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Minireview

Effects of Dorzolamide-Timolol Fixed Combination on Intraocular Pressure and on Ocular and Systemic Vascular Parameters

Teresa Rolle*, Lorenza Malinverni

Eye Clinic, Department of Surgical Sciences, University of Torino, via Cherasco 23, 10126 Torino, Italy

Corresponding author: Teresa Rolle, Eye Clinic, Department of Surgical Sciences, University of Torino, via Cherasco 23, 10126 Torino, Italy

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Abstract

Glaucoma is a progressive neurodegenerative disease and is one of the world's leading causes of irreversible vision loss. The goal of glaucoma therapy is to lower intraocular pressure (IOP) by means of topical drugs, laser and surgical procedures. Among the first-line treatments, Dorzolamide-Timolol Fixed combination (DTFC) has been used for more than ten years in the treatment of glaucoma. Alongside its proven effectiveness in reducing intraocular pressure, a hemodynamic action has been observed over the years at the level of the retinal microcirculation, the optic nerve head, the choroid and the cardiovascular system. The purpose of the minireview is at first to report and summarize the main studies on the relationship between systemic parameters and glaucoma. Furthermore, the literature data about the effects of DTFC on intraocular pressure, ocular perfusion pressure, in particular ocular diastolic perfusion pressure, and the latest evidences are indicated regarding its hypotensive and vascular effects.

Keywords: glaucoma, intraocular pressure, eye hemodynamics, Dorzolamide-Timolol, systemic vascular parameters, ocular diastolic perfusion pressure

Introduction

Glaucoma is a multifactorial, progressive optic neuropathy characterized by a loss of retinal ganglion cells (RGCs) which results in characteristic visual field defects. The etiology of glaucomatous damage has not yet been fully understood. Increased intraocular pressure (IOP) is the primary risk factor for the onset and the progression of glaucomatous optic neuropathy; however, other risks participate in the progression of glaucomatous damage, in particular in patients with low IOP values [1-5]. Up to now, there are evidences that perfusion abnormalities in the retina and in the optic nerve head (ONH) are related to the pathogenesis of glaucoma even though their real role is still being debated. Studies by Flammer et al. [6] hypothesized that primary open-angle glaucoma (POAG), in particular the NTG type, is associated with vascular dysregulation (Flammer's syndrome). This condition may contribute to glaucoma progression despite low IOP values and it consists of an alteration of the autoregulation with an abnormal blood flow response to perfusion pressure changes.

Several population-based, experimental and clinical research studies have evaluated the relationship between systemic pressure and glaucoma. In the Egna-Neumarkt Study [7-8], a positive correlation was reported between systemic blood pressure and IOP, and an association was found between POAG diagnosis and systemic hypertension; lower diastolic perfusion pressure was associated with a marked, progressive increase in the frequency of hypertensive glaucoma. Topouzis et al. [9] in a cross-sectional, population-based study on the association of POAG and PEXG with ocular perfusion pressure status reported a relationship between low diastolic perfusion pressure and increased POAG risk also in patients treated for systemic hypertension. Moreover, correlations between POAG and systemic hypotension and hypertension were proved [10]. In a Korean population, high fluctuations in systolic blood pressure were outlined as a major systemic risk factor for POAG development [11]. A recent meta-analysis [12] on the relationship between ocular perfusion pressure, risk of development and progression of POAG outlined that an impairment of the vascular supply (i.e. low OPP) to the ONH may increase its susceptibility to glaucomatous structural damage also in HTG POAG eyes. The severity of glaucoma is related to ocular perfusion pressure (OPP); in advanced POAG vs early and moderate mean OPP was low [13]. Dallanis et al. reported an association between obstructive sleep

apnea/hypopnea syndrome with glaucomatous structural damage and ocular blood flow in particular with Resistance Index (RI) [14]. More recently Jammal et al. [15] studied the effect of systemic arterial blood pressure on the progression of structural damage in glaucoma. During follow-up (> 4 years), significant associations were found between lower mean arterial pressure (MAP), diastolic arterial pressure and faster rates of RNFL loss. In a retrospective study on early open-angle glaucoma eyes, Lee et al. [16] analyzed the association between systemic arterial stiffness predicted by brachial-ankle pulse wave velocity (PWV) and initial location of structural damage progression: PWV was proved to be a significant predictor of the site of structural damage progression; also the autonomic nervous system dysfunction was proven to participate to the POAG progression [17].

Dorzolamide-timololol fixed combination (DTFC) hystory

Preserved DTFC (COSOPT®) was released commercially in 1998 and the formulation preservative- free (PF) was available in 2012. Dorzolamide is a potent CA-II inhibitor (also CA-XII and CA-IV) and it reduces the formation of bicarbonate ions. The IOP-lowering effect of Dorzolamide is dependent on the decrease in aqueous secretion with an efficacy between 17% and 32%, particularly during sleep. Animal studies showed that topical carbonic anhydrase inhibitors can be detected in the retina. Since 1977, Timolol maleate has been proven to be an efficacious and safe topical drug for long- term IOP lowering. It reduces ciliary body blood flow and cAMP production; IOP reduction has been demonstrated to be 20–28%. In general, the topical side effects of Timolol are relatively uncommon and generally mild. However, the systemic adverse effects are relatively common and potentially life-threatening as a result of the effective systemic absorption of Timolol via the nasal mucosa.

It is very complex to analyze the data relating to ocular hemodynamic studies because they use different tools and techniques so the data can hardly be compared with each other. In addition, some of these have had improvements over time, others are no longer used, others have entered the field of research and not the one of clinical practice yet.

Studies on the effects of dorzolamide, timolol and DTFC on IOP and on ocular and systemic vascular parameters

As mentioned before, the effects of topical antiglaucomatous drugs on ocular blood flow were analyzed using different instruments: Pulsatile Ocular Blood Flow and Pulse Amplitude, Laser Doppler Flowmetry (HRF), Laser Doppler Velocimetry, Laser-interferometric measurement of Fundus Pulsation, Scanning Laser Ophthalmoscopy (SLO), Color Doppler Imaging (CDI) and recently Optical Coherence Tomography Angiography (OCT-A). Moreover, in the studies regarding the evaluation of ocular perfusion, different types of perfusion pressure measurement have been used which are not exactly the same and above all the diastolic ocular perfusion pressure has not always been evaluated. The most common systemic vascular parameter used is Ocular Perfusion Pressure (OPP) which can be defined as the systolic, diastolic, or mean OPP. The Mean Ocular Perfusion Pressure (MOPP) is estimated as 2/3 of the mean arterial BP-IOP, where the MAP = DBP + 1/3 (SBP − DBP), where DBP is diastolic blood pressure, and SBP is systolic blood pressure. The ratio 2/3 considers the fall in BP between the brachial artery and ophthalmic artery when sitting. Systolic OPP is measured as the difference between SBP and IOP. The diastolic OPP (ODPP) matches the systemic DBP-IOP. The ODPP describes the lowest OPP values and it is considered an independent risk factor for POAG.

In supplementary table 1 were summarized the more relevant studies regarding the effects of Dorzolamide, Timolol and Dorzolamide-Timolol Fixed Combination on intraocular pressure and on ocular and systemic vascular parameters.

In the first studies that analyzed the effects of topical antiglaucomatous drugs, CDI, SLO and HRF were used. Harris et al. using CDI and SLO in healthy volunteers after 2 hours from Dorzolamide instillation reported IOP reduction and unaltered blood velocity or resistance index (RI) in any retrobulbar vessel and accelerated capillary dye transit in the macula and ONH [18]. Pillunat el al. [19] in healthy subjects treated with Dorzolamide three times daily for 3 days observed a decrease in IOP values but no changes in ONH blood flow. Different results were reported by Martinez et al. [20]: after Dorzolamide, several hemodynamic parameters of intraocular and periocular vessels improved in both normal and POAG eyes, especially the peak-systolic velocity of the central retinal artery, the end-diastolic velocity of the ophthalmic and central retinal arteries, and the minimum velocity of the central retinal vein. The RI was significantly lower in the ophthalmic and central retinal arteries in all groups after Dorzolamide (20). Schmidt et al. proved the hypotensive effect of Timolol in POAG eyes using Ocular Pulse Amplitude (OPA); this effect was additively enhanced by Dorzolamide: it significantly increased OPA (not Timolol), while vascular systemic parameters were unvaried [21]. In a pilot study we compared the effects on IOP and retinal blood flow of the fixed combination Timolol+Dorzolamide (COSOPT®) vs Timolol in monotherapy in POAG eyes using HRF. All the HRF hemodynamic parameters (volume, flow and velocity) increased in the eyes treated with DTFC in the regions analyzed, not with Timolol. These results, though not statistically significant, may indicate that Dorzolamide 2% has a positive action on retina hemodynamics [22]. Lubeck et al. with the same instrument did not observe significant changes in the HRF parameter flow as compared with baseline, either after 3 weeks of Timolol treatment or 2 hours after Timolol instillation. The heart rate (HR) and arterial systolic and diastolic blood pressure values showed no alteration after Timolol therapy [23]. Arend et al. in a prospective, randomized, cross-over study, compared the vascular effects of Timolol, Dorzolamide and Latanoprost in newly diagnosed POAG patients using fluorescein angiography: Dorzolamide significantly shortened AVP times, whereas Timolol and Latanoprost did not [24]. An increase of blood flow in the ONH and in the choroid after 6 months of treatment with Dorzolamide, but not with Timolol was reported by Fuchsjager-Mayrl et al. in a controlled, randomized, double-blind study with HRF and fundus pulsation amplitude (FPA) [25].

Martinez et al. compared the effect of the Latanoprost/Timolol fixed combination (LTFC) and the Dorzolamide/Timolol fixed combination (DTFC) on retrobulbar hemodynamics and IOP in POAG patients using CDI in the ophthalmic artery (OA)

and posterior ciliary arteries (PCA); OPP was measured. DTFC significantly increased EDV in OA the PCA and significantly decreased RI in OA and in the PCA. LTFC significantly decreased the EDV and significantly increased RI in PCA. No statistically significant differences in the IOP values were showed between both treatments. The results confirmed that DTFC has a positive vascular effect on retrobulbar vessels in POAG (26). Quaranta et al. evaluated the effect of DTFC and Latanoprost 0.005% on 24-hour IOP, SBP and DBP, and ODPP in POAG patients. 24-hour IOP decreased significantly with both therapies but the major drop was seen after DTFC. Significant decreases in mean 24-hour SBP and DBP were observed after DTFC, not with Latanoprost. 24-hour ODPP raised significantly after both treatments [27]. In a comparative, randomized, open label, study we compared the effect of Dorzolamide hydrochloride 2%, Timolol maleate 0.5%, and their fixed combination on IOP, ODPP and retinal and ONH perfusion in 28 POAG patients with early to moderate glaucomatous damage. The patients after washout (T1) were divided into two groups: group I Dorzolamide BID for 4 weeks, group II Timolol BID for 4 weeks (T2). Both groups passed to DTFC for 4 weeks (T3). Retinal and ONH blood flow was measured with HRF using Automatic Full Field Perfusion Image Analyzer software (AFFPIA-SLDF 3.3; G Michelson, Erlangen, Germany). IOP decreased between T1 and T2 in group I (-12.03%; P<0.001) and in group II (-13.70%; P<0.001); between T1 and T3 in group I (-21.40%; P<0.001) and in group II (-21.25%; P<0.001); a significant decrease of IOP between T2 and T3 in group I (-10.60%; P<0.001) and in group II (- 8.80%; P<0.001). ODPP increased significantly after Dorzolamide (+ 7.24%; P<0.01), in group II (+6.08%; P<0.05), and in both groups globally (+6.71%; P<0.001); ODPP after DTFC was significantly increased (+2.60%; P<0.01). HRF parameter Flow values after Dorzolamide increased (+11.89% at rim level; NS). between T1 and T3 at rim level in group I (+30.03%; P>0.05) and when all patients were considered globally (+20.81%; P<0.05). At the end of the study, only patients previously treated with Dorzolamide showed an increase in blood flow: the reason could be a possible positive hemodynamic effect of Dorzolamide increased by a further drop in IOP with Timolol supplement [28]. In a meta-analysis of 24-Hour Intraocular Pressure studies evaluating patients with POAG, exfoliative glaucoma and ocular hypertension (OH) Dorzolamide showed a 19% 24-hour pressure reduction and DTFC 26% [29]. Januleviciene et al. outlined that after 12-months treatment with LTFC or DTFC resulted in similar IOP lowering effects and visual function and structure were comparable: the DTFC group showed lower vascular resistance in retrobulbar vessels compared to the LTFC group [30]. Fuchsjager-Mayrl et al. reported the effects of Dorzolamide and Timolol on ocular pressure/flow relationships to test the hypothesis that they improve autoregulation. The results indicated that IOP reduction with Timolol or Dorzolamide is associated with the normalization of the ocular pressure/flow relationship. If this is related to the beneficial effects of hypotensive therapy in glaucoma remains to be established [31]. In 2011 Januleviciene et al. evaluated hemodynamic parameters as possible predictors for glaucoma progression. DTFC group had higher OPP, DPP, and lower vascular resistivity indices as compared to the LTFC. Progressing patients had higher nerve fiber index, lower SBP, OPP, DPP, higher ophthalmic and central retinal artery vascular resistance, and lower pulse volume [32].

The short-term effects of Dorzolamide/Timolol on OPP and retrobulbar blood flow were studied in patients with pseudoexfoliative glaucoma (PXG). The results showed that DTFC has a less important hemodynamic action with a good hypotonic activity [33]. In NTG patients DTFC showed an important hypotensive effect with no significant action on OPP, and ODPP [34]. The same group studied the vascular activity of Latanoprost vs DTFC: diurnal OPP and ODPP showed no statistically significant difference between the groups at all time points [35].

In the past two years, a new interest has arisen regarding the vascular effects of antiglaucoma drugs and new studies have been published using a new instrument the Optical Coherence Tomography Angiography (OCT-A). 131 NTG patients 80 Carteolol-treated eyes, 27 Brimonidine-treated eyes and 24 Dorzolamide-treated eyes were analyzed with OCT-A 6 months after treatment. Among the treatments, only Dorzolamide increased the Vessel Density (VD) of the peripapillary retina [36].

OPP was studied in non-glaucomatous volunteers treated with Latanoprost or Timolol and it was evaluated with 3 commonly used formulas, based on IOP and BP. Both Timolol and Latanoprost significantly increased ODPP. OSPP increased with Latanoprost, not with Timolol. Nevertheless, the difference between the two treatments in the effects on OPP calculated with MAP was not significantly different [37].

The use of DTFC (COSOPT®) three times a day led to a reduction in IOP of 40% without systemic adverse effect. The possibility of nocturnal hypotension, not studied yet, represents a major problem for administering the fixed association three times a day [38].

Park et al. compared the efficacy, patient-reported satisfaction, and safety of preservative- free (PF)-Tafluprost, PF-Dorzolamide/Timolol and preservative-containing (P)-Latanoprost in Korean glaucoma patients with ocular surface disease (OSD). At 12 weeks, the mean total OSDI scores significantly improved from baseline with PF-Tafluprost and PF-Dorzolamide/Timolol, but not with P-Latanoprost. IOP changes were comparable among all three treatment groups [39].

Conclusions

The Dorzolamide-Timolol Fixed Combination has shown to have a significant ocular hypotensive effect in POAG HTG and NTG eyes and in the preservative-free form it is very well tolerated locally. As for the effects on local and systemic vascular parameters, it must be borne in mind that the association is made up of two completely different active ingredients which, however, have the same mechanism of action in the eye i.e. both reduce the secretion of aqueous humor through different ways.

Dorzolamide, a topical Carbonic Anidrase Inhibitor, lowers IOP by reducing the synthesis of HCO_3 in the ciliary body, thereby decreasing aqueous humor production. It has few systemic side effects and locally can give eye irritation, blepharitis, sense of bitterness in the mouth. Timolol Maleate is a non-selective beta-blocker that has few local side effects (dry eye) but through absorption, mainly through the nasal mucosa, it has important

systemic side effects and should not be used in patients with pulmonary and heart problems in particular bradycardia, hypotension, second and third-degree atrioventricular block and heart failure. Recently, Tuleski et al. reported that in healthy cats, one drop of Timolol 0.5% ophthalmic solution reduced systolic function, and standard echocardiographic variables; about diastolic evaluation, Timolol decreased HR but it did not separate the mitral diastolic waves [40].

From the oldest to the most recent studies present in literature, the hypotensive efficacy of this fixed association is clear and indisputable, which has now been demonstrated for over 22 years. As regards the vascular effects, it is more difficult to reach a precise definition of the action of the DTFC on ocular and systemic hemodynamics due to the extreme variety of methods and techniques used. ODPP was measured in a few studies and generally was increased due to the hypotensive effect (in particular of Timolol) but, as reported in clinical studies and also based on personal results, Dorzolamide plays a decisive role.

Certainly, the possibility of using more advanced tools such as OCT-A could provide new data. Furthermore, researches are focused on new carbohydrate-based sulfonamide derivatives selective carbonic anhydrase II inhibitors containing glucosamine moieties. These new molecules presented a good water solubility and pH values are neutral, instead of Dorzolamide that is more lipophilic with a pH of 5.5 [41]. In normotensive rabbits on the hydrophilic derivatives with potent and selective inhibition of hCA II isoforms, the conjunctival absorption predominates over the corneal one and presents greater chances of being tied to sustained-release nanoparticles [42]. The introduction of these new molecules into clinical practice could further improve the hypotensive efficacy of CAI and their favorable action on the vascular ocular and systemic parameters.

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References

1. Flammer J. The vascular concept in glaucoma. Surv Ophthalmol 1994; 38:3–6.
2. Flammer J, Orgul S, Costa VP et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res 2002;21:359–93.
3. Drance S, Anderson DR, Schulzer M. Risk factors for progression of visual field abnormality in normal tension glaucoma. Am J Ophthalmol 2001;131:699–708.
4. Grunwald JE, Sinclair SH, Riva CE. Autoregulation of the retinal circulation in response to decrease of intraocular pressure below normal. Invest Ophthalmol 1982;23:124–129.
5. Galassi F, Nuzzaci G, Sodi A, et al. Possible correlation of ocular blood flow parameters with intraocular pressure and visual field alterations in glaucoma. A study by means of color Doppler imaging. Ophthalmologica 1994; 208: 304–308.
6. Flammer J, Konieczka K. The discovery of the Flammer syndrome: a historical and personal perspective. EPMA J. 2017 May 22;8(2):75-97. doi: 10.1007/s13167-017-0090-x. PMID: 28725290; PMCID: PMC5486542.
7. Bonomi L, Marchini G, Marraffa M, et al. The relationship between intraocular pressure and glaucoma in a defined population. Data from the Egna-Neumarkt Glaucoma Study. Ophthalmologica. 2001 Jan-Feb;215(1):34-8. doi: 10.1159/000050823. PMID: 11125267.
8. Bonomi L, Marchini G, Marraffa M, et al. Vascular risk factors for primary open angle glaucoma: the Egna-Neumarkt Study. Ophthalmology. 2000 Jul;107(7):1287-93. doi: 10.1016/s0161-6420(00)00138-x. PMID: 10889099.
9. Topouzis F, Wilson MR, Harris A, et al. Association of open-angle glaucoma with perfusion pressure status in the Thessaloniki Eye Study. Am J Ophthalmol. 2013 May;155(5):843-51. doi: 10.1016/j.ajo.2012.12.007. Epub 2013 Feb 6. PMID: 23394905.
10. Chung HJ, Hwang HB, Lee NY. The Association between Primary Open-Angle Glaucoma and Blood Pressure: Two Aspects of Hypertension and Hypotension. Biomed Res Int. 2015;2015:827516. doi: 10.1155/2015/827516. Epub 2015 Oct 18. PMID: 26557702; PMCID: PMC4628713.
11. Lee NY, Jung Y, Han K, et al. Fluctuation in systolic blood pressure is a major systemic risk factor for development of primary open-angle glaucoma. Sci Rep. 2017 Mar 6;7:43734. doi: 10.1038/srep43734. PMID: 28262703; PMCID: PMC5338023.W,
12. Kim KE, Oh S, Baek SU, et al. Ocular Perfusion Pressure and the Risk of Open-Angle Glaucoma: Systematic Review and Meta-analysis. Sci Rep. 2020 Jun 22;10(1):10056. doi: 10.1038/s41598-020-66914-w. PMID: 32572072; PMCID: PMC7308312.
13. Ch'ng T, Chua CY, Ummi Kalsom MA, et al. Ocular Perfusion Pressure and Severity of Glaucoma: Is There a Link? J Curr Glaucoma Pract. 2021 May-Aug;15(2):78-85. doi: 10.5005/jp-journals-10078-1305. PMID: 34720497; PMCID: PMC8543740
14. Dalianis G, Trivli A, Limnopoulou A, et al. Association of obstructive sleep apnea/hypopnea syndrome with glaucomatous optic neuropathy and ocular blood flow. Exp Ther Med. 2021 Jun;21(6):657. doi: 10.3892/etm.2021.10089. Epub 2021 Apr 20. PMID: 33968187; PMCID: PMC8097189.
15. Jammal AA, Berchuck SI, Mariottoni EB, et al. Blood Pressure and Glaucomatous Progression in a Large Clinical Population. Ophthalmology. 2022 Feb;129(2):161-170. doi: 10.1016/j.ophtha.2021.08.021. Epub 2021 Aug 30. PMID: 34474070; PMCID: PMC8792171.
16. Lee JS, Bae HW, Park S, et al. Systemic Arterial Stiffness Is Associated With Structural Progression in Early Open-Angle Glaucoma. Invest Ophthalmol Vis Sci. 2022 Mar 2;63(3):28. doi: 10.1167/iovs.63.3.28. PMID: 35353125; PMCID: PMC8982628.
17. Liu B, Zhao Y, Zhang H. The Effect of Autonomic Nervous System Dysfunction on the Progression of Primary Open-Angle Glaucoma. Int J Gen Med. 2022 May 2;15:4565-4573. doi: 10.2147/IJGM.S362275. PMID: 35528285; PMCID: PMC9075998
18. Harris A, Arend O, Arend S, et al. Effects of topical dorzolamide on retinal and retrobulbar hemodynamics. Acta Ophthalmol Scand 1996;74:569–72.
19. Pillunat LE, Böhm AG, Köller AU, Schmidt KG, et al. Effect of topical dorzolamide on optic nerve head blood flow. Graefes Arch Clin Exp Ophthalmol. 1999 Jun;237(6):495-500. doi: 10.1007/s004170050268. PMID: 10379611.
20. Martinez A, Gonzalez F, Capeans C, et al. Dorzolamide effect on ocular blood flow. Invest Ophtalmol Vis Sci 1999; 40(6): 1270–1275.
21. Schmidt KG, von Rückmann A, Becker R, et al. Ocular pulse am-

plitude, intraocular pressure and beta blocker/carbonic anhydrase inhibition in combined therapy of primary open-angle glaucoma. Klin Monbl Augenheilkd. 1999 Dec;215(6):361-6. German. doi: 10.1055/s-2008-1034733. PMID: 10637801

22. Brogliatti B, Rolle T, Vizzeri GM, et al. Comparison of the efficacy on intraocular pressure and retinal blood flow of a beta-blocker (timolol maleate) against the fixed association of a topical carbonic anhydrase inhibitor (dorzolamide) and a beta-blocker (timolol maleate). Acta Ophthalmol Scand 2000; 78: 47–49.
23. Lübeck P, Orgül S, Gugleta K, et al. Effect of timolol on anterior optic nerve blood flow in patients with primary open-angle glaucoma as assessed by the Heidelberg retina flowmeter. J Glaucoma. 2001 Feb;10(1):13-7. doi: 10.1097/00061198- 200102000-00004. PMID: 11219633.
24. Arend O, Harris A, Wolter P, et al. Evaluation of retinal haemodynamics and retinal function after application of dorzolamide, timolol and latanoprost in newly diagnosed open-angle glaucoma patients. Acta Ophthalmol Scand. 2003 Oct;81(5):474-9. doi: 10.1034/j.1600- 0420.2003.00122.x. PMID: 14510794.
25. Fuchsjäger-Mayrl G, Wally B, Rainer G, et al. Effect of dorzolamide and timolol on ocular blood flow in patients with primary open angle glaucoma and ocular hypertension. Br J Ophthalmol. 2005 Oct;89(10):1293-7. doi: 10.1136/bjo.2005.067637. PMID: 16170119; PMCID: PMC1772863.
26. Martinez A, Sanchez M. Retrobulbar haemodynamic effects of the latanoprost/timolol and the dorzolamide/timolol fixed combinations in newly diagnosed glaucoma patients. Int J Clin Pract. 2007 May;61(5):815-25. doi: 10.1111/j.1742-1241.2006.01126.x. Epub 2007 Mar 2. PMID: 17343668.
27. Quaranta L, Miglior S, Floriani I, et al. Effects of the timolol-dorzolamide fixed combination and latanoprost on circadian diastolic ocular perfusion pressure in glaucoma. Invest Ophthalmol Vis Sci. 2008 Oct;49(10):4226-31. doi: 10.1167/iovs.08-1744. Epub 2008 May 23. PMID: 18502991.
28. Rolle T, Tofani F, Brogliatti B, et al. The effects of dorzolamide 2% and dorzolamide/timolol fixed combination on retinal and optic nerve head blood flow in primary open-angle glaucoma patients. Eye (Lond). 2008 Sep;22(9):1172-9. doi: 10.1038/sj.eye.6703071. Epub 2008 Jan 18. Erratum in: Eye (Lond). 2009 May;23(5):1244-5. PMID: 18202708.
29. Stewart WC, Konstas AG, Nelson LA, et al. Meta-analysis of 24-hour intraocular pressure studies evaluating the efficacy of glaucoma medicines. Ophthalmology. 2008 Jul;115(7):1117-1122.e1. doi: 10.1016/j.ophtha.2007.10.004. Epub 2008 Feb 20. PMID: 18082886.
30. Januleviciene I, Ehrlich R, Siesky B, et al. Visual function, optic nerve structure, and ocular blood flow parameters after 1 year of glaucoma treatment with fixed combinations. Eur J Ophthalmol. 2009 Sep-Oct;19(5):790-7. doi: 10.1177/112067210901900517. PMID: 19787599.
31. Fuchsjäger-Mayrl G, Georgopoulos M, Hommer A, et al. Effect of dorzolamide and timolol on ocular pressure: blood flow relationship in patients with primary open-angle glaucoma and ocular hypertension. Invest Ophthalmol Vis Sci. 2010 Mar;51(3):1289-96. doi: 10.1167/iovs.09-3827. Epub 2009 Oct 22. PMID: 19850848.
32. Janulevičiene I, Ehrlich R, Siesky B, et al. Evaluation of hemodynamic parameters as predictors of glaucoma progression. J Ophthalmol. 2011;2011:164320. doi: 10.1155/2011/164320. Epub 2011 Apr 10. PMID: 21577269; PMCID: PMC3090719.
33. Eliacik M, Karaman Erdur S, Baltepe Altıok I, et al. Effects of dorzolamide/timolol fixed combination on retrobulbar hemodynamics in pseudoexfoliative glaucoma. Kaohsiung J Med Sci. 2016 Jan;32(1):38-43. doi: 10.1016/j.kjms.2015.12.004. Epub 2016 Jan 23. PMID: 26853174.
34. Lee NY, Park HY, Park CK. Effects of a dorzolamide/timolol fixed combination on diurnal intraocular pressure, heart rate, blood pressure, and ocular perfusion pressure in normal- tension glaucoma. Jpn J Ophthalmol. 2016 Sep;60(5):377-82. doi: 10.1007/s10384-016- 0455-z. Epub 2016 Jun 16. PMID: 27312903.
35. Lee NY, Park HY, Park CK. Comparison of the Effects of Dorzolamide/Timolol Fixed Combination versus Latanoprost on Intraocular Pressure and Ocular Perfusion Pressure in Patients with Normal-Tension Glaucoma: A Randomized, Crossover Clinical Trial. PLoS One. 2016 Jan 12;11(1):e0146680. doi: 10.1371/journal.pone.0146680. PMID: 26756747; PMCID: PMC4710520.
36. Lin YH, Su WW, Huang SM, et al. Optical Coherence Tomography Angiography Vessel Density Changes in Normal-tension Glaucoma Treated With Carteolol, Brimonidine, or Dorzolamide. J Glaucoma. 2021 Aug 1;30(8):690-696. doi: 10.1097/IJG.0000000000001859. PMID: 33927152.
37. Kolli A, Toris CB, Reed DM, et al. The Effects of Topical Timolol and Latanoprost on Calculated Ocular Perfusion Pressure in Nonglaucomatous Volunteers. J Ocul Pharmacol Ther. 2021 Dec;37(10):565-574. doi: 10.1089/jop.2021.0068. Epub 2021 Oct 4. PMID: 34610254; PMCID: PMC8713568
38. Pakravan M, Naderi Beni A et al. Efficacy and safety of timolol-dorzolamide fixed-combination three times a day versus two times a day in newly diagnosed open-angle glaucoma. J Drug Assess. 2021 Aug 23;10(1):91-96. doi: 10.1080/21556660.2021.1967642. PMID: 34447609; PMCID: PMC8386705.
39. Park SW, Lee J, Kook MS. Efficacy, Safety and Patient-Reported Outcomes with Preservative-Free (PF) Tafluprost or PF-Dorzolamide/Timolol Compared with Preserved Latanoprost: A Prospective Multicenter Study in Korean Glaucoma Patients with Ocular Surface Disease. Pharmaceuticals (Basel). 2022 Feb 7;15(2):201. doi: 10.3390/ph15020201. PMID: 35215313; PMCID: PMC8874539.
40. Tuleski GL, Pscheidt MJGR, Dos Santos JP, et al. Timolol 0.5% ophthalmic solution influences cardiac function in healthy cats. J Feline Med Surg. 2022 Apr 26:1098612X221083372. doi: 10.1177/1098612X221083372. Epub ahead of print. PMID: 35470745.
41. Hou Z, Cai Q, Cheng MS. Novel carbohydrate-based sulfonamide derivatives as selective carbonic anhydrase II inhibitors: Synthesis, biological and molecular docking analysis. Bioorg Med Chem Lett. 2021 Nov 1;51:128291. doi: 10.1016/j.bmcl.2021.128291. Epub 2021 Jul 26. PMID: 34324968.
42. Kalinin S, Kovalenko A, Valtari A, et al. 5-(Sulfamoyl)thien-2-yl 1,3-oxazole inhibitors of carbonic anhydrase II with hydrophilic periphery. J Enzyme Inhib Med Chem. 2022 Dec;37(1):1005-1011. doi: 10.1080/14756366.2022.2056733. PMID: 35350949; PMCID: PMC8973362.

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