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Comparative effectiveness of commonly used drugs in primary open angle glaucoma in Indian eyes

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Abstract

Aim: Objective of this study to compare effectiveness of first line of topical drugs commonly used in POAG and to see the percentage of the IOP lowering effect of different drugs in Indian eyes.

Design: This study was conducted in one of the zonal hospital in north India. The study design was a randomized control trial and sample size of 60 patients was included.

Methods: We included Randomized controlled trial of three commonly used drugs (Latanoprsot, Timolol, Brimonidine) for established cases of POAG, NTG and Pigmentary Glaucoma. Patients were followed up for 06 months and IOP recording was done in phase manner for four visits. Data were analyzed using SPSS software over 15.0

Results*:* At the end of six months, Latanoprost eye drops have the highest percentage of reduction (33%), compare to Timolol (27%) and Brimonidine (25%) group. Latanoprost eye drops also have better patient compliance as a once a day regime.

Conclusion: All active first line of drugs is effective in lowering intraocular pressure at the end of 06 months. However Latanoprost eye drops has greater IOP reduction compared to Timolol and Latanoprost group. All these drugs can be chosen as a first line of drugs depending upon patient age factor, the degree and type of glaucoma, compliance of drugs, cost and side effect of these drugs.

Keywords: Brimonidine, Glaucoma, Indian eyes, Latanoprost, Timolol

Introduction

Glaucoma is the commonest cause of blindness and it has been estimated that in the beginning of this millennium, 66.8 million individuals in the world would have glaucoma, and of which 60% will be in Asia.[(1)] In the countries like India, glaucoma is emerging as a major cause of blindness and adds to already a severe backlog of needles blind due to cataract. The predominant form of primary glaucoma is open angle. Recently well designed population based survey have been conducted in India, which have highlighted the relative prevalence of glaucoma and consequent visual impairment. The Andhra Pradesh eye study[(2)] had reported prevalence of POAG to be 2.52% in those aged 50 years or more. This prevalence is similar to slightly more than that in Caucasians in North America and significantly less prevalence of POAG in a population of Africa. 93% of individuals diagnosed with glaucoma have not been previously diagnosed and 48% had severe visual impairment, including 16% who were blind in one or both eyes due to disc damage. The Arvind Comprehensive eye Care study is similar population based prevalence study in rural population in south India, which also reported the prevalence of POAG to be about 2.6% in the individual aged 40 years and above and 93% of those diagnoses of POAG were unaware of these studies prior to study (unpublished data). 75% of individual with glaucoma in this survey had severe visual impairment in one or both eyes based on visual and/or visual field defect. The Vellore Eye Study[(3)] however, reported POAG prevalence in urban population to be 0.41% in those aged between 30 years to 60 years. The reason for the discrepancy between these studies could be due to the fact the only50% of individuals with suspected glaucoma had actually performed the fields. Moreover, this study has excluded individuals aged 60 years or above.

Glaucoma, whether manifesting as primary open angle glaucoma, angle closure or congenital disease is leading cause of blindness in developing countries. The prevalence of glaucoma in the eastern population of India is not carried out in details. However the large population was under diagnosed and a large proportion of these having a definite POAG already had severe glaucomatous damage. The most common type POAG develops insidiously, without any outward signs

There are many medical management options are available for treating glaucoma patients. The safety and efficacy of latanoprost have been reported in several studies[(4,5)] and it is well known fact that there may racial differences in the effect of any particular drug. The present study is carried out to see the IOP lowering effect of Latanoprost eye drops in Indian eyes.

Materials and Method

This study was done in of the zonal hospital in North India

Selection of cases: A total of 60 patients of either gender diagnosed as primary open angle glaucoma, pigmentary glaucoma or normal tension glaucoma was enrolled from Nov 2013 to Oct 2014.Written permission was obtained from the hospital ethical

committee and patients were enrolled after their consent.

Inclusion and exclusion criteria: To be eligible for study the patient had to be over 18 years. At least one eye of patients had to meet the following criteria for POAG and pseudoexfoliation glaucoma

1. Mean IOP (3 readings) more than 21 mm of Hg
2. The angle to be to grade II and above (posterior trabecular meshwork visible)
3. Visual field defect in Humphry perimetry

For NTG visual field defect in Humphry Perimetry with 24 Hrs IOP in high teens.

Exclusion criteria were if the patient were on medication for glaucoma, angles considered to be gonioscopically occludable, history of previous intraocular surgery. History of ocular inflammation or infection in last three months, ocular condition precluding Goldman applanation tonometry and known sensitivity to any vehicle component. Those patients who have advance cupping and advance visual field loss in perimetry is also excluded as they require aggressive therapy.

Study design and plan: The patient was first visited on day 1 (visit 1). The treatment period for each drug is for six months, each drug required for visits IE baseline, day 14 (visit 1), week 6 (visit 2) and week 14 (visit 3) 6 month (visit 4). A total of 60 patients were enrolled in this study that fulfill above criteria.

20 patients were given Timolol eye drops, 20 patients given Brimonidine and 20 patients were given Latanoprost by randomized technique. No systematic medication was given during the study period.

Informed consent of the patient was obtained from the patient. A complete ophthalmic history and examination was performed, which includes a) Subjective and objective refraction b)Best corrected visual acuity c)Slit lamp examination d) Applanation tonometry e)Gonioscopy f)Detailed fundus examination with 90D Lens g) visual fields with HFA using SITA programme.

For base line IOP is measured with GAT, It was measured at 900 hrs,1100 hrs, 1300 hrs and 1500 hrs and mean was taken and in subsequent follow ups IOP is measured by GAT in same phase protocol manner.

During subsequent visits a deviation of +/-2 days for visit 2 and +/- 1 week for subsequent visit is accepted. All patients were followed up for one year Descriptive and inferential statistical analysis has been carried out in the present study. Results of continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.

Observation

Out of 60 patients, 7 patients (2 from Latanoprost group, 1 from timolol and 2 from brimonidine group) lost in follow up and in 2 patients, we have to add or switch with another group of anti-glaucoma drug as IOP was not reached at target level. A total of 53 patients had completed the study.

Demography and drug distribution of each drug was shown in (Table 1).

Table 1: Shows patient demography

Gender	Latanoprost	Timolol	Brimonidine	Total
Female	9(45%)	9(45%)	6(30%)	24(40%)
Male	11(55%)	11(55%)	14(70%)	36(60%)
Total	20(100%)	20(100%)	20(100%)	60(100%)

P=0.535, Not significant by Chi-Square test

Mean Base line IOP in latanoprost group is 23.27 mm of Hg, Timolol group is 24.41 mm of Hg and Brimonidine group is 24.27 mm of Hg (Table 2).

Table 2: Shows baseline IOP in each group

	IOP(mean)
Latanoprost	23.27mm of Hg
Timolol	24.41mm of Hg
Brimonidine	24.27mm of Hg

P Value for base line is 0.151(not significant)

(Table 3) shows mean IOP at various visit in different group.

Table 3: IOP reduction in each visit of different group

IOP	Latanoprost	Timolol	Brimonidine	Total	P value
Baseline	23.27±0.31	24.41±2.66	24.27±2.16	23.99±2.02	0.151
Visit 1	16.22±0.21	18.30±1.07	18.88±1.25	17.80±1.49	<0.001**
Visit 2	15.75±0.30	18.11±0.97	18.35±1.04	17.37±1.44	<0.001**
Visit 3	15.68±0.29	18.00±0.94	18.12±1.00	17.22±1.39	<0.001**
Visit 4	15.47±0.23	17.85±1.00	18.13±1.13	17.10±1.49	<0.001**
Drop of IOP from baseline					
Visit 1	7.049	6.112	5.397	6.186	0.001**
Visit 2	7.520	6.307	5.949	6.592	0.002**

Visit 3	7.591	6.362	6.155	6.703	0.005**
Visit 4	7.808	6.505	6.146	6.820	0.002**

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

(Table 4) shows the percentage reduction at various visits.

Table 4: Shows percentage IOP reduction at various visits

IOP	Latanoprost	Timolol	Brimonidine
Visit 1	29.81%	25%	22.43%
Visit 2	30.79%	26%	24%
Visit 3	30.77%	26%	25%
Visit 4	32.97%	27%	25%

(Table 5) shows the percentage reduction in the mean IOP at 6 monthly follow up. It shows Latanoprost group has percentage reduction of 33% (highest from others) 27% reduction in timolol group and 25% reduction in Brimonidine group.

Table 5: Shows long term follow up results(6 monthly)

	Latanoprost	Timolol	Brimonidine
IOP(mean)mm of Hg	15.46	17.82	18.12
Percentage reduction	33%	27%	25%

P<0.001 significant

(Table 6) shows the percentage of patients who has reached IOP of less than 17 mm of Hg.

Table 6: Shows percentage of patients who reached the specific target IOP at 6 months

	Latanoprost n=18	Timolol n=17	Brimonidine n=18
<17 mm of Hg	55% (10 patients)	41% (7 patients)	34% (6 Patients)

Discussion

A large body of evidence has established the importance of IOP reduction in the management of glaucoma.[6] Other targets of intraocular therapeutic intervention, such as improving the blood flow under the protection of neuroglial cell are under investigation, but IOP lowering remains the mainstay of treatment. Recent evidence suggested that IOP near 17 or 18 mm of Hg do not lead to the progressive field loss in many patients.[7] This support the increasing aggressive effort to lower the IOP as low as possible especially in patients with the rapidly increasing disease.

The OHTS study[8] has demonstrated that the lowering of IOP by 20% of base line delays or prevents the onset of glaucomatous in OHT patients. The CIGTS[9] study has demonstrated that the patients with an IOP consistently above 17.5 mm of Hg over their first six month visits experienced rapidly progressing disease over the consequent six years.

This study also shows that patients with consistently 16 mm of Hg at every visits over the six year follow up experienced a mean change from baseline in visual field is close to zero. The degree of IOP control throughout the day and night is another important indication of drug efficacy. IOP is known to have typical circadian rhythm, with greater than normal fluctuations in patient with glaucoma patients.[10] So ideal glaucoma medication should ensure that IOP remain consistent throughout 24 hours.

In the study at our center, Latanoprost reduced mean IOP reduction of 33% compared to 27% with Timolol group. The quantum of reduction and difference was maintained at 6 month follow up. At subsequent visit, latanoprost reduced the IOP significantly more than the timolol and brimonidine group.

IOP reduction <17 mm of Hg was achieved in a high no of eyes(55%) as compared to timolol(41%) and brimonidine(34%).

The lack of response was less likely to latanoprost as a single day regime, so latanoprost provide greater IOP control over timolol and brimonidine group.

It is reported that the action of latanoprost starts with first two weeks maximeses in six weeks and then stabilizes without short term and long term drift.[11] Our results are similar, except that due to the short-term nature of study we cannot comment on the long term drift. Different article has shown IOP reduction ranging from 25% to 32% with latanoprost eye drops.[12,13] However, one study reported that the black population was less responsive to medical management.[14] In our study newly diagnosed patients with POAG or OHT with increased IOP when given latanoprost, the mean IOP reduced significantly. The mean base line IOP of 23.27 mm of Hg was reduced to 15.45 mm of Hg.

We have not countered iris pigmentation or conjunctival hyperaemia in treated with latanopost patient probably because of the very small sample size as well as short duration of study. Conjuntival Hyperaemia is most common side effect of latanoprost noted by others.[15] Timolol was widely used since its introduction in USA in 1978.With long term treatment with timolol very known complication of this drug has been reported.[16] It has also got the systemic side effects.[17]

Summary and Conclusion

In the treatment of glaucoma, the goal must be to preserve the visual field with no or minimal side effects, for the expected life of patients, without any disruption of his/ her activities at the sustainable cost. We can do a medical therapy, but if we do the medical therapy, the IOP should be controlled for 24 hours. The drug should have no long term and short term drift and it should be convenient for patient to use that the compliance is good.

In the study at our centre the latanoprost significantly reduces the IOP as compared to timolol and brimonidine group and it also maintains the IOP <17 mm of Hg in 55% of cases.

So to conclude the pressure lowering effect of latanoprost is more than the timolol land brimonidine eye drops with long term IOP control, with better compliance as once a daily administration. The problem for latanoprost is its cost and availability in remote areas. Patient selection like age, type of glaucoma, severity of glaucoma and compliance to drug must also be kept in mind.

The short come of this study is shorter duration and small number of patients included in study. We have to look for long term effects of latanoprost in controlling IOP and its side effects.

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