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PRIMARY OPEN ANGLE GLAUCOMA;

COMPARISON OF THE OCULAR HYPOTENSIVE EFFICACY OF 0.004% TRAVOPROST & 0.2% BRIMONIDINE

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ABSTRACT… Introduction: Glaucoma constitutes a group of ocular diseases characterized by optic nerve damage and loss of visual field, usually associated with elevated IOP. Although the elevation of IOP beyond normal values is not necessary for the occurrence of glaucomatous damage, it is currently thought to be a major risk factor. Glaucoma is one of principal causes of blindness in the world. The primary aim of POAG treatment is to prevent functional visual impairment with in patient's life time by slowing the rate of ganglion cell loss closer to that of normal population (approximately 5000/year). Medications for glaucoma have changed notably over the past 2 decades with increase in efficacy, better dosing regimens, improvement in safety, and reduction in side-effects. **Purpose of study:** The purpose of this study is to compare the IOP lowering efficacy of the (Travatan) Travoprost 0.004%ophthalmic solution and (Alphagan) brimondine 0.2% ophthalmic solution in primary open angle glaucoma. **Duration:** The duration of study was six months from June 2009 to November 2009. **Material and methods:** The study was conducted on 60 patients with primary open angle glaucoma (POAG) divided into two groups randomly.. Each patient was examined regarding visual acuty, refraction, slit lamp biomicroscopy, IOP with Goldmann Applanation Tonometer, Gonioscopy, fundoscopy and Perimetry. **Results:** GROUP A had 30 patients with 60 eyes there were 25 male (83.33%) patients and five females (16.67 %) patients. The eye drops travoprost 0.004 % one drop at night was used. The average IOP reduction was 7mmhg from base line, GROUP B also had 30 patients with 60 eyes there were 27 male (90%.) and 3 females (10 %) The eye drops brimonidine tartarate 0.2 % was instilled twice a day one drop in the morning and one drop in the evening. The average IOP reduction was 5.5mmhg from base line. **Conclusions:** In conclusion both latanoprost and brimonidine reduce IOP effectively in POAG. Mean IOP lowering is better with latanoprost.

Key words: Glaucoma, primary open angle glaucoma (POAG)

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INTRODUCTION

Glaucoma constitutes a group of ocular diseases characterized by optic nerve damage and loss of visual field, usually associated with elevated IOP. Although the elevation of IOP beyond normal values is not necessary for the occurrence of glaucomatous damage, it is currently thought to be a major risk factor[1]. The initial treatment for POAG is usually medical. Filtration surgery is traditionally reserved for individuals in whom maximally tolerated medical therapy fails to control the disease. Eye sight is one of the greatest gift from God. Glaucoma is a silent thief of this precious gift. Glaucoma effects as many as 67 million people word wide and is a leading cause of vision loss and blindness[2]. Glaucoma cases are accepted to hit 80 million by 2020, Women and people in Asia and Africa will be most affected[3]. Based on epidemiologic surveys, open angle glaucoma (OAG), the most common form of glaucoma, affects approximately 1.86% of US population over the age of 40.OAG is more prevalent in Blacks, Hispanics and in the elderly[4].

The primary aim of POAG treatment is to prevent functional visual impairment with in patient's life

time by slowing the rate of ganglion cell loss closer to that of normal population (approximately 5000/year). Currently the best method of achieving this goal is to lower the IOP to target pressure which can be accomplished through medical therapy, laser treatment, or surgery[5].

Medications for glaucoma have changed notably over the past 2 decades with increase in efficacy, better dosing regimens, improvement in safety and reduction in side-effects[6]. Although beta-blockers continue to be the primary initial treatment for POAG but they have the potential to cause serious cardiovascular and respiratory side effects[7,8].

Newer agents, for example topical carbonic anhydrase inhibitors, topical adrenergic agonists (œ2 agonists), and topical prostaglandins are also prescribed[9].

Travoprost like the other prostaglandin analogues latanoprost and bimatoprost, is a synthetic analogue of prostaglandin F2a. The travoprost molecule is an ester pro-drug that is hydrolyzed by corneal esterases into its active free-acid form. Once hydrolyzed in the eye, travoprost acid then binds to prostaglandin FP receptors in both the ciliary muscle and the trabecular meshwork.The results of these FP receptor-mediated intracellular signals include increased production of several matrix metalloproteinases (MMPs). Remodeling of the extracellular matrix of the ciliary body is hypothesized to lower IOP by creating or increasing spaces between the ciliary muscle fiber bundles, thus increasing outflow through the uveoscleral pathway[10].

Brimonidine is a highly selective α2-adrenergic agonist approved for the treatment of open-angle glaucoma. One of the primary risk factors for glaucoma is elevated intraocular pressure. When applied to the eye, brimonidine activates α2-adrenergic receptors, resulting in decreased aqueous humor production and increased uveoscleral outflow. These effects on aqueous humor dynamics lead to a reduction in intraocular pressure[11]. Although it has been well established that IOP is a major risk factor for the development of glaucoma and that reducing IOP slows the progression of disease. However, in many patients it has been found that in spite of adequate control of IOP with medical therapy, visual fields continues to deteriorate. It means that there are some other factors in glaucoma like IOP fluctuation and Retinal nerve fiber layer damage which causes visual fields deterioration.

Hong S and colleagues have shown in their study that intraocular pressure fluctuation was associated with a progressive increase visual fields in the deterioration even though patients with glaucoma maintained their IOP after the triple procedure[12]. In clinical practice, IOPs are measured during the day and decisions about treatments are based on these findings. However, important events occur during sleep that may precipitate the development of or exacerbation of glaucomatous optic neuropathy. These events include nocturnal systemic hypotension, and possibly, increased IOP at night is apparent that the need for IOP control is at least important during the day[13].

This study was designed to compare the pressure lowering effects of 0.004% Travoprost and 0.2% Brimonidine in patients with primary open angle glaucoma.

PURPOSE OF STUDY

The purpose of this study is to compare the IOP lowering efficacy of the (Travatan) Travoprost 0.004%ophthalmic solution and (Alphagan) brimondine 0.2% ophthalmic solution in primary open angle glaucoma.

Study design

Quasi experimental study.

Duration

The duration of study was six months from June 2009 to November 2009

MATERIAL AND METHODS

A comparative study of 60 patients with 120 eyes was carried out in the department of

ophthalmology of Allied Hospital Faisalabad. The patients of POAG were selected and registered from the out patient department for treatment and divided randomly into two groups A and B each having 30 patents and 60 eyes. The age of patents varied between 45 to 60 years. The study period was between June 2009 to November 2009. Each patients was examined regarding visual acuity and refraction ,slit lamp examination, IOP (with goldman applanation, with instillation of Alcain and Fluorescein drops), Gonioscopy with goldman goniolens and fundoscopy with 90D was performed. Perimetry was done with Humphrey filed analyzers where was required.

The follow up was carried out as Day one ,One week and 4 weeks.

STATISTICAL ANALYSIS

The collected data were analysed using SPSS. The frequencies with percentages were find out for qualitative data and mean with standard deviations were calculated for quantitative data. For comparison between two treatments of Travoprost and brimonidinr tatrate "t-test, was applied.

Inclusion criteria

The inclusion criteria was as follows.

- No sex discrimination
- Age 45years to 60 years.
- IOP above 21 mmHg.
- C/D ratio more than 5.
- Visual field defect
- Angle of anterior chamber of grade 3 or above

Exclusion Criteria

The following patients were excluded from the study

- Patients below 45 years or above 60 years. IOP less then 21mmHg.
- C/D < 0.5.
- Narrow angle.
- History of diabetes, hypertension and trauma.
- History of previous cataract or glaucoma surgery
- Inability to undergo applanation tonometery
- Clinically significant progressive retinal diseases
- Significant hypersensitivity to prostaglandin and it's analogue and brinzolamide
- Ocular inflammation and infection within past three months.

RESULTS

A total one hundred and twenty eyes of sixty patients with primary open angle (POAG) who met the inclusion criteria were enrolled. The patients were randomly divided into two groups, A and B. Informed consent of each patient was taken. The IOP lowering effect of two drugs was noted after instilling them in eyes with POAG.

Group A

This group has 30 patients with 60 eyes. There were 25(90%) males and 5(10%) females patients. (Figure No. 1) In this group Travatan (Travoprost 0.004%) eye drops was instilled once a day, in the night . The average reduction of IOP was 7 mmHg from base line.(Table No I)

Avg. range of base line IOP	No. of Eyes	Average IOP reduction from base line	Total average reduction from base line
22 to 33 mmHg	20	8 mmHg	7 mmHg
24 to 26 mmHg	18	7 mmHg	
27 to 28 mmHg	12	6 mmHg	
29 to 31 mmHg	10	7 mmHg	
Total	60	28	

Table-I. IOP record of patients on treatment with Travoprost 0.004%

Group B

This group has 30 patients with 60 eyes. There were 27 male and 3 female patients. (Figure No. 1) In this group Alphagan (brimondine 0.2%) eye drops twice a day one drop in the morning and one drop in the evening were instilled in eyes. The average reduction of IOP was 5.5 mmHg from base line.(Table No II)

Age range in group A & B

45-60 years

Male: Female ratio in Group A
83.33% : 16.67%(Fig-1)
Male: Female ratio in Group B
90%:10%(Fig-1)
Total Average reduction of IOP in Group A
7mmHg(Table I)
Total Average reduction of IOP in Group B
5.5mmHg(Table II)
Mean reduction of IOP in Group A
7.15 mmHg(table III)
Mean reduction of IOP in Group B
5.87 mmHg(table III)
SD in Group A SD:0.76(table III)
SD in Group B SD:1.02(table III)

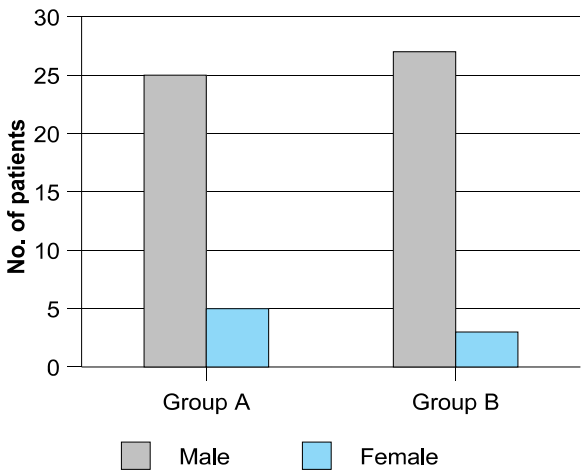

Fig-1. Sex distribution

Avg. range of base line IOP	No. of Eyes	Average IOP reduction from base line	Total average reduction from base line
22 to 33 mmHg	22	5.6 mmHg	5.5 mmHg
24 to 26 mmHg	20	7.0 mmHg	
27 to 28 mmHg	15	5.0 mmHg	
29 to 31 mmHg	03	4.4 mmHg	
Total	60	22.0	

Table-II. IOP record of patients on treatment with brimonidine tatrate 0.2% ophthalmic solution

DISCUSSION

This study was designed to study the IOP lowering effects of 0.004% travoprost and 0.2% Brimonidine tatrate as primary monotherapy for open angle glaucoma. Lowering the IOP is the only treatment that effectively preserves optic nerve function and stability of visual fields[14]. However several studies have demonstrated that IOP variation is an independent risk factor for progression of glaucoma[15].

In recent years, the mono therapy for medical treatment of glaucoma have increased with development of many new drugs like 0.004% travoprost and 0.2%Brimonidine tartarate[16].

We were very concerned about the different medications being used to lower IOP as uncontrolled IOP leads to irreversible visual loss. The main focus of our study was to compare the IOP lowering efficacy in POAG of the two drugs concerned.

All major clinical trials such as Ocular hypertension treatment study (OHTS), Early manifest glaucoma trial (EMGT) and advanced glaucoma intervention study (AGIS) showed that reduction of IOP slows down glaucoma damage. So IOP level is very important in determining visual field loss. Question is which level of IOP is safe? The European glaucoma society guidelines suggest that treatment should aim at achieving at least a 20% reduction from the initial pressure at which damage occurred or in advanced glaucoma, to lower IOP to a level below 18mmHg.Studies have shown that maintaining IOP below this pressure reduces the risk of both the development and progression of glaucoma[17].

In our study 0.004%Travoprost reduced mean IOP by 7 mmHg while Goldberg and colleagues in their study, have shown that mean intraocular pressure reductions ranged from 6mmHg to 8.1mmHg for 0.004% travoprost compared with timolol ,which ranged from 4.7 to 7.1mmHg[17].

Fellman et al reported that mean IOP reductions ranged from 6.5 to 8.0 mmHg with travoprost

Group	Treatment	Number	Mean	Std. Deviation	Std. Error Mean	t	Propabability
22 to 23	Travoprost Brimonidine	20 22	8.03 5.59	0.23 0.55	0.05 0.12	18.47**	0.000
24 to 26	Travoprost Brimonidine	18 20	7.00 7.03	0.18 0.60	0.04 0.14	-0.20^{NS}	0.841
27 to 28	Travoprost Brimonidine	12 15	6.01 5.01	0.18 0.34	0.05 0.09	9.09**	0.000
29 to 31	Travoprost Brimonidine	10 3	7.01 4.40	0.20 0.23	0.06 0.13	19.10**	0.000
Total	Travoprost Brimonidine	60 60	7.15 5.87	0.76 1.02	0.10 0.13	7.81**	0.000

Table-III. Comparison between Travoprost 0.004 % and Brimonidine tatrate 0.2 % ophthalmic solution regarding IOP reduction from base line

*** =Highly Significant(P<0.01); NS=Not-significant(p>0.05)*

0.004% vs 5.2 to 7.0 mmHg with timolol 0.5%[18]. While Cantor et al, reported mean IOP reductions for travoprost ranged from 4.6 to 7.2 mmHg (19%–29%) vs 7.4–8.8 mmHg (34%–36%) for bimatoprost[19].

0.2% Brimonidine tartarate ophthalmic solution instilled twice daily, one drop in the morning and one drop in the evening reduced baseline IOP to 5.5mmHg.Of the previous studies on brimonidine, in one study Joel SS and the brimonidine group had mean IOP lowering range from 6.3 to 7.6 mmHg[20]. While, Serle JB the Brimonidine Study Group III reported that when the efficacy of brimonidine was compared with betaxolol the mean decrease in IOP with brimonidine was 5.5–6.2 mmHg and with betaxolol was 3.5-4.1[21]. Dubiner et al found that the mean reduction of IOP from baseline at month 3 was 6.8mmHg with brimonidine and 6.5mmHg with lantanoprost[22]. Various other studies have reported a mean IOP reduction of 20 – 35% with latanoprost; and 16-26% with brimonidine[23,24].

In our study, both drugs were well tolerated. In travoprost group, two patients developed conjuctival hyperemia and in brimonidine group one patient developed conjuctival hyperemia but there was no need to discontinue treatment. None of our patients had iris hyperchromia, a known side effect of latanoprost. The short duration of treatment precludes any comment on this[25]. The slight variation of our results from previous studies, may be due to type of glaucoma, as our study was limited to POAG.

CONCLUSIONS

In conclusion both latanoprost and brimonidine reduce IOP effectively in POAG. Mean IOP lowering is better with latanoprost. No patient had any significant side effects requiring withdrawal of either study medication. So both the drugs were generally well tolerated and safe for use in newly diagnosed patients of primary open angle glaucoma.

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