

## Update on Congenital Glaucoma

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### ABSTRACT

**Background:** primary infantile glaucoma, commonly termed congenital glaucoma or trabeculodysgenesis, is an unusual, inherited congenital anomaly of the trabecular meshwork and anterior chamber angle which leads to obstruction of aqueous outflow, increased intraocular pressure, and optic nerve damage. Primary congenital glaucoma is a worldwide diagnostic and therapeutic challenge. Although medical management is often a temporizing measure, early surgical intervention is the definitive treatment.

**Keywords:** Congenital glaucoma, Goniotomy, Trabeculotomy, Trabeculectomy, Glaucoma drainage implants, Cyclodestructive procedures, Deep sclerotomy.

### INTRODUCTION

It is thought that goniotomy was first described in 1893 by Carlo de Vincentiis; however it was performed without visualization of the angle and resulted in poor outcomes<sup>(1)</sup>. It was not until 1938 when Otto Barkan performed the first goniotomy utilizing gonioscopy and a knife to incise the trabecular tissue<sup>(2)</sup>. Although goniotomy was difficult or impossible in eyes with significant corneal edema, it became the standard of treatment for PCG. Trabeculotomy, which could be performed in the presence of corneal opacity, was later developed by Smith in 1960<sup>(3)</sup>.

Laser therapy has a limited role in developmental glaucomas. The most effective and definitive form of treatment of most developmental glaucoma is surgical trabeculotomy, although combined trabeculotomy with trabeculectomy may be useful in certain populations with a high risk of failure of goniotomy or trabeculotomy. Refractory pediatric glaucomas may be managed by trabeculectomy with anti-fibrosis drugs, glaucoma drainage implants and cyclodestructive procedures<sup>(4)</sup>.

Deep sclerotomy non penetrating surgery has attracted more interest during last two decades for its potential to decrease IOP without some of immediate postoperative hypotony and long term bleb complication of traditional filtering surgery<sup>(4)</sup>.

The study was approved by the Ethics Board of Al-Azhar University.

### Developmental Glaucoma:

Axenveld-Rieger syndrome and aniridia are both inherited in an autosomal dominant manner. Approximately 50% of individuals who carry genetic mutations will develop early-onset glaucoma. Mutations in the PITX2 and FOXC1 genes are associated with Axenveld-Rieger syndrome, and PAX6 mutations cause aniridia and Peters anomaly. Each of these genes encodes

transcription factors involved in the eye's development. Genetic testing is available for all three genes. A novel therapy for aniridia is being investigated that is based on the molecular biology of PAX6 genetic mutations<sup>(5)</sup>.

Ataluren is an investigational new drug that works by reducing ribosomal sensitivity to premature stop codons. Postnatal topical application of a drug formulation containing ataluren can reverse corneal, lenticular, and retinal defects in a mouse model of aniridia, which suggests that ataluren may be available therapeutic option for patients with PAX6 genetic mutations<sup>(6-7)</sup>.

### Management:

#### a-Medical therapy:

As discussed, medical therapy usually plays a supportive role.

**Beta-blockers:** Beta-blockers reduce IOP by decreasing aqueous secretion. Timolol in 0.25% and 0.5% solutions maybe used cautiously in young glaucoma patients. The drug should be used with extreme caution in neonates due to the possibility of apnea and other systemic side effects. Cardiac abnormalities and bronchial asthma should be specifically excluded before its use. Use of 0.25%, rather than 0.5%, is recommended in children in order to reduce its side effects; however, the 0.25% formulation is not widely available. Hence, 0.5% timolol can be used with punctal occlusion. For this reason, selective beta-blocker (e.g., betaxolol) is preferred over non selective ones<sup>(8-9)</sup>.

**Carbonic anhydrase inhibitors (CAIs):** are chemically related to sulfonamides. They lower IOP by inhibiting aqueous secretion. Systemic CAIs would be expected to have similar side effects in children as compared to adults. In addition, growth suppression in children has been associated with oral acetazolamide therapy, and infants may experience a severe metabolic acidosis. Topical versus oral CAI therapy has been evaluated for pediatric glaucoma in

a crossover design study. The mean IOP was reduced by 36 and 27% compared with baseline, after treatment with oral acetazolamide and topical dorzolamide, respectively. All eyes showed an increase in IOP when switched from systemic acetazolamide to topical dorzolamide, with a mean increase of 3.7 mmHg. At present, topical CAIs are more commonly prescribed compared with systemic CAIs. For older children, the fixed combination of dorzolamide with timolol may simplify medical regimen, reducing the number of drops instilled per day<sup>(10)</sup>.

**Prostaglandin analogues:** This group has sustained IOP lowering effect which probably extends for several days. Latanoprost are F2-alpha analogues that as selective agonists of the FP prostanoid receptor, both of these enhance aqueous outflow through uveoscleral route. Some studies on children show a significant ocular hypotensive effect with latanoprost<sup>(11)</sup>.

Parents should be advised about the possibility of local side effects, including iris pigmentation, eyelash elongation and hyperemia<sup>(11)</sup>.

**Alpha-2 agonists:** decrease IOP by both decreasing aqueous secretion and enhancing uveoscleral outflow. Because of central nervous system mediated side effects, brimonidine should be used with caution in pediatric patients, and only be used in older children<sup>(12-13)</sup>.

**Other drugs:** In pediatric patients, the use of pilocarpine is limited. Osmotic drugs like mannitol may be administered to reduce the IOP before surgery in patients with developmental glaucoma with IOPs that are high even with standard medical therapy<sup>(14)</sup>.

## **b- Surgical treatment:**

### **Angle Surgeries:**

Angle surgery is the first procedure for patients with the following features: no other ocular or systemic abnormalities, disease noted before one year of age, and with corneal diameters less than 14mm.

Angle surgery consists of either goniotomy or trabeculotomy ab externo. Goniotomy (if the cornea is clear enough for adequate visualization of the goniotomy knife passing across the anterior chamber and incising the trabecular meshwork) or trabeculotomy ab externo if the cornea is cloudy enough to preclude a safe goniotomy (or when the surgeon prefers this technique due to prior training or more experience with the procedure even when the cornea is clear). Both procedures presumably work by allowing a more direct access of aqueous humor into Schlemm's canal and the outflow system<sup>(15)</sup>.

### **Goniotomy:**

Goniotomy represented an important breakthrough in ophthalmology because for the first time it was possible to treat congenital glaucoma in a successfully and reasonably safe way. Although initially used by De Vincentis, in 1893 for all type of glaucoma, the pioneering work of Dr. Barkan<sup>(15)</sup> and others, with gonioscopy to perform successful goniotomies.

### **Trabeculotomy:**

Trabeculotomy first described by Burian in 1960 who unroofed Schlemm's canal through an incision radial to the limbus and entered it with a specially made instrument that he called trabeculotome. He called the procedure trabeculotomy ab externo in contrast to goniotomy which was considered a trabeculotomy ab interno. In 1966, Harms modified the technique by dissecting a superficial scleral flap similar to the one used in trabeculectomy and then making the radial incision to identify Schlemm's canal and opening it with a modified instrument (Harm's trabeculotome)<sup>(16)</sup>.

Some believe that 360-degree trabeculotomy with a lighted probe offers significant advantages over the traditional trabeculotomy technique in children. In contrast with traditional trabeculotomy, this procedure adds certainty with regards to adequate identification and probing of Schlemm's canal for the whole 360-degree circumference in a single session<sup>(17)</sup>.

### **Trabeculectomy:**

Trabeculectomy is a procedure that most ophthalmologists are familiar with and is technically easier than goniotomy or trabeculotomy, and it has been advocated by some as a primary procedure in congenital glaucoma. Its mechanism of action is bypassing the aqueous from the anterior chamber to a subconjunctival fistula<sup>(18)</sup>. The modifications that have been suggested to improve the outcome of this surgery in pediatric patients have been the use of a fornix base flap because of its lower rates of bleb-related infections, use of releasable sutures, and use of Healon GV left into the anterior chamber at the end of the procedure to prevent early postoperative hypotony and shallow anterior chamber<sup>(19, 20)</sup>.

### **Combination Trabeculotomy Ab Externo and Trabeculectomy**

The intended mechanism of action for combining these two procedures is to gain access to dual outflow, through Schlemm's canal and/or the trabeculectomy fistula<sup>(21)</sup>.

### **Glaucoma Drainage Implants (GDIs):**

Glaucoma drainage implant has role in managing infants and other children with glaucoma refractory to angle surgery and trabeculectomy. The first

glaucoma drainage implant used in the pediatric population was the Molteno implant in 1973, followed by the Baerveldt implant and Ahmed valve implant (AGV). The Ahmed valve implant has a unidirectional valve restriction flow mechanism, designed to open when the aqueous pressure is higher than 8mmHg. This is highly effective in reducing the risk of early postoperative hypotony compared to nonvalved implants (Molteno, Baerveldt), which require special surgical maneuvers to reduce the flow or a two-stage procedure to avoid this problem. Baerveldt, and Ahmed implants have been the most common devices used in children<sup>(22)</sup>.

#### **Cyclodestructive Procedures:**

Cyclodestructive Procedures in pediatric glaucoma are usually used for those challenging cases that have failed multiple more conservative treatments and for those patients with anatomic abnormalities that preclude traditional surgeries. Their mechanism of action is through ablation of the ciliary body and resultant reduction of aqueous production<sup>(23)</sup>.

**-Cyclocryotherapy:** This procedure decreases the intraocular pressure by freezing and destroying the ciliary body epithelium. Although cyclocryotherapy was utilized for refractory and poor visual potential pediatric patients, it is not a preferred cyclodestructive procedure any longer because it has been gradually replaced by less aggressive and more targeted procedures such as laser cyclophotocoagulation which result in less inflammation and complications<sup>(23)</sup>.

#### **-Transcleral Diode Laser Cyclophotocoagulation:**

Transcleral diode laser cyclophotocoagulation had a convenient compact design and less side effects, in particular avoiding the occurrence of sympathetic ophthalmia, a dreaded complication of YAG transcleral cyclophotocoagulation<sup>(24)</sup>.

#### **Endolaser Cyclophotocoagulation (ECP)**

First described by Uram in 1992 for neovascular glaucoma, this procedure accomplishes cycloablation through direct visualization. It uses a 20 gauge instrument, with endoscopic view through a monitor and a diode laser treating each individual ciliary process until whitening and shrinkage is observed<sup>(25)</sup>.

#### **Deep Sclerectomy:**

Deep sclerectomy is non penetrating surgery has attracted more interest during the last decade for its potential to decrease intraocular pressure without some of the immediate postoperative hypotony and long-term bleb complications of traditional filtering

surgery<sup>(4)</sup>. The procedure involves the dissection of a deep scleral flap, deroofing of Schlemm's canal, and preserving the structural integrity of the trabecular meshwork. Its mechanism of action is not entirely clear, but a combination of a more diffuse filtering bleb formation and uveoscleral and transcleral flow have been cited<sup>(26)</sup>. It has been proposed by some as an alternative to other procedures in high risk pediatric glaucoma cases such as Sturge-Weber syndrome, where it is desirable to minimize sudden hypotony and the resultant possibility of massive choroidal serous or hemorrhagic detachments, which can lead to catastrophic outcomes<sup>(27)</sup>.

#### **Viscocanalostomy:**

The American Academy of Ophthalmology<sup>(28)</sup> (AAO, 2001) stated that non-penetrating glaucoma surgery (viscocanalostomy is one of the 2 major variations of this procedure) has the potential to reduce IOP while minimizing the risk of postoperative relative hypotony and the complications associated with hypotony.

Although there are a variety of viscocanalostomy techniques, the procedure basically involves production of superficial and deep scleral flaps, excision of the deep scleral flap to create a scleral reservoir, and unroofing of Schlemm's canal. A high-viscosity viscoelastic, such as sodium hyaluronate, is used to open the canal and create a passage from a scleral reservoir to the canal. The superficial scleral flap is then sutured watertight, trapping the viscoelastic until healing takes place<sup>(28)</sup>.

#### **Viscocanaloplasty:**

Recently, a glaucoma canaloplasty (enhanced viscocanalostomy) has been introduced, which involves modification of the viscocanalostomy procedure. Canaloplasty uses viscoelastic and a specialized micro catheter to forcibly open the Schlemm's canal. The procedure is intended to restore the natural drainage of fluid from the eye, thus reducing IOP in persons with glaucoma<sup>(29)</sup>.

#### **CONCLUSION**

The management of pediatric glaucoma in its different forms is still quite challenging. The visual and long-term results variable depending on the severity and type of disease. The number and type of newer surgical procedures and modifications to traditional ones have improved our choices and capability to treat this condition. Although it is generally agreed that angle surgery is the best initial approach for milder cases of primary congenital glaucoma, the surgical procedure to use for more severe cases, secondary glaucomas, or failed angle surgery cases is less clear cut.

## REFERENCES

1. **Mandal AK and Chakrabarti D(2011):** "Update on congenital glaucoma," *Indian Journal of Ophthalmology*, 59 (1): S148–S157.
2. **Ou Y and Caprioli J(2012):** "Surgical management of pediatric glaucoma." *Developments in Ophthalmology*, 50: 157–172.
3. **Smith R (1960):** "A new technique for opening the canal of Schlemm. Preliminary report," *The British Journal of Ophthalmology*, 44: 370–373.
4. **Razeqhinejad MR, Fudemberg SJ, and PAETH GLS (2012):** "the changing conceptual basis of trabeculotomy; a review of past and current surgical techniques" *survey of ophthalmology*, 57(1):1-25.
5. **Ton CC, Hirvonen H, Miwa H et al.(1991):** Positional cloning and characterization of a paired box- and homeobox-containing gene from the aniridia region. *Cell*, 67(6): 1059-1074.
6. **Gregory-Evans CY, Wang X, Wasan KM et al.(2014):** "Postnatal manipulation of Pax6 dosage reverses congenital tissue malformation defects." *Journal Clinical Investigative*, 124(1): 111-116.
7. **Sahel JA, Marazova K(2014):** Toward postnatal reversal of ocular congenital malformations. *Journal Clinical Investigative*, 124(1): 81-84.
8. **Samant M, Medsinghe A, Nischal KK(2016):** Pediatric glaucoma: Pharmacotherapeutic options, 18(3):209.
9. **Hoskins HD, Jr, Hetherington J, Jr, Magee SD, Naykhin R, Migliazzo CV(1985):** Clinical experience with Timolol in childhood glaucoma. *Archives Ophthalmology*, 103: 1163–5.
10. **Portellos M, Buckley EG, Freedman SF(1998):** Topical versus oral carbonic anhydrase inhibitor therapy for pediatric glaucoma. *Journal AAPOS.*, 2: 43–7.
11. **Enyedi LB, Freedman SF, Buckley EG(1999):** The effectiveness of Latanoprost for the treatment of pediatric glaucoma. *J AAPOS.*, 3: 33–9.
12. **Enyedi LB, Freedman SF(2001):** Safety and efficacy of brimonidine in children with glaucoma. *Journal AAPOS.*, 5: 281–4.
13. **Bowman RJ, Co. pe J, Nischal KK(2004):** Ocular and systemic side-effects of brimonidine 0. 25% eye drops (Alphagan in children) *Eye*, 18: 24–6.
14. **Epstein DL, Allingham RR, and Schuman JS(1996):** Chandler and Grant's Glaucoma, chapter 70 (Freedman SF), Williams and Wilkins, Baltimore, Md, USA, 4th edition. <https://www.amazon.com/Chandler-Grants-Glaucoma-Malik-Kahook/.../1556429541>
15. **Barkan O(1938):** "Technique of goniotomy," *Archives of Ophthalmology*, 19: 217–221.
16. **Burian HM(1960):** "A case of Marfan's syndrome with bilateral glaucoma. With description of a new type of operation for developmental glaucoma (trabeculotomyabexterno)," *American Journal of Ophthalmology*. 50(6): 1187–1192.
17. **Jose Morales, Sami Al Shahwan, Sami Al Odhayb, Ibrahim Al Jadaan, and Deepak P. Edward(2013):** "Current Surgical Options for the Management of Pediatric Glaucoma". *Journal of ophthalmology*. article ID763735. <https://www.hindawi.com/journals/joph/2013/763735/>
18. **Fulcher T, Chan J, Lanigan B, Howell R, and O'Keefe M(1996):** "Long term follow up of primary trabeculectomy for infantile glaucoma," *British Journal of Ophthalmology*, 80(6): 499–502.
19. **Wells AP, Cordeiro MF, Bunce C, and Khaw PT(2003):** "Cystic bleb formation and related complications in limbus- versus fornix-based conjunctival flaps in pediatric and young adult trabeculectomy with mitomycin C," *Ophthalmology*, 110(11): 2192–2197.
20. **Low S, Hamada S, and Nischal KK(2008):** "Antimetabolite and releasable suture augmented filtration surgery in refractory pediatric glaucomas," *Journal of AAPOS.* , 12(2):166–172.
21. **Elder MJ(1994):** "Combined trabeculotomy-trabeculectomy compared with primary trabeculectomy for congenital glaucoma," *British Journal of Ophthalmology*, 78(10): 745–748.
22. **O'Malley Schotthoefler E, Yanovitch TL, and Freedman SF(2008):** "Aqueous drainage device surgery in refractory pediatric glaucomas: I. Long-term outcomes," *Journal of AAPOS.*, 12(1): 33–39.
23. **Al Faran MF, Tomey KF, and Al Mutlaq FA(1990):** "Cyclocryotherapy in selected cases of congenital glaucoma," *Ophthalmic Surgery*, 21(11):794–798.
24. **Kirwan JF, Shah P, and Khaw PT(2002):** "Diode laser cyclophotocoagulation: role in the management of refractory pediatric glaucomas," *Ophthalmology*, 109(2):316–32, .
25. **Uram M(1992):** "Ophthalmic laser microendoscopic process ablation in the management of neovascular glaucoma," *Ophthalmology*, 99(12): 1823–1828.
26. **Rohit, Ahmad A (2015):** "Advanced glaucoma surgery". Publishing Switzerland . New York .p.57-60. <https://www.scribd.com/document/209850386/Glaucoma-Surgery>
27. **Audren F, Abitbol O, Dureau P et al.(2006):** "Non-penetrating deep sclerectomy for glaucoma associated with Sturge-Weber syndrome," *Acta OphthalmologicaScandinavica*, 84(5):656–660.
28. **Young YU, Zhi-LiLiu, Lei Cao, Qing-Zhu Nie(2012):** Clinical effect of improved viscocanalostomy for the treatment of primary congenital glaucoma, 4: 466-468.
29. **Tian B, Kaufman PL(2013):** Transitional vision science, *tvst, arvo Journals. Org. technology*, 23:23-25.