

Outcome of Single Suture Trabeculectomy for Primary Congenital Glaucoma with Mitomycin C in an African Country

Adedayo Adio* and Ejele IOI

Pediatric eye clinic, University of Port Harcourt teaching hospital, Rivers state, Nigeria

***Corresponding Author:** Adedayo Adio, Consultant Pediatric Ophthalmic Surgeon, Pediatric eye clinic, University of Port Harcourt teaching hospital, Rivers state, Nigeria.

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Abstract

Background: Primary congenital glaucoma is a significant (but not common) cause of irreversible blindness, particularly when adequate surgical skills and facilities for determined follow-up are suboptimal. The often grim outcome of treatment is worsened by relatively late presentation of patients who suffer from the bilateral form. This study is to determine the clinical presentation, demographics and outcome of single suture trabeculectomy with Mitomycin C of patients presenting with features of primary congenital and infantile glaucomas (PCG) at the University of Port Harcourt teaching hospital, Rivers state, Nigeria.

Methodology: Records of patients seen at the UPTH eye clinic diagnosed to have primary congenital glaucoma between the period of July 2008 and July 2012 were requested for and details about their vital statistics and clinical presentation were documented. Eyes were graded complete success, qualified success and complete failure according to standard definitions. Data was analyzed and presented in form of simple proportions.

Results: Within the 4-year period reviewed, 38 eyes of 22 patients (2.38% of all glaucoma patients seen) were diagnosed to have PCG. Two folders could not be traced leaving 36 eyes of 20 patients, 15 males and 5 females (M: F ratio of 3:1). Mean age at presentation 4.5m (SD \pm 8.1m) ranging from 5 days and 24months with mean history of duration of 4 months ranging from 5 days to 13 months. Only 21 eyes consented to EUA. Horizontal corneal diameter averaged 12.5 mm (range 11.5 to 15.5 mm). Mean IOP was 24 mmhg (SD \pm 9.3) range 14 to 46mmhg. Haab striae was present in 14 eyes. CDR ranged from 0.5 to 1.0. Gonioscopy and A scan could not be carried out in these patients due to lack of equipment. Out of these, 17 had single suture fornix based triangular flap trabeculectomy with MMC. Two eyes required injections of 5 FU subconjunctivally postoperatively. All 17 had complete success at 1 month post-operative. Only 6 eyes remained after 2 months in FU. Of these, 3 eyes had complete success, 1 eye had qualified success and 2 eyes failed completely.

Conclusion: Though not common, early recognition and intervention in patients with PCG can lead to restoration of visual development and function. In our series, single suture trabeculectomy with Mitomycin C had complete success in majority of the patients in the first 1 month but poor FU affected full evaluation of the final outcome. Social services need to be effective in reaching out. However, among those still in FU after 2 months, majority had complete success. Regular planned EUAs was a rate limiting step in the FU due to hospital cost issues. Allocation of adequate resources to equip centers with eye care workers with world class training will help to improve the visual future of these children.

Keywords: Primary congenital glaucoma; Single suture trabeculectomy; Mitomycin C; African; Developing country; follow-up

Introduction

Primary congenital glaucoma (PCG) (also referred to as trabeculodysgenesis) though relatively rare when compared with adults is actually technically present at birth but most times not evident at the time. However, it may appear anytime during the first three years of life. Its importance is precisely because of the age of the patient as it frequently leads to irreversible blindness if left untreated and these are individuals that can potentially live up to a minimum of 70 years. In developing countries, this condition frequently leads to blindness due to a paucity of skilled manpower, lack of appropriate equipment, late presentation due to long distances to travel, difficulties in its management, initial and sustained payment for care and lack of sustained follow up. Some studies have shown that a significant number of those attending schools of the blind are there because of this condition [1-3].

With an onset at birth to early infancy, PCG is highly prevalent in inbred populations and consanguinity is strongly associated with the disease. It is a heterogeneous autosomal recessively inherited condition which has been genetically linked to some mutations in North African studies. To date, PCG has been linked to three loci: 2p21 (GLC3A), for which the responsible gene is CYP1B1, and 1p36 (GLC3B) and 14q24 (GLC3C) [4]. Specifically, the CYP1B1 gene mutation (a member of the P450 cytochrome) at g.4339delG [5], and a novel mutation which is homozygous E173K and heterozygous N498D and G61E [6,7] harbours mutations in PCG.

A new locus (GLC3D) harbouring the LTBP2 gene has since been mapped [8]. Null mutations in this gene (mapping to chromosome 14q24.3 which is around 1.3 Mb near the documented GLC3A locus) has been found to cause PCG in four consanguineous families from Pakistan and in patients of Gypsy ethnicity. LTBP2 is the largest member of the latent transforming growth factor (TGF)-beta binding protein family, which are extracellular matrix proteins with multidomain structure. It is similar to fibrillins and is said to have roles in cell adhesion and as a structural component of microfibrils. It has been localized in the anterior segment of the eye, ciliary body, and particularly the ciliary process and therefore may be essential for normal development of the anterior chamber of the eye, where it is said to maintain ciliary muscle tone [9].

PCG thus occurs in children due to the abnormal development of the trabecular meshwork and the anterior chamber angle [10,11]. Histopathological studies of the AC angle shows partial absence and retrodisplacement of Schlemm's canal, hypoplasia of the trabecular meshwork, broad attachment of ciliary muscle to the meshwork, and anterior insertion of hypoplastic iris with the formation of a pseudo membrane [9].

In a study carried out in north central Nigeria, PCG was found in 1.4% of school children examined [12] and also accounted for 21.3% of cases requiring examination under anaesthesia(EUA) in the same area [13] making it the commonest reason for such a procedure. Other studies examining glaucoma patients over a 2-year period, found congenital glaucoma accounting for 0.7% and 1.7% of cases seen [14,15]. Studies of congenital eye disorders reported 14.3% and 22.2% [16,17]. In the northern part of Nigeria, it was as high as 38% of those seen over a 5-year period [18].

However, in Ghana, only one case was found among 957 school children examined [19]. An Ethiopian study found 2% (33of 1586 glaucoma patients) were congenital [20] in Congo, 1.7% [21] akimbo, 9% in Zaire [22].

In the UK, the incidence of PCG is 5.41 per 100,000 (1 in 18,500) live births and in Ireland 3.3 per 100,000 (1 in 30,500) [23].

In the Middle east, of all the glaucoma presenting in children, PCG accounted for 80% of them over a 2-year period [24].

These patients usually present with buphthalmic eyes that may be opaque (due to the development of breaks in Descemet, s membrane and associated stromal edema), watering and marked photophobia [25]. Others present with squinty eyes.

In terms of management, surgical rather than medical therapy is the mainstay of treatment. However, treatment with antiglaucoma medications particularly using lower concentrations of selective beta blockers [26] has a role in temporarily reducing the IOP prior to surgery? Trabeculectomy is the commonest surgical procedure employed in Nigeria with significant control of intraocular pressure in most cases between 60 to 100% in skilled hands [26-29]. Though most of them may require a repeat trabeculectomy [27]. A meta-analysis has found that children less than 6 months tend to do poorly with trabeculectomies [26].

However, in other parts of Africa, goniotomy is a more frequent procedure with similar published good results of up to 80% [26,29,30]. The possible advantage of this procedure is the preservation of conjunctiva for a future filtering procedure and its shorter operating time. It is worthwhile to note that some of the patients in this African study who underwent goniotomies later still needed to have trabeculectomies carried out to achieve a control [30].

This surgical option is worthwhile learning however as the cloudy cornea precluding clear view into the eye (most times the reason given for this surgery to be avoided) that often accompanies the presentation in these patients can be surmounted by debriding the corneal epithelium with 100% ethanol or glycerine soaked cotton swabs before the procedure leaving a clear view to perform the procedure [30].

The use of Trabectomes to perform ab interno surgeries has also been tried by some workers with up to 100% success rates in cases. Though there is a higher incidence of hyphema and higher chance of further surgery following this procedure, it has proven to be useful [31]. Also trabeculotomy performed with an ab externo approach has been documented with up to 97% success rate [26]. It is possible to do this procedure even when visualization of angle structures is difficult and is performed using either a trabeculotome which is a rigid curved probe (or the double parallel pronged Harm, s trabeculotome), suture or an illuminated microcatheter [26].

However, more recently, better results have been documented combining trabeculotomy and trabeculectomy (Trab-Trabs) together [32-34]. However, it has been pointed out by Dr. mandel that these procedure works best when it is carried out as a primary procedure within 6 months of birth. Thereafter it may become difficult to perform the trabeculotomy aspect. However, this combined procedure even when carried out in infants as young as 1 month of age is quite effective [35,36]. Other publications have however have stated that this surgical combination even with the addition of antifibrotic agents has not been found to be significantly better in performance or offer any added advantage [26].

In addition, bilateral simultaneous trab trabs have been found to be very useful in order to obviate the need for a repeat anaesthesia in these patients which may cause more morbidity and risk of mortality and is also less expensive on the long run to patients and families [34,37].

These procedures are more effective if combined with antifibrotic agents like 5 Fluoruracil [33,38,39]. Though most will only use these adjuncts only after a failed primary procedure because of the lifelong risk of bleb related endophthalmitis.

The use of drainage shunts (Baerveldt, Moletno and Ahmed devices) and cyclodestructive procedures are reserved for those cases considered to be refractory and unresponsive to other known surgical and medical therapies and have a success rate of between 32-85% [33,40,41].

Transscleral cyclophotocoagulation also has a significant role to play in refractory cases especially when there is very little visual potential [42]. Laser has a very limited role in eyes with good visual prognosis. Other surgical modalities that are in play include the use of Seton implantation, Visualized cannulation and deep Sclerectomy [42].

It is important to report how children presenting with this condition currently respond to available treatment modalities since there are very few reports available yet in this area.

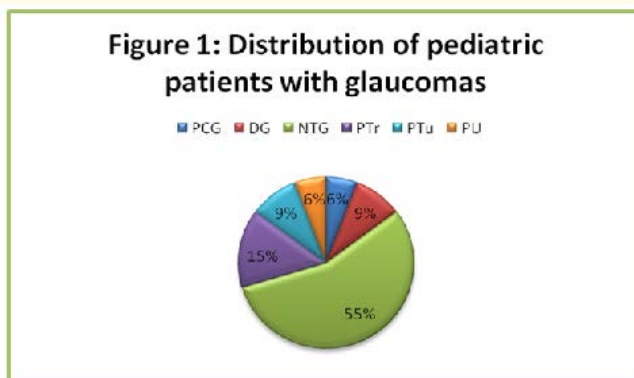
This study was therefore undertaken to determine the clinical presentation, demographics and response to management of patients with primary congenital glaucomas at the University of Port Harcourt teaching hospital, Rivers state which will add to currently available information in order to influence the acquisition of appropriate equipment and training of human resources to handle the challenge of its care.

Methodology

This retrospective descriptive study approved by the ethical committee of the University of Port Harcourt teaching hospital, Rivers state focussed on the period between July 2008 and July 2012. All folders of patients diagnosed and managed for PCG were retrieved and details about their demographics, clinical presentation and their management and the responses to management were documented. These also included visual acuity, optic disk cupping, intraocular pressure (IOP), corneal diameter, Pachymetry, visual fields, refraction, strabismus, glaucoma management, and ocular co morbidity. If an eye did not require medication for IOP control of 21 mmHg or less, clear cornea and absence of progressive glaucomatous optic disc changes, it was called a “complete” success, and if antiglaucoma medication was needed to achieve this endpoints, it was designated a “qualified” success [26,38]. All information was filled in a specialized form and analysed with the aid of a statistician using EPI INFO version 17 and presented in the form of proportions and percentages.

Results

Within the 4-year period under review, 13,440 glaucoma patients were seen in the glaucoma outpatient clinics of which 381 children were diagnosed to have glaucoma of different etiologies (2.83%). PCG was responsible for 22 patients (38 eyes, 16 of 22 were bilateral), developmental glaucoma was responsible for 29 patients (58 eyes). NTG was responsible for 180 (360 eyes), posttraumatic causes were responsible for 96 cases (96 eyes) while post tumorous (like retinoblastoma) causes were responsible for 24 cases (58 eyes, 17 of 24 were bilateral) and postuveitic causes responsible for 30 cases (30 eyes).



Key: PCG (primary congenital glaucoma) DG (developmental glaucoma) NTG (normal tension glaucoma) PTr (post traumatic glaucoma) PtU (glaucoma following intraocular tumors) PU(postuveitic glaucoma)

Primary congenital glaucoma

For those diagnosed with PCG (38 eyes of 22 patients), 16 patients had bilateral disease while the remaining 6 had unioocular disease, with 4 affecting the right eye only and 2 affecting the left eye only. Two folders of the unioocular cases were missing and could not be traced both from the cases affecting the RE only, leaving a total of 20 patients with 36 eyes.

Demographics

Of the 20 patients reviewed, there were 15 males and 5 females giving a male female ratio of 3:1. Age at presentation ranged between 5 days and 2 years (Mean is 4.5 months; SD \pm 8.1).

Clinical Presentation

Duration of history ranged between 5 days and 13 months with a mean of 4 months at first visit. The clinical presentation was in order of frequency: buphthalmos (24 eyes, 66.7%), photophobia (21 eyes, 58.3%), tearing (20 eyes, 55.6%), whitish discoloration of the eye (9 eyes, 25%) itching/excessive rubbing of the eyes (4 eyes, 11.1%) and squinty eye (4 eyes, 11.1%). Most of the patients had more than one pattern of presentation. The combination of buphthalmos and photophobia was the most common (62.5%).

There was bilateral involvement in most (30 eyes of 15 patients, 83.3%) followed by the RE only (4 eyes of 4 patients; 11.1%) and LE only (2 eyes of 2 patients; 5.6%).

Examination under anaesthesia/Surgery

Permission for examination under anaesthesia (EUA) was given in 21 eyes of 36 eyes, 58.3%) and of this number, 17 eyes had surgery (47.2%).

Of those who allowed an EUA, there was Haab, s striae in 14 eyes (38.9% of 36 eyes) and total corneal opacity in 3 eyes (8.3% of 36 eyes) from chronic stromal edema. The remaining 4 eyes had clear cornea. The corneal diameters ranged from 11.5 mm to 15.5 mm (Figure 1 with the highest corneal diameter of 15.5 mm) with an average of 12.5 mm (SD \pm 0.81) while the intraocular pressures (IOP) ranged from between 14 mmHg to 46 mmHg with a mean of 24 mmHg (SD \pm 9.3). At first EUA, 13 eyes had been started on antiglaucoma medications (36.1% of 36 eyes) an average of 2 weeks prior to EUA.

Gonioscopy and Pachymetry were not carried out in these group of patients that permitted EUA as the instruments were not available. A-scan was also not carried out as the machine was faulty.

The funduscopy showed clear media in 18 eyes with corneal haze responsible for non-clarity in the remaining 3 eyes. The cup-disc ratios ranged from 0.5 to 1.0 with a healthy neuroretinal rim at first EUA in the 18 eyes where it was visible.

Fornix based single suture Trabeculectomy with Mitomycin C(MMC) was carried out in all the 17 eyes operated on. Postoperative sub-conjunctival 5 Fluorouracil (5FU) given opposite to the site of surgery (surgical site at 12 'o' clock) was given to 2 eyes (11.8% of 17 eyes) that were extremely refractory after surgery.

There was immediate reduction in IOP in all cases when checked 2 days postoperative under light sedation with well formed anterior chambers and good pupillary dilatation. Mean IOP at 1st day postoperative was 6mmhg (SD \pm 2.2) with a range of 2 mmHg to 8 mmHg. The corneal haze disappeared in all cases that had such, prior to surgery.

Of the 17 eyes, 7 were bilateral, and 3 eyes were unilateral (1 was involving LE only).

All 17 eyes attended first follow-up (FU) after 2 weeks and IOP was found to still be within acceptable limits- within complete success, average of 11 mmhg (SD \pm 2.9) with a range of 8 to 15 mmhg without any medications.

At second FU, 4 weeks postoperative, 11 eyes (64.7% Of 17 eyes) did not come, leaving 6 eyes.

These 6 patients had a mean IOP of 19 mmHg (SD \pm 3.9) with a range of 16 mmHg to 26 mmHg. Two of the eyes with high IOPs was a bilateral case (24 and 26 mmHg) and he was started on antiglaucoma medications. The other 4 eyes had IOPs of 14 mmHg, 14 mmHg, 16 mmHg and 20 mmHg at that visit. The unioocular case with 20 mmHg was also started on antiglaucoma medications (making 3 eyes). Gentle massaging was also started at this point in these 3 patients) along with 5FU injections for the bilateral case.



Figure 2: Patient with advanced unioocular primary congenital glaucoma.

Weekly FU appointments were kept for these 6 patients till 2 months postop and 3 of the eyes maintained complete success and stopped coming. The unioocular eye with 20mmHg retained an IOP range of between 16 and 21 mmHg with massaging and 1 anti-glaucoma medication (qualified success) (Figure 3). The bilateral refractory case turned out to be a complete failure with increasing myopic shift of up to -6D in both eyes, increasing horizontal corneal diameter (15.5 mm) and haze along with photophobia despite the use of 3 antiglaucoma medications and antifibrotic injections given up to 6 times twice a week over 3 weeks. The IOP went up to as high as 36 mmHg and he was subsequently referred to another hospital to have glaucoma drainage implant surgery.



Figure 3: A successfully treated unioocular primary congenital Glaucoma patient.



Figure 4a: Patient with bilateral primary congenital glaucoma preoperatively.



Figure 4b: A failed post-trabeculectomy patient (same patient as figure 3a).

Discussion

PCG is uncommon in our locality [19,20,43] because inbreeding or consanguineous practices rarely if ever happens as is common in some other countries [44-48]. Most of our PCG patients were male as is well documented [49,50] and the age at presentation in this study (4.5 months) is comparable to that elsewhere (4.4 months) [24,51] (3.8 month). Non acceptance of surgery and even accepting EUA is a difficult challenge as most of the parents did not come back for a full evaluation under EUA in our series (only 29.2% had EUA). A similar finding was encountered in another Nigerian study where out of the 8 patients seen, only 2(25%) eventually had surgery [43]. However, there are other studies outside Nigeria within Africa with good uptake of surgery of up to 83% [49].

However evidently this does not appear to be a challenge in developed countries with patients strongly followed up after surgery for up to 40 years in some cases [52]. In fact, most of the schools for the visually impaired in these countries no longer have high numbers of those who are blind from congenital glaucoma as was the case in earlier years when cases were not being followed up closely [53].

Follow-up in this condition is however lifelong because the IOP needs to be checked on a regular basis for the lifetime of the patient even after apparently successful treatment [54]. This is however a significant problem in developing countries as most are lost from lack of counselling and suboptimal social services to follow-up patients in a matter of months (and in some cases, weeks) as in this study [43]. Most probably feel that the surgery is the only treatment, not considering that it is just the beginning of the treatment in this unpredictable disease. Studies have shown that IOP can still rise (without any symptomatology) years even after successful surgery [52,55]. However medical therapy may have a role to play. Even though surgical therapy is the widely preferred method of control of IOP in PCG, the BIG study in UK published that most of its PCG was controlled adequately with medications in 94% of cases [23]. In our series however we used medical therapy only as a temporary measure or to augment the surgical procedure carried out.

The clinical picture needs to be evaluated properly in order to make a diagnosis as even a large mean corneal diameter of 12.5 mm was found in some normal infants without associated congenital glaucoma in a south west Nigeria study [56]. They went further to conclude in that study that African mean corneal diameters in infants are slightly higher than that reported among other infant populations.

The mean age of presentation of 4.5 months in this study is much younger than that seen in other studies-8.1 months [49]. This might indicate either a more severe clinical course or increased awareness among caregivers of our patients.

The mean preoperative IOP in this study is slightly lower than that documented in other African studies 29.4 mmHg [49].

Postoperatively however, the mean IOP attained in this study is higher than documented in some studies (13.6 mmHg \pm 4.3) [52]. The cup disc ratios also were slightly higher in our study as against 0.7 ± 0.3 in the same study [52].

The IOP can be affected by the CCT which though it was not measured in our cohort (due to non-availability) is a significant part of the evaluation of these patients. It is usually significantly thicker in these patients when compared to patients without glaucoma [57].

Ultrasound Biomicroscopy (UBM) and high resolution anterior segment optical coherence tomography show characteristic features. Though not carried out in our patients, thin, stretched-out ciliary bodies and abnormal tissue at the iridocorneal angles were features seen in 90% of UBM scans of affected eyes. Iris thickness and stretched zonules correlated with the axial length ($r = -0.6$ and 0.58 , respectively; $p = 0.04$) but not with the mean corneal diameter. Abnormal insertion of the ciliary body to the posterior surface of the iris was noted in eight eyes (17%) [10].

Caregivers for these children have a significant emotional and psychological burden and may exhibit depression tendencies and this may play a significant role in the uptake and continuance of care of these patients [58]. This may possibly partly explain the loss to FU of over 70% in this series. Regular EUAs are also required for adequate FU payment for which was a challenge for most caregivers. At the time this paper was written, there was no subsidization or free services available in federal hospitals for medical or surgical care in this African country.

Overall, PCG has been documented to have better prognosis compared with other Pediatric glaucomas in terms of visual function provided appropriate and timely diagnosis is made and the currently available better treatment modalities is present [59]. This has largely been achieved in developed countries and this is what we should strive to attain in developing countries.

Conclusion

Appropriate and timely diagnosis and intervention in patients with PCG can lead to restoration of visual development and function. In our series, single suture trabeculectomy with Mitomycin C had qualified success in majority of the patients in the first 1 month but poor FU affected full evaluation of the final outcome. Effective social services are important. However, among those still in FU after 3 months, majority had complete success. Regular planned EUAs are necessary but was a rate limiting step in the FU of these patients. Further efforts

are needed to provide effective, subsidized/free timely screening of children and allocate adequate resources to equip centers and allow health care workers have world class training to reduce the rate of avoidable blindness from PCG in developing countries.

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Declaration of competing interests

We the authors declare we have no competing interests.

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