ORIGINAL RESEARCH PAPER

Volume-6 | Issue-10 | October-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Evaluation of Safety and Efficacy in a Comparative Study between Dorzolamide 2% eye drops v/s Alphagan 0.2% eye drops in cases of POAG and Ocular Hypertension

Ophthalmology

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ABSTRACT

Topical CAI was approved for ophthalmic clinical use in 1994. One of them is commercially available Dorzolamide 2% eye drops. This group of drugs act by inhibiting the action of the enzyme CAI in the ciliary processes, thereby slowing the formation of bicarbonate ions, subsequently reducing the sodium and fluid transport. This decreases the aqueous formation and therefore reduces IOP. In our study with regular checkup of 3 months, patients on antiglaucomatous drugs showed mean IOP reduction to be always higher in topical dorzolamide group with least side effect, when compared with drugs like Brimonidine Tartarate.

KEYWORDS

Dorzolamide, Alphagan, IOP, POAG

Introduction:
Glaucoma is one of the leading cases of blindness in the world and account for approximately 15% of all cases. Commonly used antiglaucomatous drugs have their own side effects. Topical Carbonic Anhydrase Inhibitors were approved for use in 1994. This group of drugs acts by inhibiting the action of the enzyme CAI in the ciliary processes, thereby slowing the formation of bicarbonate ions, subsequently reducing the sodium and fluid transport. This decreases the aqueous formation and therefore reduces IOP. It minimizes the systemic side effects frequently encountered with oral drugs from this group (Example: Acetazolamide) such as fatigues, diuresis, abnormalities in taste, paresthesias etc.

Brimonidine (Brand Name: Alphagan) is a highly selective alpha-2 adrenergic agonist used for IOP lowering in ocular hypertension or glaucoma. It is an effective IOP lowering agent when used as monotherapy. It's mechanism of IOP lowering includes dual action by decreasing aqueous production and increasing uveo-scleral outflow. It binds to receptors and signals the cells to carry out neuroprotective function.

Patients and Methods:
The study was conducted in the Department of Ophthalmology, Seth G.S. Medical College & K.E.M. Hospital in Mumbai for a period of 6 months between October 2011 and March 2012. A written Informed Consent was taken from all the patients prior to their enrolment in the study. The study Design was randomized, prospective, open and unicentric.

Inclusion Criteria:
Patients above 18 years of age, of either gender, diagnosed with POAG/OHT where IOP was found to be more than 21 mm of Hg on atleast three different occasions, willing to voluntarily sign the written informed consent for the study which includes:

(a) POAG suspect, where the risks and benefits of treatment need to be weighed against the developing glaucomatous disc changes.
(b) Ocular Hypertensives - patients with repeated Raised IOP in high twenties even without the presence of risk factors.

Exclusion Criteria:
- Prior History of hypersensitivity to any of the drugs that will be used in the study.
- Secondary glaucoma and Narrow Angle glaucoma
- Any corneal abnormality that will cause difficulty in accurate IOP measurement.
- Pregnant, lactating or nursing mothers
- Any patient with uncontrolled systemic disease.

Baseline Evaluation and Follow up:
Subjects fulfilling the above criteria underwent detailed ophthalmic and medical history taking and a detailed physical examination. All relevant laboratory investigations including blood sugar levels were carried out. The ophthalmic examination included measurement of visual acuity, IOP, slit lamp microscopy, detailed dilated fundus examination and recording of visual fields.

Drug Administration:
Patients meeting the above criteria with respective IOP changes were given one drop of Dorzolamide 2% eye drops 3-4 times a day depending on the severity of glaucoma and Alphagan 0.2% eye drops twice a day. Patients were also allowed artificial tears as concomitant medication. Sixty patients were divided into Group A and Group B. The Dorzolamide eye drops were instilled every four hours in patients of Group A while Alphagan eye drops were instilled into eye twice daily in patients of Group B.

Efficacy Parameters:
The primary efficacy parameter was the reduction of IOP from the baseline. Also, meeting the target IOP necessary for maintaining the quality of vision was studied.

Assessment of Safety:
Patients were enquired about occurrence of any adverse effects thought to be drug related every visit and any discontinuation of therapy because of the above, was noted.

Statistical Analysis:
Results of patients who had completed atleast one week of therapy were included in the analysis. Non parametric Wilcoxans rank sum test was used to compare the IOP levels and changes in visual fields.

Results:
Sixty patients were enrolled in the study. The mean age of the subjects was 47.48 ± 11.57 years. 50% of these patients were males, and remaining 50% were females. Both the groups comprised of thirty patients each. The patients needed to complete atleast one week of therapy with Dorzolamide and Alphagan eyedrops.

Sixty patients meeting the above criteria were considered for analysis[Table 1].

IOP reduction and clinical success:
Even Though both drugs produced significant reduction in IOP from baseline ($p < 0.001$)at one month visit, 27 of 30 patients(90%) treated with Dorzolamide eye drops achieved a >15% reduction from baseline IOP as compared to 23 of 30 (80%) treated with Alphagan ($p=0.144$).The mean reduction from baseline IOP at month one was 4.60 ± 0.62 mm og Hg(22.8%) in Dorzolamide treated patients [Table 2] vs 3.43 ± 0.62 mm Hg (17.2%, P= 0.219 between groups) in Alphagan treated patients [Table 3].

The reduction in mean IOP at one month in clinically successful patients who had achived a ≥15% reduction from baseline IOP, was

5.32 ± 0.63 mm Hg (26.8%,n-27) with Dorzolamide treatment compared with 5.07 ± 0.45 mm Hg (24.5%, n-23) with Alphagan treatment (p= 0.48).

For the patients who did not achieve the IOP lowering goal in the first month, the mean reduction from baseline IOP was 0.50 ± 0.66 mm Hg (n=7) in Alphagan group. The frequency distribution of percentage reduction from baseline IOP at month one[Table 3] revealed that 5 patients in Alphagan group failed to achieve even 10% reduction in IOP, compared to 2 patients in Dorzolamide group.

For the patients, who achieved the IOP lowering target of 15% from baseline by first month, on initial regimen, IOP remained successfully lowered from baseline with either Alphagan or Dorzolamide for the remaining duration of the study with no significant differences in any further study visit.

Table 1: Patient's Demographics

Parameter	Values
No of Patients	60
Mean Age(years) ± SD	47.48 ± 11.57
Sex	
Males	30
Females	30
Antiglaucoma drugs Used	
Dorzolamide 2%	Four times a day
Alphagan 0.2%	Twice or thrice a day

Table 2: Mean (±SEM reduction in IOP at peak drug effect) Dorzolamide (x-30)

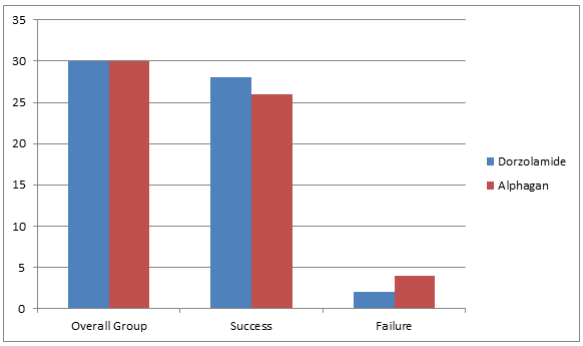
Number(%)	Mean IOP (mm Hg)	Mean(mm)
Total 30	20-20	-
Baseline 1 month	15-60	4.60 ± 0.62
Responders(27)	19.85	-
Baseline 1 month	14.53	26.80
Non Responders	22.17	-
2 months	21.67	2.26

Table 3: Alphagan (n=30)

Number(%)	Mean IOP (mm Hg)	Mean(mm)	Mean Decrease (%)
Total 30	19.98	-	-
Baseline 1 month	16.55	3.43 ± 0.62	17.2
Responders(23)	20.88	-	-
Baseline 1 month	15.81	5.07 ± 0.45	24.5
Non Responders	18.29	-	-
2 months	17.23	0.36 ± 0.66	1.97

Efficacy [Fig 1]

Fig 1.



Adverse Events

Both Dorzolamide and Alphagan were well tolerated as adjunctive agents and produced quite low rates of adverse events causing discontinuation of therapy. 2 patients (10%) in the Alphagan group presented as ocular allergic reaction with symptomatic allergic follicular conjunctivitis leading to discontinuation.

Discussion:

The current study compared Dorzolamide and Alphagan in treatment of Glaucoma using the achievement of a≥ 15% reduction in IOP as a primary clinical end point. Such an end point can help in defining the success of therapy as it reflects the individualized IOP target goals typically set in patients of ophthalmic practices. Glaucoma is a progressive optic neuropathy and success in its management might ideally be defined as lack of progression of neuropathy. However because of slow disease progression and variable measure of neuropathy and visual field loss glaucoma progression (or lack of progression) cannot be effectively measured in a short term trial. Therefore IOP reduction is considered as an alternative measure of clinical success.

In our study, 85% of patients treated with Dorzolamide achieved the target IOP reduction as compared to 65% of Alphagan treated patients (p=0.144). As expected both Dorzolamide and Alphagan produced significant reduction in average IOP. The overall mean reduction in IOP was greater in Dorzolamide treated patients than patients treated with Alphagan.

Both the study medications were well tolerated and associated with very few side effects. The adverse event that led to discontinuation was occurrence of ocular allergic conjunctivitis in two patients treated with Alphagan after one month of assessment. The current results demonstrating success of Dorzolamide in meeting the goal of 15% IOP reduction are consistent with the previous clinical effectiveness trails using an end point of clinical success. Dorzolamide has shown a notable clinical success in this study as it successfully lower the IOP in glaucoma patients even after failure of other agents. Hence, it represents a versatile option for therapy in patients of glaucoma.

Conclusion :

Although both the drugs , Alphagan and Dorzolamide were well tolerated and effective in reducing IOP in majority of the patients, 85% of patients treated with Dorzolamide achieved clinical success where as Alphagan was successful in 65% of patients. Ophthalmologists may be able to design better and more reliable therapies for patients suffering from Glaucoma and ocular Hypertension by considering the clinical success rates of these and other available medications. Our study suggests that Dorzolamide is a better treatment option than Alphagan for treating patients of glaucoma who needed more than one agent to control their IOP. Further comparative trials conducted in larger populations are clearly warranted.

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