24-Hour Intraocular Pressure Control between Travoprost/Timolol Fixed Combination, Latanoprost/ Timolol Fixed Combination and Standard Timolol in Primary Open Angle Glaucoma and Ocular Hypertension

Pongsak Pachimkul MD*,
Kanokwan Yuttitham MD*, Peerapong Thoophom MD*

** Department of Ophthalmology, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand*

***Objectives**: To evaluate the efficacy between Travoprost 0.004%/Timolol 0.5% fixed combination, Latanoprost 0.005%/ Timolol 0.5% fixed combination once a day in the morning and Timolol 0.5% twice a day in a 24-hour intraocular pressure control (IOP).*

***Material and Method:** The patients with primary open angle glaucoma and ocular hypertension was subjected. After 2-4 weeks of washout period, patients with daytime IOP $\geq$ 21 mmHg and $\leq$ 36 mmHg were admitted to the hospital for 24-hour IOP monitoring every 3-hour interval starting from 9 am to 9 am the next day. The patients were randomly received Travoprost-Timolol fixed combination, Latanoprost-Timolol fixed combination once a day or Timolol twice a day in the studied eyes. Another 24-hour IOP monitoring was taken again 2 weeks later.*

***Results:** 59 eyes from 32 patients were subjected. The mean initial IOP at 9 am was 21.6 mmHg. The mean reduction of IOP ranging from 1.6 to 7.3 mmHg for Travoprost-Timolol group, 1.5 to 8.2 mmHg for Latanoprost-Timolol group and 2.2 to 5.6 mmHg for Timolol group. All three groups produced statistically significant reduction ($p < 0.05$) in mean IOP at all test times except; at 3 am for the Travoprost-Timolol group; at 3 am, 12 midnight-and 6 pm in the Latanoprost-Timolol group; and at 3 am and 9 pm in the Timolol group. The effects of IOP reduction of the combination drugs were greatest between 9 am and 3 pm with the morning dose of both combinations. There was no statistically significant difference in mean IOP reduction at any test time between the 2 combination drug groups but they were both better than Timolol alone at 9 am and 3 pm.*

***Conclusion:** A fixed combination of Travoprost 0.004% and Timolol 0.5% is as effective as a fixed combination of Latanoprost 0.005% and Timolol 0.5% and are better than Timolol 0.5% in 24-hour IOP control.*

***Keywords:** 24 hour intraocular pressure, Fixed combination antiglaucoma drug*

J Med Assoc Thai 2011; 94 (Suppl. 2): S81-S87
***Full text. e-Journal:** http://www.mat.or.th/journal*

Glaucoma is a progressive optic neuropathy that an intraocular pressure (IOP) was known to be an independent risk factor for the development and progression of disease[1-3]. The reduction of IOP is still the key to the glaucoma management[4-6]. The mechanisms in reduction of IOP are mainly concentrated by both reducing the aqueous production and improving the aqueous outflow. The beta-blocker has been primarily used as the first-line drug for over 20 years. The effectiveness of this group of medication in term of good efficacy for aqueous suppression and lower intraocular pressure was addressed[7]. In 1990, the prostaglandins analogue was introduced as another mechanisms to lower intraocular pressure and was claimed to be more effective than the beta blocker[8-10]. Since over 45% of glaucoma patients were unable to achieve adequate control of IOP with single medication[11] and majority of them were elderly and took several oral medications for the general health, there were some major concerns to be addressed, *e.g.*, compliance to dosage and drugs, and side effect from the topical eye

Correspondence to:
Pachimkul P, Department of Ophthalmology, Rajavithi Hospital, 2 Phayathai Road, Ratchathewi, Bangkok 10400, Thailand.
Phone: 0-2354-8080 ext. 3423, Fax: 0-2354-8080
E-mail: pongsakpachimkul@gmail.com

drops[12]. The fixed combination of prostaglandin and beta blocker aimed to address these concerns. In addition, the efficacy of fixed combination drugs was seen as equally effective as or superior to the concomitant usage of each drug[13,14]. The maximum effect of prostaglandin analogs on timing of IOP lowering and the short half-life of beta-blocker seemed to synergize and proved to be a better solution for 24 hour IOP controlled. The fixed combination of beta blocker and prostaglandins analogs that was available commercially was Latanoprost/Timolol fixed combination,Travoprost/Timolol fixed combination and Bimatoprost/Timolol fixed combination.

Among them, the combination of 0.004% Travoprost and 0.5%Timolol proved to be an effective anti-glaucoma medication that superior to concomitant use of each drug in term of lowering IOP, improving compliance and reducing side effect[15]. The aim of this study was to compare the efficacy of 24-hour IOP reduction by observing the circadian pattern of IOP between the combination of 0.004% Travoprost and 0.5% Timolol, the combination of 0.005% Latanoprost and 0.5% Timolol and Standard Timolol 0.5%.

Material and Method

The study was approved by the Research Ethics Committee of the Rajavithi hospital. We enrolled patients from the glaucoma clinic of the Ophthalmology Department, Rajavithi Hospital. The inclusion criteria were primary open angle glaucoma (POAG) and ocular hypertension (OHT) patients who were using topical anti-glaucoma medications to control the disease. Their medical records were carefully reviewed with regard to the pattern of IOP control, type of medications, visual field test and optical coherence tomography (OCT). We included patients with mean IOP $\geq$ 18 mmHg for screening. Patients who had a history of filtering surgery, phacoemulsification and medically uncontrolled Argon laser trabeculoplasty (ALT) in the last three months were excluded. Cases of severe glaucoma with advanced cupping of more than 0.8 or severe visual field loss in either eye were also excluded. The participants were informed about the schedule for admission and the interventional plan in the next two weeks. Consent was obtained in all cases. After a 2 to 4 week washout period (two weeks for miotics, alpha adrenergic agonists, carbonic anhydrase inhibitors; four weeks for beta-blockers and prostaglandin analogues), the patients with IOP $\geq$ 21 mmHg and $\leq$ 36 were admitted to the hospital for 24-hour IOP measurement. On the eligibility visit, the patients had complete ocular examinations at 8 am. The IOP measurements were scheduled for every 3 hours, starting at 9 am up to and including 9 am of the next day. Daytime IOP was measured at 9 am (admission), 12 noon, 3 pm, 6 pm, and 9 am (Discharge day). The measurements were administered using the Goldmann applanation tonometer (GAT) with the patient in the upright position in the daytime, whereas the night time IOP at 9 pm, 12 midnight, 3 am and 6 am were obtained by using the handheld Perkins applanation tonometer (PAT), with the patient in the supine position. We assumed that gently waking the patient during the night would not interfere with the IOP value. The IOP at each test time in the eligibility visit served as the baseline IOP. Before discharge, the patients were randomized to receive the Travoprost/Timolol fixed combination (Duotrav = D), Latanoprost/Timolol fixed combination (Xalacom = X) to be instilled at 8 am once daily or standard 0.5% Timolol (Timolol = T) to be instilled at 8 am and 8 pm for two weeks. The follow-up 24-hour IOP measurement was done again after 2 weeks in the interventional visit. The patients were advised to take the same bottle of eye drops on the second admission in order to check compliance.

Statistical Analysis

The descriptive statistics were used for the basic characteristic of the subjects. Chi-square or Fisher's exact test was employed to compare baseline data for categorical data and ANOVA for continuous data. We mainly focused on the mean IOP of each visit and the IOP difference (changes in IOP readings between two visits) in the three groups of patients (D, X and T). A pair t-test was adopted to determine whether the mean scores of pressure in each patient were significantly different. The p-value of 0.05 will be established to indicate if the relationship is statistically significant. There were two different types of measure. First and foremost, an overall measure of performance of each drug in a "before" and "after" use of drug on the same patient by using a paired-sample t-test. Secondly, a comparison of differences in IOP readings after each drug use in order to assess whether drug performance among the three types showed any differences by using an independent-sample t-test.

Results

Out of 40 participants, 39 patients completed both visits. One patient pulled out after the first admission due to uncomfortable sleep. Seven patients were excluded due to a diagnosis of normal tension

glaucoma. Of 32 patients, five patients were only eye. The authors conducted one eye as one event assumed each eye was independent. In total, 59 eyes were included in the study. An average age of subjects in the study is 55.6 ± 17.5 years, range from 18 to 82. There are 12 female and 20 male. Among them, 29 are POAG and 3 are OHT. The demographic data is shown in Table 1. The mean IOP at the eligibility visit was 21.59 ± 5.45 mmHg. The 24-hour IOP at baseline ranged from 10-46 mmHg. The mean baseline IOP, mean IOP after drug use and IOP differences of the three groups are shown in Table 2. The courses of IOP variation before and after drugs use are presented in Fig. 1.

Testing the difference (before and after using) in each drug

There were significant differences found during the period of 9 am, 12 noon, 3 pm, 6 pm, 9 pm, 12 midnight, 6 am and 9 am of the following day (except at 3 am) among the group using drug D on the dependent measures ($p < 0.05$), as shown in Table 2. Similarly, lower IOP was found significantly at the test times of 9 am, 12 noon, 3 pm, 6 pm, 12 midnight, 6 am and 9 am (not at 9 pm or 3 am) in the group using drug T (Table 2). Finally, significant IOP reduction was found at 9 am, 12 noon, 3 pm, 9 pm, 6 am and 9 am (not at 6 pm, 12 midnight or 3 am) by the group using drug X (Table 2). The IOP differences of each drug are represented in Fig. 2.

Comparing differences after each drug use

When comparing between D and T groups as shown in Table 2, statistically significant differences were found at the period of 3 pm ($p = 0.012$). In the same effect, there were statistically significant between X and T groups at 9 am and 3 pm ($p = 0.025$ and 0.019 respectively). Interestingly, there was no statistically significant difference among D and X groups.

Discussion

The increased intraocular pressure and the increased diurnal intraocular pressure variation are addressed as risk factors of prevalence, incidence and progression of open angle glaucoma[16]. The higher the intraocular pressure, the greater the likelihood that an individual has open angle glaucoma. There has been an increasing tendency to discount the relative importance of intraocular pressure variation and fluctuation as risk factors for glaucoma progression[17]. There has been many publications supporting the idea that difference in intraocular pressure in the period of 24 hour is an independent risk factor for glaucoma[18].

However, there are also numbers of studies that do not prove that point. Bengtsson and Heijl revealed that mean IOP was strongly correlated with deterioration of glaucoma whereas IOP fluctuation was not found to be independent risk factor for progression[19]. The long-term IOP variation was not significantly associated with the risk of developing

Table 1. Demographic statistics by treatment group (32 cases: 59 eyes)

	Total (n = 32)	D group (n = 12)	X group (n = 10)	T group (n = 10)	p-value
Age					0.406++
Years (mean ± SD)	55.62 ± 17.53	63.92 ± 10.67	50 ± 16.79	51.3 ± 22.14	
Range (years)	18-82	37-76	18-70	18-82	
Sex:					0.344+
Male n (%)	20 (62.5)	6 (30)	6 (30)	8 (40)	
Female n (%)	12 (37.5)	6 (50)	4 (33)	2 (17)	
Type of OAG:					0.304+
POAG n (%)	29	11 (37.9)	8 (27.6)	10 (34.5)	
OHT n (%)	3	1 (33.3)	2 (66.7)	0 (0.0)	
Systemic diseases					0.756+
DM n (%)	4	1 (25)	1 (25)	2 (50)	
HT n (%)	5	3 (60)	1 (20)	1 (20)	
None n (%)	23	8 (34.8)	8 (34.8)	7 (30.4)	

+ = p-value from Chi-square test/ Fisher's exact test
++ = One way analysis of variance

Table 2. Mean IOP at baseline, Mean IOP after drug use and IOP differences from baseline

		Time								
		9 AM (admit)	12 PM	3 PM	6 PM	9 PM	12 AM	3 AM	6 AM	9 AM (discharge)
Baseline										
Drug IOP (n = 59 eyes)										
D	Mean ± SD	20.48 ± 4.93	20.30 ± 7.12	21.83 ± 5.14	21.26 ± 5.23	22.39 ± 6.06	20.87 ± 4.36	21.91 ± 3.56	21.30 ± 4.48	20.65 ± 7.89
T	Mean ± SD	22.72 ± 7.29	27.17 ± 7.38	26.89 ± 6.76	24.83 ± 6.35	25.78 ± 8.88	26.78 ± 8.15	27.33 ± 6.46	29.22 ± 7.88	26.17 ± 9.00
X	Mean ± SD	21.89 ± 7.72	23.83 ± 8.10	24.11 ± 7.62	21.06 ± 6.55	22.50 ± 8.01	22.00 ± 10.65	22.61 ± 7.45	24.39 ± 9.59	22.17 ± 5.32
Second visit (n = 59 eyes)										
D	Mean ± SD	14.83 ± 5.88	14.61 ± 6.19	15.57 ± 4.2	15.48 ± 3.16	16.74 ± 3.35	18.61 ± 4.18	20.30 ± 4.65	18.09 ± 3.79	14.67 ± 5.61
T	Mean ± SD	19.61 ± 6.53	22.56 ± 8.98	24.67 ± 5.85	20.67 ± 6.61	22.44 ± 7.12	21.44 ± 5.70	23.89 ± 7.01	25.11 ± 6.76	20.56 ± 7.83
X	Mean ± SD	13.28 ± 3.72	17.44 ± 6.92	16.94 ± 6.38	18.06 ± 6.58	18.06 ± 7.25	19.83 ± 7.59	21.06 ± 6.48	19.89 ± 6.81	16.78 ± 6.86
IOP difference (n = 59 eyes)										
D	diff (mmHg)	5.65	5.70	6.26	5.78	5.65	2.26	1.61	3.26	7.26
	p-value	0.000*	0.001*	0.000*	0.000*	0.000*	0.001*	0.134	0.001*	0.001*
T	diff (mmHg)	3.11	4.61	2.22	4.17	3.33	5.33	3.44	4.11	5.61
	p-value	0.005*	0.000*	0.033*	0.005*	0.136	0.018*	0.099	0.027*	0.024*
X	diff (mmHg)	8.16	6.05	6.79	2.84	4.21	2.05	1.47	4.26	5.11
	p-value	0.000*	0.002*	0.000*	0.071	0.009*	0.099	0.116	0.013*	0.002*

* Significant at $p < 0.05$, p-value from Pair t-test $p< 0.05$, diff= IOP difference (mmHg)
D = Travoprost /Timolol fixed combination
T = Timolol
X = Latanoprost/Timolol fixed combination

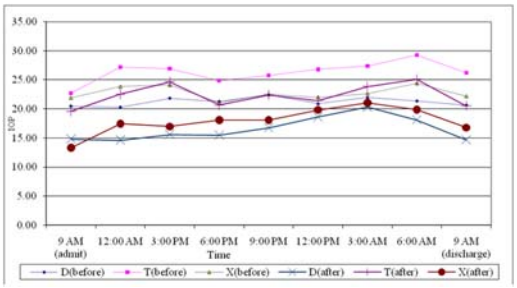

Fig. 1 Mean IOP before and after drugs use

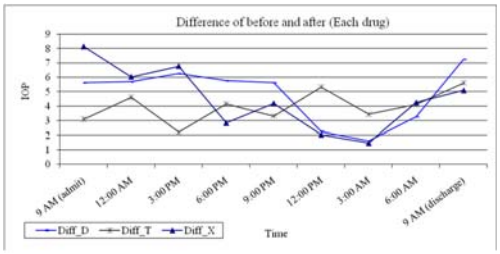

Fig. 2 IOP differences after each drug use

glaucoma in untreated ocular hypertension subjects[20]. There are some consensuses among glaucoma experts by modified Delphi process that 66% agree about the important of short-term and long-term intraocular fluctuation and reduction and the care of patients with glaucoma should include reduction of short-term (24 hours) intraocular pressure fluctuation[21]. The prostaglandin analogs Latanoprost and Travoprost have been shown to reduce intraocular pressure within 24 hours, though the effect of drugs was more potent during daytime with evening doses[22]. Latanoprost's 24-hour effect on IOP was shown to be relatively uniform throughout the circadian cycle and was found to be more effective than Timolol and Dorzolamide. Konstas et al showed that evening dosage of Latanoprost provided a daytime IOP lower than provided by morning dosage[23]. Konstas et al also demonstrated that when Latanoprost was given with Timolol in seperated bottles, evening dosage provided lower daytime pressure than morning dosage[24].

Travoprost is a newer prostaglandin analog that has efficacy similar to Latanoprost. Dubiner et al have examined the 24-hour efficacy of Travoprost and showed that the IOP was reduced at each individual time period in both morning and evening dosage[25]. The fixed combination of the prostaglandin analog and beta blocker was shown to produce greater IOP reduction than its components alone but have benefits of once a day dosage.

In our study, we compared 24-hour IOP pre and post dosage of 2 fixed-combination drugs-0.004% Travoprost /0.5% Timolol and 0.005% Latanoprost/0.5% Timolol. We found the significant difference ($p < 0.05$) in IOP reduction of both fixed combinations at all time point except at 3 am is common. Both fixed-combinations were not significant different in reduction of IOP at all time point, but significant different to Timolol alone. This confirms previous studies that beta-blockers have limited efficacy in lower IOP at night whereas prostaglandin analogs demonstrated such lowering effect[25].

All 3 drugs are poorly controlled on the IOP peak in the early morning hours (3 am to 6 am). Although the relative importance of IOP peaks remains unclear, the authors do not know whether some patients are more susceptible to IOP peaks and what level of IOP peak is required to cause glaucomatous damage. Despite these unanswered questions, some treatments would be added to control the IOP peaks in early morning hours, balancing the risk of visual loss in patients received fixed-combinations in one single regimen.

In conclusion, results of the present study seem to indicate that the two fixed-combinations; Travoprost/Timolol and Latanoprost/Timolol are equally effective in reducing 24-hour IOP especially in diurnal period and both are also better than Timolol. The fixed-combination Travoprost/Timolol is insignificantly better control of nocturnal IOP than the fixed-combination Latanoprost/Timolol.

Potential conflicts of interest

None.

References

1. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol 2000; 130: 429-40.
2. Asrani S, Zeimer R, Wilensky J, Gieser D, Vitale S, Lindenmuth K. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. J Glaucoma 2000; 9: 134-42.
3. Bengtsson B, Heijl A. A long-term prospective study of risk factors for glaucomatous visual field loss in patients with ocular hypertension. J Glaucoma 2005; 14: 135-8.
4. Collaborative Normal-Tension Glaucoma Study

Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. Am J Ophthalmol 1998; 126: 498-505.
5. Kass MA, 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.
6. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol 2003; 121: 48-56.
7. Dailey RA, Brubaker RF, Bourne WM. The effects of timolol maleate and acetazolamide on the rate of aqueous formation in normal human subjects. Am J Ophthalmol 1982; 93: 232-7.
8. Camras CB. Mechanism of the prostaglandin-induced reduction of intraocular pressure in humans. Adv Prostaglandin Thromboxane Leukot Res 1995; 23: 519-25.
9. Schachtschabel U, Lindsey JD, Weinreb RN. The mechanism of action of prostaglandins on uveoscleral outflow. Curr Opin Ophthalmol 2000; 11: 112-5.
10. Goldberg I, Cunha-Vaz J, Jakobsen JE, Nordmann JP, Trost E, Sullivan EK. Comparison of topical travoprost eye 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.
11. Reardon G, Schwartz GF, Mozaffari E. Patient persistency with topical ocular hypotensive therapy in a managed care population.Am J Ophthalmol 2004; 137 (1 Suppl): S3-12.
12. Broadway DC, Grierson I, O'Brien C, Hitchings RA. Adverse effects of topical antiglaucoma medication. I. The conjunctival cell profile. Arch Ophthalmol 1994; 112: 1437-45.
13. Fechtner RD, Realini T. Fixed combinations of topical glaucoma medications. Curr Opin Ophthalmol 2004; 15: 132-5.
14. Higginbotham EJ, Diestelhorst M, Pfeiffer N, Rouland JF, Alm A. The efficacy and safety of unfixed and fixed combinations of latanoprost and other antiglaucoma medications. Surv Ophthalmol 2002; 47 (Suppl 1): S133-40.
15. Gross RL, Sullivan EK, Wells DT, Mallick S, Landry TA, Bergamini MV. Pooled results of two randomized clinical trials comparing the efficacy and safety of travoprost 0.004%/timolol 0.5% in fixed combination versus concomitant travoprost 0.004% and timolol 0.5%. Clin Ophthalmol 2007; 1: 317-22.
16. Boland MV, Quigley HA. Risk factors and open-angle glaucoma: classification and application. J Glaucoma 2007; 16: 406-18.
17. Nouri-Mahdavi K, Hoffman D, Coleman AL, Liu G, Li G, Gaasterland D, et al. Predictive factors for glaucomatous visual field progression in the advanced glaucoma intervention study. Ophthalmology 2004; 111: 1627-35.
18. Caprioli J. Intraocular pressure fluctuation: an independent risk factor for glaucoma? Arch Ophthalmol 2007; 125: 1124-5.
19. Bengtsson B, Leske MC, Hyman L, Heijl A. Fluctuation of intraocular pressure and glaucoma progression in the early manifest glaucoma trial. Ophthalmology 2007; 114: 205-9.
20. Medeiros FA, Weinreb RN, Zangwill LM, Alencar LM, Sample PA, Vasile C, et al. Long-term intraocular pressure fluctuations and risk of conversion from ocular hypertension to glaucoma. Ophthalmology 2008; 115: 934-40.
21. Lee PP, Sultan MB, Grunden JW, Cioffi GA. Assessing the importance of IOP variables in glaucoma using a modified Delphi process. J Glaucoma 2010; 19: 281-7.
22. Orzalesi N, Rossetti L, Bottoli A, Fogagnolo P. Comparison of the effects of latanoprost, travoprost, and bimatoprost on circadian intraocular pressure in patients with glaucoma or ocular hypertension. Ophthalmology 2006; 113: 239-46.
23. Konstas AG, Nakos E, Tersis I, Lallos NA, Leech JN, Stewart WC. A comparison of once-daily morning vs evening dosing of concomitant latanoprost/timolol. Am J Ophthalmol 2002; 133: 753-7.
24. Konstas AG, Maltezos AC, Gandi S, Hudgins AC, Stewart WC. Comparison of 24-hour intraocular pressure reduction with two dosing regimens of latanoprost and timolol maleate in patients with primary open-angle glaucoma. Am J Ophthalmol 1999; 128: 15-20.
25. Orzalesi N, Rossetti L, Invernizzi T, Bottoli A, Autelitano A. Effect of timolol, latanoprost, and dorzolamide on circadian IOP in glaucoma or ocular hypertension. Invest Ophthalmol Vis Sci 2000; 41: 2566-73.

การศึกษาเปรียบเทียบความดันตา 24 ชั่วโมง ระหว่าง Travoprost/Timolol fixed combination และ Latanoprost/Timolol fixed combination กับ standard Timolol ในผู้ป่วยต้อหินชนิดมุมเปิดและภาวะความดันตาสูง

พงศ์ศักดิ์ ปัจฉิมะกุล, กนกวรรณ ยุติธรรม, พีระพงษ์ ธูปหอม

วัตถุประสงค์: *เพื่อเปรียบเทียบประสิทธิภาพของยา Travoprost 0.004%/Timolol 0.5% fixed combination และ Latanoprost 0.005%/Timolol 0.5% fixed combination หยอดวันละครั้งกับ standard Timolol 0.5% หยอดเช้า-เย็นในการควบคุมความดันตา 24 ชั่วโมง*

วัสดุและวิธีการ: *หลังจากหยุดยาลดความดันตาทุกชนิดเป็นเวลา 2 ถึง 4 สัปดาห์ ผู้ป่วยที่มีความดันตาระหว่าง 21 ถึง 36 มม. ปรอทจะได้รับเข้าไว้ในโรงพยาบาลเพื่อวัดความดันตาตลอด 24 ชั่วโมง โดยวัดทุก ๆ 3 ชั่วโมง จากนั้นผู้ป่วยจะได้รับยาอย่างใดอย่างหนึ่งใน 3 ชนิด ได้แก่ Travoprost 0.004%/Timolol 0.5% fixed combination หรือ Latanoprost 0.005%/Timolol 0.5% fixed combination หยอดเวลา 8.00 น. หรือได้รับยา Timolol 0.5% หยอดเวลา 8.00 น. และ 20.00 น. เป็นเวลา 2 สัปดาห์ หลังจากนั้น ผู้ป่วยจะได้รับเข้าไว้ในโรงพยาบาลเพื่อวัดความดันตาทุก ๆ 3 ชั่วโมง ตลอด 24 ชั่วโมงอีกครั้งหนึ่ง*

ผลการศึกษา: *ทั้งหมด 59 ตา จากผู้ป่วย 32 คน มีความดันตาเฉลี่ยเริ่มต้นที่ 21.6 มม. ปรอท ความดันตา 24 ชั่วโมงแรกรับ อยู่ในช่วงระหว่าง 10 ถึง 46 มม. ปรอท หลังจากหยอดยาที่ทำการทดลองมา 2 สัปดาห์ ความดันตาเฉลี่ยที่ลดลงอยู่ระหว่าง 1.6 ถึง 7.3 มม. ปรอท ในกลุ่ม Travoprost 0.004%/Timolol 0.5% fixed combination และ 1.5 ถึง 8.2 มม. ปรอทในกลุ่ม Latanoprost 0.005%/Timolol 0.5% fixed combination และ 2.2 ถึง 5.6 มม. ปรอทในกลุ่ม Timolol 0.5% ซึ่งลดลงอย่างมีนัยสำคัญทางสถิติเมื่อเปรียบเทียบกับก่อนหยอดตาทั้ง 3 ชนิด ผู้ป่วยมีความดันตาลดลงอย่างมีนัยสำคัญ ($p < 0.05$) ที่เกือบทุกช่วงเวลา คือยกเว้นที่เวลา 3.00 น. ในผู้ป่วยที่ได้รับยา Travoprost 0.004%/Timolol 0.5% fixed combination และช่วงเวลา 18.00 น., 24.00 น. และ 03.00 น. ในกลุ่ม Latanoprost 0.005%/Timolol 0.5% fixed combination และช่วงเวลา 3.00 น., 21.00 น. ในกลุ่ม Timolol 0.5% ที่ความดันตาเฉลี่ยลดลงไม่แตกต่างกัน พบว่าผลของยา fixed combination สามารถลดความดันตาได้ดีที่สุดในช่วงระหว่าง 9.00 ถึง 15.00 น. ในแต่ละวันโดยไม่มีความแตกต่างในประสิทธิภาพของยาทั้ง 2 ชนิด แต่พบว่าดีกว่าการใช้ยา Timolol ชนิดเดียวที่ 9.00 น. และ 15.00 น.*

สรุป: *Travoprost/Timolol fixed combination และ Latanoprost/Timolol fixed combination สามารถลดความดันตา 24 ชั่วโมง ได้ดีเกือบทุกช่วงเวลาทั้ง 2 ชนิด ไม่แตกต่างกันและดีกว่าการใช้ยา Timolol หยอดเพียงชนิดเดียว*