The reduction of intraocular pressure after instillation of travoprost compared with timolol in chronic primary angle-closure glaucoma

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Abstrak

Tujuan tulisan ini adalah untuk membandingkan penurunan tekanan intraokuler (TIO) setelah pemberian obat tetes mata Travoprost 0,004% dengan setelah pemberian timolol 0,5% pada glaukoma primer sudut tertutup kronik. Penelitian prospektif yang dilakukan dari April 2005 sampai Juli 2005 di Departemen Mata Rumah Sakit Cipto Mangunkusumo (RSCM) Jakarta pada pasien glaukoma primer sudut tertutup kronik. Subjek dibagi secara acak menjadi 2 grup: grup pertama diberi tetes mata Travoprost 0,004% sekali sehari, dan grup ke dua diberi timolol 0,5% dua kali sehari. Dua minggu sesudah pengobatan dengan obat yang pertama, obat diganti dengan obat yang kedua. Tekanan intraokuler dicatat sebelum pengobatan dimulai, pada hari 1, hari 7 dan hari 14. Masa wash out dilaksanakan selama tiga minggu sebelum terapi awal dan setelah dilakukan cross over. Enam belas pasien (32 mata) memenuhi kriteria inklusi dan diikut-sertakan pada penelitian ini. Sebelum terapi, TIO pada grup Travoprost sebesar 25,38 ± 3,01 mmHg, sedangkan pada grup timolol sebesar 25,88 ± 2,55 mmHg (p=0,354). Pada hari ke 7 pengobatan, TIO untuk masing-masing grup sebesar 16,75 ± 1,92 dan 21,25 ± 3,09 (p=0,001). Sedangkan pada hari ke 14 pengobatan, TIO untuk masing-masing grup sebesar 13,94 ± 2,02 dan 19,25 ± 2,18 (p=000). Dengan demikian Travoprost secara statistik bermakna menurunkan TIO lebih cepat dan besar dari pada timolol (p<0.05). Tetes mata Travoprost 0,004% menurunkan tekanan intraokuler lebih cepat dan lebih besar daripada tetes mata timolol 0,5%. ***(Med J Indones 2006; 15:242-5)***

Abstract

The objective of this study is to compare the reduction of intraocular pressure (IOP) after instillation of Travoprost compared with timolol in chronic primary angle-closure glaucoma. A prospective randomized, crossover study was conducted from April 2005 to July 2005 at Department of Ophthalmology, National Central General Hospital (RSCM) Jakarta on subjects with chronic primary angle-closure glaucoma. Subjects were randomly divided into 2 groups: those taking Travoprost once daily and those taking timolol twice daily. Two weeks after treatment with the first drug, the second drug was substituted. Intraocular pressure was recorded before therapy, at day 1, day 7, and day 14. There was a wash out period of three weeks prior to initial treatment and after the cross over. Sixteen subjects (32 eyes) met the inclusion criteria and were included in this study. The mean baseline IOP in the Travoprost group was 25.38 ± 3.01 mmHg, while in the timolol group it was 25.88 ± 2.55 mmHg (p=0.354). At day 7, the IOP were consecutively 16.75 ± 1.92 mmHg and 21.25 ± 3.09 mmHg (p=0.001) and at day 14 IOP were 13.94 ± 2.02 mmHg and 19.25 ± 2.18 mmHg (p=000). This showed that Travoprost decreased the IOP faster and greater than timolol. The mean baseline IOP was 25.38 ± 3.01 mmHg was decreased to 11.44 ± 1.90 mmHg with Travoprost. In the timolol group, the mean baseline IOP of 25.88 ± 2.55 mmHg was decreased to 6.63 ± 2.25 mmHg. Statistically, Travoprost significantly reduced the IOP faster and greater than timolol (p<0.05). Travoprost eye drops reduced the IOP faster and greater than timolol. ***(Med J Indones 2006; 15:242-5)***

Keywords: *chronic primary angle closure glaucoma, intraocular pressure, Travoprost, timolol.*

At present time, timolol an adrenergic beta-blocker, is the first line drug for chronic primary angle closure glaucoma (CPACG) treatment.[1] Timolol works by reducing the production of aqueous humor without affecting its outflow. The IOP lowering effect of timolol 0.5% twice a day occurs after two hours of administration and lasts for 24 hours. The IOP lowering effect is about 4-6 mmHg.[1] The Advanced Glaucoma Intervention Study (AGIS) has reported that timolol 0.5% cannot be used as a single therapy on 50% of glaucoma cases, and additional antiglaucoma agent is needed.[2]

Presently, there is a prostaglandin analog group of drugs for the lowering of IOP in glaucoma. The mechanism of action of this drug in lowering IOP is

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by improving aqueous humour outflow through the uveoscleral path.[3] A previous report from a multi-center study on the use of prostaglandin analog (latanaprost) on CPACG for 12 weeks showed that latanaprost reduced IOP greater than timolol.[4] The effect of latanoprost in lowering IOP is not influenced with wider peripheral anterior synechia.[5] Another prostaglandin analog is Travoprost which also showed effectiveness in lowering IOP on primary open angle glaucoma and ocular hypertension.[6-8] During six-month trial in a clinical testing phase III, Travoprost was found to be more effective in reducing IOP compared to timolol. The IOP reduction was about 30% - 33% or an average of less than 17 mmHg, and there was no tendency for IOP to rise.[6] Pivotal studies showed that Travoprost was an effective single therapy and optimal effect was achieved when Travoprost was given at night.[4-7]

In an other study comparing Travoprost, latanoprost and bimatoprost for 12 weeks on subjects with primary open angle glaucoma and ocular hypertension, all three drug were found to have the same potency in reducing IOP, but no study of the effect of Travoprost on primary angle closure glaucoma has been done.[8] Compared to other prostaglandin analogs which are partial agonist, Travoprost is a full agonist, which meant the drug has a high affinity to prostaglandin receptor and will produce maximal effect.[8] A further advantage is that Travoprost is more stable compared to latanaprost in room temperature.[5] At the present time, there is insufficient data regarding the use of Travoprost on CPACG.

The objective of this study was to compare IOP reduction after instillation of travoprost 0.004% eye drops with that of timolol 0.5 % on CPACG.

METHODS

This study was a cross-over intervention, randomized double blind trial. Subjects were derived consecutively from all subjects with previously treated CPACG at the Glaucoma Division, Department of Ophthalmology Faculty of Medicine of the University of Indonesia / National Central General Hospital Jakarta from April 2005 to July 2005.

The inclusion criteria for subjects were: CPACG subject, aged 40 years or more; initial CD ratio between 0.5 – 0.7; who had undergone peripheral iridectomy with IOP between 21 mmHg - 30 mmHg without medical therapy; CPACG subject who had undergone trabeculetomy IOP between 21 mmHg - 30 mmHg with no therapy; and subject who had undergone peripheral iridectomy with or without trabeculectomy IOP 21 mmHg or less, and receiving medical therapy. All subjects were washed out and evaluated every week for three weeks with IOP between 21 mmHg - 30 mmHg, and willing to sign a consent form.

The exclusion criteria were: CPACG subject with no compliance to a treatment regimen; subject with no compliance to scheduled follow up; subject contra-indicated for Travoprost and timolol; and subject with serious systemic drug side effects (asthma, cardiac disorder).

Subjects of the study were randomly divided into A and B group. The subject in group A received Travoprost 0.004% eye drop once a day, while subjects in group B received timolol 0.5% twice a day. Every subject of the study from both group were given two bottles of eye drops identical in form and size. The first bottle was labeled "morning" and the second bottle was labeled "night". Subjects in group A were given a bottle labeled "morning" containing placebo and the bottle labeled "night" containing Travoprost 0.004%. Subjects in group B were given 2 bottles labeled "morning" and "night", both containing timolol 0.5%.

Anamnesis was taken regarding age, gender, occupation, and history of systemic as well as topical drug use. Visual acuity was examined using the Snellen chart, anterior segment was examined by slit lamp, anterior chamber angle by slit lamp and goniolens (to grade angle closure according to Shaffer) and IOP was measured with Goldmann aplanation tonometry. Evaluations of compliance and applanation tonometry for IOP were performed on day 1, 7, and 14.

The data were analyzed by Wilcoxon, paired T, unpaired T tests for the appropriate data set using SPSS version 10.

RESULTS

Sixteen subjects (32 eyes) met the inclusion criteria and were included in this study. Out of the 16 subjects meeting the inclusion criteria of the study, 9 (56.75%) subjects were post laser peripheral iridectomy, 4 (25%) were post trabeculectomy, and 3 (18.25%)

subjects were post peripheral iridectomy and trabeculectomy. The subjects were comparable on entry for this study (Table 1).

Table 1. Some demographic characteristics of subjects

	Mean ± SD	Range	p
Age (years)	63.19 ± 5.36	49 - 71	
Gender			
Men	4 (25%)		
Women	12 (7 5%)		
Visual acuity (log MAR)	0.39 ± 0.36	1.10 - 0.00	
Initial IOP pre-therapy (mmHg)			
Travoprost	25.25 ± 2.87	22 - 30	0.621
Timolol	25.75 ± 2.25	21 - 30	
Initial IOP pre-cross over (mmHg)			
Travoprost	25.50 ± 3..34		0.867
Timolol	26.00 ± 2.98		
Cup disk ratio	0.59 ± 0.08	0.5 - 0.7	

Our study did not find serious systemic side effect in both groups. Table 2 shows that mean IOP on day 1, day 7 and day 14 after therapy in both groups were decreased. However, reduction of IOP was greater in the Travoprost group. Mean IOP on day 1, day 7 and day 14 reached 21 mmHg in the Travoprost group while in the timolol group this value was achieved only by day 14. Average IOP between the two groups on each follow up showed that reduction in IOP were faster and greater in the Travoprost than the timolol group.

Table 2. Average IOP (mmHg) pre- and post-Travoprost and timolol therapy

Time	Group of treatment		p
	Travoprost (mean ± SD) n=16	Timolol (mean ± SD) n=16	
Pre-therapy	25. 38 ± 3.01	25.88 ± 2.55	0.354
Post-therapy			
Day 1	21.00 ± 1.93	24.13 ± 3.32	0.004
Day 7	16.75 ± 1.92	21.25 ± 3.09	0.001
Day 14	13.94 ± 2.02	19.25 ± 2.18	0.000

DISCUSSION

Some limitations in this study were: (1) the study was conducted in one hospital (Central General Hospital in Jakarta) only; (2) the number of subject was small; (3) the duration of the observation was short; and (4) IOP was measurement only taken once on each follow-up, without measuring diurnal variation. It was realized that a single measurement of IOP may be not enough for optimal management of glaucoma, and IOP measurement need to be performed several times within 24 hours, especially to observe diurnal IOP variation as stated by a previous study.[9]

For diurnal fluctuation, IOP measurements need to be conducted at least four times a day with the subjects hospitalized. In this study IOP measurement was conducted only once, that is on every follow up, and therefore IOP diurnal fluctuation cannot be evaluated. This was due to the fact that most of the subjects in this study were women who refused to be hospitalized because of family responsibilities, such as taking care of their children and husbands. Other reasons were the great distance between their homes and the hospital making it impossible to come to the hospital several times a day for follow ups. This was why the time for IOP measurement was between 8 -10 o'clock in the morning of each follow up, when the IOP rise is expected to be the highest.

In this study, the average IOP between the two groups on each follow up showed that the decrease in IOP were faster and greater in the Travoprost group than in the timolol group. No other study was found regarding this finding on CPACG. However, previous studies have revealed that Travoprost was more effective than timolol in primary open angle glaucoma.[6]

There were no serious systemic side effects in both groups. However, a previous study noted that the reduction in IOP after administration of timolol was not up to expectation and some serious systemic side effects were found; timolol was also unable to suppress diurnal fluctuation.[11.12] In another study lasting for three months, there was a reduction of 6.1 ± 0.2 mmHg from the initial IOP in CPACG.[13] While in another study where timolol was administered for 2 weeks, there was a reduction of 5.7 ± 0.7 mmHg or 23% in IOP in CPACG.[11]

In this study, IOP reduction in the timolol group on day 14 was 6.63 ± 2.25 mmHg compared to baseline IOP or 25.35%. This finding supports a previous study which found that timolol 0.5% reduced IOP by 25% to 30%.[6] The ocular hypotensive effect can decrease (long term drift) with long term (a few months/years)

administration of timolol.[9,10] IOP will reach a stable phase of 25% reduction of pre-treatment IOP.

The findings in this were based only on a single IOP measurement taken between 8.00 to 10.00 AM, while a previous study lasting 12 months on open angle glaucoma and ocular hypertension comparing Travoprost, Latanoprost and timolol, where IOP was measured on the second week and then every month, measurements were conducted at 8 o'clock in the morning, 10 o'clock in the morning and 4 o'clock in the afternoon. IOP reduction for the Travoprost group was significant for each measurement when compared to pretreatment initial IOP. Average IOP reduction showed that Travoprost reduced IOP all day long and produced significantly greater IOP reduction at 4 o'clock in the afternoon.[14]

In conclusion, both Travoprost 0.004% and timolol 0.5% eye drops can reduce IOP in chronic primary angle closure glaucoma, but Travoprost reduced IOP faster and greater when compared to timolol.

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