

A COMPARATIVE TEST OF EYEDROPS TIMOLOL 0.5% AND BETAXOLOL 0.5% IN THE REDUCTION OF INTRAOCULAR PRESSURE IN PRIMARY OPEN-ANGLE GLAUCOMA IN DR SOETOMO HOSPITAL, SURABAYA

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ABSTRACT

Significant intraocular pressure reduction in each group was found in week 1 and week 2, which was 7.4 mmHg in Betaxolol and 8.4 mmHg in Timolol 0.5%. Insignificant intraocular pressure reduction occurred in week 1 - 2, 0.1 mmHg in Timolol and 0.4 mmHg in Betaxolol. Comparative test on the reduction of intraocular pressure in two groups, both in premedication pressure reduction until week 1 and week 2, revealed no significance. Comparative test on intraocular pressure change between both groups also revealed no significance.

Keywords: *Timolol, Betaxolol, intraocular pressure, primary open-angle glaucoma, Dr Soetomo Hospital*

INTRODUCTION

Since 1967 blindness has been declared as national disaster, as it may result in social, economic, and psychological effects that may become a burden not only for the individual himself, but also for the society and the nation as well. Based on the survey of blindness morbidity by the Department of Health in 1982, glaucoma, which affects 0.1% of the population, is the third major cause of blindness after cataract and corneal turbidity. It is the tenth of ten eye diseases in Indonesia, with prevalence rate of 0.4%, indicating that the number of glaucoma patients in Indonesia today is around 740,000 individuals. From this number, 20 - 80% become blind. A proportion of 90% of primary glaucoma is primary open-angle glaucoma that has bilateral and slowly progressive characteristics, asymptomatic at early stage, and if vision and visual field impairment has occurred, the visual outcome cannot be saved (Krupin T, 1989; Kolker AE, 1983; Oka PN, 1985). The objective of medication in primary open-angle glaucoma is principally to prevent further impairment in optic nerve papilla using medicaments by continuously reducing intraocular pressure with minimal side effects, infrequent administration, and safe for longer period.

Timolol is a non-selective beta-adrenergic inhibitor, introduced firstly in 1978 and used until today to reduce intraocular pressure. Although side effects rarely occur, the use of timolol may result in serious

sequelae. Its inhibitory effect may slow down the heartbeat, reduce blood pressure and bronchoconstriction. Chronic obstructive pulmonary diseases, particularly asthma, is contraindicated. Sole P et al (1990), in their study using timolol 0.5% in 40 patients with ocular hypertension, found intraocular pressure reduction of 40.6% and humoral aqueous production of 39%. Richard L et al (1983) suggest that there was a reduction in pressed expiratory volume in asthmatic bronchitis patients, 1 hour after given with timolol eye drops. Steinert et al (1981) in a study using timolol 0.5% for 41 patients with primary open angle glaucoma found that it was effective in reducing intraocular pressure for 3 years.

Betaxolol is an acceptable novel alternative for glaucoma treatment. This is an also beta adrenergic inhibitory agent with additional benefits, such as selective effect on beta-1 receptor, so that its systemic side effect tends not to result in bronchoconstriction, particularly the recurrence of reactive respiratory diseases, as indicated by the results of several clinical trials. However, side effects on heart and metabolism remains possible. Until recently, clinical experience on betaxolol is limited. Dunn et al stated that betaxolol is effective to reduce intraocular pressure and has less effect on patients with pulmonary function disorder. Leibowitz dan Berrospi (1985) found an intraocular reduction of 29.4X - 35 % using betaxolol eye drops for 12 glaucoma patients. Berry and Stewart et al (1984) in a comparative study proved that timolol and betaxolol had similar effectiveness. However, Allen et al (1984) found that timolol was more effective than betaxolol, while both had no effect on pupillary width or the tone of ciliary muscle. This study was aimed to find the difference in effectiveness of betaxolol hydrochloride 0.5% and

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timolol maleate 0.5% in reducing intraocular and globe pressure in patients with primary open angle glaucoma treated at Dr Soetomo Hospital, Surabaya, and to confirm that betaxolol 0.5% eye drop can be used as alternative medication to reduce intraocular pressure.

METHODS

Using double blind randomized clinical design, this study was carried out at Ophthalmology Outpatient Clinic, Dr Soetomo Hospital, Surabaya. Population was patients with primary open angle glaucoma admitted at the clinic. Samples were taken totally from those population, namely the patients who came between July and December 2000 and who met the inclusion criteria, such as intraocular pressure of 21 - 30 mmHg, no active infection, no COPD, heart failure, and allergic bronchial asthma,

not taking beta blocker inhibitors, and no previous use of timolol and betaxolol. A number of 14 patients (25 eyes) were found to be eligible. The name, age, sex, and visual acuity of patients who met these criteria were recorded and they were consulted to the Departments of Pulmonary Disease and Internal Medicine. They were subsequently given in random with timolol or betaxolol that had been coded A and B. Prior to eyedropping, intraocular pressure was measured using Schiottz' tonometer and Goldmann's three mirror examination was also carried out. Eyedropping was carried out twice, at 7 a.m. and 7 p.m., while intraocular pressure was measured at 9 p.m at week I and II. Collected data were tabulated and analyzed by means of paired t test and independent t test.

RESULTS AND DISCUSSION

Table 1. Sex and age of the patients

Age (year)	Sex		Total
	Male	Female	
40-49	-	1 (7.14%)	1(7.19%)
50-59	2 (19.29%)	1 (7.14%)	3(21.43%)
60-69	3 (1.43%)	3 (21.93%)	6(42.86%)
70-79	3 (21.43%)	1 (7.14%)	4(28.17%)
Total	8 (57.15%)	6(42.85%)	14(100%)

As seen in the table, male patients were 8 (57.15%), mostly aged 9 and female patients were 6 (42.85%), mostly of 60 - 79 years old (21.43%). The youngest was 45 years and the oldest was 77 years. These data indicate that the prevalence of primary open angle chronic glaucoma between male and female patients

was similar. As the youngest age was 45 years, this was in line with the theory that glaucoma is often found in those of more than 40 years old. Therefore, routine intraocular pressure examination is necessary for this age group.

Table 2. Intraocular pressure reduction in week 1 and 2 after Timolol 0.5% administration

TIO	Mean	SD	p
Pra	27.69	± 1.494	0.000
M 1	18.7538	± 3.177	0.000
M 2	18.6154	± 2.577	(S)

TIO PRE : pre-Timolol administration

TIO M1 : 1 week after

TIO M2 : 2 weeks after

S : significant p : level of significance

Table 3. The difference of intraocular pressure in week 1 - 2 after Timolol administration

TIO	Mean	SD	P
M 1	18.7538	± 3.177	0.784
M 2	18.6154	± 2.577	(NS)

NS: Not Significant

Intraocular pressure reduction after Timolol 0.5% administration for 1 week was averagely 8.3 mmHg, while after 2 weeks it was 8.4 mmHg. Paired t test with t value of 10.92 to these data showed that the reduction was significant ($p < 0.05$). Varied intraocular reduction in individuals can be seen from high values of standard deviation. Using the same test with t value of 0.28, a minute intraocular pressure reduction, averagely 0.1 mmHg between

week 1 and 2 (Table 2 and 3), was found to be not significant ($p > 0.05$). These results confirm the findings of some authors, such as Berry, Van Buskirk, Caldwell, that a high intraocular pressure reduction in week 1 occurs because peak concentration in blood plasma is reached 2 hours after topical administration, and this concentration is maintained along the first week until the maintenance dose in blood plasma is reached.

Table 4. Intraocular pressure reduction in week 1 and 2 after betaxolol 0.5% administration

TIO	Mean	SD	P
Pra	27.1538	± 3.215	0.000
M 1	20.18,16	± 3.359	0.000
M 2	19.7231	± 2.505	(S)

Table 5. The difference of intraocular pressure reduction in week 1 and 2 after betaxolol 0.5% administration

TIO	Mean	SD	P
M 1	20.1846	± 3.359	0.221
M 2	19.7231	± 2.506	(NS)

The results of paired t test showed significant reduction in intraocular pressure after betaxolol administration for 2 weeks, with $p = 0.000$ ($p < 0.05$). Insignificant reduction in intraocular pressure was also found between week 1 and 2 ($p > 0.05$). Betaxolol 0.5% administration for 2 weeks resulted in average intraocular reduction of 7.4 mmHg or 27% from the initial pressure. Berry et al. (1984) studied primary open angle chronic glaucoma patients for 26 weeks, and found intraocular reduction as much as 33.6%. These findings were

different from those in this study, as Berry et al. applied additional therapy, such as Pilocarpin, for certain patients. They might also use different duration or samples. As can be seen in Table 5, the change of the pressure in week 1 - 2 after Betaxolol administration is averagely 0.4 mmHg, while the reduction 1 and 2 weeks after Timolol administration was averagely 0.1 mmHg (Table 3). This is because the half life of Betaxolol is longer than that of Timolol.

Table 6. Comparative test of intraocular pressure between 2 treatment groups in week 1 and 2

TIO	Pra	M 1	M 2
Timolol	27.0969 ± 1.949	18.7538 ± 3.177	18.6154 ± 2.517
Betaxolol	27.1538 ± 3.215	20.1846 ± 3.359	19.7231 ± 2.506
p	0.942 (NS)	0.276 (NS)	0.276 (NS)

Table 7. Comparative test of the change of intraocular pressure between 2 treatment groups

TIO	Pra - M 1	Pra - M 2	MI-M2
Timolol	8.3231 ± 2.747	8.4615 ± 2.825	0.1385 ± 1.785
Betaxolol	6.9692 ± 0.715	$7.43b8 \pm 1.151$	0.4615 ± 1.288
p	0.108 (N S)	0.241 (NS)	0.602 (NS)

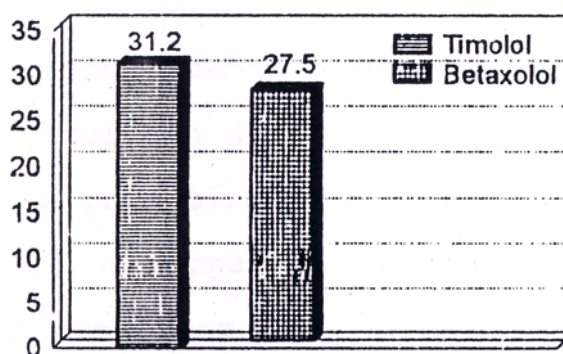


Figure 1. Intraocular pressure reduction (%)

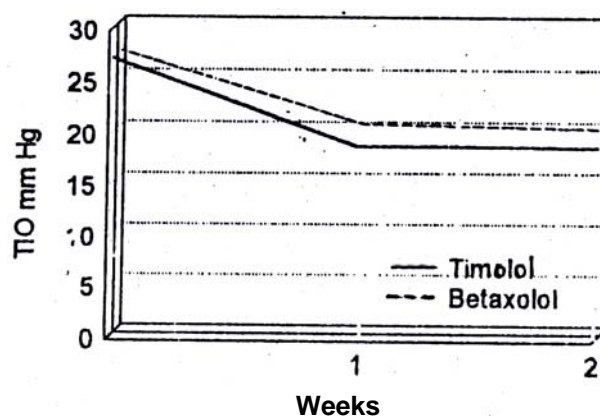


Figure 2. Intraocular pressure reduction (mmHg)

By using paired t test with level of significance of 0.05, and t value of -0.7, it was found that $p = 0.94$ ($p > 0.05$). This indicated that intraocular pressure between 2 groups, either pre-, 1 week post-, and 2 weeks post-treatment, showed no significant difference, or, in other words, the pressure between both groups was homogeneous. Results of comparative test of intraocular pressure reduction in groups receiving Timolol and Betaxolol in week 1 and 2 showed no significant difference. However, a significant reduction was marked in week 1 and 2 between each treatment groups (Table 6).

Comparative test of the difference of intraocular pressure reduction between 2 groups using paired t test with level of significance of 0.05 and t value of 1.72 revealed $p = 0.108$, suggesting no significant difference from pre-treatment to week 1. The same test with the same level of significance from pre-treatment to week 2 between both groups also showed no significant difference. The p value was 0.41 ($p > 0.05$). All of these results demonstrate that Timolol and Betaxolol are drugs with capacity to reduce intraocular pressure, although the reduction after Timolol was 31% while that after Betaxolol was 27%. Nevertheless, these difference was statistically not significant (Table 7 and Figure 1).

Those findings can be explained as follows: Timolol is a drug consisting of beta 1 and beta 2 adrenergic antagonists, while Betaxolol is a beta 1 selective adrenergic antagonist. Ciliary corpus is an organ producing humoral aqueous where most of beta 2 receptors reside here, so that these receptors are inhibited more by Timolol, as compared to Betaxolol. However, intraocular pressure reduction after the administration of beta adrenergic antagonists remains uncertain. Figure 2 shows that the highest reduction of intraocular pressure after Betaxolol and Timolol was in week 1, while the reduction in week 2 was slight.

CONCLUSION

No significant difference between Betaxolol 0.5% and Timolol 0.5% eye drops in the reduction of intraocular pressure in primary open angle chronic glaucoma patients treated at Ophthalmology Outpatient Clinic, Dr Soetomo Hospital, Surabaya. Therefore, Betaxolol can be used as alternative therapy for these patients.

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