ISSN: 0975-5160

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2021; 11(6);170-178

Original Research Article

Prospective Study Comparing Topical Travoprost 0.004% and Dorzolamide 2% in Primary Open Angle Glaucoma

Prerana Agarwal[1], Suryadev Tayal[2], Rinky Agarwal[3]

[1]Associate Professor, Department of Ophthalmology, Ananta Institute of Medical Sciences (Rajsamand) Rajasthan

[2]Professor, Department of Ophthalmology, Saraswathi Institute of Medical Sciences, Hapur. U.P (India)

[3]Department of Ophthalmology, Saraswathi Institute of Medical Sciences, Hapur. U.P (India)

Received: 24-10-2021 / Revised: 28-11-2021 / Accepted: 06-12-2021

Corresponding author: Dr. Prerna Agarwal

Conflict of interest: Nil

Abstract

Background: To compare the efficacy and safety of travoprost 0.004% with dorzolamide 2% eye drops in naive primary open-angle glaucoma (POAG)

Design: Prospective, randomized, comparative, interventional study

Setting: Tertiary eye-care centre

Methods: 40 systemically healthy adult patients with newly diagnosed unilateral POAG with intraocular pressure (IOP) between 22-36mmHg were divided into two groups (n=20 each). One group was administered travoprost 0.004% at 9:00pm while the other was instilled dorzolamide 2% at 6:00am, 2:00pm and 10:00 pm). IOP was measured at baseline, 2 weeks and 6 weeks follow-up at 9:00am and 4:00pm. All patients were monitored for any side effects.

Results: Both groups were comparable in baseline parameters such as age, gender and IOP. The mean IOP at the baseline, 2 weeks and 6 weeks follow-up was 25.02±1.40mmHg and 20.12±0.99mmHg, 17.85±0.80mmHg in travoprost group, and 23.40±1.10mmHg, and 20.90±1.12mmHg and 19.35±1.14mmHg in dorzolamide group respectively. The mean reduction in IOP at final follow-up was significantly higher in travoprost group (7.17±1.12mmHg) when compared to dorzolamide group (4.0±0.81mmHg) (p =0.0021). The incidence of ocular side-effects was marginally lower in travoprost group (6/20; foreign body sensation (4), conjunctival hyperemia (2)) when compared to dorzolamide group (7/20; foreign body sensation (2), conjunctival hyperemia (2), stinging (1), headache (1), and dryness of eye (1)).

Conclusion: Both travoprost 0.004% and dorzolamide 2% may be employed as primary monotherapy in POAG eyes. However, travoprost shows greater reduction in IOP when compared to dorzolamide.

Keywords: Glaucoma; Travoprost; Dorzolamide; IOP

Introduction:

Glaucoma is defined as a group of progressive optic neuropathies characterized by the degeneration of retinal ganglion cells which results in optic nerve head changes and subsequent irreversible visual field loss.[1,2] Raised intraocular pressure (IOP) is one of the strongest and most modifiable risk factors for the development of glaucoma.[3] Hence, the main aim of glaucoma management involves effective control of IOP and various anti-glaucoma agents can be used for this purpose. Major classes of antiglaucoma drugs presently available for commercial use include beta blockers, alpha agonists, prostaglandin analogues (PGAs), sympathomimetics and carbonic anhydrase inhibitors (CAIs). Numerous studies have compared the action of different antiglaucoma agents either singly or in combination.[4-9]

PGAs and CAIs are widely used as first line-agents for management of primary open angle glaucoma (POAG). PGAs act by increasing the uveoscleral outflow either by increasing the permeability of tissues in ciliary muscle or by an action on episcleral vessels. Currently available PGAs include latanoprost, travoprost, bimatoprost, and tafluprost. CAIs suppress aqueous production by limiting the generation of bicarbonate ion in the ciliary epithelium.[10-12] Commercially available topical CAIs include dorzolamide and brinzolamide. Various authors have compared the action of different classes of PGAs with each other and with dorzolamide combined with timolol.[4-9]

Similarly, travoprost has also been compared with fixed combination of dorzolamide with timolol.[4-9] However, no study till date has compared the action of this agent with dorzolamide alone. In this study, we prospectively compare the efficacy and safety of topical travoprost 0.004% with topical dorzolamide 2% in patients with POAG.

Material and methods

Present study was designed as a 6 week, prospective, comparative, randomized, interventional study conducted at tertiary eye-care centre comparing the efficacy and safety of topical travoprost 0.004% with topical dorzolamide 2%. Institutional ethics committee approval was obtained and the study was conducted according to the declaration of Helsinki. Signed, informed consent was obtained from all patients before starting the study.

Patient selection

All consecutive patients presenting to ophthalmic outpatient department between November2019 to February 2020 were screened for unilateral POAG. Inclusion criteria included patients with age ≥18 years who were willing to participate & follow up, with newly diagnosed unilateral POAG with baseline IOP >21 mmHg and not on any prior systemic or topical medications. All patients were subjected to a thorough eye examination inclusive of visual acuity assessment, refraction, slit-lamp examination, dilated fundoscopy (using tropicamide 1%), automated perimetry (Humphrey field analyser program 30-2 equipped with STATPAC, Carl Zeiss Meditec AG, Jena Germany) and IOP measurement (calibrated Goldmann applanation tonometry). At each time point, three separate measurements were taken and their mean was calculated for further analysis. POAG was defined as either visual field defect or glaucomatous changes of the optic nerve head (neural rim loss, disc asymmetry, blood vessel changes, peripapillary atrophy) in association with an elevated IOP (>21mmHg).

All eligible patients were required to have an IOP between 22mmHg and 36mmHg in one eye (the same eye for all visits) at 9am and 4pm at three eligible visits. Forty patients who met the criteria were randomly allocated into two groups using a computer randomized program. One group (n=20) was administered topical travoprost 0.004% once daily at 9:00pm) (Travo, Microlabs, India) and other group (n=20) was advised topical dorzolamide 2% three times per day at 6:00am, 2:00pm, 10:00pm (Dorzox, Cipla, India). The fellow eye of all patients was administered preservative free lubricant eye drop three times a day. Patients were instructed how to instill the medications. Patients with IOP >36mmHg in the affected eye, best-corrected visual acuity <0.6 log MAR, cup disc ratio >0.8, gonioscopy measured angle grade <2 (Shaffer classification), severe central visual field loss, a history of chronic and recurrent inflammatory eye disease, presence of ocular surface disease or any other ophthalmic pathology (retinal disease, etc.,), any abnormality limiting reliable applanation tonometry, ocular trauma, using topical or systemic medications that can affect IOP, laser procedures or intraocular surgery within 6 months of screening, secondary glaucoma (pseudoexfoliation, pigment dispersion, etc.,), ocular hypertension and normo-tension glaucoma were excluded from the study. Pregnant or lactating women and patients with severe unstable or uncontrolled cardiovascular, hepatic or renal diseases, bronchial asthma or chronic pulmonary diseases; or hypersensitivity to any components of the study medications were also excluded.

Follow-up

The patients were followed up at 2 weeks and 6 weeks and IOP was again recorded at this visit at 9am and 4pm with the same applanation tonometer (used preoperatively) by a single observer to avoid inter-observer bias. This observer was blinded for the type of drug administered to avoid intra-observer bias. Effectiveness of the drugs was calculated in terms of mmHg fall in mean IOP. An adverse event was defined as any undesirable event occurring in a subject and a serious adverse event was defined as an event that was potentially fatal, life threatening or sight threatening. Flare, if present, was graded as none (0–2 cells), mild (3–5 cells), moderate (6–20 cells), or severe (>20 cells) based on number of anterior chamber cells in a 2mm slit. Conjunctival hyperemia, foreign body sensation, blurred vision, dry eye sensation, stinging, pruritus, eyelash changes, iris pigmentation, superficial keratitis, follicular conjunctivitis, herpetic reactivation, taste abnormalities, and headache were noted at each follow-up.

Statistical analysis

The data were coded and were entered in Microsoft excel sheet. Statistical analysis was performed using Statistical Package for the Social Sciences. Appropriate statistical tests were applied for comparing categorical and continuous data. p-value less than 0.05 was considered statistically significant.

Results

Demographic characteristics

A total of 40 eyes of 40 patients were included in the study and divided into two groups of 20 each. The mean age of patients was 43.4±8.91 years and 43.25±9.14 years respectively in travoprost & dorzolamide eye drop groups respectively. The gender distribution in travoprost group (10 male, 10 female) comparable to dorzolamide group (9 female, 11 male). There was no statistical difference between the treatment groups for sex, diagnosis, visual acuity, gonioscopy values, horizontal and vertical cup-disc ratio. No patients were lost to follow-up.

Mean IOP values

The mean baseline IOP was 25.02±1.40mmHg in travoprost group and 23.40±1.10mmHg in dorzolamide group respectively. The mean baseline IOP at 9:00am was 24.90±1.44mmHg and 23.35±1.18mmHg in taravoprost and dorzolamide group respectively. The mean baseline IOP at 4:00pm was 25.15±1.38mmHg and 23.45±1.05mmHg in travoprost and dorzolamide group respectively. The overall mean baseline IOP in control eye in travoprost group was 17.30±1.20mmHg and in dorzolamide group was 17.50±1.50mmHg at the time of enrolment in study.

At the end of 2 weeks, change in IOP from baseline was 4.90±0.81mmHg and 2.50±0.67mmHg in travoprost & dorzolamide groups respectively. While at the end of 6 weeks, change from baseline was 7.17±1.12mmHg and 4.0±0.81mmHg in travoprost & dorzolamide groups respectively. A statistically significant difference was noted in reduction of IOP between 2 weeks & 6 weeks values in travoprost & dorzolamide groups (Table 1, Figure 1). The mean reduction in IOP was significantly higher for travoprost compared to dorzolamide ($p < 0.01$). At the end of 2 and 6 weeks, the overall mean IOP in control eye was 17.52±1.31mmHg and 17.73±1.45mmHg, in travoprost group and 17.68±1.62mmHg and in 17.87±1.65mmHg dorzolamide group respectively.

Adverse effects

In travoprost group, 6/20 participants had adverse effects, out of which 4 had foreign body sensation and 2 had conjunctival hyperemia. In dorzolamide group, 7 participants suffered from adverse effects, out of which 3 had foreign body sensation, 2 had conjunctival hyperemia, and remaining participants (one each) suffered from stinging, headache, and dryness of eye. No anterior segment inflammation, blurred vision, eyelash changes, iris pigmentation, superficial keratitis, follicular conjunctivitis, herpetic reactivation and taste abnormalities were seen in any patient.

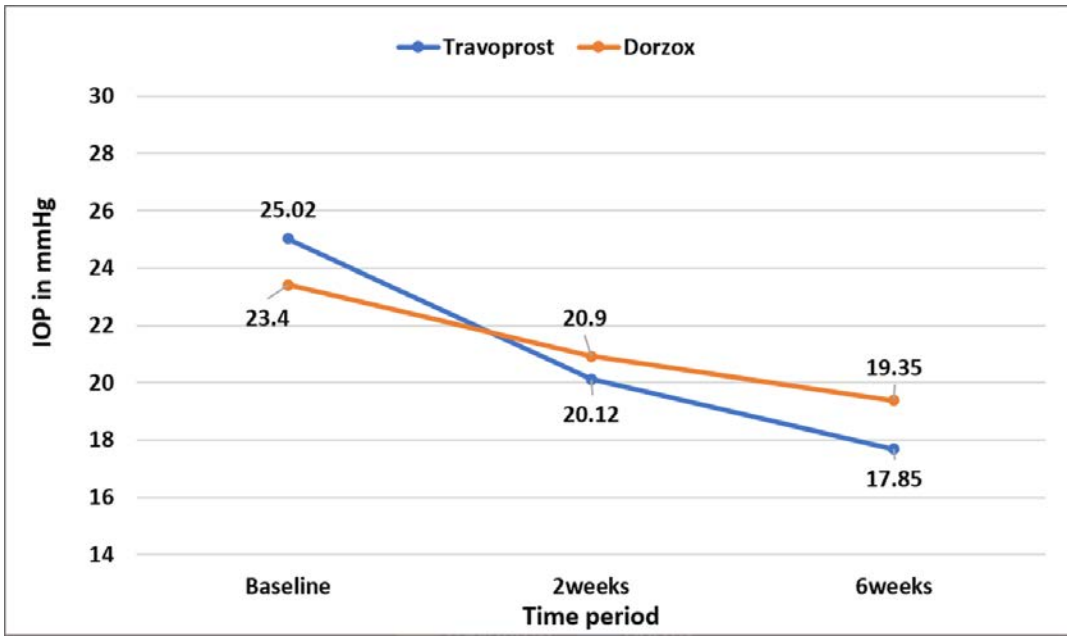

Figure 1: Graph showing IOP changes with Travoprost and dorzolamide

Table 1: Intraocular pressure changes (mmHg) with Travoprost 0.004% and Dorzolamide 2%

	Baseline	Week 2	Week 6
Travoprost group (n=20)			
9:00am	24.9±1.44	20.15±1.13	17.90±0.91
4:00pm	25.15±1.38	20.1±0.85	17.80±0.69
Overall	25.025±1.40	20.12±0.99	17.85±0.80
Dorzolamide group (n=20)			
9:00am	23.35±1.18	20.95±1.14	19.35±1.13
4:00pm	23.45±1.05	20.85±1.13	19.40±1.18
Overall	23.40±1.10	20.9±1.12	19.35±1.14
p-value	0.811	**0.045**	**0.0021**

Discussion

Elevated IOP is the most important modifiable risk factor of glaucoma and a lot of present-day research focuses on modalities that aid in lowering the IOP. In the present times, topical pharmacotherapy with currently available anti-glaucoma agents remains the primary mode of management of patients with POAG.[13, 14] To the best of our knowledge, this remains the first study comparing the safety and efficacy of travoprost with dorzolamide monotherapy as a primary mode of therapy in naive POAG patients, especially pertaining to Indian eyes.

Numerous prior studies have compared the effect of travoprost with fixed combination of dorzolamide hydrochloride and timolol maleate in eyes with POAG.[4-9] We believe that our study is more representative of reliable comparative results as individual agents were compared with each other (travoprost with dorzolamide). This avoids the confounding effect of the second agent, timolol, on IOP reduction. Also, it avoids unnecessary ocular and systemic side-effects of topical beta blockers. Besides, studies with monotherapy are better than fixed dose combination as complications if any can be attributed to specific agent and scrutinized accordingly.

In the present study, statistically significant reduction in mean IOP was noted in both the groups at 2 weeks as well as at 6 weeks follow-up. Presently, the percentage of IOP reduction in our study was 28.67% and 17.09% in travoprost and dorzolamide group respectively. This corroborated well with prior studies. A recent study on topical PGAs reported 30% and 26.5% reduction of IOP from baseline by travoprost and latanoprost, respectively.[15,16] Dixit et al noted a significant reduction ($p < 0.001$) in IOP by 6.56 mmHg (27.99%) after 12 weeks of travoprost instillation.[17] Another meta-analysis on topical PGAs in reducing IOP by Denis and colleagues demonstrated a decrease by 30% for travoprost therapy.[18, 19] Studies have proven an efficacious role of topical dorzolamide in reducing the IOP by 10–26% as a monotherapy agent.[20-22] In a metanalysis by Stewart et al reported a 19% 24-hour IOP reduction with dorzolamide, while Li et al reported an IOP reduction of 2.49mmHg with dorzolamide. Even in our study, while dorzolamide produced maximum reduction in first 2 weeks after instillation with only minimal decrease thereafter, travoprost continued to reduce IOP even after 2 weeks. This indicates that the treating ophthalmologist should wait for at least 6 weeks to guage the maximum effect of travoprost to show in any patient.

As seen in our study, travoprost fared better than dorzolamide in controlling IOP. Besides, at final follow-up, the overall mean

IOP in the affected eye equated with the control eye better in the travoprost group (17.85±0.80 vs 17.73±1.45mmHg) when compared to the dorzolamide group (19.35±1.14 vs 17.87±1.65mmHg). It also demonstrated marginally better side-effect profile. While use of a topical CAI eliminates most of their systemic adverse effects, repeated dosing may increase cost of therapy and decrease compliance. Once daily dosing with travoprost overcomes these limitations. This may also decrease IOP spikes associated with missed medication and washout effect of repeated dosing.

An evening dose of PGAs is typically used as monotherapy to decrease IOP.[19] Latanoprost is a well-established monotherapy to treat open-angle glaucoma during the initial two years of diagnosis.[23] Other authors have also proven superior role of other PGAs such as latanoprost and tafluprost over dorzolamide.[24,25] Similarly, although our study suggests that both travoprost and dorzolamide can be used as an effective primary therapy in naive POAG cases, travoprost may be preferred over dorzolamide due to its superior efficacy. Besides, both travoprost and dorzolamide had a relatively low frequency of manageable adverse effects following treatment. Although travoprost had marginally lesser side-effects, role of preservatives used in both medications on these side-effects need to be explored further (polyquad in Travo is less oculo-toxic than benzalkonium in Dorzox).

It is reported that glaucoma patients can have their peak IOP outside office hours.[26] A retrospective review by Hughes et al also showed that the peak diurnal IOP was on average 4.9mmHg higher than the maximum IOP conventionally measured in a clinic. In the same study comparing 24-hour IOP monitoring with the conventional office-hour IOP measurements, the implementation of 24-hour IOP monitoring even resulted in a change of clinical management in 79.3% of the patients.[27] Clinicians may thus choose different antiglaucoma monotherapy or drug combinations according to the distinct circadian rhythm in each glaucomatous subtype or as reflected by the individual IOP profile.[28] We believe that 9:00am and 4:00pm measurements of IOP in our study allowed enough time for action of both travoprost and dorzolamide. In a 5-year trial by Riva et al, travoprost proved efficacious in long-term in providing 24-hour IOP control in patients with POAG.[29] Even in our study, once daily dosing of travoprost and thrice daily dosing of dorzolamide allowed effective control of IOP at different timings without causing dramatic ups and downs in IOP.

Certain limitations of our study include relatively short duration and limited sample size. Although early results support convincing results in our study, larger, long-term studies are needed to assess the clinical effects, and particularly the safety, of these medications. Also, caution is to be exercised while extrapolating the results of the present study to other types of glaucomas due to variable pathophysiology and to other brands of same active chemicals due to their variable efficacy. While we tried to minimize the false positive results by taking fellow eyes as controls, cross-over studies or paired-eye comparisons are recommended for obtaining accurate results.

Conclusion

To conclude, both travoprost 0.004% and dorzolamide 2% eye drops are safe and efficacious in controlling IOP and may be effectively employed as a monotherapy in naive POAG eyes. However, travoprost had greater reduction in IOP and was found marginally safer than dorzolamide with lesser patients reporting ocular surface related problems. However, the final choice of

therapy lies on the clinical discretion of the treating ophthalmologist.

References

1. Xu SC, Gauthier AC, Liu J. The Application of a Contact Lens Sensor in Detecting 24-Hour Intraocular Pressure-Related Patterns. J Ophthalmol. 2016;2016:4727423.
2. McMonnies CW. Glaucoma history and risk factors. J Optom. 2017 Apr-Jun;10(2):71-78.
3. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006 Mar;90(3):262-7.
4. Lafuma A, Berdeaux G. Costs and effectiveness of travoprost versus a dorzolamide + timolol fixed combination in first-line treatment of glaucoma: analysis conducted on the United Kingdom General Practitioner Research Database. Curr Med Res Opin. 2007 Dec;23(12):3009-16.
5. Babić N, Andreić V, Miljković A, Grković D, Jovanović P. Comparison of the efficacy and safety of fixed combination travoprost/timolol and dorzolamide/ timolol in patients with primary open-angle glaucoma and ocular hypertension. Srp Arh Celok Lek. 2013 Jul-Aug;141(7-8):441-6.
6. Suzuki ER Jr, Franklin LM, da Silva LJ, Figueiredo CR, Netto JA, Batista WD. Comparison of the efficacy and safety of travoprost with a fixed-combination of dorzolamide and timolol in patients with open-angle glaucoma or ocular hypertension. Curr Med Res Opin. 2006 Sep;22(9):1799-805.
7. Suzuki ER Jr, Suzuki CL. Efficacy and safety of travoprost alone or in combination with other agents for glaucoma and ocular hypertension: patient considerations. Clin Ophthalmol. 2010 Oct 21;4:1165-71.
8. Teus MA, Miglior S, Laganovska G, Volksone L, Romanowska-Dixon B, Gos R, Holló G. Efficacy and safety of travoprost/timolol vs dorzolamide/timolol in patients with open-angle glaucoma or ocular hypertension. Clin Ophthalmol. 2009;3:629-36.
9. Netland PA, Landry T, Sullivan EK, Andrew R, Silver L, Weiner A, Mallick S, Dickerson J, Bergamini MV, Robertson SM, Davis AA; Travoprost Study Group. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2001 Oct;132(4):472-84.
10. Sharif NA, Kelly CR, Crider JY. Human trabecular meshwork cell responses induced by bimatoprost, travoprost, unoprostone, and other FP prostaglandin receptor agonist analogues. Invest Ophthalmol Vis Sci. 2003 Feb;44(2):715-21.
11. Singh K, Shrivastava A. Medical management of glaucoma: principles and practice. Indian J Ophthalmol. 2011 Jan;59 Suppl(Suppl1):S88-92.
12. Siesky B, Harris A, Cantor LB, Kagemann L, Weitzman Y, McCranor L, Marques C, Werne A, Stefansson E. A comparative study of the effects of brinzolamide and dorzolamide on retinal oxygen saturation and ocular microcirculation in patients with primary open-angle glaucoma. Br J Ophthalmol. 2008 Apr;92(4):500-4.
13. Schwartz K, Budenz D. Current management of glaucoma. Curr Opin Ophthalmol. 2004;15:119–126.
14. Allingham RR, Damji KF, Freedmam S, Moroi SE, Rhee DJ. Shields Textbook of Glaucoma. 6th ed. Philadelphia, PA: Wolters Kluver Plublisher; 2010:176-85.

15. Lee AJ, McCluskey P. Clinical utility and differential effects of prostaglandin analogs in the management of raised intraocular pressure and ocular hypertension. Clin Ophthalmol. 2010 Jul 30;4:741-64.
16. Parikh RS, Parikh SR, Navin S, Arun E, Thomas R. Practical approach to medical management of glaucoma. Indian J Ophthalmol. 2008 May-Jun;56(3):223-30.
17. Dixit A, Ashish A, Sharma R. A comparative study on efficacy of fixed combination timolol/brinzolamide versus travoprost monotherapy in drug-naïve open-angle glaucoma patients. Ther Adv Ophthalmol. 2020 Apr 28;12:2515841420909666.
18. Denis P, Lafuma A, Khoshnood B, Mimaud V, Berdeaux G. A meta-analysis of topical prostaglandin analogues intra-ocular pressure lowering in glaucoma therapy. Curr Med Res Opin. 2007 Mar;23(3):601-8.
19. Denis P, Launois R, Devaux M, Berdeaux G. Comparison of diurnal intraocular pressure control by latanoprost versus travoprost : results of an observational survey. Clin Drug Investig. 2006;26(12):703-14.
20. Stewart WC, Konstas AG, Nelson LA, Kruft B. Meta-analysis of 24-hour intraocular pressure studies evaluating the efficacy of glaucoma medicines. Ophthalmology. 2008 Jul;115(7): 1117-1122.e1.
21. Kimal Arici M, Topalkara A, Güler C. Additive effect of latanoprost and dorzolamide in patients with elevated intraocular pressure. Int Ophthalmol. 1998;22(1):37-42.
22. Li T, Lindsley K, Rouse B, Hong H, Shi Q, Friedman DS, Wormald R, Dickersin K. Comparative Effectiveness of First-Line Medications for Primary Open-Angle Glaucoma: A Systematic Review and Network Meta-analysis. Ophthalmology. 2016 Jan;123(1):129-40.
23. Garway-Heath DF, Crabb DP, Bunce C, Lascaratos G, Amalfitano F, et al. Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. Lancet. 2015 Apr 4;385(9975):1295-304. doi: 10.1016/S0140-6736(14)62111-5. Epub 2014 Dec 19. Erratum in: Lancet. 2015 Jul 11;386(9989):136.
24. Konstas AG, Boboridis KG, Kapis P, Marinopoulos K, Voudouragkaki IC, et al. 24-Hour Efficacy and Ocular Surface Health with Preservative-Free Tafluprost Alone and in Conjunction with Preservative-Free Dorzolamide /Timolol Fixed Combination in Open-Angle Glaucoma Patients Insufficiently Controlled with Preserved Latanoprost Monotherapy. Adv Ther. 2017 Jan;34 (1):221-235.
25. Luque Aranda R, Cabarga Del Nozal C, Silva Silva G, Vázquez Salvi A, García Campos JM. Estudio del efecto hipotensor del latanoprost frente a la asociación timolol-dorzolamida [Study on hypotensive effect of latanoprost vs timolol-dorzolamide association]. Arch Soc Esp Oftalmol. 2002 Apr;77 (4):205-10.
26. Quérat L, Chen E. Monitoring daily intraocular pressure fluctuations with self-tonometry in healthy subjects. Acta Ophthalmol. 2017 Aug;95(5): 525-529.
27. Hughes E, Spry P, Diamond J. 24-hour monitoring of intraocular pressure in glaucoma management: a retrospective review. J Glaucoma. 2003 Jun;12(3): 232-6.
28. Cheng JW, Cheng SW, Gao LD, Lu GC, Wei RL. Intraocular pressure-lowering effects of commonly used

fixed-combination drugs with timolol: a systematic review and meta-analysis. PLoS One. 2012;7(9):e45079.

29. Riva I, Katsanos A, Floriani I, Biagioli E, Konstas AG, Centofanti M, Quaranta L. Long-term 24-hour intraocular pressure control with travoprost monotherapy in patients with primary open-angle glaucoma. J Glaucoma. 2014 Oct-Nov;23(8):535-40.