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Approach to primary congenital glaucoma: A perspective

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Abstract:

Primary congenital glaucoma (PCG) occurs worldwide and has a broad range of ocular manifestations. It poses a therapeutic challenge to the ophthalmologist. A proper diagnostic evaluation under anesthesia is advisable for all children who do not cooperate for an office examination. Medical therapy only serves as a supportive role, and surgical intervention remains the principal therapeutic modality. Angle incision surgery such as goniotomy or trabeculotomy ab externo is the preferred choice of surgery in the Caucasian population. Primary combined trabeculotomy-trabeculectomy with or without antifibrotic therapy is the preferred choice in certain regions such as India and the Middle East where the disease usually presents with severe forms of corneal edema along with megalocornea. In refractory cases, trabeculectomy with antifibrotic therapy or glaucoma drainage devices are available options in the armamentarium. Cycloablative procedures should be reserved for eyes with poor visual potential. Myopia is common among children with PCG, and appropriate optical refractive correction in the form of glasses or contact lenses should be provided. Amblyopia therapy should be instituted to ensure overall visual development in the early developmental years. Low-vision rehabilitation services should be provided to children with vision impairment. Long-term follow-up is mandatory and carers of children with PCG should be counseled and educated about this need. Regardless of the visual outcomes, clinicians should emphasize the need for education of these children during the clinic visit. The overall goal of the management should be to improve the overall quality of life of the children with PCG and their carers.

Keywords:

Goniotomy, primary combined trabeculotomy-trabeculectomy, primary congenital glaucoma, trabeculectomy with mitomycin C, trabeculotomy, transscleral cyclophotocoagulation

Introduction

The field of pediatric glaucoma management has seen major changes in the last few years. Primary congenital glaucoma (PCG) is primarily a surgical disease, and most children will require surgery at some point of time. From a seemingly untreatable disease with very few surgical options, the pediatric glaucoma surgeon now has several options in his/her surgical armamentarium to choose from. In this article, we highlight the changing trends and recent advances in PCG. We will also discuss the quality of life (QoL) issues for these children, a topic that is often overlooked but has gained tremendous importance in recent years because of the holistic approach to the child as a whole, encompassing both the physical and mental aspects of development of a growing child with a lifelong challenge and its enormous effect on the parents and caregivers.

Classification

PCG is the most common nonsyndromic glaucoma in infancy. The Collaborative Glaucoma Research Network (CGRN) classifies childhood glaucoma into the following categories:[1,2]

1. Primary childhood glaucoma
2. Secondary childhood glaucoma

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a. Glaucoma associated with nonacquired ocular anomalies (e.g., Axenfeld–Rieger anomaly/syndrome, Peters anomaly, aniridia)
b. Glaucoma associated with nonacquired systemic disease or syndrome (e.g., Down syndrome, mucopolysaccharidosis, and Sturge–Weber syndrome)
c. Glaucoma associated with acquired condition (e.g., uveitis, trauma, steroid-induced, tumor, and retinopathy of prematurity)
d. Glaucoma following cataract surgery.

The first category includes two conditions: PCG and juvenile open-angle glaucoma.

PCG is classified according to age of onset into: (1) neonatal or newborn onset (0–1 month), (2) infantile onset (>1–24 months, and (3) late onset or late recognized (>2 years). Figure 1 depicts the typical clinical appearance of neonatal-onset bilateral PCG in a 1-week-old child. Cases with normal intraocular pressure (IOP) and optic disc but typical signs of PCG, such as buphthalmos and Haab striae are classified as spontaneously arrested PCG.

Epidemiology

PCG is the most common nonsyndromic glaucoma in infancy, but its prevalence has a distinct geographical and ethnic variation. A higher prevalence has been observed in cultures and groups with an increased rate of consanguinity, especially in those groups in which cousin-cousin marriage is common.[3] PCG occurs in 10,000–20,000 live births in Western countries.[4] The incidence rises in the Middle East to 1:8200 live births in Palestinian Arabs[4] to 1:2500 live births in Saudi Arabians.[5] The prevalence of PCG is one in 3300 live births, and PCG accounts for 4.2% of all childhood blindness in Indian population.[6] The highest reported incidence is 1:1250 in Slovakian Gypsies.[7] PCG is usually bilateral (70%) with the severity of involvement frequently asymmetrical.[8,9] The male gender has a slightly higher prevalence, but familial cases tend to have an equal sex distribution.[8,9] In races with a higher incidence, the presentation of PCG occurs at an earlier age compared to other races with lower incidence. The mean age of presentation ranges from 3 to 4 months among Asians, Saudi Arabians, and Indians to 11 months in Western countries.[10]

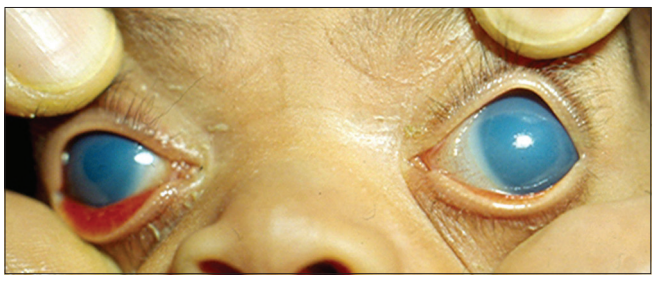

Figure 1: Typical appearance of a child with bilateral neonatal-onset primary congenital glaucoma

Genetics

PCG is a genetically heterogeneous condition. Overall PCG is either inherited as an autosomal recessive trait with variable penetrance, or it may occur as a sporadic condition.[11] Mutations in the CYP1B1 gene encoding the cytochrome P450 at the GLC3A locus are the most common genetic causes of PCG.[11] However, CYP1B1 alone cannot explain the overall genetic contributions in PCG. The exact role of this gene in the pathophysiology of the disease remains unknown, and those devoid of mutations in CYP1B1 would be great interest from the genetic standpoint.

A study from India on 146 Indian PCG patients tried to correlate the genotype of patients screened for 6 different mutations (Ins376 A, P193 L, E229K, R390C, G61E, and R368H) to disease severity.[12] Accordingly, a severity index was prepared that included corneal diameter, IOP, cup-to-disc ratio, corneal clarity, and last recorded visual acuity (VA). Cases with frameshift mutation (Ins376A) had the worst phenotype followed by those with homozygous R390C mutation. In addition, 80% of the cases with E229K, 72% with R368H, 66.7% with G61E, and 62.5% with P193 L exhibited a severe phenotype in at least one eye.[12]

Recently, advances in the genetic understanding of PCG have been made. The developing picture of CYP1B1 gene could lead to an effective screening test for the condition, as well as the possible application of gene therapy.[13,14] Proper screening and genetic counseling would be a crucial part of a worldwide effort to more effectively treat PCG, as consanguineous relationships are frequently cited as one reason for areas with high prevalence rates.

Pathogenesis

Although many theories have been proposed over the years, the pathogenesis of PCG remains uncertain.

Obstruction to outflow was popularly thought to be due to the presence of an impermeable membrane, Barkan membrane, but this has never been verified histopathologically. With time, the site of obstruction was found to be trabecular, rather than pretrabecular.[8,9] Isolated maldevelopment of the trabecular meshwork (TM) (isolated trabeculodysgenesis) is considered to be the basic pathology.[8,9,15]

The immature angle appearance is currently thought to result from the developmental arrest of tissues derived

from the neural crest cells in the third trimester of gestation. The severity of angle abnormality depends on the stage at which angle development is arrested.

Pathophysiology is postulated to be due to thick, compacted trabecular sheets, which coalesce and prevent the posterior "sliding" of the iris which occurs during the development of the anterior segment. These trabecular sheets suspend the iris more anteriorly which results in the typical appearance of the "high" insertion of iris in children with PCG.

Presentation

1. Age: PCG usually presents in neonates or infants, with the majority presenting less than the age of 6 months
2. History: Ask about age of onset, family history, history of parental consanguinity, and any systemic issues
3. Symptoms and signs: Epiphora (without discharge), photophobia (earliest symptom), blepharospasm, corneal haze/opacification (usually the first sign noticed by the parents), and enlarged eyeball size (buphthalmos). Epiphora, photophobia, and blepharospasm result from corneal edema resulting from elevated IOP and constitute the classical triad. Rarely, the disease may present with acute corneal hydrops.[16]

Assessment

1. Vision is assessed by age-appropriate VA tests, whenever possible
2. A detailed examination can only be obtained by examination under anesthesia (EUA). The key points to note during EUA are refraction, corneal findings, IOP, gonioscopy, and ophthalmoscopy; these findings will guide the decision for surgery, if possible, in the same sitting. The requisites for EUA are pediatric speculum, fluid for irrigation, calipers, tonometer (Perkins/Tono-Pen/iCare), direct and indirect ophthalmoscope, retinoscope, angle evaluation by direct goniolens like Koeppe's/Swan-Jacob or by RetCam, ultrasound pachymetry, and ultrasonography B-scan. All anesthetics and sedative agents lower IOP, with the exception of ketamine, chloral hydrate, and benzodiazepines. Sevoflurane is the most commonly used inhaled agent due to its convenience and safety profile
3. IOP should be recorded the moment the child stops moving after inhaled anesthesia and prior to intubation to avoid erroneous measurements. An IOP >21 mmHg in one or both eyes on at least two occasions is considered abnormally elevated. In general, normal eye IOPs in children are 12.02 ± 3.74 mmHg.[17] Physiological IOP in children is lower than adults and increases with age. General anesthesia decreases IOP by about 30%, and the measurement only balances after a few minutes of intubation (less if a laryngeal mask is used).[18] Regarding the type of tonometers, Goldmann applanation tonometer (GAT) and Perkins are the gold standard. Tono-Pen overestimates IOP compared to Perkins in normal children and in those with glaucoma. iCare portable rebound tonometer does not need topical anesthesia. The same instrument should be used for follow-up
4. Corneal haze: This is representative of severity and is usually more centrally. Corneal haze can be graded according to the visualization of the pupillary margin, iris details, fundus vessels, etc., Corneal edema in PCG is initially simple epithelial edema due to elevated IOP; subsequently, there is permanent stromal edema. Untreated, the edema progresses to stromal scarring and irregular corneal astigmatism
5. Corneal diameter: Corneal enlargement secondary to elevated IOP usually occurs before 3 years. The white-to-white horizontal visible corneal diameter is documented. Normal value is 10 mm at birth. Abnormal values are ≥11 mm in a newborn, >12 mm in a child <1 year of age, and >13 mm at any age
6. Haab striae: Horizontal lines of Descemet's membrane rupture (Haab striae) are often present and may persist even after IOP reduction.[8,9,15] These horizontal lines are classically distinguished from those observed after corneal trauma (by forceps delivery in particular) that appear as vertical splits on slit-lamp biomicroscopy. Haab striae may be concentric to limbus in periphery but are more typically horizontal centrally near or across the visual axis. Figure 2 depicts the classical appearance of Haab striae in a 6-month-old child with PCG. They can be distinguished from the Descemet's breaks in forceps injuries as they are typically vertical,

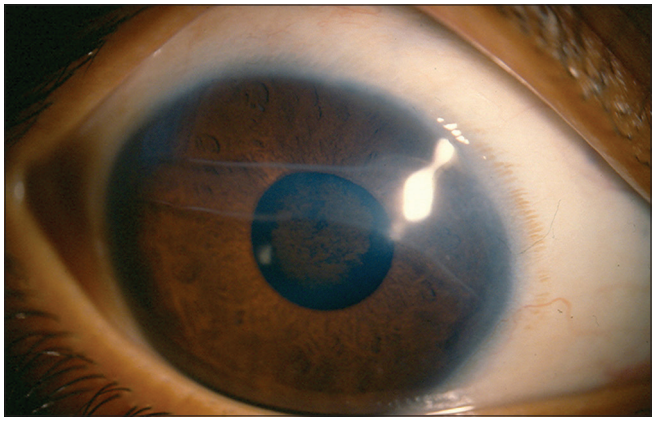

Figure 2: Haab striae

unilateral, central, with normal corneal diameter and often associated with periocular bruising
7. Gonioscopy: In PCG, gonioscopy reveals a flat and high iris insertion and the absence of an angle recess. A thin and hypopigmented iris stroma might be detected as well as peripheral scalloping of the posterior pigmented iris layer and easily visible, hyperemic iris vessels with circumferential vessels running tortuously in the peripheral iris
8. Fundus examination: Binocular indirect ophthalmoscopy should be performed in all cases. The optic disc should be examined for cupping and focal areas of rim loss. A cup: disc ratio of >0.3 in an infant or >0.5 in an older child is suspicious. Striking reversal of cupping may result in IOP reduction after successful glaucoma surgery[19]
9. Pachymetry: Central corneal thickness (CCT) may influence the accuracy of GAT and may artifactually overestimate or underestimate true IOP. The definitive role of pachymetry in the evaluation of childhood glaucoma is uncertain. CGRN recommends that CCT should not be used to "adjust" an IOP measurement but rather taken into consideration in the overall context
10. Axial length: Absolute value may not be important, but serial documentation is useful. Increase in axial length on sequential examination is a sensitive indicator of glaucoma progression.[20]

Mimickers/Differential Diagnoses

1. Differential diagnoses (D/D) of epiphora: Nasolacrimal duct obstruction, conjunctivitis, corneal abrasion, keratitis, and uveitis
2. D/D of Congenital corneal clouding (mnemonic: STUMPED)
   - S: Sclerocornea
   - T: Tears in Descemet's membrane: PCG and birth trauma
   - U: Ulcer: herpes simplex virus, bacteria, and neurotrophic
   - M: Metabolic corneal opacities: mucopolysaccharidosis, mucolipidosis, and cystinosis
   - P: Posterior corneal defect: Posterior keratoconus, Peters anomaly, and staphyloma
   - E: Endothelial dystrophy: Congenital hereditary endothelial dystrophy, posterior polymorphous dystrophy, and congenital hereditary stromal dystrophy
   - D: Dermoid.
3. D/D of enlarged cornea: High axial myopia and megalocornea
4. D/D of congenital disc anomaly: Optic nerve hypoplasia, tilted disc syndrome, optic nerve coloboma and morning glory disc anomaly, etc.

Management

Surgical treatment is the mainstay of management in cases of PCG; however, medical therapy has a significant role in several clinical scenarios such as to lower the IOP initially till the surgical intervention is possible or in between surgeries in cases requiring repeat interventions.

Medical treatment

The safety and efficacy of glaucoma medication in the pediatric population is an important concern.[21] Beta-blockers like timolol maleate 0.5% and topical carbonic anhydrase inhibitors (dorzolamide or brinzolamide) are the usually preferred agents for their safety and efficacy. Pilocarpine 1%–2% can be used twice or thrice daily preoperatively in angle surgery to improve angle visualization and postoperatively for 2–3 weeks after angle surgery to induce miosis and reduce anterior synechiae formation (which can potentially occlude the goniotomy cleft). Side effects such as diarrhea can occur in neonates with higher concentration and frequency. Prostaglandin analogs like latanoprost can serve as useful adjuncts. Rho-kinase inhibitors are relatively newer glaucoma medications, but their safety has not been established in young children. Brimonidine must be avoided in neonates, infants, and young children for the risk of apnea.

Surgical treatment

Brief history

In the early 1900s, congenital glaucoma was considered untreatable and Anderson commented: "The future of patients with hydrophthalmia is dark" and "one seeks in vain for a best operation in the treatment of hydrophthalmia."[22] However, the introduction of goniotomy in 1938 by Barkan had dramatically changed the poor prognosis of congenital glaucoma.[23] However, goniotomy was not feasible in cases with hazy corneas. The next major advance in angle surgery came in 1960 with trabeculotomy.[24-26] It was simultaneously and independently described in 1960 by Smith (nylon filament trabeculotomy)[26] and by Allen and Burian and Burian (using an instrument called trabeculotome).[24,25] Subsequently, to target a wider area of angle pathology, circumferential trabeculotomy (CT) using a blunted 6-0 Prolene was introduced in 1995 by Beck and Lynch.[27] In India, primary combined trabeculotomy-trabeculectomy (CTT) was introduced by Sood in 1976.[28] In 1979, Luntz reported that CTT provides better outcomes in congenital glaucoma with cicatrized angle.[29] In 1980, Maul *et al*. described CTT in an infant with severe bilateral PCG who had failed goniotomy.[30] Trabeculectomy was introduced by Cairns in 1968 for the treatment of adult glaucoma but came to be performed also in children who had repeatedly failed angle or other types of surgery.[31] The use of a glaucoma

drainage device in children was first described by Molteno *et al*. in 1973.[32] The introduction of illuminated microcatheter by Sarkisian revolutionized the surgical technique of CT as it enables continuous visualization of the device during the procedure and several successful series have been reported.[33-35] In 2022, Mandal described a novel technique combining illuminated microcatheter passage-assisted CT and trabeculectomy (IMPACTT) as a safe and effective surgical procedure for the management of advanced PCG.[36] Several other surgical procedures have also been described.

Choice of surgery

Early surgical intervention is of prime importance in the management of patients with developmental glaucoma. In some parts of the world, such as the USA, patients may have only mild or moderate corneal edema at presentation, and these patients may be candidates for goniotomy, which has a high success rate in this population. By comparison, in some parts of the world, such as India or the Middle East, the majority of the children present with corneal clouding and goniotomy is technically impossible. In these situations, external trabeculotomy is the initial procedure of choice. When initial trabeculotomy has a poor success rate, trabeculotomy may be combined with trabeculectomy. Another important factor is that although most patients have symptoms suggestive of congenital glaucoma at birth or within 6 months of birth, they often present late due to various nonmedical factors.[37] In such advanced cases, we prefer to perform ab externo CTT which offers the best hope of success.[8,38-42]

Goniotomy

Goniotomy consists of an incision of the trabeculum (using a needle-like knife) under direct visualization with a gonioscopic lens (e.g., Swan-Jacob goniolens). An adequate visualization of the anterior chamber angle is essential; hence, the cornea must be sufficiently clear. The surgical technique consists of the following steps: The goniotomy knife or needle knife enters the Anterior chamber (AC) through peripheral clear cornea, approximately 1 mm inside the corneoscleral junction; once in the AC, the knife is guided parallel to the iris, away from the pupil, toward the TM; the tip of the knife is engaged slightly anterior to the middle of the TM and can be seen to indent the TM before it is cut by circumferential movement of the knife. As the incision proceeds, a white line develops behind the blade, the iris falls posteriorly, and the angle deepens. By rotation of the globe by the assistant, approximately 4–6 clock hours of meshwork can be excised. The reported results of goniotomy surgery show a success rate of 80% in infantile glaucoma.[9] It appears that goniotomy is most successful in patients whose glaucoma is recognized early and treated between 1 month and 1 year of age.[15]

Trabeculotomy ab externo

Trabeculotomy ab externo has a number of advantages over the alternative operation of goniotomy.[43] It can be done even if the cornea is hazy, can accomplish rupture of the inner wall of the Schlemm's canal and TM with anatomical precision, does not require the introduction of sharp instruments across the AC, and can be done with standard microsurgical technique without the need of having to adapt with the view of goniotomy lens.

The procedure essentially involves creation of a fornix-based or limbus-based conjunctival flap, creation of a triangular or rectangular superficial scleral flap, deroofing the Schlemm's canal by incising at the junction of the bluish-gray zone anteriorly and the white scleral zone posteriorly, then introducing the metal trabeculotome on each side and entering into the AC after rupturing the inner wall of the Schlemm's canal, followed by suturing the scleral flap with 10-0 nylon and the conjunctival flap with 8-0 Vicryl suture. Several studies have reported that as the initial procedure, trabeculotomy enjoys a higher success rate than goniotomy, but some studies showed that they are equally effective.[8,9,15]

Primary trabeculectomy

Trabeculectomy is a procedure that most ophthalmologists are familiar with and is technically easier than goniotomy or trabeculotomy. However, many authors do not consider it as a first-line procedure in congenital glaucoma in view of a higher incidence of complications and lower success rate. Nevertheless, several reports have documented successful results following primary trabeculotomy for congenital glaucoma, which are comparable to goniotomy or trabeculotomy.[44]

Combined trabeculotomy with trabeculectomy

Theoretically, combining trabeculotomy with trabeculectomy (with or without anti-scarring agents) as an initial procedure provides two major outflow pathways and should improve the results for PCG. The basic steps are creating a fornix-based/limbal-based flap, constructing a superficial triangular/rectangular scleral flap, putting a radial incision in the sclera to identify the Schlemm's canal ("where white meets blue, Schlemm's canal waits for you"), introducing one arm of the metal trabeculotome into the Schlemm's canal and rotating it into the AC on each side, thus rupturing about 90°–120° of the inner wall of the Schlemm's canal. Then, trabeculectomy and iridectomy are performed in the usual manner as is done in adults. Superficial scleral flap is closed with one 10-0 nylon suture at the apex of the triangular scleral flap and the knot is buried. Conjunctival closure is completed with the help of 8-0 Vicryl suture in a continuous manner. Figure 3a-h illustrates the surgical steps of primary CTT.

Figure 4a and b illustrates the preoperative and 6-month postoperative appearance of a child with neonatal-onset PCG operated at the age of 3 days. Whether CTT is superior to trabeculotomy alone is debatable. Dietlein *et al*. investigated the outcome of trabeculotomy, trabeculectomy, and CTT; although initially the combined procedure seemed to have a favorable outcome, after 2 years this difference was not statistically significant.[45] Mandal *et al*. reported long-term outcome of 299 eyes of 157 patients who underwent CTT; the success rate of 63.1% was maintained until 8 years of follow-up.[39]

There is a paucity of studies regarding the long-term outcomes of CTT in PCG.[46] However, in the recent past, there have been a few reports from India and other parts of the world.[28,39,41,46-48] Recently, we evaluated the long-term visual and surgical outcomes, and associated risk factors for poor outcomes in patients with PCG over a 21-year period.[46] We reviewed the medical records of children who underwent CTT as the first surgical procedure by a single surgeon (by one of the authors, AKM) between January 1990 and December 2010. Data on diagnosis and surgical procedures were extracted. The primary outcome measure was complete success defined as IOP <16 mmHg in patients examined under general anesthesia or <21 mmHg in patients who were old enough to be examined with the slit-lamp and when there was no progression of disc cupping or enlargement of corneal diameter at last follow-up. Qualified success occurred if one ocular antihypotensive agent was required to maintain these criteria. We used the World Health Organization (WHO) criteria of vision loss to categorize the visual outcomes. The cohort included 653 consecutive PCG patients (1128 eyes; mean age, 26.34 months) of whom 475 (73%) underwent simultaneous bilateral CTT. Kaplan–Meier survival analysis revealed 1-, 5-, 10-, 15-, and 19-year complete success rates of 92.6%, 75.5%, 55.9%, 44.7%, and 21.6%, respectively. Multivariate analysis revealed independent associations between failure, preoperative corneal clarity, and prior glaucoma surgery. Of the VA data obtained at the last follow-up (n = 333, 51%), 92 (28%) had no visual impairment, 145 (43%) had low vision, and 96 (29%) were blind. We concluded that primary CTT may be safely employed to control IOP and may provide long-term benefits in PCG patients.

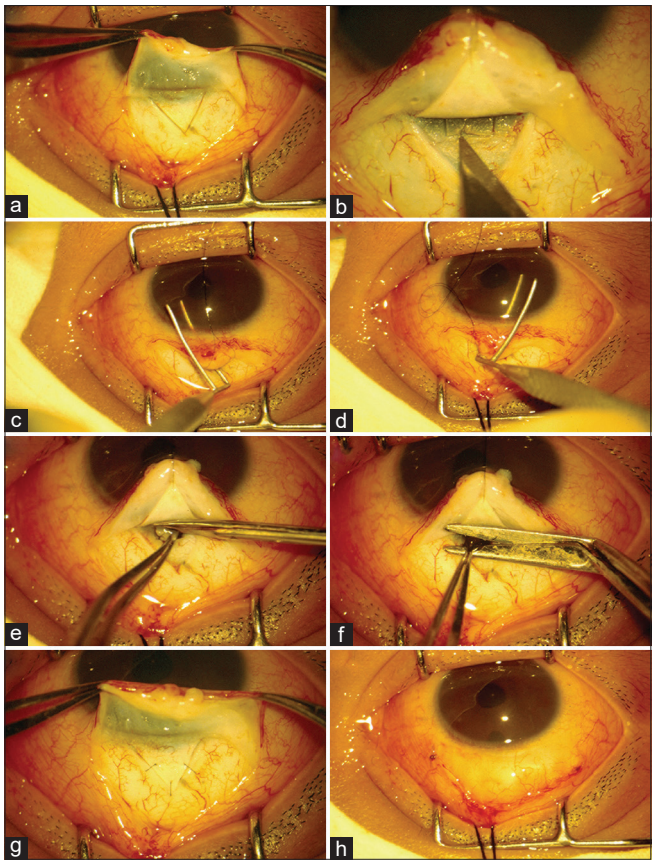

Figure 3: Steps of primary combined trabeculotomy-trabeculectomy. (a) Triangular scleral flap delineated, (b) Surgical landmarks of the limbal region are clearly identified and Schlemm's canal opened by a central radial incision, (c) Trabeculotomy performed on the left of the radial incision, (d) Trabeculotomy performed on the right of the radial incision, (e) Trabeculectomy performed, (f) Iridectomy performed, (g) Superficial scleral flap closed with 10-0 nylon sutures, (h) Conjunctival closure performed with 8-0 Vicryl suture

Circumferential trabeculotomy

The further development of standard trabeculotomy into 360° trabeculotomy or CT almost initiated a new era.[26] The procedure was performed by rupturing the entire circumference of the TM and the inner wall of Schlemm's canal, using a polypropylene suture. This seemed to establish a near-to-normal aqueous outflow that gained at least as low IOP as standard trabeculotomy and goniotomy. In their retrospective study, Beck and Lynch reported on 12 months results which were promising as 85% of the eyes met the criteria of success.[27] Later reports suggested that the IOP appeared to be better controlled than after goniotomy or standard trabeculotomy, and the VA somewhat better.[49,50] However, there were reports on complications such as misdirection of the suture into the suprachoroidal or subretinal spaces as well as lasting hypotony.[51-53] In 2010, Sarkisian described the use of an illuminated microcatheter.[34] This technical advancement appears to have reduced the adverse events.

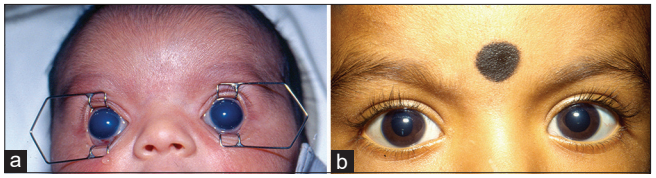

Figure 4: (a) Preoperative appearance of the cornea in a child with neonatal-onset primary congenital glaucoma operated on the 3rd day of birth, (b) Six-month postoperative appearance of the same child showing clear corneas in both eyes

Circumferential trabeculotomy with trabeculectomy

In 2022, Mandal described a novel technique combining IMPACTT as a safe and effective surgical procedure for the management of advanced PCG.[36]

In patients with advanced PCG, the collector channels and the aqueous veins needed to carry the aqueous to the episcleral veins are more likely to be anomalous or atrophic in addition to the primary pathology, i.e., trabeculodysgenesis. Assessment of the collector channels and functional efficiency of the distal outflow system is beyond the scope of clinical evaluation. In such a situation, angle surgery even in the form of CT is bound to yield suboptimal results. A poorly functioning distal outflow pathway will necessitate an additional surgical step that bypasses it, like trabeculectomy. Hence, adding trabeculectomy to CT will have theoretical advantage of dual outflow pathway ensuring better drainage of aqueous and normalization of IOP. Therefore, IMPACTT is safe and effective, and further prospective randomized studies are required to determine the perceived superiority of IMPACTT over the contemporary surgical techniques for the management of PCG.

Management of Refractive Pediatric Glaucoma

When the IOP is not controlled after the first surgery, the surgical options are filtration surgery with anti-fibrosis drugs, glaucoma drainage implants, or cyclodestructive procedures.

Trabeculectomy with mitomycin-C

When one or more angle procedures (and medications) have failed to achieve IOP control in refractory primary infantile glaucoma cases, filtering surgery is often undertaken. Although most glaucoma filtration surgery in children was standardly performed using a limbus-based conjunctival flap, many surgeons now advocate fornix-based flaps in both infants and children.

The use of intraoperative mitomycin-C (MMC) has somewhat enhanced the success of this procedure, although not without significant and, as yet, unquantifiable risk.[54] Mandal *et al*. reported success of 66% at 30 months in a series of 38 eyes, most of which had refractory PCG.[55]

Figure 5 illustrates the preoperative and 1-year postoperative appearance of a child who underwent second glaucoma surgery in the form of MMC-augmented trabeculectomy following failure of primary CTT.

Glaucoma drainage implants

These may be characterized as open-tube (nonrestrictive) devices such as the Molteno and Baerveldt implants

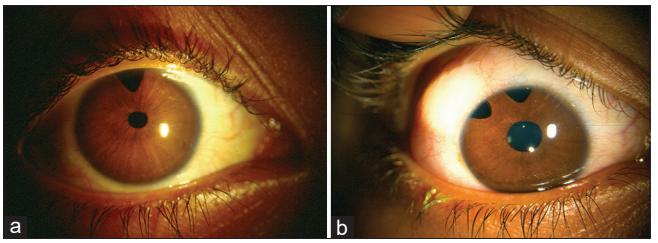

Figure 5: (a) Preoperative appearance of an eye with failed primary combined trabeculotomy-trabeculectomy, (b) 1-year postoperative appearance of the bleb following repeat glaucoma surgery (trabeculectomy with mitomycin-C)

or the Aurolab aqueous drainage implants (AADI), or valved (flow-restrictive) devices such as Krupin implant or Ahmed glaucoma valve. The flow-restrictive devices are intended to reduce the incidence of complications associated with hypotony during the immediate postoperative period. Both the Baerveldt and Ahmed (S3 and FP8) implants (most commonly used) come in smaller sizes, which may be more fitting for the pediatric eye. Children may be particularly prone to extrusion and exposure of the implant. Senthil *et al*. reported good success rates of Ahmed glaucoma valve implant in refractory pediatric glaucoma.[56] Aurolab aqueous drainage implants (AADIs) have also been successfully used in the management of refractory pediatric glaucoma.[57,58] Reported complications of implants include hypotony with shallow AC and choroidal detachments, tube-cornea touch, obstructed tube, exposed tube or plate, endophthalmitis, and retinal detachment.

Cyclodestructive procedures

The most commonly performed cyclodestructive procedures are cyclophotocoagulation (transscleral Nd: YAG, transscleral diode, and endoscopic diode) and cyclocryotherapy. When available, the former is preferable because of less postoperative inflammation and possibly less incidence of phthisis. Success rates range from 28% to 79%.[38] An intraocular technique employing an endoscope with endolaser (endoscopic cyclophotocoagulation) has been described for more precise delivery of laser energy to the target tissue. In general, cyclodestructive procedures are often unpredictable as to the extent of IOP control, have limited success rates, often require re-treatment, and may be associated with vision-threatening complications.

Figure 6a-c illustrates the long-term follow-up of a child operated for infantile-onset PCG and who presented with acute corneal hydrops in the left eye. The child underwent primary CTT in the left eye. At 10-year follow-up, the child had a spectacle-corrected VA of 20/20 in the left eye (compound myopic astigmatism) and right eye (emmetropia).

Whatever surgery is performed, the responsibility of the surgeon does not end with the surgery and care

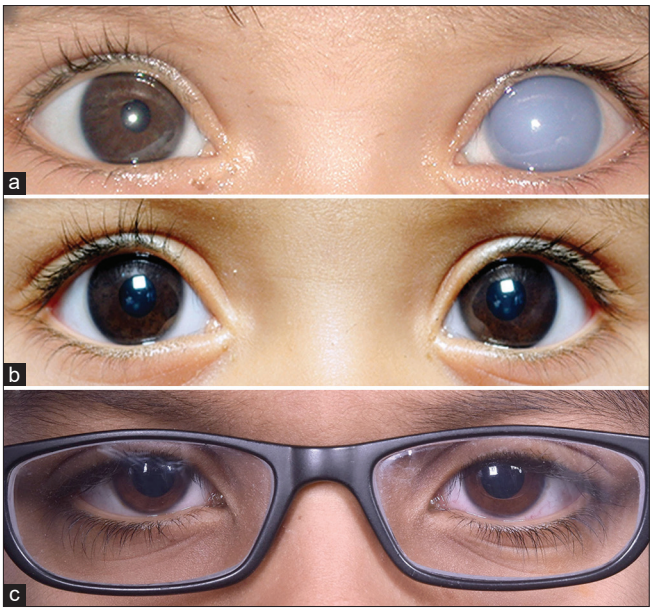

Figure 6: (a) Clinical appearance of a 3-month-old child with infantile-onset primary congenital glaucoma showing acute corneal hydrops in the left eye, (b) Six-month postoperative appearance of the same child showing normal corneal transparency of the left eye, (c) 10-year postoperative appearance of the same child showing clear cornea and using spectacles for compound myopic astigmatism and having a visual acuity of 20/20 in both eyes

must be taken to manage amblyopia for optimum visual rehabilitation of the child. Myopia and astigmatism are often present in infants with PCG. In unilateral cases, the affected eye is usually more myopic. Astigmatism often results when Haab striae cross the visual axis. The amblyopia can be attributed to stimulus deprivation (due to corneal haziness) and anisometropia. Following successful surgery, glasses should be prescribed after refraction, and amblyopia should be treated by patching – more important for unilateral cases.

Unfortunately, even with the best treatment in the best centers, many children with congenital glaucoma have low vision. Visual rehabilitation and low-vision devices can help these children compete with their normally sighted peers. After appropriate assessments, telescopes (handheld or spectacle mounted) may be prescribed to improve distance vision, while hand or pocket magnifiers (×2 to ×3) may be prescribed to improve near vision. Structured training programs in the use of these devices should be planned and discussed with the child and parents.[15,59]

Quality of Life of Children with Congenital Glaucoma and Their Caregivers

PCG and its treatment may have an impact not only on visual functioning (VF) but also on the overall well-being of the person, the "QoL." QoL has been defined by the WHO as "an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns".

Gothwal *et al*. designed, developed, and validated a novel Caregiver's Congenital Glaucoma QoL questionnaire for use with caregivers of children with PCG.[60] Caregivers of children with PCG have significant emotional and psychological burden, and moderate-to-severe depression may be present in one-third of the caregivers.[61] Using the Kidscreen-27 questionnaire, Gothwal *et al*. explored the health-related QoL (HRQoL) of children operated for PCG.[62] Despite undergoing successful glaucoma surgery, children with PCG reported reduced HRQoL. Gothwal *et al*. assessed parent–child agreement regarding child's HRQoL in children operated for PCG.[63] The results demonstrated that the perspectives of children with PCG and their parents regarding the child's HRQoL vary widely, with parents under- or overestimating their child's own report. Gothwal *et al*. compared the VF and vision-related QoL (VRQoL) of children aged 8–18 years treated for PCG and secondary childhood glaucoma.[64] Children with treated PCG experienced significantly better VF and VRQoL than those with secondary childhood glaucoma, despite comparable VA and IOP. Further, Gothwal and Mandal examined the QoL and life satisfaction (LS) outcomes in 82 patients with PCG operated during early childhood and who were transitioning into adulthood, and the results suggested that QoL and LS of treated patients with PCG during adult life are generally good and appear to be driven by factors other than clinical indices, most importantly the educational achievement.[65] Patients with PCG were found to be gainfully employed across various professions such as medicine, engineering and technology, IT sector, pharmacy, educational sector, and chartered accountancy.[65] The authors recommended that clinicians should emphasize the importance and need for education in the continued care of these patients.

Conclusion

Once considered virtually untreatable, pediatric glaucoma has now become reasonably manageable in most cases, thanks to scientific advances. Awareness about the role of consanguineous marriages can reduce the burden of this disease and awareness about the symptoms can help in early detection of this disease. Referral to a center routinely performing these surgeries can have the best possible outcomes. Ongoing research, particularly in the field of genetics and surgical innovations, will hopefully paint a brighter picture for children who are afflicted with this disease, which still remains one of the most challenging glaucoma to be treated by glaucoma specialists and ophthalmologists.

Declaration of patient consent

The authors certify that they have obtained all appropriate consent forms from the legal guardians of the patients. In the form, the guardians have given the consents for the images and other clinical information of the patients to be reported in the journal. The guardians understand that the names and initials of the patients will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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