

Management of Primary Congenital Glaucoma

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Abstract

To study management of primary congenital glaucoma in a defined population of the Qalyubia governorate ,Egypt. Patients and methods The present study was a retrospective chart review of 28 children(48)eyes, who presented with PCG and were operated upon between January 2013 and December 2017 at the Ophthalmology Department of Benha University Hospital.The charts were reviewed for demographics as well as clinical data. Postoperative data were retrieved till the end of the follow-up period. Complications were noted, and success rates were studied. Results The mean age±SD (range) of the study population at presentation was 9.1±17.5 months, and of the follow-up period was 17.5±10.8 months.The most common primary glaucoma surgical procedure performed trabeculectomy with mitomycin C (36 procedures). The mean values (range) of preoperative intraocular pressure (on no intraocular pressure lowering therapy), corneal diameter and cup/disc ratio of the study eyes were 26.2 ±5.4 mmHg,13.6±0.8mm, 0.66± 0.1, respectively, and postoperatively at last follow-up were12.9±4.7mmHg, 12.9±0.9mm, 0.41±0.2. The most common complications were peaked pupil (10.5%), followed by cataract (8.4%) and tube endothelial touch (6.3%). Conclusion Most PCG patients present in the first 6 months of life, so that the most commonly performed procedure was trabeculectomy augmented with mitomycin-C. Meticulous, continuous and prolonged follow-up is mandatory for all operated cases to ensure long-term success.

Keywords: Combined trabeculectomy, Congenital, glaucoma, Primary, Trabeculotomy.

1. Introduction

Primary congenital glaucoma (also called primary infantile glaucoma) is a rare congenital anomaly of the anterior segment of the eye, typically presenting prior to 12 months of age, with raised intraocular pressure, loss of corneal transparency, photophobia and buphthalmos [1]. Initial treatment of primary congenital glaucoma is always surgical. Angle surgery in the form of goniotomy (if an adequate view can be obtained through the cornea) or trabeculotomy (if view through the cornea was impaired) has been recommended as first-line treatment. Other forms of glaucoma surgeries such as trabeculectomy with adjunctive mitomycin-c, glaucoma drainage devices and cyclodestructive procedures have still maintain their role in the management of primary congenital glaucoma [2,3].

2. Patients and methods

The present study was a retrospective chart review of 28 children (48) eyes, who presented with PCG and were operated upon between January 2013 and December 2017 at the Ophthalmology Department of Benha University Hospital. All surgeries were performed by a single surgeon (MFF), with the informed consent of the parents of all patients. The study was approved by the Ethics Committee for Human Research at Benha University Hospital. Data retrieved from the patients' charts included the following: demographic data such as age at surgery, sex, laterality and family history such as parental consanguinity, affected siblings and positive family history for similar conditions; details of the clinical examination, whether office examination or examination under general anaesthesia (EUA), including findings such as intraocular pressure (IOP, measured by Perkin's tonometer during EUA), corneal diameter (white to white, by callipers), clarity and thickness, cup/disc ratio and ; operative details including type(s) of

surgical procedure(s) for glaucoma; complications; and postoperative data of the eyes at monthly intervals . PCG was diagnosed clinically when a child presented with an enlarged cornea and/or corneal haze with an elevated IOP (>21 mmHg) under sedation or inhalational general anesthesia and optic nerve cupping in the absence of any associated ocular or systemic anomalies or secondary conditions known to be associated with or to cause glaucoma. All surgical procedures were performed under general anesthesia. The choice of surgical technique depended on some factors which include corneal clarity, level of IOP, systemic general health, surgeon's experience and preferences. Our preferred starting procedure is trabeculotomy. In advanced cases with very high IOP in which the success of isolated trabeculotomy was not anticipated, we used combined trabeculotomy and trabeculectomy with the use of mitomycin-C. In cases where trabeculotomy was difficult or failed, we use trabeculectomy augmented with mitomycin-c application. If failed, trabeculectomy or combined trabeculotomy-trabeculectomy, the procedure could be repeated for one more time.

2.1 Postoperative regimen

All patients were treated with topical 1% cyclopentolate twice daily for 1 month and the corticosteroid-antibiotic preparation (0.1% dexamethasone and tobramycin) five times a day, tapered gradually over a 6-week period. All patients were examined 1 and 3 days after surgery, followed by examination in the office at the end of 1, 4, and 6 weeks and in the office every 3 months thereafter.

2.2 Data collection

All preoperative, surgical, and postoperative parameters were entered in a computer-friendly data

entry form. Any intra- and perioperative surgical complications and retreatments were also recorded.

2.3 Outcome measures

The outcome measures included preoperative and postoperative IOPs, corneal clarity, horizontal corneal diameter, cup/disc ratio, refractive errors, success rate, and complications.

2.4 Success criteria

Surgical success and failure were defined before data analysis. The surgery was considered a complete success when the IOP was less than 21 mmHg without medication and when there was no progression of disc cupping or corneal diameter. Qualified success was defined as cases in which such pressure was maintained with topical antiglaucoma medications. Failure was defined as IOP greater than 21 mmHg or the development of hypotony-related maculopathy or other sight-threatening complications.

2.5 Statistical analyses

The collected data were tabulated and analyzed using SPSS version 20 soft ware (SpsInc, Chicago, ILL Company). Categorical data were presented as number and percentages, Fisher's exact tests was used to analyze them. Quantitative data were tested for normality using

Shapiro-Wilks test assuming normality at $P>0.05$. Normally distributed variables were expressed as mean \pm standard deviation and analyzed by Student "t" test for 2 independent groups, while non parametric data were presented as median and inter-quartile range (IQR), and analyzed by Friedman;s test for matched variables more than 2. Significant friedman's was followed by Wicoxon test to detect the significant pairs. Non parametric variables among 2 independent groups were analyzed by Mann Whitney U test. Kaplen Meier curve was drawn to show the probabilities of success over the period of the study. Binary logistic regression analysis was run to detect the significant predictors of outcome. ROC curves were constructed for the significant predictors to assess their performance.

3. Results

This study included 28 children (48) eyes, who presented with PCG and were operated upon between 2013 and 2017. The demographic data are shown in table 1 The mean age of patients was 9.1 ± 17.5 months. There were 16 female patients (57.1%) and 12 males (42.9%). The majority of patients had no history of consanguinity (85.7%) while only 32.1% had positive family history. The right eye was affected in 21.4% of patients, the left in 7.1%, while 71.4% of patients had bilateral disease.

Table (1) Demographic data of the studied patients.

Variable		No. (N=28)	% (100%)
Age (months)	Mean \pm SD	9.1 \pm 17.5	
	Median (Range)	5.5 (1-96)	
Sex	Male	12	42.9
	Female	16	57.1
Consanguinity	Negative	24	85.7
	Positive	4	14.3
Family history	Negative	19	67.9
	Positive	9	32.1
Laterality	Right eye	6	21.4
	Left eye	2	7.1
	Bilateral	20	71.4
no. of eyes=48	Right	26	54.2
	Left	22	45.8

The mean IOP decreased significantly ($p<0.001$) from 26.2 ± 5.4 mmHg preoperatively to 13.7 ± 4.8 mmHg at the 1st postoperative week, 15.5 ± 5.2 mmHg at the 1st postoperative month, 16.8

± 7.9 mmHg at the 3rd postoperative month, 14.7 ± 5.7 mmHg at the 6th postoperative month and to 12.9 ± 4.7 mmHg at the last postoperative follow up visit as shown in table2.

Table (2) Changes in IOP of the studied sample of eyes over the period of the study.

Variable	IOP (n=48)					P value (Wilcoxon test)			
	Mean	\pm SD	Median	IQR	Range				
Preoperative	26.2	5.44	26.0	22.2-30	14.0-37	ref.			
1 st week postoperative	13.7	4.80	13.5	10.0-17	4.9-24	<0.001 (HS)	ref.		
1 st months postoperative	15.5	5.23	15.0	12.0-19.5	5.0-28	<0.001 (HS)	0.007 (S)	ref.	
3 rd months postoperative	16.8	7.90	14.0	12.0-20.7	3.5-40	<0.001 (HS)	0.011 (S)	0.21	ref.

Table (2) Continue

6th months postoperative	14.7	5.71	13.5	11.0-16	7.0-33	<0.001 (HS)	0.20	0.51	0.23	ref.
Last visit	12.9	4.73	12.0	10.1-14.7	0.0-28	<0.001 (HS)	0.67	0.023 (S)	0.005 (S)	0.19
Friedman's test (P)	100.8 (<0.001, HS)									

Regarding the change in horizontal corneal diameter (HCD) of the studied sample of eyes over the period of the study, the mean horizontal corneal diameter decreased significantly (p<0.001) from 13.6±0.8 mm preoperatively to 13.4±0.8 mm at the 1st

week postoperative, 13.3±0.7 mm at the 1st month postoperative, 13.2±0.9 mm at the 3rd months postoperative, 13.1± 0.8mm at the 6th month postoperative, and to 12.9±0.9 mm at the last postoperative visit Table (3).

Table (3) Change in horizontal corneal diameter of the studied sample of eyes over the period of the study.

Variable	Corneal diameter (n=48)					P (Wilcoxon test)				
	Mean	± SD	Median	IQR	Range					
Preoperative	13.6	0.87	13.5	13-14.5	10.5-15.5	ref.				
1st week postoperative	13.4	0.81	13.5	13-14	11-15.5	0.001 (HS)	ref.			
1st months postoperative	13.3	0.79	13.25	13-14	11-15	<0.001 (HS)	0.061	ref.		
3rd months postoperative	13.2	0.95	13.0	12.5-14	10.5-15.5	<0.001 (HS)	0.029 (S)	0.25	ref.	
6th months postoperative	13.1	0.88	13.0	12.5-13.5	10.5-15.5	<0.001 (HS)	0.023 (S)	0.15	0.91	ref.
Last visit	12.9	0.93	13.0	12.5-13.4	10.5-15.5	<0.001 (HS)	0.013 (S)	0.03 (S)	0.26	0.23
Friedman's test	44.5 (<0.001, HS)									

Regarding the change in cup to disc ratio (CDR) of the studied sample of eyes over the period of the study, the mean CDR decreased significantly (p<0.01) from 0.66± 0.1preoperatively to 0.55±0.2 at the 1st week

postoperative, 0.56±0.2 at the 1st month postoperative, 0.52±0.2 at the 3rd months postoperative, 0.5±0.2 at the 6th month postoperative, and to 0.41±0.2 at the last postoperative visit Table (4).

Table (4) Findings of CDR over the period of the study.

Variable	Mean	± SD	Median	IQR	Range	P (Wilcoxon test)				
Preoperative	0.66	0.19	0.70	0.55-0.8	0.1-0.9	ref.				
1st week postoperative	0.55	0.26	0.70	0.3-0.75	0.1-0.9	0.002 (S)	ref.			
1st months postoperative	0.56	0.23	0.70	0.35-0.7	0.1-0.9	0.003 (S)	0.78	ref.		
3rd months postoperative	0.52	0.22	0.50	0.4-0.7	0.1-0.8	0.001 (HS)	0.72	0.011 (S)	ref.	
6th months postoperative	0.50	0.20	0.50	0.35-0.7	0.1-0.8	<0.001 (HS)	0.043 (S)	0.01 (S)	0.19 (S)	ref.
Last visit	0.41	0.21	0.40	0.3-0.6	0-0.8	<0.001 (HS)	0.022 (S)	0.009 (S)	0.004 (S)	0.018 (S)
Friedman's test	32.9 (<0.001, HS)									

Regarding outcomes of surgical interventions among the studied sample of eyes; 70.8% of patients showed true success, 20.8% of patients showed qualified success

and 8.3% of patients were considered failure Table (5), Fig (1). Survival probabilities of success were shown as Kaplan-Meier curve in Fig (1).

Table (5) Outcome among the studied sample of eyes.

Variable	No. (N=48)	% (100%)
Outcome		
True success	34	70.8
Qualified success	10	20.8
Failure	4	8.3

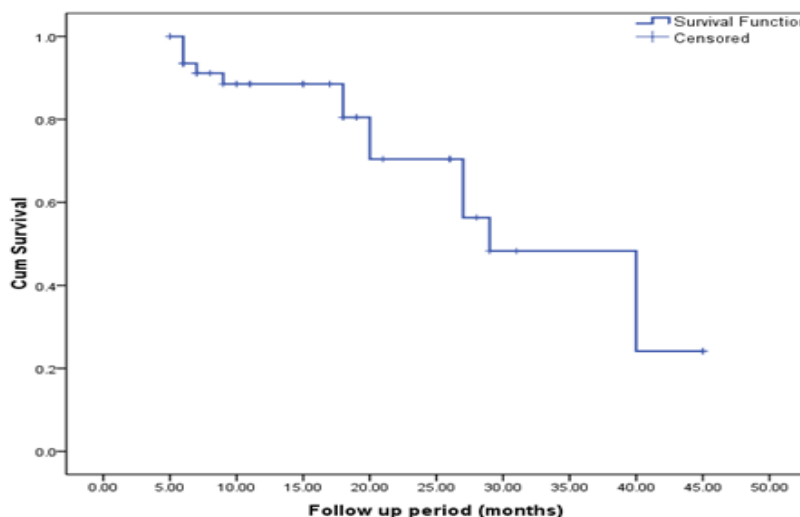


Fig (1) Kaplan Meier curve showing the cumulative probability of success and over the period of follow up.

The most common complications were peaked pupil (10.5%), followed by cataract (8.4%) and tube endothelial touch (6.3%) Table (6).

Table (6) Types of complications.

Variable	No. (N=28)	% (100%)	
Complications	Cataract	4	8.4
	corneal abrasion	1	2.1
	corneal edema	1	2.1
	hyphema	2	4.2
	Hypotony	2	4.2
	orbital cellulitis	1	2.1
	peaked pupil	5	10.5
	posterior synechia	1	2.1
	Shallow anterior chamber	1	2.1
	valve extrusion	1	2.1
	Endothelial touch	3	6.3

Table (7) show number of surgeries per eye per patient among the studied patients. Most eyes (68.8%)

underwent one surgery, while (25.0%) underwent two surgeries.

Table (7) Number of surgeries and complications among the studied sample of eyes.

Variable	No. (N=48)	% (100%)	
Number of surgeries	One	33	68.8
	Two	12	25.0
	Three	1	2.1
	Four	1	2.1
	Seven	1	2.1
Complications	Yes	18	27.5
	No	30	62.5

4. Discussion

The incidence of PCG varies substantially in different ethnic groups from 1 in 1250 births in Slovakian Roms [4] to 1:20,000 in Scandinavian regions [5]. In the West, the average incidence is about 1 in 10,000 births[6], but appears to be higher in Asians. In Saudi Arabia, it is reported to be 1:2500 [7], while Indian data from Andhra Pradesh reported an incidence of 1:3300[8].

Despite its infrequent incidence, PCG accounts for 7–20% of childhood blindness [9-13],this disproportionate share of pediatric blindness may be because diagnosis is frequently delayed, resulting in an unnecessarily poor outcome despite appropriate treatment. Once the disease has advanced due to delayed diagnosis, little can be done in terms of visual rehabilitation of these children [11].

Although not a nation-wide figure, yet it clearly agrees with previous reports of PCG being more common in inbred communities with more consanguineous marriages, such as in Egypt, Saudi Arabia [13], India [11] and among Slovakian Gypsies [10,12,14].

In our study female is dominant, 16 (57.1%) were females and 12 (42.9%) were males. This is in agreement with, a recent report from Saudi Arabia revealed a slight female preponderance in PCG cases, which was accounted for by a selection bias in data collection [15]. Nevertheless, the study of Prashant Bhushan was reported that 72.22% children were male and 27.7 % were female [16].

Laterality distribution in the current study demonstrates that bilateral cases are predominate, which is in agreement to other reports in the literature, which emphasize the predominantly bilateral nature of the disease [17,18,15,19]. It might be possible that the disease phenotype is more severe in some populations than in Egypt, which may be related to the nature of the causative mutations in these populations, although there are no published studies of any genotype difference between unilateral and bilateral PCG cases.

Parental age does not seem to be a factor related to the occurrence of PCG as there were no extremes of parental age detected in this series. There is no mention of parental age in published reports on PCG.

The mean age of patients was 9.1 ± 17.5 months in our study. However the study of Dave [20] reported that the mean age at surgery was 15.4 ± 4.9 months. It was slightly higher than that reported from other parts of the world – namely, Saudi Arabia the mean age was 7.9 ± 15.6 [15] and India the mean age was 8.6 ± 12.9 [21,22] – further emphasizing the notion of a more severe disease phenotype in these populations (which both present earlier) than in the current locale of the study in Benha City of Egypt; after all, the current study locale may not be generalizable to the whole of Egypt. Nevertheless, in the current series, the cases that needed more than one glaucoma surgical procedure presented earlier, supporting the hypothesis that the more severe the disease the earlier the presentation and the more difficult the treatment.

In our study observed the mean IOP decreased significantly ($p < 0.001$) from 26.2 ± 5.4 mmHg preoperatively to 13.7 mmHg at the 1st postoperative week, 15.5 mmHg at the 1st postoperative month, 16.8 mmHg at the 3rd postoperative month, 14.7 mmHg at the 6th postoperative month and to 12.9 mmHg at the last postoperative follow up visit. However results of the current study could be compared with the study of Mandal et al [21] that included 299 patients with primary congenital glaucoma in whom, mean IOP significantly decreased from 26.6 ± 6.2 mmHg to 14.4 ± 4.9 mmHg at last follow up visit.

The present study showed that the mean horizontal corneal diameter decreased significantly ($p < 0.001$) from 13.6 mm preoperatively to 13.4 mm at the 1st week postoperative, 13.3 mm at the 1st month postoperative,

13.2 mm at the 3rd months postoperative, 13.1 mm at the 6th month postoperative, and to 12.9 mm at the last postoperative visit. However the study of Helmy [23] showed that the postoperative diameter slightly reduced.

The mean CDR decreased significantly ($p < 0.01$) from 0.66 preoperatively to 0.55 at the 1st week postoperative, 0.56 at the 1st month postoperative, 0.52 at the 3rd months postoperative, 0.5 at the 6th month postoperative, and to 0.41 at the last postoperative visit. In agreement with our findings, a Cohort study performed by Mandel et al [21], mean CDR decreased from 0.67 preoperatively to 0.54 at the 6th month postoperatively.

The observed reversibility of cupping with successful IOP control in PCG is again demonstrated well, which is in agreement with other reported results in previous studies [24–25]. Of note, the average age at surgery in the current series matched what was reported in previous reports in which, reversibility of optic disc cupping was observed.

Most eyes (68.8%) underwent one surgery, while the majority of eyes had no complications. There were no serious intraoperative or postoperative complications compared to other studies that serious complication occurs as in Al-Hazmi et al [26]. The most common complication was peaked pupil (10.5%), followed by cataract (8.4%), endothelial touch (6.3%). There was no incidence of bleb leakage, bleb-related infection or endophthalmitis as occurred in the study of Mandel et al [27]. Based on these results, we believe that simultaneous bilateral surgery can be undertaken safely in these patients. However, strict intraoperative asepsis is mandatory and the second eye should be operated as if performing a surgical procedure on a different patient [27]. The only case of flat AC encountered resolved spontaneously within the first postoperative week.

The criteria of total success are fulfilled in 70.8% of the cases, partial success in 20.8% and 8.3% of patients were considered failure. A study in Tunisia reported a success rate of 64.2% after postoperative monitoring for one year [28]. These relatively unsatisfactory results could be explained by the delay in the diagnosis of their patients. As for the postoperative functional result, it is difficult to assess due to the young age of the patient. The need for IOP-lowering medications in some cases after the surgery to control the IOP – the so called by some authors ‘qualified success’ – is much less than the reports from other studies [26,14].

The aim of this study was to evaluate the surgical outcome of infants with developmental glaucoma who were operated within 6 months of birth. Kaplan–Meier survival analysis demonstrated the success probabilities along the period of follow-up. Our success rate with initial surgery is significantly better than most of the reported results of initial goniotomy or trabeculotomy ab externo. Similarly, Mendicino et al [29] reported a success rate of 87% over a mean follow-up of 38.422.5 months. Studying the success rates among operated eyes, for all study eyes and for those requiring more than one surgical procedure reveals a clearly declining success

rate (with an increase in qualified success rates) over time. Intractable childhood glaucoma generally reported to require more than one glaucoma surgical procedure with poor reported success rate [30,31,32]

It was found that no relation between outcomes and family history, consanguinity, gender and laterality, but there was significant relation with (age, preoperative IOP and number of surgeries). In the BIG study, Papadopoulos et al [14] failed to find an association between IOP control and initial IOP, sex, ethnicity, time to surgery from diagnosis, corneal diameter, or the age of diagnosis.

Lower IOP, smaller corneal diameter, and corneal clarity at presentation were predictors for good outcome but not earlier age at presentation by itself.

Results showed the median age of patients with true success was 6.5 months, while in patients without true success, the median age was 2.25 months, with statistical difference between groups ($p < 0.001$) and the mean preoperative IOP of patients with true success was 24.9 mmHg, while in patients without true success, the mean IOP was 29.4 mmHg, with statistical difference between groups ($p = 0.008$). *st. "t"*; student t-test.

It was found that age (positive correlation; the older the age, the better the outcomes) and preoperative IOP (negative correlation; the lower the preoperative IOP, the better the outcomes) are the predictors for true success, $p = 0.024$ and $p = 0.033$, respectively.

ROC curve analysis showed that age and preoperative IOP can significantly predict true success, $AUC = 0.794$ and $AUC = 0.743$, respectively.

5. Conclusion

Congenital glaucoma is a polygenic disorder characterized by the improper development of aqueous outflow system of the eye, hence resulting into a rise in intraocular pressure which is often present at birth. When recognized early and appropriate therapy applied, there can be significant improvements to the visual future of the children. The most commonly performed procedure was trabeculectomy augmented with mitomycin-C followed by isolated trabeculotomy and combined trabeculotomy-trabeculectomy.

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