivier and colleagues [31] conducted a small prospective case series (35 eyes, n= 35 patients) for the management of those with medically uncontrolled POAG or PXF glaucoma and cataracts. They performed combined phacoemulsification and implantation of the Ex-PRESS R-50. There was reduction in IOP from 19.3mm Hg preoperatively to 13.3mm Hg, and number of medications reduced (57% reduction) at 4 years of follow-up. Complications reported were conjunctival erosion and tube obstruction (each 11.4%); besides further surgery for tube removal was recommended in 28.6% (n=10 patients). The Ex-PRESS shunt device was placed underneath a partial thickness scleral flap instead of only underneath the conjunctiva to reduce rates of conjunctival erosion [31].

Traverso and coworkers [16] looked at the long-term results of the Ex-PRESS when placed subconjunctivally and combined with phacoemulsification surgery. They reported reduction of IOP at 35%, 29%, and 22% at 1, 2, and 3 years of follow-up, respectively. The overall surgical success, defined as IOP </21mm Hg with or without glaucoma medications, was reported to be 76.9%. Postoperative hypotony was reported in 6 eyes (with IOP <5mm Hg), which did not encounter further clinically adverse effects. Whereas erosion of the conjunctiva was reported in 3 eyes (11.5%). The authors determined that the Ex-PRESS implant is a clinically safe and effective procedure when performed with phacoemulsification surgery [16].

Cataract surgery with glaucoma drainage implant

Hoffman and coworkers [32] conducted a retrospective case series of 33 patients who performed combined phacoemulsification and Baerveldt glaucoma implant; they reported improvement in IOP control and reduction in glaucoma medications.

The commonest indication for the implant surgery was a precious unsuccessful trabeculectomy surgery [32].

Complications reported were tube retraction, recurrent uveitis, cystoid macular oedema, fibrin plugging of the tube, and macular striae and choroidal effusion.

Augmented phacotrabeculectomy is currently the most standard and the traditional choice for management of combined OAG and cataracts. If more lowering of IOP is required, then trabeculectomy alone may be suggested.

Cataract surgery alone may be the best option for those who require the quickest visual rehabilitation and minimal postoperative care and who do not object taking glaucoma medications. However, combining cataract surgery with one of the newer glaucoma techniques may be an option for those who require a mild to moderate reduction of IOP [32].

Discussion

The novel glaucoma surgical techniques and devices are still in the initial stage of clinical and surgical experience. Currently there are no sufficient published randomised studies comparing these novel procedures with trabeculectomy or with other novel procedures. Further, the literature is lacking studies comparing these novel glaucoma surgical procedures combined with phacoemulsification cataract extraction with cataract extraction alone. Thus, the clinical studies evaluated in this review are limited to the available published data and literature review on non-randomised, retrospective or prospective, interventional, clinical case series, generally classified as providing only level III evidence in support of the procedures. This review showed that the novel glaucoma procedures show some potential as alternative treatments to trabeculectomy in the management of OAG. Based on the favorable efficacy findings and high safety profile reported, MIGS with multiple iStent implantation has the potential to be a valid alternative to multiple medications for moderate glaucoma, as evidenced by the lower IOP and medication reduction [27].

Considering the apparently comparable efficacy and safety of the Ex-PRESS shunt and standard trabeculectomy procedures, surgeons should consider the economic difference between the two procedures. Longer-term, prospective and multi-centre studies would reveal whether the EX-PRESS glaucoma filtration device provides better safety and comparable efficacy compared to trabeculectomy for a wider population of patients.

Nevertheless, canal surgery does not lower IOP as much as in trabeculectomy. The Trabectome, Canaloplasty, and Trabeculotomy seem to lower IOP to clinically satisfactory levels with minimal reported complications.

A comparative clinical research conducted by O'Brart and co-workers revealed that IOP decreased more dramatically with augmented trabeculectomy as opposed to viscocanalostomy [33].

Trabectome is a preferable option in open angle patients and in those who do not require low IOP. If Trabectome surgery failed to control IOP to the desired level, or there is further glaucoma progression, then the surgeon could simply opt for the more traditional trabeculectomy without the problems of scarred conjunctiva [20].

However, Trabectome does have a learning curve but surgeons with goniotomy experience should transition rapidly. This surgery requires open angle. Narrow angles, with peripheral anterior synechiae, or non-pigmented trabecular meshwork will be tougher for Trabectome procedures [20].

Strengths and Limitations of the Study

Although this review was conducted in a thorough, methodical manner, it is possible that some studies may have been overlooked by not searching the 'grey' literature which refers to research that is either unpublished or has been published in non-commercial form, e.g. conference proceedings, pre-prints and post-prints of articles, theses and dissertations or research reports.

The review had judicious external validity-the studies identified comprised different glaucoma populations and various interventions. The search for studies covered the period between January 1985 and January 2019 and comprised different study designs and recruiting participants. However, the reviewer acknowledges the potential limitations of deficiency of RCTs, time frame and language restrictions.

Meaning of the study: Implications for clinicians and policymakers

Glaucoma specialists need to be aware that indications for MIGS are different and classically do not involve patients with very severe disease or those who need a very low postoperative IOP.

This work provided the clinicians and other academic researchers and reviewers with insight on glaucoma surgery, comparing the standard trabeculectomy procedure with the new armamentarium in glaucoma surgery. This would help the clinicians to better understand and manage their patients with more insight on decision-making for the management of their glaucoma patients.

Unanswered questions and recommendations for future studies

The current literature suggests that well-designed studies providing evidence-based comparisons of the trabeculectomy and the novel glaucoma procedures are lacking.

Conclusion

The studies provide the base for potential comparative and randomised trials of existing glaucoma surgical techniques and other novel procedures. It is not possible to conclude whether these new procedures are better, equal to, or substandard to trabeculectomy or to one another.

Larger long-term trials are therefore required to determine whether the novel glaucoma procedures have a better risk-benefit ratio compared with established augmented trabeculectomy surgery.

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Volume 12 Issue 12 December 2021