THE EFFECTIVENESS OF LEVOBUNOLOL VERSUS TRAVOPROST IN REDUCING INTRAOCULAR PRESSURE; A COMPARATIVE STUDY CONDUCTED IN A TERTIARY CARE HOSPITAL OF PESHAWAR

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ABSTRACT

Objective: To compare the therapeutic efficacy of Levobunolol and Travoprost for lowering intra-ocular pressure (IOP) in patients with primary open-angle glaucoma and ocular hypertension.

Materials and Methods: A Quasi experimental study was conducted in the ophthalmology department of Khyber Teaching Hospital, Peshawar. One-hundred and twenty patients of both genders and age between 18-80 years with primary open angle glaucoma or ocular hypertension requiring single pressure lowering drug were enrolled in the study. Subjects were divided into two groups (60 in each). One group was treated with Travoprost eye drops (0.004%, OD) while other group with Levobunolol eye drops (0.5%, OD). After initial screening visit where demographic data and baseline IOP was recorded on the structured proforma, three follow-up visits were arranged each at 02 weeks interval. At each follow-up visit, IOP was recorded by standard protocol to evaluate and compare the ocular hypotensive efficacy of the study drugs by calculating mean IOP change from the baseline. Only patients with no missing IOP measurements for all visits were considered eligible for efficacy evaluation.

Results: A total of 120 patients were observed having age range from 18 years and above with mean age 52.16 ± 9.56 years and predominance of male gender. Upon comparative analysis, no significant statistical difference (p value >0.05) was observed in the ocular hypotensive ability of Levobunolol and Travoprost measured at each follow-up visit, indicating both drugs as equally effective. Moreover, age groups did not reveal any significant statistical impact on the treatment outcome of patients treated with either study drug.

Conclusion: Clinical data revealed that both study drugs reduced the intraocular pressure (IOP) without any significant difference and were found equally effective in primary open angle glaucoma and ocular hypertension.

Keywords: Levobunolol, Travoprost, Glaucoma, Ocular hypertension, Intra ocular pressure.

INTRODUCTION

Glaucoma is a neurodegenerative disease which causes progressive and irreversible visual impairment by affecting the optic nerve and related structures. It is one of the principal causes of blindness all over the world[1-3].

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In 2013, globally 64.3 million people were affected by glaucoma with expected increase to 76 million by the year 2020 and 112 million by 2040. According to epidemiological surveys, it is more common in Asian countries and contribute 60% of the total prevalence of glaucoma, worldwide [4]. Pakistan too is in the race as the overall prevalence of glaucoma here is 3.9% and continue to increase[5].

There are two types of glaucoma i.e. Open angle glaucoma and angle closure glaucoma. Approximately three-quarters of all glaucoma occur in individuals with open angles. Although some forms of open-angle glaucoma occurs secondary to other phenomena, the majority is idiopathic, known as primary open angle glaucoma. POAG is regarded as the most prevalent type and asso-

ciated with raised IOP [6]. Consistent elevation of IOP often leads to degeneration of the optic nerve, which may be followed by loss of visual field. Previous research has shown that the extent of damage to optic nerve depends on the degree of IOP raised [7]. The only treatment strategy for glaucoma is reduction of intra ocular pressure to halt the disease progression and preserve vision [8]. This can be achieved by a variety of pressure lowering medications [2,9]. Over the past three decades, a number of different drugs have become available with proven effectiveness in glaucoma including topical alpha 2 agonists, beta blockers, carbonic anhydrase inhibitors, prostaglandin analogues, parasymathomimetics (meiotic) and hyperosmotic agents (mannitol) [10-12]. The availability of wide variety of pharmacological treatment options make it difficult for the clinicians to choose appropriate and specific regimen.

Different drugs decrease the intra ocular pressure through different mechanisms, leading to different efficacies with regard to lowering IOP. Topical beta-adrenergic receptor blocking agents, such as Timolol was introduced in the late 1970s and have been widely accepted as a first line anti-glaucoma therapy. Levobunolol, a drug of same class reduces IOP by slowing the rate of formation of aqueous humor. In the recent years, a new family of drugs called prostaglandin analogues has gain popularity for its remarkable IOP lowering ability. Unlike beta-blockers, Travoprost reduce IOP by increasing both uveoscleral and conventional aqueous humor outflow [13].

In a number of studies, both drugs have proven their effectiveness individually but data regarding their comparative efficacy was scarce [14]. Our study attempts to evaluate and compare the therapeutic effectiveness of these two commonly available anti-glaucoma drugs for reducing IOP in local population. Such a thorough understanding would possibly help the clinicians in better management of patients.

MATERIALS AND METHODS

A Quasi experimental study was conducted in the Ophthalmology department of Khyber Teaching Hospital, Peshawar from Sept 2014 to Aug 2016. After taking approval from the institutional review board, 120 patients of both genders and age between 18-80 years with Primary Open Angle Glaucoma (POAG) or Ocular Hypertension (OH) were identified. Only subjects with recorded IOP of 21-26 mmHg in both eyes and requiring single pressure lowering drug (monotherapy) were included in the study. Patients with IOP above 26 mmHg or having uveitis, cystoid macular edema, inflammatory glaucoma or any other ocular condition preventing reliable applanation tonometry or those with congestive heart failure, bradycardia, bronchial asthma, obstructive airway disease or hypersensitive to either study drug were excluded from the study. The sample size was taken on the basis of cure rates of study drugs with 95% confidence interval (CI) and

power of 80 [15,16].

After taking informed consent, patients were counseled to sit straight with both eyes open and local anesthetic drops were instilled in their eyes to record the IOP by specialist ophthalmologist using standard protocols [17]. All the patients were randomly divided into two groups (60 in each). One group was treated with Travoprost eye drops (0.004%, OD) while other group with Levobunolol eye drops (0.5%, OD). After initial screening visit where demographic data and baseline IOP was recorded on the structured proforma, three follow-up visits were arranged each at 02 weeks interval. Ocular hypotensive efficacies of both study drugs were evaluated and compared by calculating the mean IOP change from baseline to each follow-up visit. Only patients with no missing IOP measurements for all visits were considered eligible for efficacy evaluation.

The collected data was entered and analyzed by SPSS version 22. Numerical variables like age, IOP and other demographics were described as Mean ± SD while categorical variables like age groups and gender were expressed in terms of frequencies and percentages. The difference between two treatment groups was determined by applying independent sample t-test whereas analysis of variance (ANNOVA) was applied for more than two groups. P-value <0.05 was considered significant.

RESULTS

One-hundred and twenty patients of open-angle glaucoma and ocular hypertension were enrolled in the study and randomly assigned to one of the two treatment groups (Travoprost or Levobunolol) to compare their efficacies in terms of lowering intraocular pressure and the results were analyzed. The distribution of age and gender is mentioned in Table 1, with mean age 52.16 ± 9.56 years and predominance of male gender.

The efficacy of study drugs in terms of reducing IOP for each follow-up visit is shown in Table 2. Patients responded quickly to both therapies with almost equal efficacy, displaying no significant statistical difference between the results of two groups (p value >0.05).

To determine the impact of various age groups on treatment outcome of patients treated with either Levobunolol or Travoprost, ANNOVA was applied. The mean reduced IOP (19.13 ± 4.884) of younger age group i.e. 30-40 years was taken as reference group whereas all the other age groups were compared with it as shown in Table 3. Results did not reveal any significant impact on the treatment outcome by different age groups.

DISCUSSION

Raised intra-ocular pressure is one of the most widely studied and important risk factor associated with

Table 1: Distribution of Age and Gender

AGE (YEARS)		30-40	41-50	51-60	>60
Drugs	Travoprost	8 (13.3%)	23 (38.3%)	17 (28.3%)	12 (20.0%)
	Levobunolol	8 (13.3%)	28 (46.7%)	16 (26.7%)	8 (13.3%)
Gender	Female	1 (2.8%)	24 (66.7%)	4 (11.1%)	7 (19.4%)
	Male	15 (17.9%)	27 (32.1%)	29 (34.5%)	13 (15.5%)

Table 2: Comparison b/w Levobunolol and Travoprost for reducing IOP

Visits	IOP (Mean ± SD)		P Value
	Travoprost	Levobunolol	
Baseline visit (Right eye)	21.68 ± 4.139	20.73 ± 4.226	0.8
Baseline visit (Left eye)	22.47 ± 3.280	22.23 ± 2.825	0.6
1st Follow-up Visit (Right eye)	18.45 ± 2.715	18.27 ± 2.863	0.7
1st Follow-up Visit (Left eye)	18.78 ± 1.851	18.87 ± 2.167	0.8
2nd Follow-up Visit (Right eye)	17.25 ± 2.384	17.83 ± 2.598	0.5
2nd Follow-up Visit (Left eye)	17.72 ± 1.698	18.30 ± 2.212	0.5
3rd Follow-up Visit (Right eye)	16.92 ± 2.346	16.67 ± 2.014	0.5
3rd Follow-up Visit (Left eye)	17.43 ± 1.619	17.53 ± 1.692	0.6

Table 3: Effect of different age groups on IOP reduction

Visits	Age Groups (Years)					
	50-31		60-51		>60	
	IOP (Mean ± SD)	P-Value	IOP (Mean ± SD)	P-Value	IOP (Mean ± SD)	P-Value
Baseline visit (Right eye)	20.92 ± 4.175	0.42	22.27 ± 3.329	0.06	21.85 ± 4.522	0.20
Baseline visit (Left eye)	21.80 ± 3.118	0.97	23.18 ± 2.920	0.70	22.50 ± 3.502	0.99
1st Follow up Visit (Right eye)	18.22 ± 2.831	0.36	19.06 ± 2.263	0.05	18.70 ± 2.922	0.22
1st Follow up Visit (Left eye)	18.75 ± 1.809	0.15	19.39 ± 2.164	0.01	19.05 ± 2.114	0.13
2nd Follow up Visit (Right eye)	17.29 ± 2.640	0.61	18.18 ± 1.845	0.09	18.00 ± 2.596	0.23
2nd Follow up Visit (Left eye)	17.90 ± 1.942	0.89	18.27 ± 2.111	0.58	18.25 ± 2.023	0.67
3rd Follow up Visit (Right eye)	16.49 ± 2.185	0.80	17.30 ± 1.741	0.16	17.40 ± 2.326	0.18
3rd Follow up Visit (Left eye)	17.43 ± 1.500	0.64	17.70 ± 1.759	0.36	17.75 ± 1.997	0.39

the development and progression of glaucoma which can be reduced by a variety of drugs [11]. Being a developing country, selection of drug should be based on effectiveness as well as its availability. Keeping the said facts in view, we conducted this study to compare IOP reducing ability of two commonly available drugs i.e. Travoprost and Levobunolol.

Our study revealed that men are more prone to develop primary open angle glaucoma as compared to women, resembling the reports presented by Song et al [18]. Increasing age did not show any difference in the degree of IOP reduction by study drugs. Also, no significant sta-

tistical difference was observed in the mean reduced IOP between two treatment groups. Similar pattern was observed in a meta-analysis published by Li T et al who compared the effectiveness of different anti glaucoma drugs showing mean reduced IOP of 4.83 mmHg in Travoprost group and 4.51 mmHg in Levobunolol group. Moreover, the mean reduced IOP by Levobunolol was found better than other competitors like apraclonidine, levobetaxolol, brimonidine, dorzolamide, brinzolamide, tefluprost, timolol, betaxolol, carteolol and unoprostone [19-21].

Contrary to our study where Levobunolol and Travoprost both has shown to have almost equal effica-

cy, some clinical trials reported Travoprost to have IOP reducing efficacy significantly better than beta blockers [22]. This superiority of prostaglandins for treating primary open-angle glaucoma was verified by van der Valk et al in a meta-analysis, followed by non-selective β-blockers, α-adrenergic agonists and finally topical carbonic anhydrase inhibitors [23]. In some clinical studies, Travoprost produced reductions in IOP of 7-8 mmHg, from a mean baseline IOP of 25-27 mmHg, which is significantly better than IOP lowering efficacy of Travoprost in our study [16]. That's why, a review article in 2019 labeled prostaglandin analogues including Travoprost as first line drugs for glaucoma management [24].

The socioeconomic impact of medical therapy in glaucoma is considerable, and treatment should be individualized to suit the educational and socioeconomic aspect of each patient. Levobunolol is cost effective than Travoprost (Rs: 150 vs Rs: 1150), so prescribing Levobunolol would improve the compliance of poor patients. In addition, beta blockers have relatively quick onset of action i.e. Levobunolol after topical administration, start its ocular hypotensive effect within 1 hour, reaches to maximum in 2-6 hours and last for 24 hours [25].

Patient safety profile is also necessary to keep in view while selecting anti-glaucoma drug. The prostaglandin analogues including Travoprost are contraindicated in conditions like uveitis, cystoid macular edema and herpes simplex virus infections, while beta blockers should be cautiously used in glaucoma patients with co-existing heart block, bradycardia, chronic obstructive pulmonary disease or asthma. Among β-blockers, Levobunolol has relatively better safety and tolerability profile as compared to other drugs of same class with the advantage of once daily dose [21, 26].

One of the major limitations of this study was non-randomized experimental design. Randomized control trial involving large sample size is recommended to achieve evidence base results of higher level for a definite conclusion. Secondly, lowering IOP is not the sole parameter for measuring drug efficacy that demands attention. To evaluate the exact disease status, perimetry and optical coherence tomography are recommended to perform along with IOP.

CONCLUSION

Both Levobunolol and Travoprost are equally effective in reducing intraocular pressure in patients of primary open angle glaucoma and ocular hypertension. If not contraindicated, Levobunolol may be started as an initial treatment because of well-established facts regarding its rapid onset of action and cost effectiveness. Travoprost may be reserved as an alternative or adjuvant therapy for patients not achieving target IOP with Levobunolol.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Naz F:	Concept designing and data collection.
Faisal MS:	Manuscript writeup.
Iqbal W:	Data and statistical analysis.
Naz M:	Management and interpretation of data.
Khan MS:	Data collection.
Hayat W:	Bibliography and critical review.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.