Original Article

Mean Change in Intra-Ocular Pressure Following Trabeculectomy with Mitomycin C in Congenital Glaucoma

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Purpose: To determine the mean change in intraocular pressure after trabeculectomy with Mitomycin C surgery in primary congenital glaucoma.

Study Design: Quasi experimental study.

Place and Duration of Study: Outpatient department of Ophthalmology Hayatabad Medical Complex, Peshawar. From Jan 20, 2016 to June 20, 2016.

Material and Methods:. Patients of both genders between age of 0-6 years with PCG and IOP of 21 mm Hg or more with and without topical anti-glaucoma medication were included in the study. Eyes with complicated or traumatic cataract and previous ocular surgeries were excluded from the study. Sample size was calculated by WHO software for sample size calculation using 77.10 % proportion of decrease in IOP and 95% confidence interval and a 7% margin of error. Diagnosis was confirmed by examination under general anesthesia. All the surgeries were done by same ophthalmologist. 0.4 mg/ml of MMC was applied below the flap for two minutes followed by copious irrigation. Follow up visit was done on 14th post-operative day. EUA was performed 2 months after surgery where the eye was examined for Bleb morphology, leakage, infection or any other complication.

Results: In this study 38 patients undergoing Trabeculectomy with Mitomycin C were followed. Out of 38 patients 24 were male and 14 were female. Average age was 1.49 ± 0.95SD years. Average pre-operative intraocular pressure (IOP) was 29.81 ± 4.80 SD while post-operative IOP was 17.21 ± 3.82 SD.

Conclusion: Intraocular pressure was decreased significantly in patients after Trabeculectomy with Mitomycin C.

Key words: Congenital glaucoma, Trabeculectomy, Mitomycin C.

Glaucoma is the leading cause of irreversible blindness worldwide[1]. It is considered the second most common cause of blindness affecting 60 million people worldwide, with an estimated 8.4 million people blind due to glaucoma. This overwhelming figure is set to increase to 80 million diseased and 11.2 million blind by 2020[2]. In Pakistan, glaucoma is the fourth most important cause of irreversible blindness[3].

In infancy, Primary congenital glaucoma (PCG) is the most common type of glaucoma with an incidence of 1 in 10,000 to 68,000 live births among different ethnic populations. Worldwide PCG is responsible for

about 18% of children in institutions for the blind and 5% of overall pediatric blindness[4]. The incidence of PCG in the Pakistani children is about nine times higher than that in Caucasians[3]. The incidence of PCG varies when high rates of consanguinity are present[5].

Medical therapy plays only an adjunctive role to the main treatment strategy, which is surgical management of congenital glaucoma. In order to maintain best visual function before permanent structural changes occur to the eye, surgery should be considered as early as possible[4]. Successful control of IOP through surgical treatment is crucial to provide a lifetime vision, in children with glaucoma[6]. In glaucoma surgery, the resistance to the aqueous outflow due to structural abnormalities in the anterior chamber angle are bypassed. Insertion of anterior ciliary body and iris overlapping the trabecular meshwork and presence of non-permeable barkan's membrane over the trabecular meshwork are the main structural abnormalities in the angle of congenital glaucoma patients[7].

Regarding surgical options, trabeculectomy is an effective treatment option in primary congenital glaucoma. It is however challenging in children and because of a vigorous healing reaction, trabeculectomy is less successful when compared with outcomes in adults[7]. This reduced surgical success rate is due to postoperative proliferation of fibroblast and scarring of the filtering bleb.

To prevent scarring of the filtration bleb numerous techniques have been applied including application of anti-metabolites, anti-VEGF agents and Beta radiation[8]. To improve the success rate, 5-fluorouracil and Mitomycin C are most commonly used as a surgical adjunct to prevent bleb scarring[9]. Mitomycin C (MMC) selectively inhibits DNA replication, mitosis, and protein synthesis. The drug inhibits the proliferation of fibroblasts, suppresses vascular in-growth. Optimum concentration and exposure time are not known and vary between 0.2–0.5 mg/ml and 1–5 min[10].

No proper data is available regarding IOP control after trabeculectomy with MMC in our community. There is limited local data available about the outcome of trabeculectomy surgery and its effectiveness in decreasing intraocular pressure. The international data available also shows a wide range of variance in decreasing intraocular pressure after trabeculectomy with MMC. This study is designed to find out the accurate mean decrease in intraocular pressure after trabeculectomy with MMC locally. The data and results will be shared with the local consultants.

MATERIAL AND METHODS

Patients attending the outpatient department of Ophthalmology Hayatabad Medical Complex, Peshawar, of both genders between age 0 - 6 years with PCG and IOP of 21 mm Hg or more with and without topical anti-glaucoma medication were included in the study. Eyes with complicated or traumatic cataract, previous ocular surgeries like repair, squint surgery, retinal detachment surgery, cataract extraction etc., previous ocular trauma, intra-operative vitreous loss, post-operative endophthalmitis and eyes which received trauma postoperatively in the follow up period, were excluded from the study.

Provisional diagnosis of congenital glaucoma was made in OPD after initial examination of all children. Diagnosis was confirmed by examination under general anesthesia. Both eyes were examined. The intraocular pressure was measured first, using Perkins Tonometer. Horizontal corneal diameter was measured with calipers. Gonioscopy was done with Swan Jacob goniolens. Further evaluation including anterior segment examination, Fundoscopy and retinoscopy (if the cornea was clear enough) was performed. The patient's condition was explained to parents and consent obtained for surgery which was performed under general anesthesia on the nearest available list. All the surgeries were done by single consultant ophthalmologist.

A limbal-based conjunctival and tenon's capsule flap was made. A rectangular (4×3 mm) partial thickness scleral flap was fashioned supero-temporally/supero-nasally with 15 size blade or crescent knife up-to clear cornea and 0.4 mg/ml of MMC was applied sub-conjunctively and below the flap for two minutes followed by copious irrigation with Balanced Salt Solution. Scleral flap was sutured using 10/0 nylon applied on corners of scleral flap. Conjunctiva was closed with 10/0 nylon suture. Topical combination of steroid and antibiotic medications was started on the first post-operative day for 8 to 12 weeks.

Every patient underwent follow up visit on 14th post-operative day. EUA was performed 2 months after surgery where the eye was examined for Bleb morphology, leakage, infection or any other

complication, which can be related to surgery along with afore-mentioned parameters.

Intraocular pressure was measured before surgery on the day of surgery and 2 months after the surgery by Perkin's tonometer to calculate the mean change.

Total sample size was 38 which was calculated using Confidence Interval (2 sided): 95%, Power: 90%, Mean Group 1: 27.40, Mean Group 2: 19.40, Mean Difference: 08, Standard Deviation Group 1: 6.3, Standard Deviation Group 2: 8.5.

Data was analyzed utilizing SPSS format of windows 20. For quantitative variables like age, preoperative and postoperative intraocular pressure mean ± standard deviation was calculated. Frequency and percentage were used for qualitative variables like gender and eye involved. Comparison of pre and post-operative intraocular pressure was done using Paired t test. To see the effect modification, pre and post-operative IOP was stratified among gender and age. To see the effect modification, post stratification pair t-test was applied. P value < 0.05 was taken as significant.

RESULTS

38 patients undergoing Trabeculectomy with Mitomycin C. were followed. In which 24 (63.15%) were male and 14 (36.84%) were female patients. Male to female ratio was 1.71:1 (Table 1). Right eye was involved in 21 (55.26%) cases while the rest of 17 (44.73%) patients had left eye involvement (Table 2).

Table 1: Gender wise distribution of patients.

Gender	Frequency	Percentage (%)
Male	24	63.15
Female	14	36.84
Total	38	100

Table 2: Laterality (side) wise distribution of patients.

Eye Involved	Frequency	Percentage (%)
Right	21	55.26
Left	17	44.73
Total	38	100

Mean pre-operative intraocular pressure (IOP) was 29.81 + 4.80 S.D while post-operative IOP which decreased in patients after Trabeculectomy with Mitomycin C to 17.21 + 3.82 S.D and was found highly significant with p-value < 0.003 (Table 3).

Table 3: Comparison of mean pre-op and post-op IOP in total patients.

IOP (mm Hg)	N	Mean	Std. Dev	P Value
Pre op IOP	38	29.81	4.80	< 0.003
Post op IOP	38	17.21	3.82	

Paired t- test applied

Stratification for pre-operative and post-operative IOP with regards to age groups showed that there was statistically significant lowering of IOP in both the age groups whether it was less than or more than 1 year of age (Table 4). Similar pattern was found when the pre-op and post-op IOP was stratified with regard to gender, as P-value was less than 0.05 indicating significance. P-value for male and female was found to be less than 0.003 and 0.005 in both the age groups respectively (Table 5).

Table 4: Stratification for pre-op and post-operative IOP with regard to age groups.

Age Group	N	IOP	Mean ±S.D	P-value
≤ 1year	14	Pre-op	30.07 ± 4.77	< 0.004
		Post -op	17.41 ± 4.11	
> 1 year	24	Pre-op	29.66 ± 4.73	< 0.005
		Post -op	17.08 ± 3.39	

Table 5: Stratification for pre-op and post-operative IOP with regard to gender.

Gender	N	IOP	Mean ±S.D	P-value
Male	24	Pre-op	29.62 ± 4.94	< 0.003
		Post -op	17.41 ± 4.1	
Female	14	Pre-op	30.14 ± 4.73	< 0.005
		Post -op	16.85 ± 3.39	

When pre-operative and post-operative mean IOP was stratified with regard to eye involved it was found significant statistically (P-value < 0.05) in both the right and left eye. P-value for right eye and left eye was less than 0.005 and 0.002 respectively (Table 6).

Table 6: Stratification for pre-op and post-operative IOP with regards to eye involved.

Side	N	IOP	Mean ±S.D	P-value
Right	21	Pre-op	30.61 ± 4.77	< 0.005
		Post –op	17.53 ± 4.1	
Left	17	Pre-op	28.8 ±4.73	< 0.002
		Post –op	17.2 ± 4.3	

DISCUSSION

Primary congenital glaucoma (PCG) is the leading cause of blindness in infancy with an incidence of 1 in 10,000 to 68,000 live births among different ethnic populations[4]. An imbalance of aqueous production and aqueous outflow via the trabecular meshwork and the uveoscleral pathway results in raised intraocular pressure. In congenital glaucoma, the pathology lies in the trabecular meshwork which exhibits a developmental defect leading to raised intraocular pressure[11]. The primary objective in the management of primary congenital glaucoma is to prevent loss of visual function and preserve the ocular integrityby normalizing and permanently controling the intraocular pressure[12].

Primary treatment option for treating congenital glaucoma is surgical with medical therapy having only an adjunctive role. Surgery should be considered as early as possible to prevent permanent visual loss[4].

Male predominance was seen in this study accounting for 63.15% of cases. The literature showed a preponderance of males in 65-80% of the cases[13]. Olusanva et al, in their study on outcome of Trabeculectomy in congenital glaucoma had a male to female ratio of 3.5:1. In their study the male population accounted for 77.7% of the total sample[14]. However, in certain ethnicities the incidence of congenital glaucoma is more in female gender. In Japan females are more affected, with a ratio of girls to boys of 3:2[15].

Average pre operative intraocular pressure (IOP) in this study was 29.81 + 4.80 SD while post operative IOP was 17.21 + 3.82 SD which was decreased in patients after Trabeculectomy with Mitomycin C and found highly significant. Our results are comparable to other similar studies. Essuman et al. reported the mean pre-operative and postoperative intra-ocular pressures of 30.3 ± 8.8 mmHg and 18.1 ± 6.8 mmHg respectively following Trabeculectomy with Mitomycin C. The difference between pre-operative and post-operative IOP in their study was statistically significant[16].

Postoperative fibrosis and scarring at the surgical wound site is a known complication and a risk factor for failure of surgery. Postoperative scarring may hamper the drainage of aqueous fluid from anterior chamber through the artificial opening made during glaucoma drainage surgery[17]. Mitomycin is an alkylating agent which reduces the fibroblast proliferation and reduces the amount of scarring[18]. Susanna et al in their study showed that the use of Mitomycin reduces post surgery fibrosis and attributed to the favourable results in casess with adjuvant use of Mitomycin C[19].

In more than 80% of cases, the onset of the clinical profile of the disease appears during the first year of life, with 25% diagnosed in the neonatal period and 60% during the first 6 months of life[20]. In our study, the highest number of cases presented during the first year of life accounting for 36.84% of the study cohort. One of the many possible explanations to the problem is lack of patient education regarding the disease. Advanced disease is a known risk factor for poor outcome in congenital glaucoma which is often associated with poor visual prognosis. Nevertheless, late presentation is a problem commonly encountered in developing countries[21]. Olusanva et al reportedly had 50% of cases presenting after first year of life[14].

We did not encounter any patient for bleb revision or repeat surgery due to raised IOP in our series. Moreover, for early postoperative bleb leaks we never had to use a bandage contact lens, as described by some authors. There was no incidence of choroidal effusion which is reported in 17-23% of cases in other studies[22].

CONCLUSION

Trabeculectomy with Mitomycin C is a safe and effective method in lowering intraocular pressure in cases of Primary Congenital Glaucoma. It is helpful by reducing the intraocular pressure and in preventing further structural changes to the eye and thus forestalling permanent visual disability. It is a convenient and economical method to manage congenital glaucoma.

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