ORIGINAL ARTICLE

Comparison of Intraocular Pressure After Water Drinking Test in Primary Open Angle Glaucoma Patients Controlled with Latanoprost and Trabeculectomy

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ABSTRACT

Purpose: To compare intraocular pressure (IOP) after water drinking test in primary open angle glaucoma patients controlled with latanoprost 0.005% and trabeculectomy.
Methods: Observational study with cross-sectional design of 28 eyes with primary open angle glaucoma (POAG) patients. Subjects were divided into two groups, 14 patients controlled with trabeculectomy and 14 patients with latanoprost monotherapy. All subjects were under clinical therapy and had an intraocular pressure (IOP) equal or lower than 18 mm Hg, monitored during the follow up period. All subjects were submitted to the water drinking test. The results of the water drinking test, which were peak and fluctuation of IOP, were then compared between groups.
Results: There were no significant difference between IOP peak between two groups (p=0.88). IOP fluctuation also showed no significant difference between groups (p=0.84). In both groups, baseline IOP strongly correlated with peak IOP in water drinking test with correlation coefficient r=0.96 (p<0.001) and r=0.71 (p=0.04), while baseline IOP in trabeculectomy group was strongly correlated with IOP fluctuation with correlation coefficient r=0.86 (p<0.001).
Conclusions: Peak and fluctuation of IOP after water drinking test in primary open angle patients controlled with latanoprost and trabeculectomy showed no significant difference.

Keywords: IOP peak, IOP fluctuation, water drinking test, trabeculectomy, latanoprost

Glaucoma refers to a group of diseases which characterized by retinal ganglion cell loss, optic neuropathy with associated visual function loss, and elevated intraocular (IOP) is one of the primary risk factors. [1] According to WHO in 2002, glaucoma is the second cause of blindness in the world, with prevalence almost 67 millon yearly. [1, 2] Primary Open Angle Glaucoma (POAG) is the most common type of glaucoma. In United States incidence of POAG is nearly 2.5 million cases and 130.000 unfortunately went blind.[2, 3]

Optic nerve and visual field changes in most cases are determined by both the level of the IOP and the resistance of the optic nerve axons to pressure damage.[1] Dynamic balance between aqueous inflow and outflow facility determines circadian fluctuation of IOP. The range in IOP variation can be extreme, with the pattern of change also varying between individuals. Patients may demonstrate diurnal or nocturnal IOP peaks.[4]

IOP fluctuation is an important risk factor in disease progression. Other factors that has been proven strongly correlated with progression were genetic and age, while central corneal thickness and *baseline* of *cup disk ratio*were still controversy.[5] Until now, IOP is the only factor that could be modified.

Open angle glaucoma patients with controlled IOP, could still showed disease progressions. This is thought due to undetected IOP peak and fluctuation during visit in office hours. A*dvanced glaucoma intervention study* (AGIS) study concluded longterm IOP fluctuations were correlated with visual field defect especially in patients with low IOP.[6] Malerbi et al and David R et al showed that IOP peak in glaucoma patients mostly occurred outside office hours.[7, 8] Asrani et al did home tonometry based measurement and found IOP fluctuation in open angle patients could reached 10 mmHg.[9] Nakakura et al assumed that IOP measurement in outpatient clinic is predictive to mean circadian IOP, but not to IOP peak and fluctuation.[10]

In daily practice, 24 hours IOP measurement is difficult to obtain and costly, while home tonometry is considered unreliable due to high variability.[9, 11] Other technique to measure IOP peak and fluctuation were modified diurnal tension curve, was found failed to detect IOP peak at night.[11]

The water drinking test is a provocative test that was widely used a few decades ago to help in the diagnosis of open angle glaucoma, but was found to be inadequate due to many false positive and negative results. However after some years, the water drinking test has been proposed as an alternative method to check the IOP control. [12] Nowadays water drinking test is proposed as a new method to estimate circadian IOP.[11-14] Kumar et al concluded that IOP peak and fluctuations in water drinking test was strongly correlated with circadian IOP peak and fluctuations.[15]

Susanna et al found that POAG patients with progressive visual field defect, 25 % experienced IOP peak > 21 mmHg during water drinking test. IOP fluctuations over 6 mmHg also found in 35,7% patients. [12] Other large study by Armaly et al, concluded from 26 factors assumed to be associated with progressive visual field defect in POAG patients, only 5 factors that proven significant, and IOP fluctuations after water drinking test was one of them. [16]

Glaucoma therapy is aimed to lower the IOP and avoid the progress of the disease. [1, 17] Latanoprost as one of the prostaglandin analog antiglaucoma drugs has been proven effective in controlling IOP fluctuations in open angle glaucoma and ocular hypertension patients. [18,19] While in uncontrolled patients after maximum medidal and laser treatment, trabeculectomy is the treatment of choice. Medeiros et al showed that trabeculectomy lower the IOP means and fluctuations compared to medically treated patients.[20] In water drinking test, trabeculectomy patients also showed a more stable IOP compared to patients with maximum antiglaucoma treatment. [21]

METHODS

From July to October 2011, a total of 28 patients were enrolled from the Glaucoma division of Departments of Ophthalmology, Kirana Eye Center, Cipto Mangunkusumo hospital, Jakarta, Indonesia. All patients were diagnosed with POAG, 14 patients were treated with topical IOP lowering monotherapy and 14 patients with trabeculectomy when enrolling this study. Approval from the Institutional Review Board Ethics Committee wass obtained for the study, which followed the principles of the Declaration of Helsinki.

All patients were submitted to the water drinking test. The patients were instructed to fast during the two-hour period preceding the test. The test was

carried out in a standardised manner: the patient was required to drink one litre of tap water over 15 minutes. After that, IOP was measured a total of three times at 15-minute intervals until 90 minutes. All IOP measurements were performed using the same Goldmann applanation tonometer (Haag–Streit, Bern, Switzerland) by experienced blinded examiners. The difference in IOP between the peak of the WDT and the baseline IOP immediately before water drinking test was considered as the IOP fluctuation.

STATISTICAL ANALYSIS

The sample size calculation was based on the assumption that a difference in mean IOP of 2.5 mm Hg is clinically relevant. In order to reach a power of 1-b = 0.90, given a = 0.05 and a SD of 2 mm Hg, 15 patients were needed. We included 20 patients in each group to achieve a power of over 90%. All calculations were performed using Stata^{TM} V 11 (Stata Corp). A p value of 0.05 or less was considered significant.

RESULTS

Twentyeight patients were included in the trial, 14 patients in the trabeculectomy group and 14 in the latanoprost group. No relevant statistically significant differences were found between the treatment groups in baseline characteristics (table 1).

In trabeculectomy group all patients had undergone trabeculectomy with mytomicin C for at least 3 months before water drinking test, with mean follow up periods 11.78 months.

Mean IOP fluctuations before and after water drinking test, which are baseline IOP, minimum IOP and peak IOP showed no significant difference. IOP fluctuations between groups also showed no significant difference (Table 2).

Table 3 showed details of IOP comparison between group during water drinking test. Peak IOP usually reached at 30 minutes, then decreased slowly and reached baseline at 90 minutes.

Table 1. Clinical characteristics of study participants

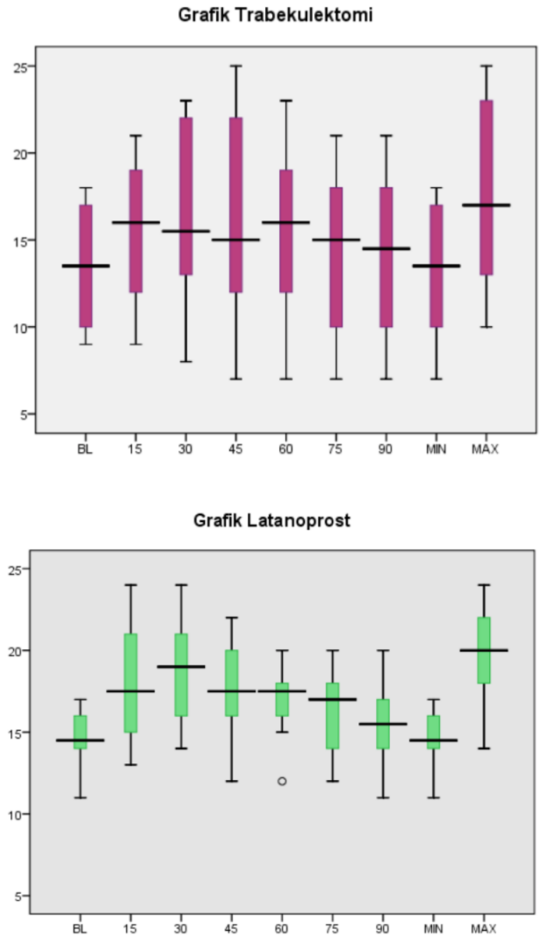
Parameter	Trabeculektomy	Latanoprost	*P* value
Number of patients (n)	14	14	
Age (y.o)	66.8 ± 1.8	62.8 ± 3.3	p = 0.15
Sex			
Female (n)	3	6	p = 0.23
Male (n)	11	8	
Baseline IOP (mmHg)	13.8 ± 3.3	14.6 ± 1.7	p = 0.80
Visual field defect (MD)	-15.6 ± 7.4	-11.4 ± 9.4	p = 0.20

Table 2. Mean of IOP peaks, minimum and fluctuations in water drinking test.

Parameter	Trabeculectomy	Latanaprost	Nilai p
Max IOP	17.5 ± 5.3	19.4 ± 2.9	p = 0.88
Min IOP	13.4 ± 3.9	14.6 ± 1.7	p = 0.85
T max– T min	4.1 ± 1.9	5.0 ± 1.8	p = 0.84

Table 3. Fluctutions during water drinking test

Parameter	Trabeculectomy group (n=14)	Latanoprost group (n=14)	*P* value
Baseline IOP	13.8 ± 3.3	14.6 ± 1.7	p = 0.80
15 minutes	15.6 ± 4.2	17.9 ± 3.5	p = 0.93
30 minutes	16.5 ± 5.3	19.0 ± 3.2	p = 0.93
45 minutes	16.2 ± 5.9	17.6 ± 2.6	p = 0.78
60 minutes	15.5 ± 5.1	17.0 ± 2.1	p = 0.84
75 minutes	14.8 ± 4.8	16.1 ± 2.2	p = 0.83
90 minutes	14.4 ± 4.7	15.7 ± 2.2	p = 0.83



Graphic 1. Comparison of IOP fluctuations between trabeculectomy and latanoprost group during water drinking test.

During water drinking test, 4 patients had an IOP fluctuations over 6 mmHg in latanoprost group and 2 patients in trabeculectomy group (p=0.36).

Table 4 showed correlation between mean baseline IOP with peak and fluctuations of IOP in each group. In both groups, baseline IOP is strongly correlated with peak IOP reached during WDT, while baseline IOP in trabeculectomy was strongly correlated with IOP fluctuations.

Table 4. Correlation between baseline IOP with peak and fluctuations of IOP with Pearson correlation rank test.

Variable	IOP peak	IOP fluctuations
Baseline IOP trabeculektomy group	R=0.96 p<0.001*	R=0.712 p=0.04*
Baseline IOP latanoprost group	R=0.86 p<0.001*	R=0.506 p=0.06

DISCUSSION

The aim of the present study was to show if fluctuations in IOP differ significantly between patients controlled by trabeculectomy, or latanoprost. Our results show that IOP varies significantly throughout the water drinking test, but this variation is not different between the groups. Trabeculectomy group showed IOP fluctuations 4.1 mmHg or increased 26.9 % from baseline IOP, while in latanoprost group 5.0 mmHg or increase 32.7% from baseline IOP. Different result were found by Monsouri et al in 2008 and Konstas et al that found medically treated patients showed less stable IOP fluctuations compared to trabeculectomy patients.[19,39]

Outside demographic factors, Monsouri and Kontas showed different baseline characteristics from our study participants. Mansouri study include patients with *normotension glaucoma* (NTG), which usually has a lower baseline and peak IOP compared to POAG patients. Monsouri also did water drinking test in the evening when latanoprost effect might be already decreased. In our study water drinking test done during office hour around 9.00 to 12.00 AM, when latanoprost effect reach its peak, 12 hours after administration.

In Konstas study, almost 50% patients with POAG, has undergone laser trabeculoplasty, which may effect to a lower nocturnal IOP fluctuations. This sudy also include patients with pseudoexfoliation syndrome that known has a higher IOP fluctuations.

Our study was using latanoprost due to its efficacy in reducing IOP fluctuations significantly. Orzalesi et al found that latanoprost can decrease IOP fluctuations higher than timolol and dorzolamide.[40] Susanna et al also found similar result that latanoprost can reduce IOP fluctuation during WDT lower than unoprostone.[41]

In this study, patients with latanoprost showed IOP fluctuations

slightly higher than trabeculectomy patients (5.0 mmHg vs 4.1 mmHg), but not statistically significant. This result could give an additional benefit of latanoprost in stabilizing IOP fluctuations in WDT as an reflection of diurnal IOP fluctuations. Brubaker[33] study found that eye capability to relieve after transient IOP elevation in WDT, based on *outflow* capacity. Phisiologically, outflow of aqueous humor that *pressure-sensitive* is through trabecular meshwork, but in the latest study uveoscleral outflow can also be pressure sensitive in certain condition, for example after treatment of topical analog prostaglandin.[18]

In a condition where otflow capacity were increased, eyes could overcome the elevation of aqueous humor volume rapidly, therefore IOP peak after WDT will be lower. In trabeculectomy group, there was a permanent bypass from anterior chamber to sclera and ends in subconjunctival and subtenon spaces, so aqueous humor volume elevation is easier to overcome.

Technique to measure the outflow of trabecular meshwork pathway or uveoscleral pathway is still lacking. Lately glaucoma experts considered WDT is beneficial to measure all the outflow capacity, through trabecular meshwork and uveoscleral pathway.

Our result also showed the baseline IOP is strongly correlated with IOP peak and fluctuations during WDT. This results is similar to Medeiros et al.[20] This result proved that the higher the baseline IOP, the fluctuations would increased as well.

In trabeculectomy patients, there was still 2 patients who had an IOP fluctuations exceed 6 mmHg. These condition might be due to a diffuse and minimal bleb morphology after trabeculectomy in both patients, eventhough the IOP could stable less than 21 mmHg 30 days after trabeculectomy. Bleb cicatrix could cause elevation of outfow resistancy.

There were few limitations of our study, which were two blinded experienced examiners were involved in this study that can caused interobserver measurement bias, but the usage of Goldmann applanation tonometry has a minimal interobserver realibility 0.4 mmHg [43], which is still below our difference of mean IOP of 2.5 mm Hg that clinically relevant. We also did not evaluate the hidration status of our patient. This factor is not also measured by the previous study. This factor is important, cause WDT is mostly affected by osmotic changes due to hidration status. We could only instructed the patients by fasting 2 hours before WDT.

CONCLUSIONS

Our study found no significant difference of the IOP peak and fluctuations between trabeculectomy and latanoprost group during WDT. This result could give additional benefit to latanoprost in stabilizing the IOP peak and fluctuations, but further equivalent study were needed to confirm this result with a bigger sample size included.

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