Title: Long Term Outcomes of Trabeculectomy Augmented with Mitomycin-C Undertaken within the First Two Years of Life

Running Head: MMC Trabeculectomy within the First Two Years of Life

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Conflict of Interest
No conflicting relationship exists for any author and all have no proprietary or commercial interest in any materials discussed.

Financial Disclosure(s)
HJ, CB, NGS, PTK and MP acknowledge a proportion of their financial support from the UK Department of Health through the award made by the National Institute for Health Research to Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology for a Biomedical Research Centre for Ophthalmology. Our work with Childhood Glaucoma is also supported in part by the Moorfields Special Trustees, Moorfields Eye Charity, Lady Helen Hamlyn, Michael and Ilsa Katz, Ron and Liora Moskovitz. HJ is currently supported by a fellowship awarded by the Fulbright Commission in association with Fight for Sight. The views expressed in this publication are those of the authors and not necessarily those of the UK Department of Health.

Précis

Contemporary pediatric trabeculectomy technique with mitomycin-C in phakic infants with glaucoma can be associated with long term IOP control off medications and with satisfactory visual outcomes.

Abstract

Purpose: To evaluate the long-term effectiveness and safety of mitomycin-C (MMC) augmented trabeculectomy undertaken within the first two years of life for the surgical management of glaucoma.

Design: Retrospective, consecutive, non-comparative case series.

Participants: All children who underwent MMC augmented trabeculectomy within two years of birth between May 2002 and November 2012.

Methods: The medical records of 40 consecutive eyes of 26 children who underwent surgery by a single surgeon were reviewed. Data collected during routine clinical care were analyzed.

Main Outcome Measures: Assessment of clinical outcomes included intraocular pressure (IOP), final visual acuity, bleb morphology, surgical complications (early and late), postoperative interventions and further glaucoma surgery performed. Surgical success was defined as 5mmHg ≤ final IOP ≤ 21mmHg, with anti-glaucoma medications (qualified success) and without (complete success), stable ocular dimensions and optic disc cupping, no further glaucoma surgery (including needling) or loss of light perception. Surgical outcomes were evaluated using Kaplan-Meier life-table analysis.

Results: 40 eyes of 26 children were studied over a mean follow up period of 62.8 months. The majority of cases (80%) were primary congenital glaucomas following failed goniotomy surgery. Cumulative probabilities of survival at 1, 5 & 7 years were 78%, 67% and 60% respectively. Of eyes regarded as successful, 96% (25/26 eyes) had controlled IOP off topical medication, and 44% achieved visual acuity of 20/40 or better. Only one of the 40 eyes developed a cystic avascular bleb with all the other eyes being non-cystic in nature (diffuse and elevated or flat) at final follow up. Sixty-four percent (9/14 eyes) of cases regarded as failures ultimately underwent glaucoma drainage device implantation.

Conclusions: Contemporary pediatric trabeculectomy technique augmented with MMC is an effective procedure in the management of glaucoma within the first two years of life, as shown by the successful long-term outcomes and low incidence of sight threatening complications. Trabeculectomy, following failed goniotomy surgery, or as a primary surgical intervention may offer a phakic infant with glaucoma an excellent opportunity to achieve long-term control of intraocular pressure off medications and be associated with optimal visual outcomes.

Introduction

Childhood glaucoma is an uncommon disorder characterized by elevated intraocular pressure (IOP) related damage to the eye that can be caused by a diverse group of conditions. The ultimate therapeutic goal in children with glaucoma is to provide a lifetime of vision, for which successful control of IOP is crucial. Medical therapy plays an important role in controlling IOP but the mainstay of treatment is surgery, which usually needs to be repeated[1-4]. Surgical intervention is often the case for glaucoma presenting in infancy, that is within the first two years of life. The surgical procedure of choice is largely determined by the type of glaucoma and may be further influenced by factors such as corneal clarity and the surgeon's experience and practice. The outcomes and longevity of surgical interventions may have a significant impact upon the future quality of life of both children and their families[5].

Primary congenital glaucoma (PCG) is the commonest glaucoma in infancy[1, 4] for which angle surgery (goniotomy or trabeculotomy) is widely regarded as the primary surgical intervention of choice[6] due to successful reported outcomes[7-9]. Poorer outcomes from angle surgery are usually reported for secondary childhood glaucomas[10, 11]. Traditionally, trabeculectomy was indicated following failed angle surgery. However, trabeculectomy surgery in children is especially challenging as it is less successful when compared to adults[12, 13] because of a vigorous healing response[14]. This has necessitated the use of adjunctive anti-scarring agents such as mitomycin-C (MMC) but at the cost of an increased risk of potentially serious complications such as hypotony and bleb related problems. [15-19] However even with MMC, the literature suggests disappointing outcomes for trabeculectomy in infants (especially less than one year of age) when compared to older children[15, 16, 18, 20] and also when compared to glaucoma drainage devices (GDD)[21]. GDD in children carry a significant risk of tube related problems such as tube-cornea touch in up to 26% cases[21-23] and tube migration or extrusion often necessitating the need for further tube related surgery

in up to a third of cases[3, 21]. Consequently, there is no consensus on the optimum surgery following failed angle surgery[6].

Contemporary trabeculectomy techniques involving fornix-based conjunctival dissection, releasable sutures and a wide area of anti-scarring application (a technique often described as the Moorfields Safer Surgery System)[24, 25] have evolved over the past 15 years with the aim of encouraging posterior aqueous flow and the development of diffuse drainage blebs. These changes were developed to reduce the high incidence of sight threatening complications, particularly bleb related problems, in children and subsequently applied to adult surgery. [26, 27] The aim of this study was therefore to evaluate the long-term safety and effectiveness of this surgical technique in infants undergoing trabeculectomy within the first two years of life.

Patients and Methods

The protocol for this project was granted institutional review board approval by the Clinical Audit Assessment Committee of Moorfields Eye Hospital. A retrospective case note review was performed on the records of all children aged two years or younger that underwent MMC augmented trabeculectomy by a single surgeon (MP) between May 2002 and November 2012. Some children underwent sequential surgery to both eyes but no simultaneous bilateral surgery was performed. In these situations, each individual eye was regarded as a separate data entity for the purpose of analysis. All cases had a minimum of 12 months of follow up.

Standard Surgical Technique

The surgical procedure involved the creation of a superior fornix-based conjunctival peritomy and a rectangular (5mm x 4mm) lamellar scleral flap with a crescent blade at the 12 o' clock position. Due to the very elastic nature of the infantile sclera, only short radial cuts were

made which enabled tight closure without the need to suture the radial edge of the flap whilst also encouraging posterior aqueous flow. A wide area of subconjunctival space (approximately 3 clock hours) was then treated with MMC soaked Merocel corneal shields (Beaver Visitec, UK), as was the undersurface of the scleral flap with a tear film strip (Sno-strips, Chauvin Pharmaceuticals Limited, UK) cut to size. MMC was applied at concentrations varying between 0.1-0.5mg/ml (at surgeon's discretion dependent upon risk factors for failure) for 3 minutes before irrigation with 20ml of balanced salt solution. 10-0 nylon (Alcon, UK) was used to preplace intralamellar scleral sutures, with a fixed suture at each corner and two releasable sutures at the posterior edge of the scleral flap. Following insertion of an anterior chamber (AC) maintainer (Lewicky, Beaver Visitec UK), the AC was entered at the anterior edge of the scleral bed. A 500μm sclerostomy was created with a Khaw Descemet membrane punch 7-101 (Duckworth & Kent, UK) followed by a surgical iridectomy. Further sutures were placed in the scleral flap, as required, with the aim of achieving no aqueous flow through the flap at the end of procedure. Tenonectomy was not performed. The conjunctiva was closed with 10-0 nylon sutures and in most cases a small volume of viscoelastic (usually Provisc® (Alcon, UK)) and sterile air were injected into the AC. Subconjunctival injections of steroid (Betamethasone) and antibiotic (Cefuroxime) were given at the end of the case. All eyes were patched overnight.

Postoperatively, all patients received daily intensive steroid drops (dexamethasone 0.1%) every 2-3 hours and ointment at night (Maxitrol – dexamethasone, neomycin sulfate and polymyxin b sulfate ointment). Topical steroids were gradually weaned over 3-5 months as dictated by the degree of conjunctival inflammation. Antibiotic drops (Chloramphenicol) four times a day were usually stopped within 2-3 weeks of surgery once all exposed sutures were removed. Cycloplegics were not routinely administered. Parents were advised to tape a plastic shield over the operated eye at night time for the first month after surgery.

Postoperative Management

All children were examined at 1 day, 1 week, three weeks and six weeks after surgery, with subsequent outpatient visits dependent upon clinical progress. Examination under Ketamine anesthesia (EUA) took place at 1, 3 and 6 weeks after surgery when releasable sutures were loosened or removed and subconjunctival steroid and/or 5-fluorouracil (5-FU) injections (0.2-0.3ml of 50mg/ml solution) administered depending upon the characteristics of the bleb and the degree of bleb inflammation. Measurements of corneal diameter and axial length were also performed. Subsequently, additional glaucoma surgery was undertaken in eyes uncontrolled by glaucoma medications.

Visual acuity, IOP, slit lamp biomicroscopy examining bleb morphology, anterior chamber depth, wound status and lens clarity were routinely performed along with evaluation of the optic nerve and retina at each postoperative visit. Quantitative visual acuity was measured when the child's age and developmental abilities allowed. IOP measurements were obtained using either Perkins applanation tonometry under Ketamine anesthesia, rebound tonometry (Icare, Finland) or Goldmann applanation tonometry as the children became older. Amblyopia was appropriately treated with refractive correction and a patching regime.

Outcome Measures

Surgical success was defined as IOP≤21mmHg and ≥5mmHg either with (qualified success) or without (complete success) topical glaucoma medications, no further glaucoma surgery (including bleb needling which was considered a failure), no devastating complications or the loss of light perception vision and stable ocular dimensions (axial length, corneal diameter) and optic disc cupping. Manipulation of the scleral flap (bleb massage), removal/adjustment of releasable sutures were not considered as criteria for failure, as these comprise routine post-surgical care with the technique employed. Complications and details of postoperative interventions following the initial trabeculectomy were noted.

Statistical Methods

Data analysis was performed using Graphpad Prism (Graphpad, USA). Demographic data were reported as the mean ± standard error with the range specified. Surgical success was evaluated by Kaplan-Meier life-table analysis. Survival curves between subgroups were compared using the log-rank (Mantel-Cox) test with Chi-Squared significance test. Parameters between the groups designated success and failure were compared using either a two-tailed unpaired *t*-test with Welch's correction or else by a Mann-Whitney Test, depending on whether the populations fitted a Gaussian distribution as shown by the D'Agostino & Pearson normality test. Retrospective contingency table analysis was performed using a two-tailed Fishers Exact Test. Statistical significance was considered for values at $p<0.05$.

Results

Patient Demographics and Preoperative Clinical Status

Forty consecutive eyes of twenty-six children were identified as having undergone MMC augmented trabeculectomy before two years of age within the designated study period. The full patient record was available for all the cases identified and the baseline demographic data of the group studied are summarized in Table 1. Children ranged in age from 1 to 19 months with a mean of 9.0 ± 0.8 months. All eyes were phakic and most had PCG that had undergone previous angle surgery in the form of goniotomy with a mean of 1.1 ± 0.1 procedures. Three eyes with PCG due to corneal edema and four eyes with secondary childhood glaucoma (2, AR anomaly and 2 aniridia) did not have goniotomies. Forty-one percent of infants with PCG had goniotomy repeated when the first goniotomy had reduced the IOP but to an unsatisfactory level. None of the secondary glaucoma cases had angle surgery repeated. The mean preoperative IOP was 24.2 ± 0.7 mmHg using an average of 2.1 ± 0.2 glaucoma medications, with no children receiving pre-operative acetazolamide. The population was predominantly white but 23% were of black descent.

Surgical Procedure and Follow-up Period

There was a standard surgical approach in all cases as detailed above, with intraoperative MMC administered at a mean concentration of 0.22 ± 0.02 mg/ml (range, 0.1 – 0.5mg/ml). Eighty-three percent of cases had either 0.1-0.2 mg/ml concentration of MMC during surgery. Higher doses of MMC, ie. 0.5mg/ml, were used in children of Black or Middle Eastern descent only. The mean duration of follow up in successful cases was 72.9 ± 5.7 months (range, 26-129 months) and failure was observed at a mean of 29.0 ± 8.2 months (range, 1-90) .

Surgical outcomes

A summary of the postoperative care and outcomes at the final follow up for groups designated as success or failure is shown in Table 2.

Twenty-six of forty eyes (65.0%) were considered successful at the time of last follow up, of which 62.5% (25/40 cases) were regarded as a complete success and 2.5% (1/40 cases) a qualified success with the use of topical medication. The mean postoperative IOP at the last follow up visit for all successful eyes was 11.9 ± 0.7 mmHg with a mean reduction of 48.8% ± 4.0% from the preoperative baseline. Eyes classed as failures had a mean IOP of 23.4 ± 1.2 mmHg at the time of failure and achieved a mean final IOP of 14.5 ± 1.0 mmHg with a 38.4% ± 5.1% reduction from baseline after additional surgery. In addition to the IOP reading, glaucoma progression was determined by clinical signs and biometric parameters. Nine out of the fourteen failures had releasable sutures removed within the first 6 weeks and in seven this was also associated with needling. There was no significant difference between the dose of MMC, duration of postoperative topical steroids, the number of EUAs, 5-fluorouracil (5-FU) or steroid injections administered to those deemed successful and those considered failures.

Kaplan-Meier life-table analysis (Figure 1) demonstrated a mean cumulative probability of success (95% confidence interval) at 6 months and 12 months (1 year) of 0.80 (0.64-0.89) and 0.78 (0.61-0.88) respectively. The cumulative probabilities of success at 60 months (5 years) (modelled on 18 eyes) and at 87 months (7.3 years) (modelled on 9 eyes) after surgery were 0.67 (0.49-0.80) and 0.60 (0.38-0.76) respectively. When analyzed according to age at surgery, there was a trend towards greater success rates at the end of follow up observed in those twelve months or younger (70.4%) compared to of those over twelve months of age (53.8%). There was no difference in underlying diagnosis between the two groups. Life-table analysis comparing outcomes of cases of primary congenital glaucoma to those with secondary childhood glaucoma showed no significant difference in survival between these etiologies over the course of follow up (Figure 2).

Data from all eyes (including 14 children with both eyes included in the study) were used for analysis. There is potential for introducing bias by analyzing fellow eyes as independent entities. In order to address this, we performed Cox Regression allowing for clustering, which produced similar results to those found ignoring non independence. Of the 14 children who had two eyes included in the study, failure was observed in both eyes in 2 children, success was observed in both eyes in 5 children. The remaining children failed in one eye but were successful in their fellow eye. A test for symmetry was conducted (p=0.7) indicating little evidence of an association (albeit with low power). These observations would suggest that our findings are robust to non-independence and justify the inclusion of data from all eyes in the analyses presented.

Final visual acuity in all eyes studied was 0.69 ± 0.1 with 34.2% achieving the equivalent of 20/40 or better, 89.5% seeing 20/200 or better and with no cases of loss of light perception. Almost half the children with successful outcomes had visual of acuity of 20/40 or better.

Surgical Complications and Postoperative Interventions

There were no recorded cases of hyphema, flat AC, early or late bleb leak, chronic hypotony, endophthalmitis or retinal detachment observed in this series. Choroidal effusions in the presence of a shallow AC and low IOP were observed in four cases (10%) with B-scan ultrasound routinely performed at one week after surgery. Only one of the cases was with the use of MMC 0.5mg/ml. Two cases resolved following intracameral viscoelastic injection, one case did not resolve following intracameral viscoelastic injection and underwent re-suturing of the scleral flap and the fourth resolved with conservative management. All four cases went on to have a successful outcome.

Only one of the 40 eyes developed a cystic avascular bleb with all the other eyes being non-cystic in nature (diffuse and elevated or flat). This specific case also suffered blebitis ten years after trabeculectomy although it responded well to topical and systemic antibiotic treatment alone with no change in IOP control or visual acuity. Diffuse, elevated bleb morphology was noted in 63% of eyes (25 eyes) and 35% (14 eyes) had a flat appearance, of which 86% (12 eyes) were observed in eyes classes as failures.

The presence of cataract, usually a small posterior subcapsular cataract, was noted in 20% (8/40) of all eyes across the study group. The presence of cataract was observed in 11.5% (3/26) eyes) in the group deemed to be successful at the end of follow up at a mean of 33.7 $\pm$ 14.4 months after trabeculectomy surgery. None of these patients required cataract surgery as their vision was not thought to have been significantly impacted by the cataract to warrant surgery (one case had visual acuity of 0.1 and the other 2 cases were unchanged at 0.8 and 0.9). The majority of observed cataract formation (5/8 cases), including a single case that required surgery, occurred in the failure group at a mean of 56.4 $\pm$ 10.5 months after trabeculectomy surgery. In these cases, cataract development occurred after further glaucoma surgeries in all cases (3 cases of needling followed by Baerveldt tube insertion, 1

case of needling followed by repeat trabeculectomy with MMC 0.5mg/ml adjacent to the original, 1 case of needling followed by cyclodiode laser).

Reasons for Failure

Postoperative interventions across the study group are summarized in Table 3. The fourteen eyes that failed all did so because of uncontrolled IOP requiring further intervention. All eyes that were considered as failures, were due to bleb needling being performed. These were performed at a mean 28.2 ± 7.5 months after trabeculectomy with an average of two needlings performed per eye. Needling alone controlled the IOP in only 21.4% (3/14 eyes) of cases. Ultimately, after failed needlings (11/14 eyes), eight eyes underwent Baerveldt implant insertion, one eye underwent a repeat trabeculectomy with MMC 0.5 mg/ml, one eye required cyclodiode laser treatment and one eye underwent cyclodiode laser followed by Baerveldt implant insertion. There was a significant association with bleb needling and further glaucoma surgery being performed (p<0.0001). However despite this group being regarded as failures, they did achieve a mean final IOP of 14.5±1.0 mmHg with a mean 38.4 ± 5.1% reduction of IOP from baseline with no loss of light perception vision, indicating that needling procedures and subsequent surgeries were largely successful in the restoration of intraocular pressure control.

Discussion

Trabeculectomy has traditionally been the procedure of choice after failed angle surgery to control IOP in children. But in contrast to adults, trabeculectomy surgery in children is associated with poorer outcomes[12, 13] due to a more aggressive healing response[14] and the potential challenges of reduced compliance and lack of co-operation with examination. Nonetheless, success of MMC trabeculectomy in children has been reported to be 59-95% (IOP $\leq$ 21mmHg) with short follow up of 2 years or less[15-18, 20, 28] reducing to 55% after 6 years mean follow up[29]. All these studies are retrospective which makes comparison difficult

as success is influenced potentially by a number of factors such as: definition of success, patient's age and race, case mix (primary and secondary glaucomas), inclusion of non phakic patients, previous surgery, surgical technique, dose and duration of MMC, use of 5-FU post operatively and duration of follow up.

In a number of studies, infancy has been shown to be a significant risk factor for failure. Reported outcomes of trabeculectomy in infants less than one year of age vary between 15-43%[15, 16, 18, 20]. Beck *et al*[20] reported that being aged less than 1 year at the time of surgery was associated with almost a six-fold risk of failure. For infants less than 2 years of age, Beck *et al*[21] reported a cumulative success rate of 36% (IOP < 23mmHg with medications) in 24 eyes at 1 year which dropped to only 19% at 6 years in a group with both primary and secondary childhood glaucoma which included aphakic and pseudophakic patients. In a larger series, Al Hazmi *et al* described a success rate of 39% (IOP < 21mmHg without topical medications) in 66 eyes (unreported follow up) in a study population mostly of PCG patients from the Middle East[15].

In comparison, our long-term outcomes of trabeculectomy with MMC for glaucoma presenting in infants less than 2 years of age are more encouraging, with a cumulative probability of success at one and seven years of 78% and 60% respectively. Almost all successful cases (25/26; 96%) were not using topical IOP lowering medications at final follow up. In infants less than one year of age, 70% were successful at the end of follow up.

The significant difference in outcomes of our study compared to published reports may relate to a number of factors. Our study group was predominantly white, PCG cases and included no patients with aphakia /pseudophakia or previous surgery involving the conjunctiva, both known to be significant risk factors for trabeculectomy failure[13, 20, 30-33]. The pre-operative IOP in our series was lower than in comparable series which may have contributed to improved outcomes. Furthermore surgical technique, namely MMC treatment

under the scleral flap also performed by other authors[15, 18] and close post-operative management with further subconjunctival 5-FU and steroid may have also played a role. It is likely the intensive post-operative bleb management achieved early diffuse posterior aqueous flow, which contributed to successful long-term outcomes. Although it could be argued that a significant number of EUAs were necessary, this has to be seen within the context of overall results and that in successful cases (65%) one operation was all that was necessary to achieve glaucoma stability over the duration of follow up. In comparison, Taylor and colleagues[1] describe children with PCG (117 patients) requiring on average of 4.3 $\pm$ 3.8 (range 0-23) operations over a 20 year observation period to manage their glaucoma.

Trabeculectomy surgery in young children has fallen out of favor not only because of reported poor outcomes but also because of the association with significant surgical complications including flat anterior chambers (10%), choroidal effusions (22%), suprachoroidal hemorrhage, retinal detachments and phthisis[18, 20]. In particular, thin avascular, cystic blebs commonly occurred,[16,18] predisposing to bleb related infection such as endophthalmitis (5-8%)[20, 29],and chronic late, bleb leaks (23%)[16]. As a consequence, contemporary pediatric trabeculectomy techniques have evolved in recent years from those used by comparative papers (e.g. limbus-based conjunctival flap and fixed sutures) with the aim of reducing the burden of complications.[24, 25,27] All cases in this series were performed using a standardized technique based on the Moorfields Safer Surgery System [24, 25] aimed at achieving posteriorly directed aqueous flow. Specific modifications for pediatric trabeculectomies include limited radial cuts to avoid anterior limbal flow and excessive flow through the flap, MMC treatment under the scleral flap as well as the subconjunctival tissue and the use of an AC maintainer in all cases.

In our study the commonest early complication was choroidal effusion at one week after surgery in 10% (4/40 eyes), which is lower than the published literature which ranges from

17-23%.[16, 20, 21] Susanna *et al*.[18] reported a 5% rate of choroidal detachment but suspected it was higher some eyes with shallow anterior chambers were not fully dilated when examined. Our observed rate of cataract development in the cohort with successful outcome (11.5% - none requiring surgery) was comparable to the existing literature for the same duration of follow up[21].

The accepted alternative to trabeculectomy following failed angle surgery is the insertion of a glaucoma drainage device (GDD). Only a few studies specifically evaluate the performance of GDD in the infant population. Success rates at one year are reported at 74-87%[21, 34] with 53% survival at 6 years after surgery[21]. Our trabeculectomy outcomes are comparable although direct comparison is difficult due to the presence of aphakic glaucoma cases in these populations. However the major difference between our findings and those reported following tube surgery is the significant associated complications often requiring surgical revision. Beck et al reported 45.7% of eyes with a GDD required one or more operations due to a complication related to the implant (most commonly tube corneal touch and exposure), in contrast to 12.5% of eyes in trabeculectomy group[21]. Tube malposition, erosion and endophthalmitis are consistently reported with greater frequency in the pediatric compared to adult population [3]. Tube malposition requiring further surgery has been reported in 26-35% of cases[21, 34]. These studies also reported corneal decompensation (9%), vitreous hemorrhage (7%), endophthalmitis (7%) and retinal detachment (7%) following GDD surgery. Overall, complications in our series were fewer than reported in comparable literature following trabeculectomy and glaucoma drainage device surgery. This is important as the technique is simple and does not require expensive special equipment. Furthermore of significance, the need for medications appears to be higher following GDD compared to trabeculectomy.[20] In one study, only 14% of infants undergoing GDD surgery achieved IOP control without topical medications[34] compared to 62.5% (25/40) of our trabeculectomy cases.

Criteria for success in glaucoma are largely based on IOP related parameters and the absence of serious complications. However, the preservation of visual function is the goal in these children and is influenced by factors other than IOP, such as corneal clarity, refractive status and amblyopia which must also be addressed. In our study, final overall visual acuity outcomes of 34.2% seeing 20/40 or better, 89.5% seeing 20/200 or better and no cases of loss of light perception were very encouraging and comparable to other published reports.[35]

This study is limited by the retrospective nature of the analysis and with the study population comprising predominantly cases of primary congenital glaucoma. A randomized, multicentre trial comparing MMC trabeculectomy and GDD would be of interest, as would a study on the optimal MMC application method, concentration and duration.

In conclusion, this study demonstrates that MMC augmented trabeculectomy using simple contemporary trabeculectomy techniques is an effective option in the management of glaucoma within the first two years of life, as shown by the successful long-term outcomes and low incidence of sight threatening complications. After failed goniotomy surgery or as primary surgery for phakic secondary childhood glaucoma cases, trabeculectomy may offer an infant with glaucoma an excellent opportunity to achieve long-term control of intraocular pressure off medications and optimal visual outcomes. The close post-operative monitoring and need for regular EUA required to achieve these results in comparison to GDD surgery is balanced by the significantly lower surgical re-intervention rate and dependence on medication for IOP control. Should failure occur later in life, the opportunity for GDD still exists and the potential complications of such surgery will be delayed, perhaps beyond the more critical period of visual maturation.

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Tables and Figures

Table 1. Baseline Demographic Information

Patients	26
Eyes	40
Age (range (mean ± SE))	1 – 19 months (9.0 ± 0.8 months)
Number of previous goniotomies (mean, SE)	1.1 ± 0.1
Diagnosis (n, %)	
Primary Congenital Glaucoma	32 (80%)
Axenfeld-Rieger Anomaly	4 (10%)
Aniridia	2 (5%)
Naevus of Ota	1 (2.5%)
Cutis Marmorata Telangectasia	1 (2.5%)
Ethnicity/Race (n, %)	
White	26 (65%)
Black	9 (22.5%)
Asian	3 (7.5%)
Middle Eastern	1 (2.5%)
Mixed	1 (2.5%)
Number of topical pre-operative medications (mean, SE)	2.1 ± 0.2
Pre-operative IOP (mean, SE)	24.2mmHg ± 0.7

SE= standard error
IOP= intraocular pressure

Table 2. Summary of Final Follow up

	Total	*Success*	*Failure*
Eyes	40	26 (65%)	14 (35%)
Time to final follow up (months)	62.8 ± 5.7 (Range 1-129)	72.9 ± 5.7 (Range 26-129)	29.0 ± 8.2 (†***) (Range 1-90)
Mean concentration of MMC (mg/ml)	0.22 (range 0.1-0.5)	0.22 (range 0.1-0.5)	0.23 (range 0.1-0.5)
Number of EUAs	3.6 ± 0.2	3.5 ±0.2	3.9 ± 0.3
Number of Needlings	0.7 ± 0.2	0	1.9 ± 0.2(†**)
Releasable Sutures Removed/Adjusted	11/40 (27.5%)	2/26 (7.7%)	9/14 (64.3%)
Number of Steroid Injections	2.0 ± 0.2	1.8 ± 0.2	2.5 ± 0.4
Number of 5-FU injections	2.1 ± 0.2	1.8 ± 0.2	2.6 ± 0.4
Duration of postoperative topical steroids (months)	3.2 ± 0.3	3.1 ± 0.3	3.4 ± 0.5
IOP at Failure (mmHg)			23.4 ± 1.2
Final IOP (mmHg)	12.8 ± 0.6	11.9 ± 0.7	14.5 ± 1.0 (‡*)
Mean % IOP Reduction from Baseline	45.2% ± 3.2	48.8% ± 4.0	38.4% ± 5.1(†*)
Final VA (logMAR)	0.69 ± 0.1	0.41 ± 0.1	1.2 ± 0.3 (†**)
20/40 or better	34.2% (13/38)	44.0% (11/25)	15.4% (2/13)
20/200 or better	89.5% (34/38)	92.0% (23/25)	69.2% (9/13)

Data shown as mean ± standard error

Table 2. Summary of data at final follow up denoting observations of the total sample (40 eyes), eyes classified as having successful outcomes and eyes classified as failure. The populations of successful eyes and those classified a failure were tested for normality using the D'Agostino & Pearson normality test and compared with a two-tailed unpaired t-test with Welch's correction (‡) if normality was shown else with a Mann-Whitney test (†). Observed significant differences are indicated in the table (*** $p<0.0004$; ** $p<0.0032$; * $p<0.04$). (EUA = Examination under anesthesia; 5-FU = 5-Fluorouracil; MMC = Mitomycin-C; VA = visual acuity; IOP = intraocular pressure)

Table 3. Post-operative Surgical Interventions

Scleral flap resuture	1/40 (2.5%)
Bleb needling	12/40 (30.0%)
Repeat Trabeculectomy	1/40 (2.5%)
Cyclodiode Laser	2/40 (5.0%)
Aqueous Shunt Insertion	9/40 (22.5%)

Table 3. Summary of postoperative procedures performed across all eyes during the follow up period. A single case of early hypotony unresponsive to an anterior chamber injection of viscoelastic required scleral flap re-suture and went on to be a success.

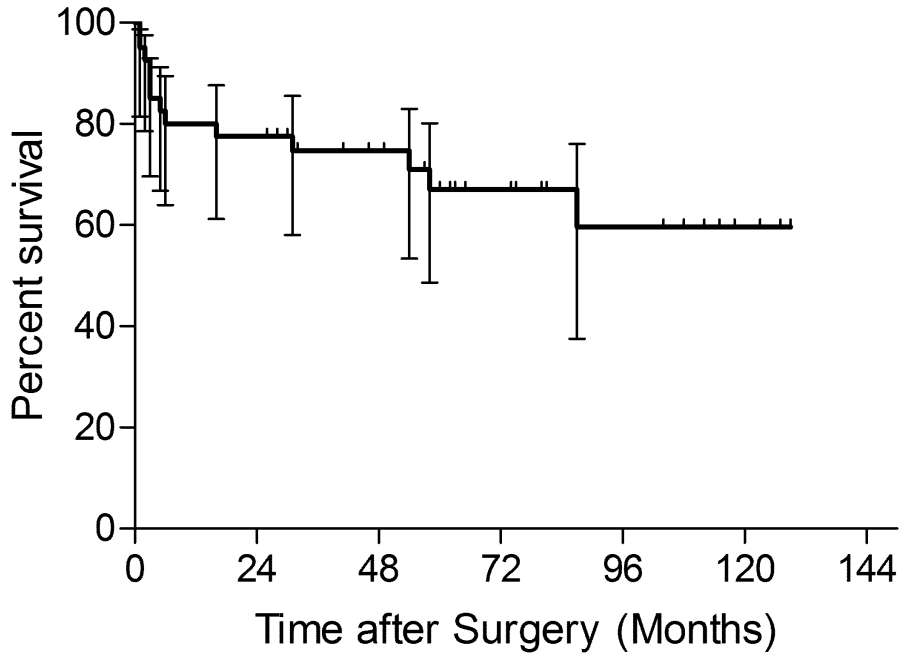

Figure 1. Cumulative surgical success after Mitomycin augmented trabeculectomy in infants by Kaplan-Meier life-table analysis. Plotted is the probability of success vs follow-up time (error bars represent the 95% confidence interval). Mean cumulative probabilities of success (95% confidence interval) at 6 months and 12 months (1 year) were 0.80 (0.64-0.89) and 0.78 (0.61– 0.88) respectively. The cumulative probabilities of success at 60 months (5 years) and at 87 months (7.3 years) after surgery were 0.67 (0.49–0.80) and 0.60 (0.38–0.76) respectively.

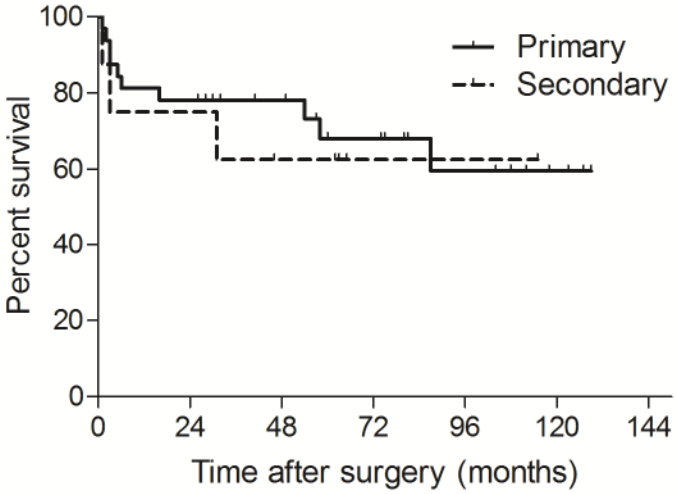

Figure 2. Cumulative surgical success by etiology after Mitomycin augmented trabeculectomy in infants by Kaplan-Meier life-table analysis. Plotted is the probability of success vs follow-up time for primary congenital glaucoma (solid line) and secondary glaucomas (dotted line). The two curves were not significantly different when compared using the log-rank (Mantel-Cox) test.