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Comparison of the Efficacy and Safety of Fixed Combination Travoprost/Timolol and Dorzolamide/ Timolol in Patients with Primary Open-Angle Glaucoma and Ocular Hypertension

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SUMMARY

Introduction Combining two medications in one bottle may improve compliance by reducing the time required to administer drops and the frequency of the total number of medication bottles.

Objective To compare the efficacy of reduced intraocular pressure (IOP) and safety of fixed combination travoprost 0.004%/timolol 0.5% vs. fixed combination dorzolamide 2%/timolol 0.5% in patients with primary open-angle glaucoma or ocular hypertension.

Methods Prospective randomized clinical study included 60 patients divided into 2 groups. Follow-up was done at day 14 and 45 and month 3. IOP measurements were taken at each follow-up examination at 8 am, 10 am and 4 pm.

Results Both fixed combinations reduced IOP significantly compared to initial values at all follow-ups ($p<0.001$). Mean pooled IOP at all visits and time points was slightly lower in the travoprost/timolol group compared with the dorzolamide/timolol group (16.13 mmHg vs. 16.15 mmHg). Mean IOP reduction from baseline ranged from -7.46 mmHg to -9.92 mmHg in the travoprost/timolol group and from -6.93 mmHg to -8.93 mmHg for the dorzolamide/timolol group. Mean (±standard error of the mean) reduction in diurnal IOP from baseline to 3rd month was 8.96±2.79 in the travoprost/timolol group versus 8.07±2.91 in patients receiving dorzolamide/timolol fixed combination ($p=0.196$). The most frequent treatment-related adverse events were conjunctival hyperemia in the travoprost/timolol group, and dry eye and foreign body sensation in the dorzolamide/timolol group.

Conclusion Travoprost/timolol fixed combination was slightly more effective than dorzolamide/timolol fixed combination in reducing mean diurnal IOP. Travoprost/timolol group resulted in an IOP reduction for up to 1.07 mmHg higher than dorzolamide/timolol group. Both fixed combinations were well tolerated and safe.

Keywords: primary open-angle glaucoma; ocular hypertension; travoprost; dorzolamide; timolol

INTRODUCTION

The first-line treatment of primary open-angle glaucoma (POAG) and ocular hypertension (OHT) comprises a single medication but over time monotherapy often fails to control intraocular pressure (IOP). As many as 40% of patients treated for glaucoma are unable to achieve adequate control of IOP with a single medication [1]. When a single medication does not adequately lower IOP, additional drug is added to the therapeutic regimen. Patients are often prescribed multiple medications from different classes of IOP-lowering therapies, including carbonic anhydrase inhibitor and α-agonist, in addition to prostaglandin analogs and β-blockers, to help maintain adequate control of IOP. The use of more than one dosing bottle is associated with several concerns, including increased preservative exposure of multiple drops, reduced compliance and potential washout [2, 3, 4]. Low compliance with prescribed long-term glaucoma therapy is common and significantly undermines treatment success [5]. Up-to-date assembled data are consistent with the idea that in glaucoma there is a direct relationship between the number of daily doses and rate of non-compliance; patients taking glaucoma medications more often than twice daily show worse compliance [5, 6]. Combining two medications in one bottle may improve compliance by reducing the time required to administer drops, the frequency of total number and the number of medication bottles [7, 8]. In certain circumstances the use of one bottle rather than two will significantly reduce the inconvenience of filling prescriptions and can also result in reduced daily cost of therapy. Fixed combination often includes timolol, a β-adrenergic antagonist that effectively decreases aqueous humor production [9, 10]. Prostaglandin analogues, another class of potent ocular hypotensive substances, reduce IOP by increasing uveoscleral outflow of aqueous humor. Eleven recent studies [12, 13, 14] showed that travoprost administrated topically once daily efficiently lower IOP in patients with POAG an OHT. The complementary mechanisms of action of a prostaglandin analog and β-blocker are likely to produce an additive IOP-

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lowering effect in combination when compared with either single agent [15, 16, 17]. Dorzolamide is carbonic anhydrase inhibitor (CAI) and it is often used with β-blockers, to achieve additional lowering of IOP. Similarly, the fixed combination of dorzolamide and timolol has been shown to lower IOP more than its individual components and has been found to be comparable to the concomitant administration of the two medications [18, 19, 20]. Few studies compared the efficacy of the fixed combination of timolol and other prostaglandin analogs with the fixed combination of dorzolamide and timolol and found greater efficacy in favor of prostaglandin and timolol fixed combination [21, 22]. However, it has been only recently studied which of new fixed combination travoprost and timolol and dorzolamide/timolol has a significantly higher efficacy in lowering of IOP [23].

OBJECTIVE

The aim of this study was to compare the efficacy and safety of the fixed combination travoprost 0.004%/timolol 0.5% versus fixed combination dorzolamide 2%/timolol 0.5% in patients with primary open-angle glaucoma or ocular hypertension.

METHODS

A three-month randomized, controlled, open-label, prospective study compared the safety and IOP-lowering efficacy of the fixed combination travoprost 0.004%/timolol 0.5% with the fixed combination dorzolamide 2%/timolol 0.5% in patients with POAG or OHT at the University Eye Clinic, Clinical Center of Vojvodina, Novi Sad, Serbia. The study was conducted in accordance with the Declaration of Helsinki. This study gained the approval of the Ethical Committee of Medical Faculty of Novi Sad, Serbia, 2008. Signed, informed consent was obtained from all patients before study enrollment.

The inclusion criteria were 18 years of age or older, newly diagnosed POAG or OHT with or without pseudoexfoliation and pigment dispersion confirmed on multiple visits over 3 months period. Glaucoma was defined as either visual field defect or glaucomatous changes of the optic nerve head (neural rim loss, disc asymmetry, blood vessel changes, perpapillary atrophy) in association with an elevated IOP (IOP above 21 mmHg). Eligible patients were required to have an IOP of 22 mmHg to 36 mmHg in one or both eyes at 8 a.m. at three eligible visits. Patients who met IOP entry criteria at two separate eligibility visits were randomized. Recruitment of patients was conducted using a computer randomized program. Sixty patients who satisfied the inclusion criteria were assigned numbers. They were then randomly delegated into either group by the program. Patients had to meet each IOP qualification criteria in at least one eye (the same eye for all visits) to be eligible for randomization. Patients with IOP >36 mmHg in either eye were excluded based on potential safety risk. Other exclusion criteria were best-corrected visual acuity (BCVA) worse than 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, severe retinal disease, any abnormality that prevented reliable applanation tonometry, ocular trauma or intraocular surgery within 6 months of screening, and laser surgery within 3 months of screening. Pregnant women or breast-feeding were excluded. Patients with severe unstable or uncontrolled cardiovascular, hepatic or renal diseases; bronchial asthma or chronic pulmonary diseases; or hypersensitivity to prostaglandins, prostaglandins analogues, topical or systemic β-blockers, topical or systemic carbonic anhydrase inhibitors; or any components of the study medications were also excluded. Safety assessments were introduced to examine the side effects associated with topical β-blockers, such as heart rate and blood pressure, topical prostaglandins, such as ocular hyperemia, iris pigmentation, eyelash changes and topical CAI, such as taste abnormalities.

The following eligibility evaluations were conducted: BCVA, biomicroscopy, gonioscopy, dilated fundus examination, cup-disc ratio, and bilateral IOP measurement at 8 a.m. at 3 eligibility assessments using Goldmann applanation tonometry and automated perimetry. The visual field evaluation was performed using the Humphrey field analyzer program 24-2 or 30-2 (Carl Zeiss Meditec AG, Jena Germany) equipped with STATPAC. Patients requiring bilateral IOP-reducing therapy were treated in both eyes, but only the eye(s) that fulfilled all the inclusion criteria and none of the exclusion criteria were designated as study eye(s). If both eyes fulfilled all inclusion criteria, then the right eye was selected for the analysis.

Sixty patients were enrolled in the study. Each patient was assigned a number, and a computer randomization program was used to delegate each patient to 1st or 2nd group to receive fixed combination of travoprost/timolol (DuoTrav; Alcon-Couvereur SA, Puurs, Belgium) once daily or fixed combination dorzolamide/timolol (Cosopt; Merck Sharp & Dohme Idea Inc., Whitehouse Station, NJ, USA) twice daily.

Patients were instructed how to instill the medications. Patients in the travoprost/timolol fixed combination group administrated 1 drop into each eye once daily in the morning at 8 a.m., and patients in dorzolamide/timolol fixed combination group administrated 1 drop into each eye twice daily at 8 a.m. and 8 p.m. The follow-up was done at 14th and 45th days and 3rd months. IOP measurements were taken at each follow-up examination at 8 a.m., 10 a.m. and 4 p.m. Patients were instructed not to take the morning dose of medication on visit days because the medication was to be administrated at the study site after 8 a.m. measurement. Two individuals (an operator and a reader) performed each IOP measurement. The operator was responsible for operating the slit lamp and the instrument dial while the reader read and recorded the results. Two consecutive IOP measurements were taken for each eye and the mean IOP was recorded. All IOP measurements were done on the same applanation tonometer.

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Table 1. Patients' demographics and baseline characteristics

Variable		Trav/Tim Group	Dorz/Tim Group	p
Number of patients		30	26	
Age (years)	Mean±SD	65.87±10.73	61.85±11.51	0.182
	Range	62–70	57–66	
Sex (n)	Male	16	14	1.00
	Female	14	12	
Diagnosis (n)	POAG	22	18	0.774
	OH	8	8	
Baseline IOP (mmHg)		25.10	24.23	0.225
Best-corrected VA (mean±SD)		0.93±0.11	0.86±0.14	0.048
Gonioscopy – Shaffer grade (mean±SD)		2.93±0.25	2.92±0.27	0.884
Optic nerve head horizontal cup/disc ratio (mean±SD)		0.41±0.14	0.48±0.16	0.110
Optic nerve head vertical cup/disc ratio (mean±SD)		0.50±0.14	0.57±0.16	0.097
Mean deviation (dB)* (mean±SD)		-5.11±4.64	-2.05±2.5	0.004

Trav/Tim – travoprost/timolol; Dorz/Tim – dorzolamide/timolol; n – number of patients; POAG – primary open angle glaucoma; OH – ocular hypertension; IOP – intraocular pressure; VA – visual acuity; * visual field indices

Ocular and systemic side effects of hyperemia, foreign body sensation, blurred vision, dry eye sensation, stinging, pruritus, iris pigmentation, eyelash changes, pulse rate changes, breathing difficulties, headaches, depression and gastrointestinal problems were documented at each visit. Ocular hyperemia was assessed by the investigator at each visit and was graded on a scale from 0 to 3. The scoring was made by comparing the hyperemia to a standard set of photographs.

The data were coded and entered in a database. Statistical analysis was performed using Statistical Package for the Social Sciences. Standard statistical parameters and methods (descriptive statistics and frequency distribution) were used. Numerical data were presented using mean values, standard deviation (SD) and 95% confidence interval (CI). Comparisons among groups were done using t test. Chi-squared test was used to test the difference in frequency distributions of observed parameters; $p<0.005$ denoted statistical significance.

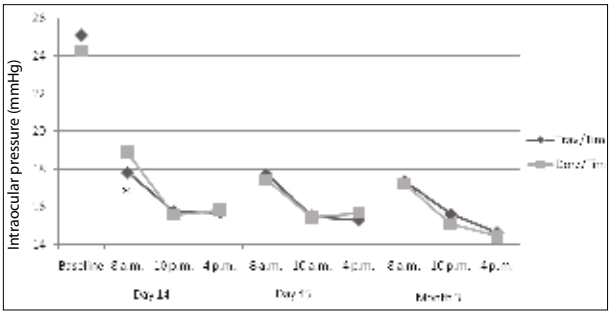
RESULTS

Sixty patients were enrolled in the study. Four patients from the dorzolamide/timolol group were excluded due to no treatment visit data. The mean age of patients in the travoprost/timolol fixed combination group was 65.87 (SD 10.73; range 62-70 years) and in the dorzolamide/timolol fixed combination group was 61.85 (SD 11.51; range 57-66 years). There was no significant difference in the mean age between the 2 groups. The demographic characteristics are shown in the Table 1. There was no statistical difference between the treatment groups for sex, diagnosis, visual acuity, gonioscopy values, horizontal and vertical cup-disc ratio, but there was a significant difference for mean deviation ($p=0.004$). Mean (± standard deviation) IOP levels in the 2 treatment groups were similar at baseline: 25.1±3.46 mmHg for travoprost/timolol fixed combination group and 24.23±1.07 mmHg for the dorzolamide/timolol fixed combination group.

Table 2. Mean intraocular pressure (IOP) and IOP reduction from baseline (%) (mean±SD)

Time		IOP (mmHg)		IOP reduction (%)	
		Trav/Tim Group (n=30)	Dorz/Tim Group (n=26)	Trav/Tim Group (n=30)	Dorz/Tim Group (n=26)
Day 14	8:00 AM	17.83±3.24	18.88±3.35	-28.65±11.58	-21.88±14.41*
	10:00 AM	15.73±2.58	15.54±2.42	-36.90±9.82	-35.74±10.45
	4:00 PM	15.67±1.95	15.81±3.02	-37.08±8.11	-34.53±13.93
Day 45	8:00 AM	17.73±1.91	17.42±2.70	-26.68±8.56	-27.96±11.58
	10:00 AM	15.47±2.27	15.42±2.41	-38.02±8.13	-36.15±10.74
	4:00 PM	15.27±2.51	15.45±2.65	-38.97±7.43	-35.19±11.69
Month 3	8:00 AM	17.33±2.13	17.19±2.40	-30.18±10.53	-28.86±10.64
	10:00 AM	15.60±1.88	15.04±2.80	-37.20±9.03	-37.76±12.15
	4:00 PM	14.60±2.55	14.42±2.30	-41.47±9.71	-40.36±9.88

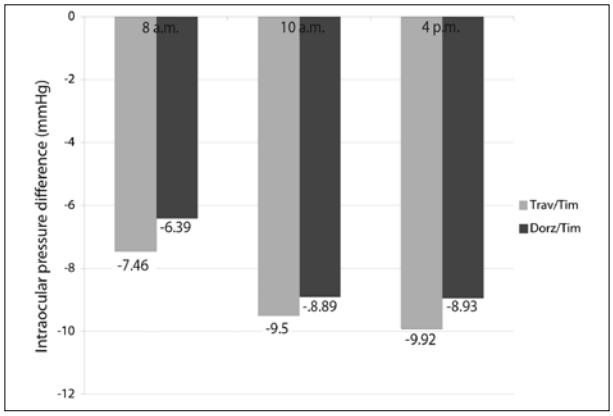
* p=0.057 for difference between groups



Graph 1. Mean intraocular pressure by treatment groups

Trav/Tim – Travoprost 0.004%/Timolol 0.5%; Dorz/Tim – Dorzolamide 2%/Timolol 0.5%

Mean diurnal IOP of all post-baseline visits at all time points ranged from 14.60 to 17.83 mmHg for the travoprost/timolol fixed combination group and 14.42 to 18.88 mmHg for the dorzolamide/timolol fixed combination group. For all visits pooled, mean diurnal IOP was 16.13 mmHg for the travoprost/timolol fixed combination group and 16.15 mmHg for the dorzolamide/timolol fixed combination group (Table 2, Graph 1). The greatest treatment difference occurred at 8 a.m. on the day 14 in favor of travoprost/timilol fixed combination group (1.05 mmHg for the mean IOP) and -6.77% of IOP reduction difference ($p<0.057$). Significant IOP reduction from baseline was achieved with both groups ($p<0.0001$). The mean reduction ranged from -7.46 to -9.92 mmHg for the travoprost/timolol fixed combination group and from -6.39 to -8.93 mmHg for the dorzolamide/timolol fixed combination group (Graph 2). Mean IOP reduction from baseline for all visits pooled was -8.96 mmHg for the travoprost/timolol fixed combination group and -8.07 mmHg for the dorzolamide/timolol fixed combination group with highest difference of -1.07 mmHg in favor of the travoprost/timolol fixed combination group but not statistically significant ($p=0.251$). Mean percentage reduction in diurnal IOP at month 3 was 36.28% in the travoprost/timolol fixed



Graph 2. Intraocular pressure change from baseline

Trav/Tim – Travoprost 0.004%/Timolol 0.5%; Dorz/Tim – Dorzolamide 2%/Timolol 0.5%

combination group and 35.66% in the dorzolamide/timolol fixed combination group (p=0.410) (Table 2).

The percentage of patients who responded to the treatment was based on a ≥25% reduction of IOP from baseline. The data were combined for all visits and time to provide an overall view how patients responded to the treatment from the beginning to the end of the study. Using these criteria at month 3, 86.7% of the patients who received travoprost/timolol fixed combination had IOP reduction >25% compared with 76.9 % of the patients receiving dorzolamide/timolol fixed combination (p=0.487).

No serious treatment-related adverse effects were reported. The most frequent ocular adverse effects in travoprost/timolol fixed combination group were hyperemia, blurred vision and pruritus. Hyperemia was observed in 50% of the patients in travoprost/timilol group and no one in the dorzolamide/timolol fixed combination group (p<0.0001). Hyperemia assessment was performed at all time points before instillation of fluorescein for IOP measurement. Blurred vision and pruritus occurred in 6.7% of the patients in travoprost/timolol fixed combination group. The most frequent ocular adverse effects among the patients in the dorzolamide/timolol fixed combination group were dry eye sensation (30.8%) and foreign body sensation (23.1%). No patient reported dry eye sensation and foreign body sensation in the travoprost/timolol fixed combination group (p<0.001 and p=0.007, respectively). Stinging was noted in 3.3 % of patients in the travoprost/timolol fixed combination group and 11.5% in the dorzolamide/timolol fixed combination group (p=0.253). Taste abnormalities occurred in 3.8% of the patients in dorzolamide/timolol fixed combination group and in 0% of the patients in travoprost/timolol fixed combination group (p=0.464). There were no observed iris pigmentation changes, eyelash changes, cystoid macular edema or systemic side effects.

DISCUSSION

This 3-month prospective study evaluated the safety and efficacy of travoprost/timolol fixed combination and dorzolamide/timolol fixed combination in patients with POAG or OH. The results show that both fixed combinations reduced IOP at all time points at all visits (p<0.001). Mean pooled IOP across visits and time points was similar between groups (16.13 vs. 16.15 mmHg). Recent study by Teus et al. [23] found greater IOP-lowering efficacy in the travoprost/timolol group compared with the dorzolamide/timolol group (16.15 vs. 17.3 mmHg). The IOP-lowering efficacy of travoprost/timolol fixed combination was up to 1.05 mmHg, slightly greater than dorzolamide/timolol fixed combination. Although the clinical relevance of such a small difference may be questioned, differences in IOP responses may be larger in some patients and even differences of 1 mmHg may be important in some patients. The Early Manifest Glaucoma Trial suggests that for each mmHg of higher IOP, the risk of progression in early glaucoma may increase by 10% over study period [24]. Also, results of the Ocular Hypertension Treatment Study suggest that each mmHg of higher IOP increases the risk of developing glaucoma in an ocular hypertensive population by similar amounts [25]. Due to the fact that the IOP-lowering effect was only slightly better for one combination than for the other, differentiation of these drugs must be based on tolerability and ease of use. In this study the mean IOP reduction from baseline was slightly greater with travoprost/timolol fixed combination (-7.46 to -9.92 mmHg) than with dorzolamide/timolol fixed combination (-6.39 to -8.93 mmHg; p=0.251). A difference in IOP-lowering efficacy was achieved between travoprost/timolol fixed combination group and dorzolamide/timolol fixed combination group at 8 a.m. at all follow-up visits (mean change of 8.96 mmHg for travoprost/timolol fixed combination group and 8.07 mmHg for dorzolamide/timolol fixed combination group). The results of other studies have shown similar IOP reduction from baseline of 6.8 to 8.2 mmHg [16] and 8.8 to 11.5 mmHg [17] for patients given travoprost/timolol fixed combination. The IOP reduction observed with dorzolamide/timolol fixed combination was similar to a previous report [21].

The 4 p.m. IOP measurement did not represent the time of maximal IOP lowering or trough for either travoprost or timolol and dorzolamide, so a comparison at this time point was more valid than at 8 a.m., which represents the trough for timolol and at 10 a.m. which represent the peak time for timolol and dorzolamide (2 hour after instillation).

Although the most frequent adverse event in the travoprost/timolol fixed combination group was ocular hyperemia (50%), the majority of patients had trace of mild hyperemia. No patients discontinued the study because of ocular hyperemia. Another study found a hyperemia rate of 23% [16]. Blurred vision and pruritus occurred in 6.7% of the patients in travoprost/timolol fixed combination group. These side effects did not appear to pose any safety issues or interfere with patients' daily activities. Iris pigmentation changes and changes in eyelash characteristics, including length, thickness, density, and color were not observed in patients receiving travoprost/timolol fixed combination although they have been observed in other studies [26].

Cystoid macular edema has been observed in some patients using prostaglandin analogues, but cystoid macular edema was not observed in any treatment groups in this study. This may be because of the stringent inclusion and exclusion criteria of this study that was designated for interpretation of the efficacy and safety without the introduction of other variables [27, 28].

Dry eye and foreign body sensation were reported in dorzolamide/timolol group (23.1% and 30.8%), which was significantly higher than for patients in the travoprost/timolol fixed combination group (0%).

Topical administration of non-selective β-blockers such as timolol is known to cause respiratory and/or cardiovascular complications. However, none of the patients in this study had serious systemic respiratory or cardiovascular effects.

Both the travoprost/timolol and dorzolamide/timolol fixed combinations are effective in lowering IOP, with only 1 mmHg greater IOP lowering efficacy in favor of travoprost/timolol fixed combination dosed once daily compared to drozalamide/timolol fixed combination dosed twice daily. Both fixed combinations were well tolerated and safe for use in this study population.

CONCLUSION

Travoprost/timolol fixed combination was slightly more effective than dorzolamide/timolol fixed combination in reducing mean diurnal IOP. Travoprost/timolol group experienced an intraocular pressure reduction up to 1.07 mmHg greater than dorzolamide/timolol group. Both fixed combinations were well tolerated and safe.

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REFERENCES

1. Kass M, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:701-13.
2. Patel SC, Speath GL. Compliance in patients prescribed eye drops for glaucoma. Ophthalmic Sur. 1995; 26:233-6.
3. Weinreb RN. Compliance with medical treatments of glaucoma. J Glaucoma. 1992; 1:134-6.
4. Tsai JC, McClure CA, Ramos SE, Schlundt DG, Picher JW. Compliance barriers in glaucoma: a systematic classification. J Glaucoma. 2003; 12:393-8.
5. Olthoff CMG, Schouten JSAG, van de Borne BW, Webers CA. Noncompliance with ocular hypotensive treatment in patients with glaucoma or ocular hypertension: an evidence-based review. Ophthalmology. 2005; 112:953-61.
6. Robin AL, Covert D. Does adjunctive glaucoma therapy affect adherence to the initial primary therapy? Ophthalmology. 2005; 112:863-8.
7. Fechner RD, Realini T. Fixed combination of topical glaucoma medications. Curr Opin Ophthalmol. 2004; 15:132-5.
8. Katz JK, Modern alchemy. Fixed combinations of glaucoma drugs. Am J Ophthalmol. 2005; 125-6.
9. Zimmermann TJ, Kaufman HE. Timolol. A beta-adrenergic blocking agent for the treatment of glaucoma. Arch Ophthalmol. 1977; 95:601-4.
10. Rafuse P. Adrenergic antagonist. In: Morrison JC, Pollack IP. Glaucoma Science and Practice. New York, Stuttgart: Thieme; 2003. p.376.
11. Weinreb RN, Toris CB, Gabelt BA, Lindsey JD, Kaufman PL. Effects of prostaglandins on the aqueous humor outflow pathways. Surv Ophthalmol. 2002; 47(Suppl 1):53-64.
12. Goldberg I, Cuhna-Vaz J, Jakobsen JE, Nordmann JF, Trost E, Sullivan KE; International Travoprost Study Group. Comparison of topical travoprost drops given once daily and timolol 0.5% given twice daily in patients with open-angle glaucoma or ocular hypertension. J Glaucoma. 2001; 10:414-22.
13. Netland P, Landry T, Sullivan EK, Anfrew R, Silver R, Weiner A, et al. Travoprost compared with Latanoprost and Timolol in patients with open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2001; 4:472-84.
14. Fellman RL, Sullivan KE, Ratliff M, Silver LH, Whitson JT, et al; Travoprost Study Group. Comparison of travoprost 0.0015% and 0.004% with timolol 0.5% in patients with elevated intraocular pressure. Ophthalmology. 2002; 109:998-1008.
15. Hughes BA, Bacharach J, Craven ER, Kaback MB, Mallick S, Landry TA, et al. A three-month, multicenter, double-masked study of the safety and efficacy of travoprost 0.004%/timolol 0.5% ophthalmic solution compared to travoprost 0.004% ophthalmic solution and timolol 0.5% dosed concomitantly in subjects with open angle glaucoma or ocular hypertension. J Glaucoma. 2005; 14:392-9.
16. Schuman JS, Katz GJ, Lewis RA, Henry JC, Mallick S, Wells DT, et al. Efficacy and safety of a fixed combination of travoprost 0.004%/timolol 0.5% ophthalmic solution once daily for open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2005; 140:242-50.
17. Barnebey HS, Orengo-Nania S, Flowers BF, Samples J, Mallick S, Landry TA, et al. The safety and efficacy of Travoprost 0.004%/Timolol 0.5% fixed combination ophthalmic solution. Am J Ophthalmol. 2005; 140:1-7.
18. Clineschmidt CM, Williams RD, Snyder E, Adamsons IA. A randomized trial in patients inadequately controlled with timolol alone comparing the dorzolamide-timolol combination to monotherapy with timolol or dorzolamide: Dorzolamide-Timolol Combination Study Group. Ophthalmology. 1998; 105:1952-9.
19. Choudhri S, Wand M, Shields MB. A comparison of dorzolamide-timolol combination versus the concomitant drugs. Am J Ophthalmol. 2000; 130:832-3.
20. Hutzelmann J, Owens S, Shedden A, Adamsons I, Vargas E. Comparison of the safety and efficacy of the fixed combination of dorzolamide/timolol and the concomitant administration of dorzolamide and timolol: a clinical equivalence study. Br J Ophthalmol. 1998; 82:1249-53.
21. Shin DH, Feldman RM, Sheu WP; Fixed Combination Latanoprost/Timolol Study Group. Efficacy and safety of the fixed combination latanoprost/timolol versus dorzolamide/timolol in patients with elevated intraocular pressure. Ophthalmology. 2004; 111:276-82.
22. Day DG, Schacknow, Wand M, Sharpe ED, Stewart JA, Leech J, et al. Timolol 0.5%/dorzolamide 2% fixed combination vs. timolol maleate 0.5% and unoprostone 0.15% given twice daily to patients with primary open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2003; 135:138-43.
23. Teus MA, Miglior S, Laganovska G, Volksone L, Romanowska-Dixon B, Gos R, et al. Efficacy and safety of travoprost/timolol vs. dorzolamide/timolol in patients with open-angle glaucoma or ocular hypertension. Clin Ophthalmol. 2009; 3:629-36.

24. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E; Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol. 2003; 121:48-56.
25. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:714-20.
26. Mashima HK, Masuada K, Kitazawa Y, Azuma I, Araie M. A comparison of latanoprost and timolol in primary open-angle glaucoma and ocular hypertension: a 12-week study. Arch Ophthalmol. 1996; 114:929-32.
27. Moroi SE, Gottfredsdottir MS, Steingardt MT, Elner SG, Lee CM, Schertzer RM, et al. Cystoid macular edema associated with latanoprost therapy in a case series of patients with glaucoma and ocular hypertension. Ophthalmology. 1999; 106:1024-9.
28. Callanan D, Fellman RL, Savage JA. Latanoprost-associated cystoid macular edema. Am J Ophthalmol. 1998; 126:134-5.

Поређење ефикасности и сигурности фиксне комбинације травопроста и тимолола са дорзоламидом и тимололом код особа с примарним глаукомом отвореног угла и очном хипертензијом

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КРАТАК САДРЖАЈ

Увод Комбинацијом два лека у једној бочици може се побољшати редовност узимања лека, смањити укупан број капи датих у току дана и смањити време потребно за примену лека.

Циљ рада Циљ истраживања је био да се упореди ефикасност снижења интраокуларног притиска (ИОП) и подношљивост фиксне комбинације травопроста (0,004%) и тимолола (0,5%) са фиксном комбинацијом дорзоламида (2%) и тимолола (0,5%) код особа с примарним глаукомом отвореног угла и очном хипертензијом.

Методе рада У проспективну, рандомизирану клиничку студију укључено је 60 испитаника сврстаних у две групе. Контролни прегледи извршени су након 14 и 45 дана, те три месеца од почетка лечења. ИОП је измерен на сваком контролном прегледу у 8, 10 и 16 сати.

Резултати Обе фиксне комбинације лекова значајно снижавају ИОП у односу на почетне вредности у свим контролним мерењима (p<0,001). Просечна вредност ИОП била је незнатно мања код испитаника који су примали травопрост и тимолол у односу на групу која је лечена дорзоламидом и тимололом (16,13 *mm Hg* према 16,15 *mm Hg*). Просечно снижење ИОП у односу на почетне вредности било је од -7,46 до -9,92 *mm Hg* за травопрост и тимолол, односно од -6,93 до -8,93 *mm Hg* за дорзоламид и тимолол. Просечно снижење ИОП од почетних вредности до трећег месеца било је 8,96±2,79 код испитаника који су примали травопрост и тимолол, а 8,07±2,91 у групи која је лечена дорзоламидом и тимололом (p=0,196). Најчешћи нежељени ефекат примене прве комбинације лекова (травопрост/тимолол) била је хиперемија вежњаче, док су суво око и осећај страног тела била најчешћа нежељена дејства примене друге комбинације (дорзоламид/тимолол).

Закључак Примена комбинације травопроста и тимолола доводи до нешто веће ефикасности снижења просечног ИОП у односу на комбинацију дорзоламида и тимолола. Разлика у снижењу ИОП између две групе испитаника била је до 1,07 *mm Hg* у корист оних који су лечени травопростом и тимололом. Обе фиксне комбинације су се показале сигурним и добро подношљивим.

Кључне речи: примарни глауком отвореног угла; очна хипертензија; травопрост; дорзоламид; тимолол

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