Evaluation of Safety and Efficacy in a Comparative Study between Actamid 5% Eye Drops v/s Alphagan 0.2% Eye Drops in Cases of POAG and Ocular Hypertension

G Kokila Kamath*

Abstract

Topical CAI was approved for clinical use in 1994. One of them is the commercially available Acetazolamide (5%) eye drops.

These drugs act by inhibiting the action of the enzyme CAI in the ciliary processes of the eye therefore slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. This decreases aqueous formation and so decreases IOP. In our study patients on anti-glaucomatous drugs showed, during periodic check up of 3 months, mean IOP reduction to be always higher in topical acetazolamide group with least side effects, when compared with drugs like Brimonidine tartrate.

Introduction

Glaucoma accounts for about 15% of total cases of blindness and it is now estimated that by the year 2007 about 10 million people will have bilateral blindness due to glaucoma. Commonly used anti glaucomatous drugs have their side effects and limitations. Topical carbonic anhydrase inhibitors was approved for clinical use in 1994. These drugs inhibit the action of the enzyme carbonic anhydrase in the ciliary processes of the eye thereby showing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. This decreases aqueous formation and IOP. It effectively minimizes systemic side effects frequently reported with oral Acetazolamide like malaise, fatigue, paraesthesias, taste abnormalities and diuretic effect.

Brimonidine is a highly selective alpha-2 adrenergic agonist indicated for lowering of IOP in patients with glaucoma or ocular hypertension. It effectively lowers IOP when used as monotherapy. It lowers IOP by a dual mechanism of action by decreasing aqueous production and increasing uveo-scleral outflow. It binds to cell receptors and signals cells to carry out neuroprotective functions.

Patients and Methods

The study was conducted in the Ophthalmology department, B.Y.L. Nair Hospital for a period of 6 months between Oct. 2006 and March 2007. A written consent was obtained from the patients prior to study enrolment. The design of the study was – open, randomized, prospective and unicentric.

Inclusion Criteria

Patients above 18 years of age diagnosed to have POAG/OHT where the IOP measures greater than 21 mm of Hg on three different occasions, willing to give voluntary written informed consent for the study, which

*Lecturer in Ophthalmology, B.Y.L. Nair Hospital and T.N.M.College, Bombay Central, Mumbai - 400 008.

includes:

1. POAG suspect, where risks and benefits of treatment need to be weighed against the risk of development of glaucomatous disc changes.
2. Ocular Hypertensives - considering it in patients with repeated increased IOPs in high twenties even without the risk factors.

Exclusion Criteria

1. History of hypersensitivity to any drugs which will be used.
2. Narrow angle glaucoma and secondary glaucoma
3. Pregnant, lactating and nursing women.
4. Any corneal abnormality that would prevent accurate IOP reading.
5. Any uncontrollable systemic disease.

Baseline evaluation and follow-up

Eligible subjects underwent detailed physical examination after a detailed ophthalmic and medical history was taken. Laboratory investigations including blood sugar levels were carried out. The ophthalmic examination included measurement of visual acuity, IOP, slit lamp microscopy and dilated fundus ophthalmoscopy and visual field recording.

Drug Administration

Patients, meeting inclusion criteria with respective IOP changes received one drop of Actamid eye drops 3-4 times a day depending on the severity of glaucoma and Alphagan eye drops twice a day. Artificial tears was allowed as concomitant medication. Thirty patients were grouped into A and B each. The Actamid eye drops were instilled into eye after every four hours in patients grouped under group A and Alphagan eye drops were instilled twice daily in patients grouped under group B.

Efficacy parameters

The primary efficacy parameter was the reduction of IOP from the baseline, on each visit. Meeting the target IOP necessary to maintain the quality of vision was studied.

Assessment of safety

At each study visit, patients were enquired regarding the occurrence of adverse events thought to be drug related and leading to discontinuation of therapy were recorded.

Statistical Analysis

Patients who had completed at least one week of therapy were included in the analysis. Non-parametric Wilcoxons rank sum test was used to compare the IOP levels and visual field changes.

Results

Sixty patients were enrolled in the study. Their mean age was 47.48 ± 11.57 years. 50% of these patients were males and 50% were females. Each group comprised 30 patients. To be evaluable for analysis, the patients needed to have completed at least one week of therapy with Actamid and Alphagan eye drops.

Sixty patients met these criteria and were considered for analysis (Table 1).

IOP reduction and clinical success

Although both drugs produced significant

Table 1 : Patients demographics

Parameter	Values
No. of patients	60
Age (yrs.) mean ± Sd	47.48 ± 11.57
Sex	
Males	30
Females	30
Antiglaucoma drugs used	
Actamid 5%	4 times / day
Alphagan 0.2%	B.D. or T.D.S.

reduction from baseline IOP ($p < 0.001$) at one month visit 27 of 30 patients (90%) treated with Actamid eye drops achieved a ≥ 15% reduction in IOP from baseline, compared to 23 of 30 patients (80%) treated with Alphagan ($p = 0.144$). The mean reduction from baseline IOP at month one was 4.60 ± 0.62 mm of Hg (22.8%) in Actamid 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 mean IOP reduction at one month in clinically successful patients, that is they who achieved a ≥ 15% reduction in IOP, was 5.32 ± 0.63 mm Hg (26.8%, n-27) with Actamid treatment compared with 5.07 ± 0.45 mm Hg (24.5%, n-23) with Alphagan treatment ($p = 0.48$).

For those patients not achieving their IOP lowering goal at month one, the mean reduction form baseline IOP was 0.50 ± 0.66 mm Hg (n=7) in Alphagan group. The frequency distribution of percentage reduction in IOP from baseline at month one (Table 3) revealed that 5 patients in Alphagan group failed to achieve even a 10% reduction in IOP, compared with 2 patients in the Actamid group.

For those patients who achieved or exceeded the IOP lowering goal of 15% from baseline by month one on the initial regimen, IOP was successfully lowered from baseline with either Actamid or Alphagan for the remainder of the study with no significant group differences at any study visit.

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

No. (%)	Mean IOP (mm Hg)	Mean (mm)
Total 30 ml	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

Efficacy (Fig. 1)

Adverse events

Both Actamid and Alphagan were well tolerated as adjunctive agents and produced low rates of adverse events leading to discontinuation. Ocular allergic reaction presenting as symptomatic, follicular allergic conjunctivitis led to discontinuation of two patients (10%) in the Alphagan group.

Discussion

The current study compared Actamid and Alphagan in glaucoma therapy using the

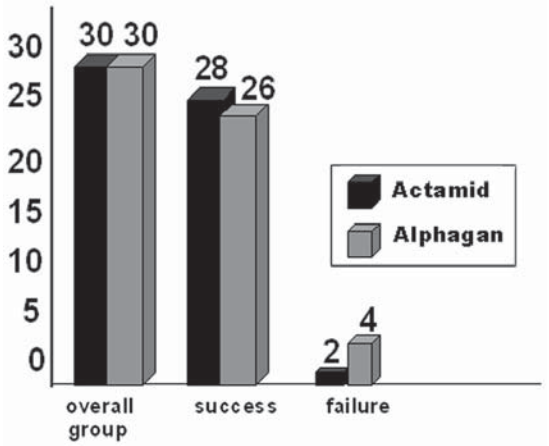

Fig. 1

Table 3 : Alphagan (n=30)

No. (%)	Mean IOP (mm Hg)	Mean (mm)	Mean Decrease (%)
Total 30 (100)	19.98	—	—
1 month			
Responders (23)	16.55	3.43 ± 0.62	17.2
Baseline	20.88	—	—
1 month	15.81	5.07 ± 0.45	24.5
Non-responders	18.29	—	—
2 months	17.23	0.36 ± 0.66	1.97

achievement of a ≥ 15% reduction in IOP as a primary clinical end point. This type of end point can be helpful in defining the success of a therapy since it reflects the individualized IOP target goals typically set for patients in ophthalmic clinical practice. Glaucoma is a progressive neuropathy, and clinical success in glaucoma management might ideally be defined as lack of progression of the neuropathy. However, because the disease progresses slowly and measures of neuropathy and visual field loss are somewhat variable, glaucoma progression (or lack of progression) cannot be measured in a short term trial. Therefore, IOP reduction is used as an alternative measure of clinical success.

In this study, 85% of Actamid treated patients achieved the target IOP reduction compares with 65% of Alphagan treated patients (p = 0.144). As expected, both Alphagan and Actamid eye drops produced significant decreases in mean IOP. The overall mean reduction in IOP was greater in Actamid treated than in Alphagan treated patients.

Both study medications were well toleratd and associated with few adverse events. The only adverse event that led to discontinuation was the occurrence of ocular allergic symptoms in two Alphagan treated subjects after one month reassessment. The current results demonstrating clinical success with Actamid in meeting a target 15% reduction in IOP are consistent with those of previous clinical effectiveness trials using an end point of clinical success. The clinical success of Actamid in the current study is particularly notable because Actamid successfully lowered IOP in patients with glaucoma, even after failure of other agents. Hence Actamid represents a valuable and versatile treated option for patients with glaucoma.

Conclusion

Although Actamid and Alphagan were well tolerated and reduced IOP in most patients, treated with Actamid eye drops was clinically successful in 85% of patients. Alphagan was clinically successful in 65% of patients. By considering the rates of clinical success of available medications, physicians may be able to design more reliable therapeutic strategies for patients with ocular hypertension and glaucoma. Our results suggest that Actamid may be more appropriate choice than Alphagan for treatment in patients with glaucoma who required ≥ 1 agent to lower IOP. Further comparative trials in larger populations are clearly warranted.

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