

Evaluation of corneal endothelial changes in Glaucomatous eyes undergoing trabeculectomy: a hospital based prospective study in north India

Lt Col (Dr) Ashok Kumar¹, Brig (Dr) Poninder Kumar²,

Col (Dr) Vinod Kumar Baranwal³

^{1,2,3} Army College of Medical Sciences & Base Hospital, Delhi Cantt, New Delhi, India-10010

Corresponding Author : Lt Col (Dr) Ashok Kumar

Introduction: Glaucoma is a disease in which a progressive loss of retinal ganglion cells is characterized by a recognizable pattern of both visual function loss & optic nerve pallor and excavation. Medical management of glaucoma has many drawbacks like lack of compliance by the patients, high cost factor, toxicity of drugs, drug resistance, continued loss of visual acuity and field despite adequate control of IOP and failure of regular follow-up visits. Glaucoma patient have decreased mean endothelial cell density. Corneal endothelial cell count has been shown to be further reduced after glaucoma filtration surgery. Decrease in endothelial cell count depends on no of factors like type of Glaucoma, Intra-operative use of mitomycin-C, post-op shallowing of anterior chamber. **Objective:** To quantify changes in corneal endothelial cell count, central corneal thickness and structural changes like pleomorphism/polymegathism in patients undergoing trabeculectomy. **Material & Methods:** Trabeculectomy was carried in 30 patients of Primary Open/Closed angle Glaucoma using standard technique. Pre-operatively and post-operatively at 01 & 06 weeks patients were evaluated by Specular microscopy, Pachymetry, IOP and best corrected visual acuity. Intra-operative Mitomycin-C in standard concentration was used in 11 patients with standard post-operative treatment regimen followed. **Results:** There was no statistically significant difference in cell count or pachymetry value change at 1 or 6 week post-operatively with a P value of > 0.05. No significant change in cell size (Polymegathism) or shape (Pleomorphism) was noted post-operatively. The IOP was well controlled in all patients post-operatively. Shallowing of anterior chamber was noted on 1st post-operative day in 3 patients (27%) whom Mitomycin-C was used which improved over next 2-3 days with conservative management without significant endothelial cell loss. **Conclusion:** Corneal endothelial cell density do decreases after Trabeculectomy like other intra-ocular surgical procedures. But there is no significant decrease in endothelial cell count or significant change in corneal thickness following Trabeculectomy when there is no prolonged shallowing of anterior chamber. **Keywords :** Glaucoma, Trabeculectomy, endothelial cell density, Mitomycin-C

Date of Submission: 28-05-2018

Date Of Acceptance: 11-06-2018

I. Introduction :

The glaucoma is a disease in which a progressive loss of retinal ganglion cells is characterized by a recognizable pattern of both visual function loss & optic nerve pallor and excavation. Untreated natural course is toward blindness or at least significant visual disability [1]. Attempts have been made to control the progressive visual loss from the disease by controlling IOP through medical, surgical and laser therapy. Medical management of glaucoma has many drawbacks like lack of compliance by the patients, high cost factor, toxicity of drugs, drug resistance, continued loss of visual acuity and field despite adequate control of IOP and failure of regular follow-up visits. These facts forced the clinician to take a recourse to surgical management more often than perusing the unsuccessful path of satisfactorily controlling IOP [2]. Trabeculectomy is a filtering surgery for eyes with glaucoma. Trabeculectomy involves creation of a lamellar scleral flap, excision of a short length of canal of schlemm and forming a filtration channel into subconjunctival space [3]. Essential function of corneal endothelial cells is to maintain corneal transparency. Endothelial cell density decreases as age progresses [4]. Certain ocular diseases and especially surgical trauma leads to reduction in endothelial cell count [5]. Glaucoma patient have decreased mean endothelial cell density [6]. Corneal endothelial cell count has been shown to be further reduced after glaucoma filtration surgery [7, 8]. There can be many causes for corneal endothelial cell damage during trabeculectomy. This damage can be compounded by the use of per-operative mitomycin-C in augmented trabeculectomy. An important factor leading to the damage of corneal endothelium is post-operative shallow anterior chamber and duration of same [9-12]. A study was therefore undertaken at a tertiary eye care centre in North India with the aim to study corneal endothelial changes in form of endothelial cell counts, central corneal thickness and structural changes like polymegathism or pleomorphism

II. Materials & Methods

A study to evaluate corneal endothelial changes was carried out among the patients undergoing Trabeculectomy at a tertiary eye care centre in north India. It was a prospective, interventional study with all patients of primary Glaucoma whether open angle or closed angle on gonioscopy fitting into criteria for filtration surgery (definitive progression of glaucoma despite being on maximal topical therapy) were included over a period of 01 year (01 Jan 2017 to 31 Dec 2017). We excluded all patients of secondary glaucoma, patients with advanced corneal diseases precluding specular microscopy,

patients who underwent Phaco-trabeculectomy, patients with pseudo-exfoliation syndrome or patients who were unable to complete follow-up.

All patients were evaluated with BCVA, IOP using Goldmann applanation Tonometer, Gonioscopy, detailed fundus examination including disc evaluation. These all patients were subjected to endothelial cell count using Topcon SP-2000P model and central corneal thickness measurement using Pachette 2 (Model DGH-550) pre-operatively and repeated at 01 week and 06 week postoperatively and compared using paired-T test for data analysis.

Surgical Procedure

All cases were operated under peri-bulbar anaesthesia by the same surgeon with good surgical experience. Irrigation of the ocular surface with 0.5% betadine solution followed by rinsing with Ringer lactate solution. Application of eye speculum & superior rectus suture done. Limbal based conjunctival flap, 8 mm post to upper limbus. Light thermal cauterization of prominent vessels on sclera. A 5 mm square partial thickness scleral flap dissected 1 mm into clear cornea. Completion of trabeculectomy by cutting 4x1 mm rectangular area of the deep sclero-trabecular lamella followed by peripheral button hole iridectomy. Repositioning of scleral flap and closure of scleral incision by 2-3 interrupted 8-0 silk sutures. Repositioning of conjunctiva-Tenon's flap and closure with 10-0 silk sutures. Sub-conjunctival injection of Dexamethasone + Amikacin given and eye patched for 24 hours. Post-operatively all the patients received oral antibiotics for 5 days, topical steroids, cycloplegics and NSAIDS.

Post-operative follow-up:- Pad and bandage were opened on 1st post-operative day. Antibiotic- steroid drops & cycloplegics instilled & eye observed for post-operative inflammation or shallowing of anterior chamber. Schedule for post-operative follow-up was- Day 1, 2, 7, 14, 28 & 42. Specular Microscopy (Fig 1) & Pachymetry (Fig 2) were performed pre-operatively, at 1 week & 6 week post-operatively (Table 1).



Fig 1: Specular Microscope



Fig 2: Pachymetry

III. Results

Total 30 patients were recruited in this study and underwent trabeculectomy procedure with standard techniques by same ophthalmologist. Out of total 30 patients, 20 (66.6%) were cases of Primary open angle glaucoma (POAG) and 10 (33.3%) were cases of angle closure glaucoma (PACG). Of total 30 patients in this study 18(60%) were male & 12(40%) were female (Fig 3). The mean age of patients included was 57.9years (ranging from 32-74 years). Vision of patients undergoing trabeculectomy ranged between 20/200 to PL+ve and IOP ranged between 22-38 mm Hg on maximal topical medication (Table 1).

Average endothelial cell count pre-operatively was 2156 ± 223.34 cells per millimeter square with cell count decreased to 2104 ± 234.67 cells per millimeter square at 1 week post-operatively with 2.4% decrease in cell counts which was not significant ($p > 0.05$). Endothelial cell count at 06 week post-operative was 2056 ± 257.27 cells per millimeter square with 4.6% decrease from baseline which was also not significant ($p > 0.05$).

In PACG group, average endothelial cell count pre-operatively was 1711 ± 232.67 cells per millimeter square, which was lower than the POAG group but no significant decrease ($p > 0.05$) was observed in endothelial cell count at 01 week and 06 week (3.2% decrease at 01 week and 6.2% at 06 weeks).

Mitomycin-C augmented trabeculectomy was done in 11(36.6%) patients. Average endothelial cell count pre-operatively in this group was 2065 ± 220.7 cells per millimeter square, which was lower than the POAG group but no significant decrease ($p > 0.05$) was observed in endothelial cell count at 01 week and 06 week (3.2% decrease at 01 week and 6.24% at 06 weeks) which was comparable to PACG group. Shallowing of anterior chamber was observed in 03(22.7%) patients in Mitomycin-C group, but they responded to conservative management in form of patching with well formed anterior chamber in 24-48 hours.

On evaluation of central corneal thickness(CCT), average CCT pre-operatively was 502 micron metre which increased to 526 micron metre at 1 week post-operatively(4.78% increase from baseline) and 533 micron metre at 6 weeks post trabeculectomy(6.17% increase) which were non significant with $p > 0.05$. No statistically significant difference in central corneal thickness was observed in sub-groups of patients treated with mitomycin-C augmented trabeculectomy or PACG patients. No obvious change in cell size (Polymegathism) or shape (Pleomorphism) was noted post-operatively.

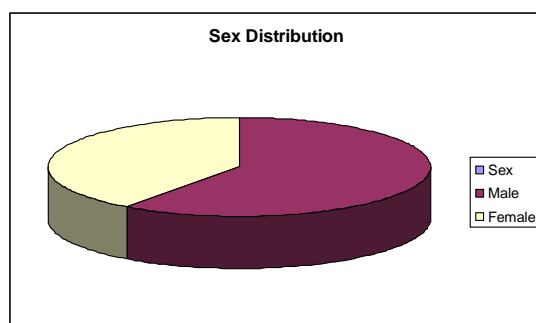


Fig 3: Sex Distribution of patients

S No	Age/Sex	Diag.	DVA	IOP	C:D ratio	Specular Count			Pachymetry (um)		
S No	Age/Sex	Diag	DVA	IOP	C:D	Pre	1 st wk	6 th wk	Pre	1 wk	6wk
1	50/F	POAG (RE)	6/60	24	0.9	2504	2430	2426	523	528	536
2	55/M	POAG (RE)	1/60	26	0.9	2418	2368	2357	514	519	521
3	68/M	POAG (RE)	PL	28	0.9	1924	1869	1854	498	501	506
4	68/M	PACG (LE)	PL	26	0.9	2140	2104	2087	507	518	524
5	54/M	POAG (RE)	6/60	24	0.8	2510	2478	2462	496	494	492
6	66/F	POAG (LE)	4/60	24	0.7	2550	2538	2506	506	503	502
7	70/M	PACG (LE)	PL	38	0.9	1836	1668	1484	528	547	556
8	32/F	PACG (LE)	PL	28	0.9	2386	2296	2284	504	511	518
9	61/M	PACG (LE)	PL	30	0.9	1868	1848	1822	536	540	542
10.	74/M	POAG (RE)	6/60	22	0.9	2238	2198	2182	526	529	530
11.	60/M	PACG (LE)	HMCF	30	0.8	2016	1964	1896	490	499	502
12.	51/F	POAG (RE)	2/60	28	0.8	2239	2208	2190	526	533	538
13.	32/M	PACG (LE)	6/60	34	0.7	2458	2408	2346	516	524	528
14.	47/F	PACG	1/60	30	0.8	2218	2164	2136	528	534	540
15.	60/F	POAG	3/60	28	0.9	2068	1986	1926	498	502	512
16.	65/F	PACG	HMCF	32	0.9	1866	1824	1738	536	542	556
17.	55/F	POAG	1/60	26	0.8	2114	2068	2004	526	532	542
18.	58/M	POAG	2/60	30	0.9	1894	1826	1746	518	524	532
19.	52/F	POAG	1/60	28	0.8	2424	2386	2294	546	548	558
20.	60/M	POAG	1/60	32	0.9	2278	2246	2228	512	516	522
21.	54/M	POAG	HMCF	30	0.9	1968	1920	1868	528	536	542
22.	56/M	POAG	3/60	28	0.8	2346	2318	2288	504	516	518
23.	60/F	PACG	HMCF	32	0.9	1892	1836	1728	496	508	524
24.	52/M	POAG	1/60	28	0.9	2006	1966	1884	548	554	558
25.	66/M	POAG	2/60	32	0.8	2236	2204	2168	544	558	562
26	65/M	POAG	1/60	32	0.8	2108	2054	1986	486	496	506
27	58/F	POAG	3/60	28	0.9	1958	1926	1872	562	574	588
28	64/M	POAG	4/60	30	0.9	2108	2052	2040	528	534	542
29	70/F	PACG	1/60	28	0.9	1856	1768	1726	544	554	568
30	56/M	POAG	3/60	26	0.8	2262	2206	2176	518	532	538

Table 1: Proforma of patients with endothelial cell counts ,central corneal thickness & clinical details

IV. Discussion

In the surgical management of glaucoma, trabeculectomy is the procedure of choice since its introduction by Cairns in 1968. Glaucoma surgery is known to induce a damage to corneal endothelium, a decrease of corneal endothelial cell density by 0.2-14.9% was reported by several authors There can be many causes for corneal endothelial cell damage during trabeculectomy. This damage can be compounded by the use of per-operative mitomycin-C in augmented

trabeculectomy. An important factor leading to the damage of corneal endothelium is post-operative shallow anterior chamber and duration of same.

Fiore and associates, reported 12% corneal endothelial cell loss in 8 eyes with shallow anterior chamber after trabeculectomy, but on the other hand, no significant decrease in cell density in 10 eyes with well maintained anterior chamber [13-16] and same has also been corroborated by our study as average endothelial cell loss at 1 week post-operative day was 52 cells per square millimeter (2.4% cell loss) which was statistically not significant ($p>0.05$) and also at 6 week post trabeculectomy when cell loss was 100 cells per square millimeter (4.6%).

Use of antimetabolites like Mitomycin-C & 5-FU decreases fibroblast proliferation and increases success rate of filtration surgery. Use of Mitomycin-C may have transient deleterious effect on corneal endothelium [17]. Sharma et al studied deleterious effects of MMC on the corneal endothelium 3 months post-operatively and average endothelial cell loss was 3.73% in standard trabeculectomy and 13.9% in trabeculectomy with MMC [18]. Our studied showed comparable results with endothelial loss 3.2% decrease at 01 week and 6.24% at 06 weeks with 03 patients showing shallowing of anterior chamber on 1st post-operative day which was managed conservatively. Dreyer et al also studied effect of MMC on anterior segment and found 7-8% corneal endothelial cell loss as compared to preoperative counts [19] which were more than this study.

In PACG group, average endothelial cell count pre-operatively was lower than the POAG group but no significant decrease ($p>0.05$) was observed in endothelial cell count at 01 week and 06 week (3.2% decrease at 01 week and 6.2% at 06 weeks). So, this was first attempt to study endothelial cell changes in different sub-groups of primary glaucoma patients undergoing trabeculectomy.

Corneal thickness is related directly to the health of corneal endothelium. Its measurement after cataract surgery and glaucoma surgery is an excellent indication of the amount of endothelial trauma sustained during surgery [20]. In our study, no statistically significant difference in central corneal thickness was observed in sub-groups of patients treated with mitomycin-C augmented trabeculectomy or PACG patients. No significant change in cell size (Polymegathism) or shape (Pleomorphism) was noted post-operatively.

Our study had advantage of studying different variable of endothelial cell changes in form of endothelial cell count, central corneal thickness and structural changes in different subgroups of patient like POAG, PACG, with use of mitomycin-C undergoing trabeculectomy. The essential disadvantage of this study is short follow-up period of 06 weeks post-operative but it helped in depicting immediate post-operative changes which will have bearing on long term effects. Patients are being followed up for evaluation of long term effects on endothelial changes.

V. Conclusion

Glaucoma patient have decreased mean endothelial cell density. Corneal endothelial cell count has been shown to be further reduced after glaucoma filtration surgery. There can be many causes for corneal endothelial cell damage during trabeculectomy. This damage can be compounded by the use of per-operative mitomycin-C in augmented trabeculectomy. An important factor leading to the damage of corneal endothelium is post-operative shallow anterior chamber and duration of same. Maintaining proper deep anterior chamber during and after surgery can reduce endothelial cell changes and subsequent complications in these patients especially when performing mitomycin-C augmented trabeculectomy.

Références :

- [1]. Ivan Goldberg. Glaucoma in the 21st century (2000) . Edited by RN Weinreb, Y Kitazawa GK Krieglstein, Mosby International Ltd.
- [2]. Duke Elder Vol. XI : System of Ophthalmology, Diseases of the Lens and Vitreous, Glaucoma and Hypotony. Henry Kimpton, London : pg 380-388
- [3]. Sihota R & Tandon R. In Parson's Disease of Eye (2007). 20th Ed. Elsevier;287
- [4]. Fernando Cesar Abib, Jackson Barretto (2001). Journal of Cataract & Refractive Surgery Oct ;Vol 27; Issue 10; 1574-1578
- [5]. Behring D, Reinhard T, Speilberg HCL (2002). Influencing factor on chronic endothelial cell loss characterised in a homologous group of patients. Br. J. Ophthalmol; 86; 35-38
- [6]. Gagnon MM, Boisjoly HM, Brunette I (1997). Corneal endothelial cell density. Cornea; 16;314
- [7]. Amavielle S, Lafontaine PO, Bidot S, Creuzot-Gacher C (2007). Corneal endothelial cell changes after trabeculectomy & deep sclerectomy. J. of Glaucoma. May; 16(3):324
- [8]. Smith DL, Skuta GL, Lindenmuth KA (1991). The effect of glaucoma filtration surgery on corneal endothelial cell density. Ophthalmic Surg ;22: 251
- [9]. S Amnavielle, PO Lofantine, S Bidot, C Creuzot-Garcher, PD>this, A M Brown (2007) . Journal of Glaucoma; Vol 16; No3; May ; 324-328
- [10]. Beckers HJ, Kinders KC, Webers CA (2003). Five-year results of trabeculectomy with mitomycin C. Graefes Arch Clin Exp Ophthalmol;241: 106
- [11]. Derick RJ, Pasquale L, Quigley HA (1991). potential toxicity of mitomycin C. Arch Ophthalmol;109: 1635
- [12]. Harish C Agarwal, V K Anuradha, J S Titiyal, Vinay Gupta (2005). Effect of intra-operative intracameral 2% Hydroxypropyl methylcellulose viscoelastic during trabeculectomy. Ophthalmic Surgery, Lasers and Imaging; Vol 36; No 4; July/Aug
- [13]. Fiore PM, Richter CU, Arzeno G, Arrigg CA, Shingleton BJ, Bellows AR, Hutchinson BT (1989). The effect of anterior chamber depth on endothelial cell count after filtration surgery. Arch Ophthalmology; 109: 1609-1611
- [14]. Korey M, Gieser D, Kass MA, Waltman SR, Gordon M, Becker BL (1982). Central corneal endothelial cell density and central corneal thickness in ocular hypertension and primary open-angle glaucoma. Am J Ophthalmol; 94: 610-616
- [15]. Smith DL, Skuta GL, Lindenmuth KA, Musch DC, Bergstrom TJ (1991). The effect of glaucoma filtering surgery on corneal endothelial cell density. Ophthalmic Surg; 22: 251-255
- [16]. Barak A, Alhalel A, Kotas R, Melamed S (1992). The protective effect of early intra-operative injection of viscoelastic in trabeculectomy. Ophthalmic Surg; 23: 206-209
- [17]. Rappaport, Liebmann, Ritch : Antimetabolites in glaucoma filtering Surgery, Advances in Clinical Ophthalmology Vol. 1, 1994, Mosby Year Book Inc.
- [18]. Sharma T, Sihota R, Agarwal HC (1998): Intraoperative Mitomycin & the Corneal endothelium, Acta Ophthalmol Scand Feb; 76 (1):80-82
- [19]. Dreyer EB, chaturvedi N, Zurakowski D (1995) : Effect of Mitomycin- C & Flurouracil supplemented trabeculectomies on the anterior segment. Arch Ophthalmol May; 113 (5): 578-80
- [20]. Daniel M Albert, Frederick A Jakobiec: Principles and Practice of Ophthalmology. 2nd edition; Chapter-60: 664-665.