Effect of Dorzolamide-Timolol Fixed Dose Combination on Central Corneal Thickness in Patients of Primary Open Angle Glaucoma Versus Normal Tension Glaucoma

Ophthalmol Pak. - Official Journal of College of Ophthalmology & Allied Vision Sciences

Aliya Ramzan[1], Saman Ali[2], Ummara Rasheed[3],
College of Ophthalmology & Allied Vision Sciences, Lahore.[1,3]
Mayo Hospital, Lahore.[2]

ABSTRACT

Purpose: To evaluate the effect of dorzolamide/timolol fixed dose combination on central corneal thickness in primary open-angle and normal tension glaucoma.

Methodology: This retrospective cohort study was approved by the Ethical Review Board of College of Ophthalmology and Allied vision Sciences (1469/23) and was conducted at Diagnostic clinic Mayo Hospital, Lahore from March, 2023 to September, 2023. Sample size was calculated by a formula whose level of significance was 5%, standard deviation 30.9 and test values of population mean was 540. Using non-probability convenient sampling method total sample size was 80 patients of age group 30 to 60 which divided into normal tension and primary open angle glaucoma of 40 each. Patients with corneal edema, diabetes, and allergic to dorzolamide-timolol fixed dose combination were excluded. Data was analyzed using SPSS version 25.00. Wilcoxon signed ranks test and chi-square test were used for the significance of the study. Data p-value <0.005 considered significant. All the tests were performed after patient's informed consent. Intraocular pressure (IOP) and central corneal thickness (CCT) were measured by Goldmann applanation tonometer and ultrasound Pachymeter respectively.

Results: IOP and CCT in right eye 16.17± 7.05 (p=0.000) and 545.50± 22.2 (p=0.098) respectively and of left eye 16.56± 7.00 (p=0.003) and 549.16± 20.0 (p=0.133) respectively. This illustrates significant difference in intraocular pressure after treatment in both eyes but insignificance difference in central corneal thickness.

Conclusion: Dorzolamide-Timolol combination successfully reduces IOP as intended and leads to no statistically significant change in central corneal thickness.

Keywords: Glaucoma, Open angle glaucoma, Normal tension glaucoma, Ultrasonography, Intraocular pressure.

How to Cite this Article: Ramzan A, Ali S, Rasheed U. Effect of Dorzolamide-Timolol Fixed Dose Combination on Central Corneal Thickness in Patients of Primary Open Angle Glaucoma Versus Normal Tension Glaucoma. Ophthalmol Pak.2024;14(2):41-46.
DOI: https://doi.org/10.62276/OphthalmolPak.14.02.83

Correspondence: Aliya Ramzan
College of Ophthalmology & Allied Vision Sciences, Lahore.
Email: aliyaramzan02@gmail.com

Received: 04-12-2023
Accepted: 19-12-2023

INTRODUCTION:

Glaucoma, a progressive optic neuropathy leading to visual impairment, with the primary treatment being the reduction of intraocular pressure (IOP) to prevent ganglion cell death.[1, 2] The irreparable damage to nerve fibre's necessitates early intervention to prevent total visual loss.[3-5] Glaucoma has various types, including primary open-angle glaucoma and normal-tension glaucoma, resulting from disrupted aqueous humour drainage.[6,7] Accurate intraocular pressure measurement is crucial, traditionally done with Goldmann Applanation Tonometry, although corneal thickness affects its accuracy.[8] Central corneal thickness (CCT) becomes pivotal in glaucoma diagnosis, as it influences intraocular pressure readings. Factors such as age, gender, and ethnicity impact central corneal thickness, and its decrease with age can lead to thinner corneas. The thin cornea is identified as a major risk factor for primary open-angle glaucoma development.[9] There is a major significance of corneal biomechanics in IOP measurement. The use of antiglaucoma drugs, specifically dorzolamide-timolol fixed combination (DTFC), is common in lowering intraocular pressure.[10,11] However, the impact of these drugs on central corneal thickness is conflicting. The study's objective was to investigate the effect of dorzolamide-timolol fixed dose combination on central corneal thickness in primary angle glaucoma and normal-tension glaucoma patients. Ultrasound pachymetry is the preferred method for measuring central corneal thickness, and the study aims to provide clarity on the contradictory findings in existing literature regarding the effect of antiglaucoma drugs on central corneal thickness. The device works by timing how long it takes for an ultrasound pulse to travel from the end of the Descemet's membrane back to the transducer. This measurement is known as the transit time.[12,13] This emphasizes the importance of measuring central corneal thickness for clinical diagnosis, accurate intraocular pressure estimation, and the detection of corneal cell affection post-treatment. It also introduces the first USA food and drug administration (FDA) approved intraocular pressure lowering fixed combination, dorzolamide-timolol fixed combination, comprising timolol and dorzolamide, known for their effectiveness and tolerability.[14] Finally, the study aims to conduct a meta-analysis and systematic review to consolidate existing evidence on the long-term impact of dorzolamide-timolol fixed dose combination on central corneal thickness in glaucoma patients.

METHODOLOGY

This retrospective cohort study was approved by the Ethical Review Board of College of Ophthalmology and Allied vision Sciences (1469/23) and was conducted Diagnostic clinic, Mayo Hospital, Lahore from March, 2023 to September, 2023. Sample size was calculated by a formula whose level of significance was 5%, standard deviation 30.9 and test values of population mean was 540.15 Using non-probability convenient sampling method total sample size was 80 patients of age group 30 to 60, later divided into normal tension and primary open angle glaucoma of 40 each after informed consent. Patients with corneal edema, diabetes, and allergic to dorzolamide-timolol fixed dose combination were excluded. Data was analyzed using SPSS version 25.00. Wilcoxon signed ranks test and chi-square test were used for the significance of the study. Data p-value <0.005 considered significant. All the tests were performed after patient's informed consent. Intraocular pressure and central corneal thickness were measured by Goldmann applanation tonometer and ultrasound Pachymeter respectively.

RESULTS

Table -1: Age Representation

Variable	N	Minimum	Maximum	Mean	Std. deviation
Age of patient	80	30.00	75.00	45.20	10.72
Valid N	80				

This table illustrates age, its maximum and minimum range and mean value of this age.

Total patients were 80 and the mean age was 45.2000.

Table -2: Comparison Of Normal Tension and Open Angle Glaucoma at 6 and 12-months Duration in Both Eyes Having Variables Like Iop and Cct.

Variables	Primary Open Angle Glaucoma			Normal Tension Glaucoma		
	Mean Value			Mean Value		
	6 months	12 months	p-value	6 months	12 months	p-value (Chi Square Test)
Pre-DTFC_IOP_OD	22.0±7.5	24.6±11.1	0.991	12.9±2.4	13.3±3.5	0.142
Post-DTFC_IOP_OD	16.0±5.0	14.3±4.57	0.437	13.7±2.6	12.5±3.0	0.091
Pre-DTFC_IOP_OS	22.2±7.5	23.6±10.4	0.985	14.0±3.9	13.6±3.9	0.012
Post-DTFC_IOP_OS	16.1±5.0	15.4±4.33	0.381	13.5±2.7	13.7±3.2	0.899
Pre-DTFC_CCT_OD	551.0±37.6	542.3±11.5	0.000	540.2±19.1	543.4±20.0	0.000
Post-DTFC_CCT_OD	527.8±58.0	555.8±36.1	0.975	544.0±22.3	550.4±37.6	0.115
Pre-DTFC_CCT_OS	551.2±37.9	544.0±18.2	0.000	543.4±16.9	545.6±13.3	0.000
Post-DTFC_CCT_OS	528.4±55.7	563.4±47.0	0.981	549.8±19.9	556.6±29.8	0.181

The table 2 illustrates mean and p-values of various variables (IOP and CCT) of both eyes (OD and OS) before using DTFC and after 6th and 12th month of DTFC usage in both primary open angle and normal tension glaucoma.

Table -3: Overall Result

Sr. #	Variables	Mean Values	p-Values (Wilcoxon signed ranks test)
1	Pre/Post-DTFC_IOP_OD	16.17± 7.05	0.000
2	Pre/Post-DTFC_IOP_OS	16.56± 7.00	0.003
3	Pre/Post-DTFC_CCT_OD	545.50± 22.2	0.098
4	Pre/Post-DTFC_CCT_OS	549.16± 20.0	0.133

This table shows overall mean and p-values of CCT and IOP variables before and after using DTFC in both eyes separately. P-values of IOP of right and left eyes before and after using DTFC is < 0.005 showing its statistical significance.

Table -4: Variables in Normal Tension Glaucoma

Sr. #	Parameter	N	CCT (mean)		IOP (mean)	
			OS	OD	OS	OD
1	Pre	40	545.00 ± 14.1	544.06 ± 22.2	13.7 ± 3.8	13.2 ± 3.2
2	Post - 6	40	549.83 ± 19.9	544.08 ± 22.3	13.50 ± 2.7	13.75 ± 2.6
3	Post - 12	40	556.6 ± 29.8	550.4 ± 37.6	13.7 ± 3.2	12.5 ± 3.0
4	P Value (Chi Square Test)		0.181	0.115	0.899	0.091

Table -5: Primary Open Angle Glaucoma

Sr. #	Parameter	N	CCT (mean)		IOP (mean)	
			OS	OD	OS	OD
1	Pre	40	546.75 ± 27.1	545.6 ± 24.6	23.15 ± 9.3	23.6 ± 9.9
2	Post - 6	40	528.4 ± 55.5	527.8 ± 58.0	16.1 ± 6.0	16.0 ± 6.0
3	Post - 12	40	563.4 ± 47.0	555.8 ± 36.1	15.4 ± 4.3	14.3 ± 4.5
4	P Value	0.981	0.975	0.381	0.437	0.437

This table 5 shows the p-values and mean values of central corneal thickness (CCT) and Intraocular pressure (IOP) of both right and left eyes in primary open angle glaucoma before and after using DTFC in duration of 6 and 12 months.

DISCUSSION

Different drugs induce different changes in central corneal thickness. This change is either increase or decrease in corneal thickness or no change in thickness at all. Some studies show the results which were similar to our study. In an article the effect of prostaglandin analogues on central corneal thickness in patients with glaucoma was documented. This research included 879 patients. The final findings of the research were the significant reduction in CCT by travoprost and bimatoprost.[16] All these researches show different effects of anti-glaucoma drugs on central corneal thickness. Similarly in another research, the effect of prostaglandin analogues on central corneal thickness was analyzed in open angle glaucoma. This included 22 patients and their prospective data was analyzed. All of them were over 18 years of age. Prostaglandins were used more than 6 months duration. The results were statistically significant reduction of central corneal thickness.[12] The results of our study were different from these above mentioned studies. Another study was done on the open angle patients who were 30 in number. The combined effect of two groups of drugs that were dorzolamide/timolol and brimonidine/timolol combinations. The patients were using them for 3 months. There was no statistically significant change with p-value=0.075 on central corneal thickness with both groups of drugs in the 3-month duration of treatment.[17] One more article reveals the corneal thickness reduction with p-value<0.001 by using anti-glaucoma medication in glaucoma patients. The medication used was beta blocker and prostaglandin. The test was performed on 125 patients.[18]

Another study showed the results similar to our study and its aim was to estimate the central corneal epithelial thickness, central corneal stromal thickness and total central corneal thickness in open angle glaucoma patients who were using timolol,

dorzolamide and brimonidine. This study included 106 patients and all these corneal changes were measured by using anterior segment optical coherence tomography. There was no statistically significant difference on central corneal thickness.[4]

In contrary to our results various other research articles also show that there is significant decrease in central corneal thickness due to prostaglandins analogues. This elaborates effect of prostaglandins analogues on central corneal thickness in glaucoma patients. In this article the aim was estimation of change in central corneal thickness after using prostaglandin analogues in patients who were using this treatment for 3 and 12 months and data was taken before and after the treatment and central corneal thickness was compared. The results showed that there was significant reduction in central corneal thickness as the p-value was <0.005.[19] Basic purpose of the study was to assess the effect of combination of topical carbonic anhydrase inhibitor and beta blocker on corneal epithelial thickness and central corneal thickness in glaucoma patients. This thickness was assessed by using optical coherence tomography. Total 80 patients were assessed. The corneal epithelial thickness was significantly reduced after using these drugs while corneal thickness was reduced in some sectors with p-value <0.001.[11] Case-control and cross sectional studies were made on 2722 patients having glaucoma and ocular hypertension. The purpose of the study was to evaluate corneal thickness changes in 2-year duration by prostaglandin analogues. The findings told that there was statistically significant thinning of corneal thickness.[20] In this study the effect of isopropyl on central corneal thickness and corneal endothelial cells was assessed in normal tension glaucoma patients using treatment for more than 6 months. There was significant change in corneal endothelial cells while no statistically significant change in corneal thickness.[21] There is another study which showing no significant changes in central corneal thickness just like our study. The purpose of this study was to compare corneal endothelial changes and central corneal thickness in patients with open angle glaucoma. 44 patients were assessed in it. Corneal endothelial changes and central corneal thickness were measured by indirect specular microscope. According to this study there was no significant change in central corneal thickness.[22]

Single centre study with retrospective view of records were main limitations of study. Authors declare no conflict of interest in this research.

CONCLUSION

The results do not provide convincing support for a meaningful change in central corneal thickness associated with the use of dorzolamide-timolol in the studied population. Authors recommend a prospective study to refine the results of this study.

Conflict of Interest: None to declare

Ethical Approval: The study was approved by the Institutional Review Board / Ethical Review Board No. COVAS-1469-23.

Author Contributions: Aliya Ramzan: Concept, Literature Search, Article Draft.

Saman Ali: Data Collection, Critical Review

Ummara Rasheed: Literature Search, Data Analysis

REFERENCES

1. Wagner IV, Stewart MW, Dorairaj SK. Updates on the Diagnosis and Management of Glaucoma. Mayo Clin Proc Innov Qual Outcomes. 2022;6(6):618-35. doi: 10.1016/j.mayocpiqo.2022.09.007.

2. Ahmad F, Deshmukh N, Webel A, Johnson S, Suleiman A, Mohan RR, et al. Viral infections and pathogenesis of glaucoma: a comprehensive review. Clin Microbiol Rev. 2023:e0005723. doi: 10.1128/cmr.00057-23.

3. Lim R. The surgical management of glaucoma: A review. Clin Exp Ophthalmol. 2022;50 (2):213-31. doi: 10.1111/j.1442-9071. 2012. 02 769.x.

4. Zembala J, Forma A, Zembala R, Januszewski J, Zembala P, Adamowicz D, et al. Technological Advances in a Therapy of Primary Open-Angle Glaucoma: Insights into

Current Nanotechnologies. J Clin Med. 2023; 12(18):5798. doi: 10.3390/jcm12185798.

5. Hamel AR, Yan W, Rouhana JM, Monovarfeshani A, Jiang X, Mehta PA, et al. Integrating genetic regulation and single-cell expression with GWAS prioritizes causal genes and cell types for glaucoma. medRxiv. 2022:20 22.05. 14.22275022.

6. Wagner IV, Stewart MW, Dorairaj SK. Updates on the Diagnosis and Management of Glaucoma. Mayo Clin Proc Innov Qual Outcomes. 2022;6(6):618-35. doi: 10.1016/j. mayocpiqo.2022.09.007.

7. Chaudhary PK, Jain S, Damani T, Gokharu S, Pachori RB, editors. Automatic diagnosis of type of glaucoma using order-one 2D-FBSE-EWT. 2022 24th International Conference on Digital Signal Processing and its Applications (DSPA); 2022: IEEE.

8. Jayaram H, Kolko M, Friedman DS, Gazzard G. Glaucoma: now and beyond. The Lancet. 2023;402(10414):1788-801. doi: 10.1016/ S01 40 -6736(23)01289-8.

9. Fiess A, Marx-Gross S, Wasielica-Poslednik J, Nagler M, Schmidtmann I, Wild PS, et al. Peripheral corneal thickness and associated factors - results from the population-based German Gutenberg Health Study. Acta Ophthalmol. 2022;100(6):e1298-e305. doi: 10. 1111/aos.15057.

10. Asiedu K, Abu SL. The impact of topical intraocular pressure lowering medications on the ocular surface of glaucoma patients: A review. J Curr Ophthalmol. 2019;31(1):8-15. doi: 10.1016/j.joco.2018.07.00.

11. Ali F, El-Gazzar HA, Tabl AA-s, Awwad MA-Z, Eleiwa TK. Effect of Topical Combined Beta-Blockers and Carbonic Anhydrase Inhibitors on Corneal Epithelial Thickness by Anterior Segment Optical Coherence Tomography. Egypt J Hosp Med. 2023;90(1):1752-9. doi: 10. 1016/j.pdpdt.2023.103728.

12. Kim JY, Yim HW. Effect of Topical Prostaglandin Analogue Therapy on Central Corneal Thickness: A Systematic Review. J Clin Med. 2022;12(1). doi: 10.3390/jcm12010 044.

13. Kadhim YJ, Farhood QK. Central corneal thickness of Iraqi population in relation to age, gender, refractive errors, and corneal curvature: a hospital-based cross-sectional study. Clin Ophthalmol. 2016;10:2369-76. doi: 10.2147/ OPTH.S116743.

14. Konstas AG, Schmetterer L, Katsanos A, Hutnik CML, Holló G, Quaranta L, et al. Dorzolamide/Timolol Fixed Combination: Learning from the Past and Looking Toward the Future. Adv Ther. 2021;38(1):24-51. doi: 10.10 07/s12325-020-01525-5.

15. Schrems WA, Schrems-Hoesl LM, Mardin CY, Horn FK, Juenemann AG, Kruse FE, et al. The Effect of Long-term Antiglaucomatous Drug Administration on Central Corneal Thickness. J Glaucoma. 2016;25(3):274-80. doi: 10.1097/ IJG.0000000000000190.

16. Kadri R, Shetty A, Parameshwar D, Kudva AA, Achar A, Shetty J. Effect of prostaglandin analogues on central corneal thickness in patients with glaucoma: A systematic review and meta-analysis with trial sequential analysis. Indian J Ophthalmol. 2022;70(5):1502-12. doi: 10.4103/ijo.IJO_1971_21.

17. MOMEN MH, MOHAMED A, SONDOS AS, RANDA HA. Comparative Study between the Effect of Dorzolamide/Timolol Fixed Combination and Brimonidine/Timolol Fixed Combination on Corneal Endothelium. Med J Cairo Univ. 2020;88:1041-46.

18. Nam M, Kim SW. Changes in Corneal Epithelial Thickness Induced by Topical Antiglaucoma Medications. J Clin Med. 2021; 10(16). doi: 10.3390/jcm10163464.

19. Park JH, Yoo C, Chung HW, Kim YY. Effect of prostaglandin analogues on anterior scleral thickness and corneal thickness in patients with

primary open-angle glaucoma. Sci Rep. 2021;11(1):11098. doi: 10.1038/s41598-021-90696-4.

20. Lu Y, Zhong E, Wu J, Cao Y. The Effect of Prostaglandin Analogs on Central Corneal Thickness of Patients with Glaucoma or Ocular Hypertension: A Systematic Review. Ophthalmic Res. 2023;66(1):431-44.

21. Lee SH, Lee WJ, Kim KW, Jeong JH, Park IK, Chun YS. Influence of 0.002% Omidenepag Isopropyl on Intraocular Pressure and the Cornea in Normal Tension Glaucoma. J Glaucoma. 2023;32(4):245-51. doi: 10.1097/IJG.0000000000002167.

22. Elagamy A, Tawashi M, Berika M. Corneal Endothelium and Central Corneal Thickness Changes in Patients with Primary Open Angle Glaucoma. J Ophthalmol. 2022;5(4):141-6. doi: 10.1097/ICO.0000000000001826.