(e) ISSN Online: 2321-9599

(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

To examine the efficacy and adverse effects of Brinzolamide and Dorzolamide in patients with elevated intraocular pressure

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ABSTRACT:
Aim: To examine the efficacy and adverse effects of Brinzolamide and Dorzolamide in patients with elevated intraocular pressure. **Material and methods:** Patients above 35 years of age, of any race and either sex, Diagnosed with either primary open angle glaucoma or ocular hypertension, in at least one eye, Best corrected visual acuity better than 6/24 in the study eye and The IOP in the study eye must have been considered controllable on one drug therapy in such a way that should assure clinical stability of vision and optic nerve through the trial were included in this study.Subjects were randomized using a random number table generator, into 2 groups:Group A: Received topical brinzolamide 1% monotherapy twice daily (8 am and 10 pm) for a period of three months, and Group B: Received topical dorzolamide 2% monotherapy thrice daily (8 am, 3 pm and 10 pm) for a period of three months. **Results:** The mean IOP after 3 weeks was 19.86 mmHg and 20.25 mmHg for the brinzolamide and dorzolamide groups respectively and after 3 months, the mean IOP was 20.53 mmHg and 20.37 mmHg in the two groups were compared, which showed that there was no statistically significant difference ($p>0.05$) between them, this infers that the maximum IOP lowering effect achieved within 3weeks.The incidence of ocular discomfort was significantly less in the brinzolamide group (10%) versus the dorzolamide group (30%). **Conclusion:** The findings of this research further demonstrate that both brinzolamide administered twice daily and dorzolamide administered three times daily resulted in a substantial and comparable reduction in intraocular pressure (IOP) in a significant proportion of individuals. For the first treatment of primary open-angle glaucoma (POAG) and ocular hypertension (OHT), we suggest using topical brinzolamide 1% as a single therapy instead of dorzolamide 2%.
Keywords: Brinzolamide, Dorzolamide,Intraocular pressure

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This article may be cited as: Bahuguna G, Chauhan A. To examine the efficacy and adverse effects of Brinzolamide and Dorzolamide in patients with elevated intraocular pressure. J Adv Med Dent Scie Res 2017;5(8):127-131.

INTRODUCTION

Glaucoma is word that does not refer to a single disease entity, but rather a group of disease that defer in their clinical presentation, pathophysiology and treatment[1].Primary open angle glaucoma is a chronic, progressive optic neuropathy in adults in which intraocular pressure (IOP) and other currently unknown factors contribute to damage of optic nerve.It is estimated that 45 million people in the world have open-angle glaucoma (OAG)[2].Glaucoma (both open- angle and angle closure)is the second leading cause of blindness worldwide, with approximately 8.4 million people blind from glaucoma. There are approximately 11.2 million persons aged 40 years and older with glaucoma in India[3]. The overall prevalence of OAG in the US population 40 years and older is estimated to be 1.86% (95% confidence interval, 1.75%-1.96%)[4]. A study shows that prevalence of POAG and OHT is more in older age group latinos than younger, there is no gender related differences in prevalence of POAG and OHT[5,6]Glaucomatous visual changes and defects are irreversible because of retinal ganglion nerve cell damage. Due to the irreversible nature of glaucomatous defects, current strategy aims at early detection through screening, and further detailed examination of 'at risk' suspects[7,8].The changes of primary open angle glaucoma are noticed by the patient after significant disease progression due to a relative lack of attendant alerting symptoms. These factors make glaucoma the 'sneak thief' of vision. Hence the need for early diagnosis, prompt treatment and lifelong compliance. Glaucoma is detected by means of a detailed eye examination including visual acuity, visual field testing for peripheral vision, dilated eye examination for inspecting the optic nerve for any signs of damage, tonometery for measuring IOP and specular microscopy for measuring central corneal thickness.

Reduction of elevated intraocular pressure is the only as yet proven approach to protect against visual field loss in patients with primary open angle glaucoma or ocular hypertension[7,8]. First line therapy for elevated IOP is typically is a single topical agent, belonging to one of the following classes of drugs: Prostaglandin analogues/derivatives, Beta blockers, Alpha-2adrenargic receptor agonists, and carbonic anhydrase inhibitors.Dorzolamide, a carbonic anhydrase inhibitor, was FDA approved in 1994[9] for the treatment of elevated intraocular pressure of

primary open angle glaucoma and ocular hypertension, is also associated with significant side effects such as ocular burning, stinging, allergic reaction, superficial punctate keratitis and others[10].Brinzolamide is another carbonic anhydrase inhibitor launched more recently, FDA approved in 1998 for the treatment of elevated intraocular pressure in primary open angle glaucoma and ocular hypertension[11].

There is paucity of studies comparing efficacy and side effect profile of dorzolamide and brinzolamide head to head, in the Indian population, the present is an attempt in that direction.

MATERIAL AND METHODS

This was a prospective, randomized, active controlled, parallel group study done by double blinding.A total of 103 patients (206 eyes) were initially enrolled in the study, according the following criteria-

Patients above 35 years of age, of any race and either sex, Diagnosed with either primary open angle glaucoma or ocular hypertension, in at least one eye, Best corrected visual acuity better than 6/24 in the study eye and The IOP in the study eye must have been considered controllable on one drug therapy in such a way that should assure clinical stability of vision and optic nerve through the trial were included in this study.

Patients with conjunctivitis, keratitis, uveitis, scleritis, any local abnormality, chronic or recurrent inflammatory eye disease, hypersensitivity to medication, pregnant, any severe medical or surgical condition, intra-ocular surgery in last 3 months, progressive retinal disease or on therapy that affect IOP or systemic blood pressure were excluded from the study. Informed consent was taken from all participants enrolled in the study.

PATIENT EXAMINATION

VISIT 0: Preliminary assessment and examination including detailed history and comprehensive medical examination [visual acuity, anterior segment slit lamp microscopic examination, gonioscopy, IOP determination].

VISIT 1: Pre-randomization assessment Baseline this involved baseline visual analogue pain/discomfort score assessment and central corneal thickness measurements with Specular microscope.

METHODOLOGY

Subjects were randomized using a random number table generator, into 2 groups:

Group A: Received topical brinzolamide 1% monotherapy twice daily (8 am and 10 pm) for a period of three months, andGroup B: Received topical dorzolamide 2% monotherapy thrice daily (8 am, 3 pm and 10 pm) for a period of three months.

Visit 2: 3 weeks post-randomization assessment :- The subjects were inquired regarding the development of any new ocular or systemic symptoms/side effects, routine follow-up best corrected vision (Snellen's) assessment, central corneal thickness measurements and Visual analogue ocular discomfort score [This score was done before administration of ocular medication, 2 minutes after administration of ocular medication at the health facility]. Diurnal variation IOP was measured with the Goldman applanation tonometer with the patient sitting, at 9am, 1pm, 5pm and 9pm(before medication instillation).

Visit 3: at 3 months post-randomization assessment- The subjects were assessed similar to the assessment done in Visit 2.

RESULTS

A total of 103 patients were initial enrolled in the study and were randomly assigned to treatment. All 103 received at least 1 week of medication in both eyes. Three patients were not available for follow- up assessments and were withdrawn from the study. Both eyes of all remaining 100 patients qualified for the purpose of the study. So a total 100 patients (200 eyes) with 50 patients in each group, completed the entire study period, and were included in the final analyses. Each individual eye was treated as a statistical unit for the purposes of the study.

Table 1: Patient Demographics

Parameter	Brinzolamide Group =50		Dorzolamide Group =50		Total =100	
	Number	Percentage	Number	Percentage	Number	Percentage
Gender						
Male	26	52	28	56	54	54
Female	24	48	22	44	46	46
Age						
31 – 40 years	2	4	1	2	3	3
41 – 50 years	9	18	12	24	21	21
51 – 60 years	12	24	14	28	26	26
61 – 70 years	20	40	18	36	38	38
71 – 80 years	7	14	5	10	12	12
Ocular Hypertensives	22	44	20	40	42	42
POAG	28	56	30	60	58	58

The mean age in brinzolamide group was 60.2 yrs and 59.48 yrs in the dorzolamide group, so the mean age of patients in the study was 59.84 yrs. In each group, the maximum number of patients were in the 51-70yrs (64%) age group. In group A (brinzolamide), 44% of the patients had ocular hypertension, and 56% of the patients had POAG, while in group B (dorzolamide), 40% of the patients had ocular hypertension, and 60% of the patients had POAG. There was no statistically difference among the two groups (p>>0.05).

Baseline Intraocular Pressure

For each patient, average IOP at baseline, average IOP at 3 weeks, and average IOP at 3 months was calculated. The mean of the IOP's was also calculated for each visit. No statistically significant differences were observed between the two groups with respect to mean IOP at baseline, or diurnal variation (p>0.05 unpaired t-test).

Intergroup comparisons

Each individual IOP measurement by time of day, at visits 2 (3 weeks) and 3(3 months) was compared with the IOP measurements at baseline. This was used to calculate the mean change in IOP (mmHg) for each treatment group by visit (2 and 3) and time of day (9am, 1pm, 5m, 9pm,) for each group. [Table 2].The mean IOP after 3 weeks was 19.86 mmHg and 20.25mmHg for the brinzolamide and dorzolamide groups respectively and after 3 months, the mean IOP was 20.53 mmHg and 20.37 mmHg in the two groups were compared, which showed that there was no statistically significant difference (p>0.05) between them (Table 2), this infers that the maximum IOP lowering effect achieved within 3weeks.

Table 2: Mean IOP by Visit and Time of Day

	Brinzolamide		Dorzolamide		
	Mean	**SD**	**Mean**	**SD**	**P value**
Baseline					
9am	26.15	1.48	24.13	1.41	0.13
1pm	25.13	1.56	23.15	1.89	0.32
5pm	24.15	2.69	22.45	2.41	0.16
9pm	22.08	2.42	24.85	2.85	0.45
Avg	22.80	2.28	22.56	1.56	0.25
3 weeks					
9am	19.26	1.55	21.56	1.85	0.18
1pm	20.69	1.88	20.12	1.36	0.43
5pm	21.01	1.67	20.23	1.96	0.21
9pm	19.52	1.96	19.85	1.25	0.37
Avg	18.85	1.81	19.52	1.90	0.23
3 months					
9am	20.85	1.32	20.25	1.62	0.16
1pm	18.75	1.81	19.96	1.68	0.14
5pm	21.94	2.02	21.58	1.41	0.31
9pm	20.23	2.74	19.23	2.54	0.33
Avg	20.88	1.66	20.85	1.47	0.15

Analysis of Ocular Side Effects

The most frequent adverse events reported included ocular discomfort (typically characterized as pain and burning sensation), transient blurred vision, conjunctivitis, and taste abnormality. The incidence of ocular discomfort was significantly less in the brinzolamide group (10%) versus the dorzolamide group (30%).

Table 3: Side effect profile of two drugs

Side Effect	Brinzolamide group =50		Dorzolamide group =50	
	Number	**Percentage**	**Number**	**Percentage**
Pain and burning sensation	5	10	12	24
Transient Blurred vision	3	6	0	0
Conjunctivitis	1	2	3	6
Taste abnormality	5	10	4	8
Foreign body sensation	2	4	2	4
Tearing	1	2	5	10

The baseline visual analog scale scores were comparable among both the groups, as was also revealed by the significance value (>0.05). The mean discomfort scores immediately post installation at 3week and 3month was 6.12 and 4.65 respectively and chronic score was 5.11 and 3.89 for brinzolamide

group compared with dorzolamide group in which immediate post installation score at 3week and 3month was14.03 and 12.21 and chronic score was 12.43 and 10.65 showed that ocular discomfort score were significantly (p-value<0.05) lower in brinzolamide group in comparison to dorzolamide group.

DISCUSSION

This study was undertaken to compare the efficacy and side effect profile of the two commercially available topical carbonic anhydrase inhibitors, Brinzolamide and Dorzolamide, in an Indian population, when used as monotherapy.Mean age in brinzolamide group was 60.2yrs and 59.48yrs in dorzolamide group, so the mean age of patients in study was 59.84yrs. These finding were supported by Hollo G et al[12]where the mean age of POAG and OHT patients were 68.8±15.3yrs and 60.3±12.6yrs respectively, which correlate with our finding that POAG and OHT is more common in people of more than 40yrs of age.The IOP-lowering efficacy of brinzolamide twice daily (administered at 8 am and 10 pm) was demonstrated by both clinically relevant and statistically significant IOP reductions at all the times of day measured. Mean baseline IOP of brinzolamide group was 24.06mmHg was compared with mean IOP at 3months 20.53mmHg (p-value<0.001) which shows a statistically significant reduction. A study conducted by Wang THet al showed that after 6weeks treatment by b.d dosing of topical brinzolamide 1% IOP 17% reduction (drooped by 4.8mmHg) achieved. Similarly, the IOP-lowering effects of dorzolamide thrice daily (administered at 8 am, 3 pm and 10 pm) was demonstrated by both clinically relevant and statistically significant IOP reductions at all times. Mean baseline IOP of dorzolamide group was 23.42mmHg was compared with mean IOP at 3months which was 20.37mmHg (p-value<0.001) showed a statistically significant reduction in IOP[13,14]A study by Wilkerson Met.al showed that 18.4% (mean baseline 26.8mmHg and after 4weeks mean IOP 21.8mmHg) reduction in IOP achieved in 4weeks with 2% dorzolamide ophthalmic solution. A four week safety and efficacy study of dorzolamide by Wilkerson M et al showed that 18.4%(mean baseline 26.8mmHg andafter 4weeks mean IOP 21.8mmHg) reduction in IOP achieved in 4weeks revealing statistically significant(p<0.05) reduction in IOP in 4weeks. The incidence of ocular discomfort was significantly less in the brinzolamide group (10%) versus the dorzolamide group (30%). In study of Tuskamoto Het al[15] incidence of ocular irritation was significantly higher (p- value<0.0001) in dorzolamide group (74%) than brinzolamide group (16%), which shows that dorzolamide causes more ocular discomfort than brinzolamide.The mean pain/discomfort score after intervention was found to be significantly higher in the dorzolamide group (p<0.05 at each follow up visit) vs the brinzolamide group. The visual analogue scale is a validated scale that has been described previously for ocular use.Shin D, Silver L.H. and Sall Ket al study have evaluated the safety of brinzolamide1% compared with dorzolamide 2% ophthalmic suspension and concluded both brinzolamide and dorzolamide have equivalent efficacy for lowering elevated IOP[16-20]

CONCLUSION

The findings of this research further demonstrate that both brinzolamide administered twice daily and dorzolamide administered three times daily resulted in a substantial and comparable reduction in intraocular pressure (IOP) in a significant proportion of individuals. For the first treatment of primary open-angle glaucoma (POAG) and ocular hypertension (OHT), we suggest using topical brinzolamide 1% as a single therapy instead of dorzolamide 2%. This recommendation is based on the fact that brinzolamide has fewer side effects and is equally effective in treating both conditions.

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