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EFFECT OF LATANOPROST/TIMOLOL AND BRINZOLAMIDE/BRIMONIDINE ON QUALITY OF LIFE IN GLAUCOMA: A COMPARATIVE STUDY

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ABSTRACT

Introduction: Glaucoma is a term used to describe group of diseases of the eye characterized by progressive and irreversible damage to the optic nerve. Glaucoma causes ocular discomfort, fatigue and visual disturbances that interfere with quality of life (QOL). This study was done to observe the effect on quality of life with latanoprost/timolol versus brinzolamide/brimonidine fixed dose combination (FDC) in primary open angle glaucoma patients. **Material & Methods:** A prospective, randomized, comparative clinical study was conducted on 50 patients and they were randomly divided in two groups of 25 each to receive either Latanoprost and Timolol FDC (0.005+0.5% w/v) ophthalmic solution once daily (Group A) or Brinzolamide and Brimonidine FDC (1% +0.15% w/v) ophthalmic solution thrice daily (Group B) intra-ocularly for 12 weeks. Quality of life assessment was done by Glaucoma quality of life (GQL-15) and Glaucoma symptom scale (GSS) questionnaire. **Results:** On intragroup analysis, at the end of 12 weeks in group A & B there was reduction in GQL-15 score by 38.07% and 31.24% respectively compared to their baseline values ($p< 0.001$). On intergroup analysis, better response was seen in group A. On intragroup analysis at the end of 12 weeks in group A & B there was increase in GSS score by 2.5% and 1.6% respectively compared to their baseline values but it was statistically significant only in Group A at the end of 12 weeks ($p<0.05$). Thus, better response was seen with group A on intergroup analysis. **Conclusion:** Latanoprost & timolol showed more improvement in quality of life than brinzolamide & brimonidine in both parameters.

KEYWORDS: Quality of life, Latanoprost, Timolol, Brinzolamide, Brimonidine, Glaucoma quality of life, Glaucoma Symptom Scale Questionnaire.

INTRODUCTION

Glaucoma is group of disorders characterised by a progressive optic neuropathy resulting in a characteristic appearance of the optic disc and a specific pattern of irreversible visual field defects that are associated frequently with raised intraocular pressure (IOP)[1] & if untreated can lead to blindness.[2]

Glaucoma is the second leading cause of blindness in world accounting for upto 8% of total blindness. In India, 1.2 million people are blind due to glaucoma out of 12 million people affected with glaucoma.[3] Primary open angle glaucoma affects 1 in100 in general population (of either sex) above the age 40 years.[4] Rise in IOP in POAG occurs due to resistance to aqueous outflow (drainage) at level of trabecular meshwork leading to decrease in aqueous outflow.[5] The disease is insidious and usually asymptomatic. Headache, eyeache of mild intensity and scotoma (defect in visual field), difficulty in reading and close work occur due to increasing accommodative failure, so patient complains of frequent change of presbyopic glasses, delayed dark adaptation, significant loss of vision and blindness.[6] The most significant consequences of glaucoma include optic neuropathy & optic disc cupping.[5] As glaucoma leads to ocular discomfort, fatigue and visual disturbances, so there is interference with quality of life (QOL) which includes aspects of physical, social, psychological functioning, daily activities and workplace productivity. It can result in difficult to perform daily activities, such as driving.[7]

Commonly used single drug therapy medications are prostaglandin analogues, topical beta blockers, adrenergic drugs and carbonic anhydrase inhibitors.[6] Monotherapy is often insufficient to achieve target IOP. As many as 40% patients need more than once medication to reach the target IOP. If one drug is not effective, then a combination of two drugs i.e. the one which decreases aqueous production (timolol or

brimonidine or dorzolamide) and other drug which increases aqueous outflow (latanoprost or brimonidine or pilocarpine) is used. Adherence is an important concern in glaucoma. Fixed dose combination leads to better adherence, decreased wash out effect of drugs, provides simplified treatment regimen, better efficacy and reduction in exposure to preservatives, thus decreased risk of corneal & ocular surface damage. Thus, this study was done to assess and compare the effect of 2 FDCs i.e. latanoprost/timolol & brinzolamide/brimonidine in patients of primary open angle glaucoma.

To the best of our knowledge, no such study involving comparison of quality of life with fixed dose combination of latanoprost/timolol versus brinzolamide/brimonidine in primary open angle glaucoma has been done worldwide. Hence, the present study was therefore taken.

MATERIAL AND METHODS

This was a prospective, open label, randomized, comparative clinical study conducted by the Department of Pharmacology and Ophthalmology, Pt. B. D. Sharma PGIMS, Rohtak on 50 patients. Study was in accordance with the principles of good clinical practice (ICH-GCP) and declaration of Helsinki. An informed consent was obtained from all patients enrolled for the study and the study was done after obtaining the ethical clearance from institutional ethical committee. No. IEC/18/pharma03 dated: 19.12.2018. Patients enrolled in the study were randomized with the help of computer generated random numbers to allocate the treatment schedule as shown in fig 1.

These 50 patients were divided in two groups of 25 patients each. The patients were randomly allocated to receive any of two different treatments. All the patients were explained about the study through patient information sheet and informed consent was obtained. The inclusion criteria included were- patient of either gender >18yrs of age, with baseline IOP more than 21 mm Hg in each eye and patient was eligible if best corrected visual acuity was at least 6/60 or better and visual field showed glaucomatous changes. Exclusion criteria included- patient with active ocular disease, hypersensitivity to study medications or other ocular medications that might have substantial effect on IOP, ocular surgeries in past 3 months, ocular inflammation and infection within past 3 months, ocular trauma within past 6 months, intraocular conventional surgery or laser surgery within past 6 months, glaucoma other than POAG, pregnant and lactating mother.

The eligible patients after screening were randomly allocated to one of the following treatments intra-ocularly for a period of 12 weeks: Group A received Latanoprost and Timolol (0.005+0.5% w/v) ophthalmic solution once daily and Group B received Brinzolamide and Brimonidine (1% +0.15% w/v) ophthalmic solution thrice daily. Available commercial preparations (same brand) of the drugs were used.

Quality of life was assessed by using Glaucoma symptom scale (GSS) questionnaire & Glaucoma Quality of life (GQL-15) questionnaire at the end of 0, 4 and 12 weeks.

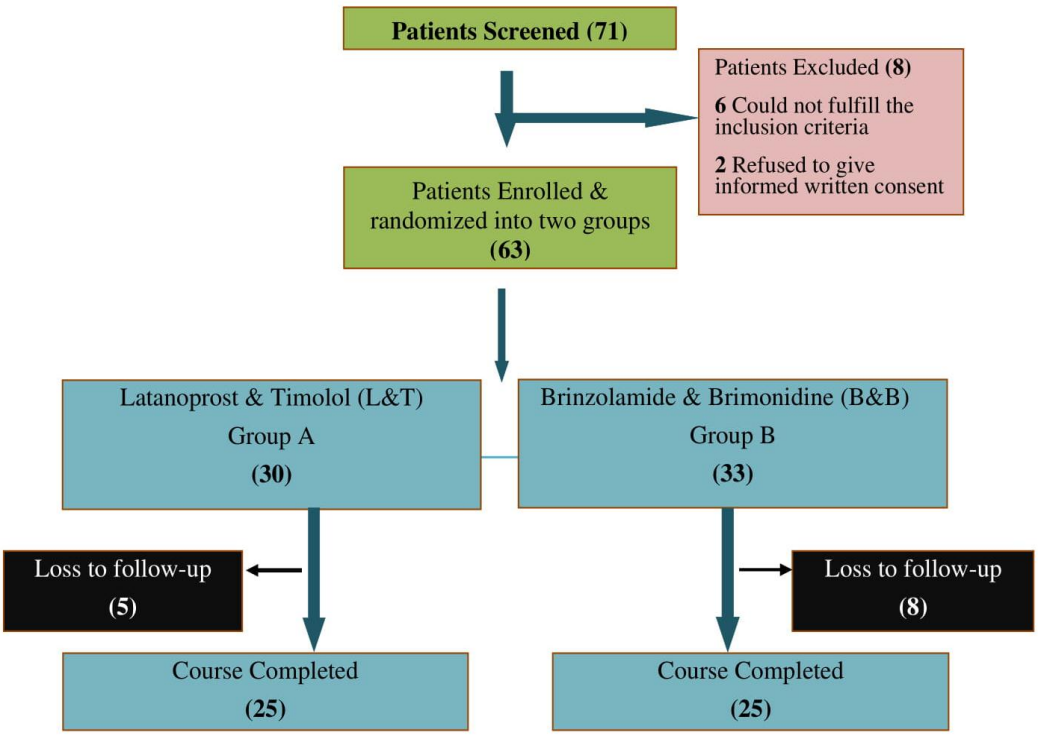

Fig 1: Enrolment of study population.

Glaucoma symptom scale (GSS) questionnaire

GSS scores ten symptoms experienced by glaucoma patients on a five point rating scale (yes very bothersome, yes somewhat bothersome, yes a little bothersome, yes but not bothersome at all and no absent). The first 6 items consist of nonvisual ocular symptoms (burning/smarting/stinging, tearing, dryness, itching, soreness/tiredness, feeling of something in the eye) whereas the last 4 items consist of visual ocular complaints (blurry/dim vision, hard to see in daylight, hard to see in dark places and halos around lights). This score was then transformed to a 0 to 100 scale, with 0 representing presence of a very bothersome problem and 100 representing absence of a problem. Final composite GSS score was average of the responses to all 10 items, averaged between the 2 eyes.[8]

Glaucoma Quality of life (GQL-15) questionnaire

It addresses 4 factors of visual disability central and near vision, peripheral vision, dark adaptation and glare and outdoor mobility. It is a 15 item questionnaire on a five point rating scale (none, a little bit, some, quite a lot and severe).[9]

Data was expressed as Mean ± SEM. Both intragroup and intergroup statistical analyses were done. Intragroup analysis for repeated measures was done using ANOVA while intergroup analysis was done using unpaired t test. A p-value <0.05 was considered as statistically significant & <0.001 was considered as statistically highly significant.

RESULTS

The patients in each group were found to be comparable at the time of their initial visit with regard to baseline characteristics such as age, weight, drug allergy and other parameters (Table 1).

Table 1: Comparison of study population characteristics.

Characteristics	GROUP A (L&T) (n=25)	GROUP B (B&B) (n=25)	'p' value
Age (years)	62.4±2.04	63.52±1.77	0.68
Weight (kg)	69.2±1.64	67.48±1.702	0.47
Gender			0.77
Females	13	14	
Males	12	11	
Education			0.08
Literate	17	22	
Illiterate	8	3	
History of drug allergy	--	--	--

Age and weight are expressed as Mean±SEM

- *Group A: Latanoprost and Timolol (L&T) (0.005+0.5% w/v FDC) ophthalmic solution once daily.*
- *Group B: Brinzolamide and Brimonidine (B&B) (1%+0.15% w/v FDC) ophthalmic solution thrice daily.*

Quality of life was assessed by using Glaucoma Symptom Scale Questionnaire (GSS) & Glaucoma Quality of life (GQL-15) questionnaire.

Assessment of GSS visual and non-visual domains was done. Each domain score of GSS was recorded in all the patients of either group before drug administration (baseline) and at end of 4 &12 weeks. Table 2 shows the changes in domain scores with the treatment. On intragroup analysis, at the end of 12 weeks there was increase in the scores of both the domains of GSS & with both the drugs. In latanoprost & timolol group, increase in composite scores was 1.08% and 2.5% at the end of 4 weeks and 12 weeks respectively as compared to baseline values. In brinzolamide/brimonidine group, increase in the composite scores of these domains was 0.14% & 1.6% at the end of 4 weeks and 12 weeks respectively, as compared to baseline values. On intergroup analysis, latanoprost/timolol showed better response than brinzolamide/brimonidine in both visual & non-visual domains. Moreover, there was statistically significant difference ($p<0.05$) in non-visual domain score between 2 groups. As there was improvement in score with latanoprost/timolol while it decreased with brinzolamide/brimonidine at the end of 12 weeks.

Table 2: Comparison of Glaucoma Symptom Scale (GSS).

GSS		L & T (Group A) (n=25)		B& B (Group B) (n=25)		p-value (Intergroup)
		Mean±SEM	Change from baseline (%)	Mean±SEM	Change from baseline (%)	
Visual Symptoms	Baseline	88.6±0.67		88.52±0.47		0.92
	4 weeks	90.28±0.67	1.8%	89.48±0.69	1.08%	0.41
	12 weeks	92.08±0.68	3.48* (3.9%)	91.96±0.72	3.44* (3.88%)	0.9
Non-Visual Symptoms	Baseline	80.6±0.67		80.52±0.47		0.92
	4 weeks	80.88±0.69	0.28 (0.34%)	79.8±0.51	-(0.72) 0.89%	0.21
	12 weeks	81.88±0.73	(1.28) 1.5%	79.88±0.49	-(0.64) 0.79%	0.02#
Composite GSS score	Baseline	84.6±0.67		84.52±0.47	0.08(0.094%)	0.92
	4 weeks	85.52±0.65	0.92(1.08%)	84.64±0.53	0.12(0.14%)	0.27
	12 weeks	86.72±0.65	2.12(2.5%)*	85.88±0.507	1.36(1.6%)	0.24

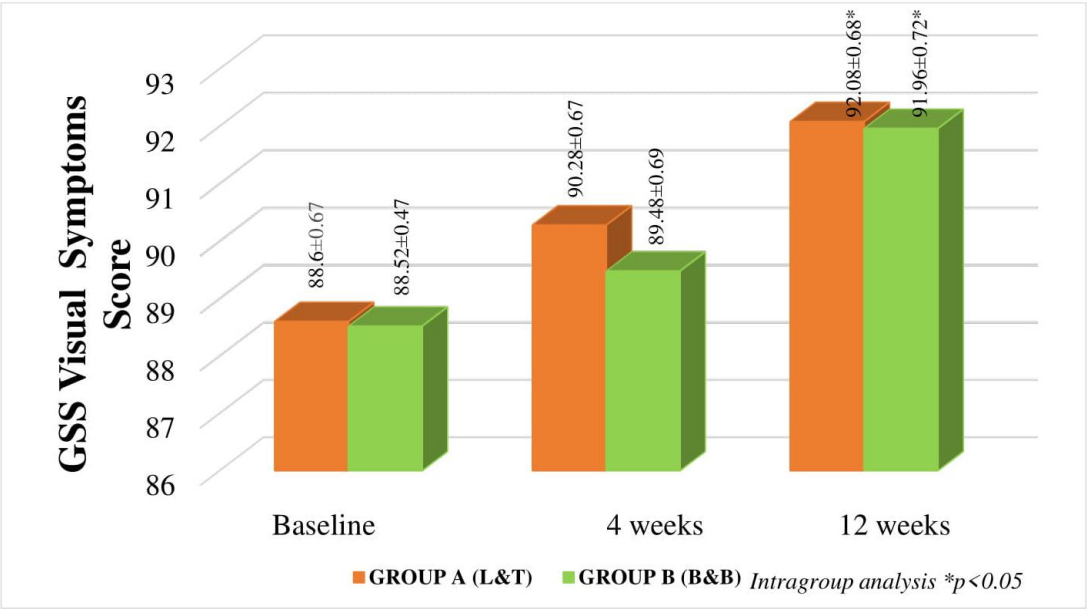

Fig 2: Comparison of GSS –Visual Symptoms Score.

** Comparison of values at end of 12 weeks with baseline values is showing statistically significant difference. (p<0.05)*

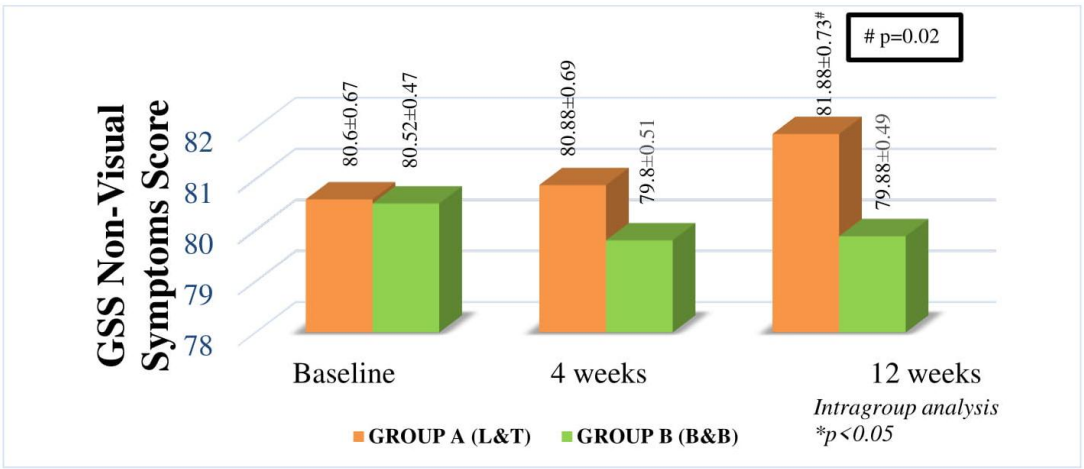

Fig 3: Comparison of GSS Non –Visual Symptoms Score.

#Comparison of values between Group A and B is showing statistically significant difference at 12 weeks(p<0.05)

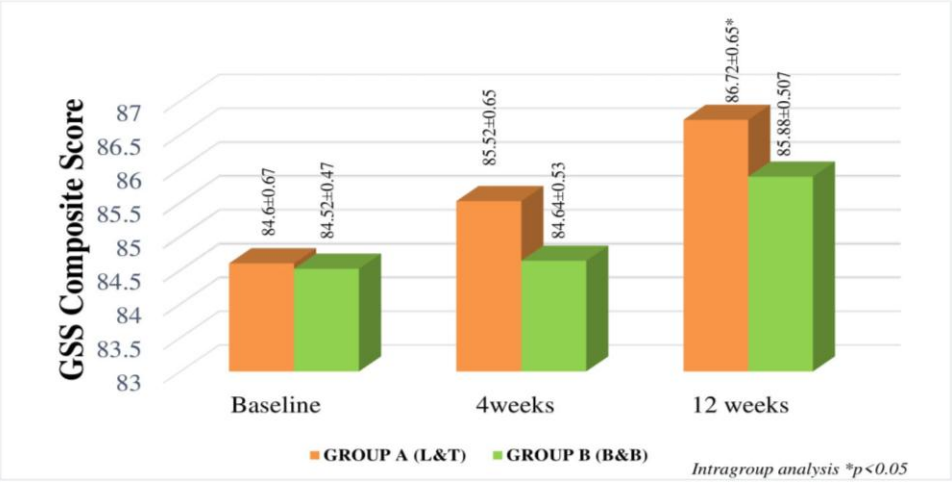

Figure 4: Comparison of GSS composite score.

INTRAGROUP ANALYSIS

** Group A at week 12 in comparison to baseline values is showing statistically significant difference (p<0.05)*

2. Assessment of Glaucoma Quality of life (GQL-15) Questionnaire

Glaucoma Quality of life (GQL-15) Questionnaire score was calculated in all the patients of either group before drug administration (baseline) and at the end of 4 &12 weeks. On intragroup analysis, in group A & B there was decrease in GQL-15 score by 15.4% & 11.67% respectively at the end of 4 weeks compared to their baseline values (p< 0.001). At the end of 12 weeks in group A & B there was still reduction of score by 38.07% and 31.24% respectively compared to their baseline values (p< 0.001). On inter-group analysis, better response was seen in group A at the end of 4 weeks as well as 12 weeks.

Table 3: Comparison of glaucoma quality of life (GQL-15).

GQL-15 Score	Group A (L & T) (n=25)		Group B (B& B) (n=25)		p-value (Intergroup)
	Mean±SEM	Reduction from baseline (%)	Mean±SEM	Reduction from baseline (%)	
Baseline	37.08±0.808		35.96±0.63		0.28
4 weeks	31.36±0.91	5.72** (15.4%)	31.76±0.82	4.2** (11.67%)	0.74
12 weeks	22.96±0.81	14.12** (38.07%)	24.72±0.45	11.24** (31.24%)	0.06

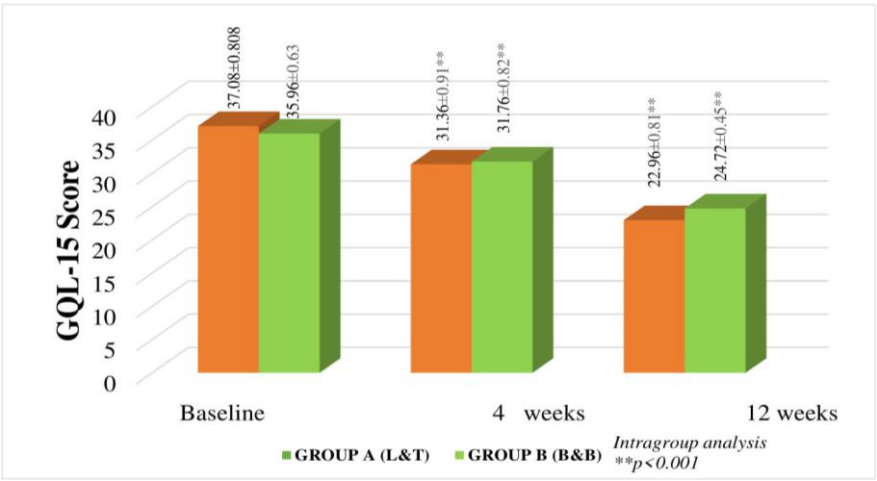

Figure 5: Comparison of GQL-15 Score.

INTRAGROUP ANALYSIS

*** Comparison of values at end of week 4 and 12 with baseline values is showing statistically highly significant difference. (p<0.001)*

DISCUSSION

Glaucoma is progressive optic neuropathy resulting in specific pattern of irreversible visual field defects that are associated frequently with raised intraocular pressure (IOP).[1] It is the second leading cause of blindness in world accounting for upto 8% of total blindness. Headache, eyeache of mild intensity and scotoma (defect in visual field) are seen in disease.[6]

Even the mere diagnosis of a chronic, irreversible, potentially blinding disorder can adversely affect the patient's sense of well-being and QOL by eliciting significant anxiety. The disease itself as well as the medical or surgical treatment can have an enormous impact on a patient's QOL.[7] Various patient reported outcomes questionnaires have been developed to assess QOL eg. Glaucoma symptom scale questionnaire (GSS) and Glaucoma Quality of life questionnaire (GQL-15) etc.

Although exact similar studies were not available in which similar treatment groups were compared for observing the effects on QOL using GSS &GQL-15. In a study done by Stephen et al in Germany, 1023 patients who were switched from previous ocular hypotensive therapies to OD schedule of latanoprost/timolol & were observed for 6 months. Results of study were that patients found it easier, didn't forget to instill the drops, were more satisfied and agreed to continue with same drops. Patients tolerated the drops better and had better quality of life. Although, assessment criteria in our study were different from above mentioned study. QOL was improved with latanoprost/timolol FDC in our study as in above mentioned study.[10]

In a study done by Jonathan et al to compare quality of life impact with brimonidine 0.2% and timolol 0.5% in newly diagnosed patients. 219 patients were enrolled & instilled medications twice daily for 4 months. Quality of life effects were assessed with the SF-36 Health Survey and Glaucoma Disability Index questionnaires. Quality of life remained stable, with no significant between group differences. Quality of life in our study improved as in above mentioned study, however we have compared FDCs of latanoprost/timolol with brinzolamide/brimonidine whereas in the above study monotherapy of brimonidine with timolol was compared.[11]

CONCLUSION

- Both treatment groups i.e. Latanoprost/timolol and Brinzolamide/brimonidine showed improved quality of life in patients suffering from glaucoma.
- Latanoprost/timolol had slightly better response on quality of life than brinzolamide/ brimonidine However, more studies observing the effect of treatment on QOL would be beneficial in order to provide guidance in making clinical decision to prescribing physicians.

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Conflicts of interest: There are no conflicts of interest.

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