Original Article

Comparison between Latanoprost and Brimonidine Efficacy and Safety in Indian Eyes

Ravi Thomas, MD; Rajul Parikh, MS; Jayaprakash Muliyil, Dr PH; Ronnie George, MS; Padma Paul, MS; Lekha M Abraham, DNB

Purpose: To compare the short-term efficacy and safety of topical latanoprost and brimonidine in Indian eyes.

Materials and Methods: Twenty-eight patients with ocular hypertension, primary open-angle, pseudoexfoliation or pigmentary glaucoma were enrolled. Following baseline measurements, latanoprost was applied topically once daily in the evening for 12-weeks. After a washout period, brimonidine was applied twice daily in all patients for 6 weeks; 16 patients continued for 12 weeks. Patients were examined at 2, 6 and 12 weeks. The primary outcome measure was the difference in mean intra ocular pressure (IOP) reduction at 6 and 12 weeks. The mean diurnal variation of IOP at baseline and at 12 weeks was also compared.

Results: Twenty-six of 28 enrolled patients completed the study. One randomly selected eye of each patient was used for analysis. At 6 weeks, the mean IOP reduction was 11.2 mm Hg (± 2.9 mmHg) with latanoprost and 6 mmHg (± 3.3 mmHg) with brimonidine. At 12 weeks this was 10.8 mmHg (± 2.8 mmHg) and 6.9 mmHg (± 3.1 mmHg) respectively. At 6 weeks 85.7% (24) eyes obtained more than 25% reduction in IOP with latanoprost compared to 13 (46.4%) with brimonidine. IOP reduction was maintained with both drugs throughout the study period. Two eyes did not show any response to brimonidine. Latanoprost reduced the diurnal variation of IOP from 5.10 to 2.90 mmHg; brimonidine reduced it from 4.70 to 3.90 mmHg. Conjunctival hyperaemia was present in one patient on latanoprost and three patients on brimonidine. Two patients experienced drowsiness with brimonidine. Neither drug produced side effects necessitating withdrawal from the study.

Conclusion: In this short-term study, both latanoprost and brimonidine effectively reduced IOP and stabilised the diurnal curve in Indian eyes. Latanoprost was more effective than brimonidine.

Key Words: Latanoprost, brimonidine, efficacy, safety, glaucoma, intraocular pressure reduction.

Indian J Ophthalmol 2003;51:123-28

Glaucoma is a chronic optic neuropathy characterised by typical optic disc and visual field changes. Raised intraocular pressure (IOP) is the only known causal risk factor for this disease and IOP reduction is the only treatment with demonstrated efficacy.[1-3] 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.

Beta-blockers are usually the first line drugs used to treat open angle glaucoma (OAG) but they have the potential to cause serious cardiovascular and respiratory side effects.[4, 5] Recently, newer medications like latanoprost and brimonidine have become available and are increasingly used in India. Latanoprost (0.005%) is a prostaglandin analogue F2µ(PGF2µ)-isopropyl ester that lowers the IOP by increasing the uveosceral outflow.[6,7] Several pre-clinical and clinical studies have indicated that latanoprost can lower the IOP by 20-36% with minimal side effects.[8-15] Brominidine (0.2%) is a new highly selective a_2 agonist. Its IOP lowering effect is due to decrease in aqueous production with some increase in uveoscleral outflow.[16] Results of a multi-centric brimonidine study trial report a mean IOP reduction of 6.5 (26.2%) mmHg compared to 6.1 (24.8%) mmHg with timolol.[17]

To the best of our knowledge (PUBMED search at the time of working) there is only one study published in the literature comparing the efficacy of latanoprost and brimonidine.[18] This 6-week multi-centric study in Caucasian eyes concluded that latanoprost produced a more consistent lowering of IOP than brimonidine and that brimonidine in a twice-daily dosage may not consistently decrease IOP 10-12 hours after the last application.[18]

L V Prasad Eye Institute (RT), Hyderabad, and Department of Ophthalmology and Community Health (RP, JM, RG, PP, LMA), Christian Medical College, Vellore, India.

Reprint requests to Dr. Ravi Thomas, LV Prasad Eye Institute, L V Prasad Marg, Banjara Hills, Hyderabad – 500 034, India. E-mail: <ravithomas@lvpeye.stph.net>

Manuscript received: 6.4.2002; Revision accepted: 7.11.2002

The present study aimed to compare the IOP lowering ability and safety of latanoprost and brimonidine in Indian patients with OAG.

Materials and Methods

Sample size calculation

The sample size was calculated to detect a difference in mean IOP reduction of 2.5 mmHg between the two drugs, with an a error of 0.05 (two-sided), power of 0.80 and a within-patient standard deviation of 3.0 mmHg. The formula used was:

$n = 2 \times std^2 \times (Z_{\alpha/2}+Z_\beta)^2/d^2 = 2 \times 3.0^2 \times (1.96 + 0.84)^2/2.5^2 = 23$

Std: standard deviation of IOP

Z_α =1.96, α = 0.05

Z_β =0.84, β = 0.2

d = difference in mean IOP reduction = 2.5 mmHg

n = 23. The sample size was 23 in each group.

This prospective study was conducted at a tertiary center. A total of 28 adult patients of either gender diagnosed as primary open angle glaucoma, pseudoexfoliation glaucoma, pigmentary glaucoma or ocular hypertension were enrolled from December 1999 to August 2000.

Inclusion and exclusion criteria

During the month preceding the study, patients had a pre-study screening and eligibility visit. To be eligible for the study the patient had to be over the age of 18 years. At least one eye of each patient had to meet the following criteria: mean IOP (3 readings) more than 21 mmHg and a diagnosis of unilateral or bilateral primary open angle glaucoma, pseudoexfoliation glaucoma, pigmentary glaucoma or ocular hypertension. The angles had to be wide open on gonioscopy. If patients were on medication for glaucoma, they had to be "controlled" with a single medication only. Patients with IOP controlled on more than one drug were not included.

Exclusion criteria were baseline IOP > 21 mmHg, angles considered to be gonioscopically occludable, angle closure glaucoma, IOP not controlled on one medication, history of ocular inflammation or infection within the last 3 months of baseline visits, history of intraocular surgery including laser procedure within 6 months of enrollment in the study, pregnant and lactating women, ocular conditions precluding Goldmann applanation tonometry and known sensitivity to vehicle component.

The diagnosis of glaucoma was based on baseline IOP more than 21 mmHg with typical glaucomatous optic disc changes and corresponding visual field defects on conventional automated perimetry.[1] Ocular hypertension was defined as IOP more than 21 mmHg with normal disc and normal visual field examination.[1]

Study design and plan

The study design was cross-over, open-label and uncontrolled. During the month preceding the study start, patients had a pre-study visit. Patients without previous glaucoma treatment could have their first visit at visit 1 (Baseline). The treatment period for each drug was three months; each drug required four visits, i.e. baseline (visit 1), day 14 (visit 2), week 6 (visit 3), and week 12 (visit 4). A deviation of ± 2 days for visit 2 and ±1 week for subsequent visits was accepted (measured from visit 1). Visit 1 and visit 4 were full day visits, while the visits in between were morning visits. Patients with persisting adverse events at study termination had a follow-up visit within 2-4 weeks after treatment ended . Patients with no persisting adverse events at study termination could be followed up by a telephone report. Interim visits could be scheduled at the discretion of each investigator.

Patients who qualified for the study using ocular hypotensive medication underwent a minimal washout period as follows: topical β- adrenoreceptor antagonist for 3 weeks, topical adrenergic agonist for 2 weeks and cholinergic agonist and systemic carbonic anhydrase inhibitor, 5 days. The washout was followed by the pre-study visit.

Systemic medications including beta-blockers were continued during the study. New systemic medications were permitted provided they had no known effect on the IOP. If a drug with a known effect on IOP was deemed necessary for the patient, the patient had to be withdrawn from the study.

Informed consent was obtained for each patient. A complete ophthalmic history and examination were performed on all patients. A medical history from each subject was obtained, including a list of all systemic medications. The examination included subjective and objective refraction, best corrected Snellen's visual acuity, slitlamp examination, Goldman applanation tonometry, gonioscopy and dilated fundus examination including stereoscopic biomicroscopic examination of the optic disc with a 60 or 90 D lens. IOP was measured with the Goldmann applanation tonometer by the same examiner on the same slitlamp. Iris color was noted at the baseline visit but photographs were not taken. All the patients underwent visual field examination at the first day and at the end of the study. Visual fields were performed on Humphrey field analyzer (30-2) using the SITA (Swedish interactive threshold algorithm) standard program unless the patient had undergone this test within last 6 months.

All patients first received latanoprost for a 12-week period, followed by brimonidine for a period of 6 weeks. Baseline IOP was obtained at the start of the study. Before starting brimonidine, baseline IOP was again obtained a month after stopping latanoprost. During this interim period patients were put on oral Diamox to control IOP if necessary; this was stopped 72 hours before obtaining the baseline IOPs. It was mandatory to obtain a mean IOP of more than 21 mmHg before initiation of any study drug. In the brimonidine group a subset of 16 patients (16 eyes) were followed up for 12 weeks. The uneven follow up was dictated by costs and logistics.

At the baseline visit IOP was measured at 09:00 Hours (±1 hour), 13:00 Hours (±1 hour), and 17:00 Hours (±1 hour). Three IOP reading were recorded and the mean used for analysis. The baseline visit included an ophthalmic

examination including visual field examination if required. Slitlamp biomicroscopy examination was done before instillation of fluorescein to look for aqueous flare and anterior chamber cellular response.

In the first phase of the study all patients were put on latanoprost once a day. They were given three vials of study drug. Two vials were dispensed at the baseline visit and the third vial at the 6-week visit. The instructions were to change the vial at the end of 4 weeks and 8 weeks. Used bottles were returned. Patients were advised to instill eye drops at bedtime, preferably at the same time every day (8 p.m.) A dummy vial was used to teach patients how to apply the medication . Patients were examined at 2 weeks, 6 weeks and 12 weeks.

In second phase of the study, following a washout period of one month all patients were put on brimonidine twice daily. This "off label" dosage reflected current clinical use. Used bottles were returned. Patients were advised to instill eye drops preferably at the same time every day (8 a.m. and 8 p.m.). Two vials were dispensed at baseline visits; one more vial was given at the 2-week visit. For patients who were followed up on brimonidine for 12 weeks, the next two vials were provided at the 6-week visit.

The examination for both phases of the study was similar. Visual acuity and refraction were recorded at 2 weeks and 6 weeks IOP was recorded at 09:00 Hour (±1 hour). Slitlamp examination was performed, especially to look for change iris color and presence of uveitis.

At 12-weeks the best-corrected visual acuity and subjective refraction were performed. IOP was measured at 09:00 Hour (±1 hour), 13:00 Hour (±1 hour), and 17:00 Hour (±1 hour). The complete ophthalmic examination included a dilated fundus examination. Visual field examination was repeated and was compared to the baseline visit field. For patients who exited at 6 weeks after brimonidine, the examination was similar to that done at the final (12-week) visit.

Adverse events (AE) were graded for severity as mild, moderate or severe as follows. *Mild*: did not interfere with the subject's usual function; *Moderate*: interfered to some extent with subject's usual function; and *Severe*: interfered significantly with subject's usual function. The occurrence of a severe AE led to withdrawal from the study.

In case of an adverse event the investigator was required to assess the relationship to the study treatment (definite, possible, unlikely or none) and report the outcome. At every visit patients were specifically asked about ocular comfort.

At baseline and at the end of study IOP was measured at 09:00 Hours (±1 hour), 13:00 Hours (± 1 hour), and 17:00 Hours (±1 hour). The effect on daytime diurnal variation was determined.

Analysis

In patients in whom both eyes were eligible for the study one randomly selected eye was included for analysis. This selection was made using computer-generated blocks. In patients with only one eye eligible for the study, this eye was used for analysis.

The primary outcome measure was the difference in mean IOP reduction between two study drugs. The study results were analysed by comparing the mean IOP at 6 and 12 weeks to mean baseline IOP using the Student's "t" test.[19] The level of significance was set at $P < 0.05\%$. The percentage reduction of IOP in both phases was also determined. Results were also analysed to determine the effect of both the drugs on diurnal variation of IOP.

Results

Patient demography is shown in Table 1. Twenty-eight patients were enrolled in the first stage (Latanoprost) of study. All patients completed this 3-month study duration . Twenty-six (26 eyes) patients completed the 6-week brimominidine study period. Two patients had uncontrolled IOP after one month of brimonidine and were withdrawn. A subset of 16 patients (16 eyes) was continued on brimonidine for 12 weeks; these results were analysed separately.

Intraocular pressure (IOP)

Table 2 shows mean IOP at various follow-up visits (up to 6 weeks) for both groups. At 6 weeks the mean IOP reduction with latanoprost was 11.2 mm Hg (41.6%) compared to 6 mm Hg with brimonidine (22.4%).

Table 3 shows the mean IOP at various follow-up visits for 16 eyes that were followed up for 12 weeks. At the 12-week follow-up the mean IOP reduction in the latanoprost group was 11.1mmHg (±2.80), a 40.95% reduction from baseline. With brimonidine the mean IOP reduction at 12 weeks was 6.9 mmHg (26.1%). Compared to baseline measurements, both the drugs produced a significant ($P< 0.001$) IOP reduction throughout the duration of therapy.

Table 4 shows the percentage IOP reduction at the 6-week and 12-week visits with the two drugs. 85.7% (24) eyes registered more than 25% reduction with latanoprost compared to 13 eyes (46.4%) with brimonidine. Table 5 shows patients achieving specific IOP level at 6 weeks and 12 weeks. 89.3% (25) eyes registered IOP of 18mmHg or less with latanoprost; 42.9% (12) eyes could achieve this with brimonidine.

Table 1. Demographic data

		n=28
Gender	Male	18 (64.3%)
	Female	10 (35.7%)
Age	Mean (standard deviation)	51.2 (12) years
Diagnosis of	POAG	20
study eye	Pseudoexfoliation glaucoma	2
	Pigmentary glaucoma	1
	Ocular hypertension	5
Study eye(s)	Right	15
	Left	13

Table 2. Mean IOP at study visits (up to 6 weeks)

Visits	Latanoprost Mean IOP (mmHg)	Brimonidine Mean IOP (mmHg)	P-value
Baseline	26.9 ± 6.1	26.5 ± 5.7	
Visit 1 (14 days)	15.8 ± 4.5	20.7 ± 6.1	<0.001
Visit 2 (6 weeks)	15.7 ± 3.7	20.5 ± 5.4	<0.001

Table 6 shows mean diurnal variation of IOP at baseline and at 12 week. Both drugs significantly reduced the diurnal variation. Latanoprost reduced diurnal variation of IOP better than brimonidine (P < 0.005).

Adverse events

Two patients in the latanoprost group and 5 patients in brimonidine group had adverse events. Table 7 shows ocular and systemic adverse events.

No patients had alteration in any of the following baseline measurements: visual acuity, slit lamp biomicroscopic examination, including anterior chamber flare or cells.

No patients had an obvious change in iris color by the end of the study in latanoprost group. (Photographs were, however, not available).

No patients had systemic side effects with latanoprost. Two patients complained of drowsiness with brimonidine. None had symptoms severe enough to require termination of the drug during the study period.

Two patients had uncontrolled IOP while on brimonidine and they had to be withdrawn from the study.

Discussion

Various studies have reported a mean IOP reduction of 20 – 35% with latanoprost; and 16-26% with brimonidine.[9-15, 18, 20-22] One study had directly compared the two drugs in the same patient population.[18] A 31% and 15.5% reduction from baseline pressure was reported for the latanoprost and brimonidine group respectively in Caucasian eyes.[18]

Table 3. Mean IOP at various Visits (up to 12 weeks): 16 eyes

Visits	Latanoprost Mean IOP (mmHg)	Brimonidine Mean IOP (mmHg)	P value
Baseline	27.1 ± 6.3	26.4 ± 5.9	
Visit 1 (14 days)	16.0 ± 4.6	20.9 ± 6.0	<0.001
Visit 2 (6 weeks)	15.9 ± 3.8	20.7 ± 5.6	<0.001
Visit 3 (12 weeks)	16.0 ± 3.3	19.5 ± 3.8	<0.001

At 6 weeks latanaprost produced a mean IOP reduction of 41.6% compared to 22.4% with the brimonidine group in the present study. The quantum of reduction and difference was maintained at the 12-week follow-up. At all follow-up visits, latanoprost reduced IOP significantly more than brimonidine. IOP reduction of >25% was achieved in a larger number of eyes (85.7%) with latanoprost as compared to brimonidine (43.1%); lack of response was less likely with latanoprost. One (3.6%) eye had IOP reduction of less than 20% with latanoprost; 11 eyes (39.3%) had IOP reduction less than 20% with brimonidine. Brimonidine had no effect on two eyes; 25 (89.3%) eyes could achieve IOP of 18 mmHg or less at the last visit with latanoprost versus 12 (42.9%) eyes with brimonidine.

It is reported that the action of latanoprost starts within the first 2 weeks, peaks within the first 6 weeks and then stabilises without short-term or long-term drift. The action of brimonidine starts with the first day, reduces by 10-15% within first 2 weeks and stabilizes within 1 month, again without long-term drift.[23] Our results were similar. The effect of both drugs was evident at the first visit and was constant during the study period; we do not have the follow-up to comment on the longterm effect. Two patients did not respond to brimonidine at any of the visits.

Large diurnal variations are an independent risk factor for glaucomatous damage.[24] Both drugs

Table 4. Percentage IOP reductions at 6 weeks and 12 weeks

IOP reduction (%)	Latanoprost		Brimonidine	
	6 weeks	12 weeks	6 weeks	12 weeks
≥ 25%	24(85.7%)	14(87.5%)	12(43.1%)	07(43.75%)
≥ 30%	20(71.4%)	12(75%)	08(28.6%)	05(31.25%)
≥ 40%	14(50%)	09(56.25%)	04 (14.3%)	03(18.75%)

Table 5. Percentage patients achieving specific IOP levels at last visit

IOP at last visit	Latanoprost		Brimonidine	
	6 weeks	12 weeks	6 weeks	12 weeks
≤21 mmHg	27(96.4%)	15(93.75%)	24(85.7%)	14(87.5%)
≤18 mmHg	25(89.3%)	14(87.5%)	12(42.9%)	07(43.75%)
≤15 mmHg	13(46.4%)	08(50%)	04(14.3%)	03(18.75%)

Table 6. Diurnal variation of IOP at baseline and 12 weeks

	Baseline IOP (mmHg)			12 week IOP (mmHg)		
	Highest	Lowest	Difference	Highest	Lowest	Difference
Latanoprost	29.7	24.6	5.1	18.1	15.0	2.9
Brimonidine	29.8	25.1	4.7	21.2	17.3	3.9

Table 7. Adverse events

Adverse event	Latanoprost	Brimonidine
Conjunctival hyperemia	1	3
Iris hyperchromia	0	0
Hypertrichosis	0	0
Drowsiness	0	2

significantly reduced diurnal variation in our patients. The amount of reduction in diurnal variation was significantly better with latanoprost than with brimonidine.

On the whole, adverse effects were uncommon. Hyperemia is a common side effect with latanaprost. Surprisingly, in our patients this was more commonly seen with brimonidine. We did not find aqueous flare or cells on slitlamp examination with latanoprost. Other studies including those using laser flare meters report similar findings.[11-13,25] None of our patients had iris hyperchromia, a known side effect of latanoprost. The short duration of treatment and purely clinical examination precludes any comment on this. [11-13]

The documented side effect of drowsiness with brimonidine was seen in this study too, but was not severe enough to withdraw the drug. None of our patients had allergy, a known side effect, again perhaps explained by the short nature of the study.[26,27]

A potential flaw in the comparison is that brimonidine was used twice daily rather than thrice as approved by the U.S. Food and Drug Administration.[28] It can be argued that IOP reduction and diurnal control might have been better with the thrice-daily dosage. We elected to compare the commonly prescribed twice-daily regimen.

In conclusion both latanoprost and brimonidine reduce IOP effectively in south Indian patients. Mean IOP lowering and stabilization of the diurnal curve is better with latanoprost. No patient had side effects requiring withdrawal of either study medication.

References

1. Wilson RM. Epidemiology of chronic open angle glaucoma. In:Ritch R, Sheilds B, Krupin T, editors. *The Glaucomas*, 2nd ed. St. Louis: Mosby Year Book, 1996. Vol 2, pp 758-68.
2. Collaborative Normal-Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. *Am J Ophthalmol* 1998;126:498-505.
3. The advanced glaucoma intervention study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. *Am J Ophthalmol* 2000;130:429-40.
4. Diggory P, Heyworth P, Chau G, McKenzie S, Sharma A, Luke I. Improved lung function tests on changing from topical timolol. Non-selective beta-blockade impairs the lung function tests in elderly patients. *Eye* 1993;7:661-67.
5. Avorn J, Glynn R, Gurwitz JH, Bohn RL, Mamane M, Everilt DE. Pulmonary effects of beta-blockers. *J Glaucoma* 1993;2:158-65.
6. Camras CB. Prostaglandins. In: Ritch R, Shields MB, Krupin T, editors. *The Glaucomas*, 2nd ed. St. Louis: Mosby- Year Book, 1996. Vol 2, pp 1449-61.
7. Alm A, Villumsen J. Ph XA34, a new potent ocular hyporensive drug, A study on dose-response relationship and on aqueous humor dynamics in healthy volunteers. *Arch Ophthalmol* 1991;109:1564-68.
8. Villumsen J, Alm A. Ph XA34, a prostagndins F2a analogue effect on intraocular pressure in patients with ocular hypertension. *Br J Ophthalmol* 1992;76:214-17.
9. Camras CB, Schumer RA, Marks A et al. Intraocular pressure reduction with Ph XA34, a new prostaglandins analogue, in patients with ocular hypertensions. *Arch Ophthalmol* 1992;110:1733-38.
10. Stjernschantz J, Alm A. Latanoprost as a new horizon in the medical management of glaucoma. *Curr Opin Ophthalmol* 1996;7:11-17.
11. Camras CB. Comparison of latanoprost and timolol in patients with ocular hypertension and glaucoma: a six-month masked, multicenter trial in the United States. The United States Latanoprost Study Group. *Ophthalmology* 1996;103:138-47.
12. Watson PG, The Latanoprost Study group. Latanoprost: Two years' experience of its use in United Kingdom. *Ophthalmology* 1998;05:82-87.
13. Alm A, Widengard, Latanoprost: Experience of 2-year treatment in Scandinavia. *Archives of Ophthalmology Scandinavia*. 2000;78:71-76.
14. Azuara-Blanco A, Katz LJ, Spaeth GL, Wilson RP, Moster MR, Flartey KJ. Effect of latanoprost on intraocular

pressure in patients with glaucoma on maximal tolerated medical treatment. *Br J Ophthalmol* 1997;81:1116.

15. Mishima HK, Masuda K, Kitazawa Y, Azuma I, Araie M. A comparison of latanoprost and timolol in primary open-angle glaucoma and ocular hypertension. A 12-week study. *Arch Ophthalmol* 1996;114:929-32.
16. Toris CB, Camras CB, Yablonski ME. Acute versus chronic effects of brimonidine on aqueous humor dynamics in ocular hypertensive patients. *Am J Ophthalmol* 1999;128:8-14.
17. Schuman JS, Horwitz B, Choplin NT, David R, Albracht D, Chen K. A controlled randomized, Multicentric Clinical Trial, A 1 year study of Brimonidine twice daily in Glaucoma and Ocular Hypertension. *Arch Ophthalmol* 1997;115:847-52.
18. Stewart WC, Day DG, Stewart JA, Schuhr J, Latham KE. The efficacy and safety of Latanoprost 0.005% Once a daily Versus Brimonidine 0.2% Twice daily in a Open-Angle Glaucoma or Ocular Hypertension. *Am J Ophthalmol* 2001;131:631-35.
19. Rao PSSS, Richard J. *An Introduction to Biostatistics*. 3rd ed. Mumbai: Prentice-Hall of India. pp. 70-75.
20. Katz LJ, The Brimonidine study group. Brimonidine tartrate 0.2 % twice daily VS Timolol 0.5 % twice daily. 1 year results in glaucoma patients. *Am J Ophthalmol* 1999:127:20-26.
21. Leblanc RP. The Brimonidine study group. Twelve-month results of an ongoing randomized, trial comparing Brimonidine tartrate 0.2 % and Timolol 0.5 % given twice daily with Glaucoma and ocular hypertension. *Ophthalmology*1998:105:1960-67.
22. Serle JB. The Brimonidine study group III. A comparison of safety and efficacy twice-daily Brimonidine 0.2 % VS betoxolol 0.25 % in subjects with elevated intraocular pressure. *Survey of Ophthalmology* 1996:41:S39-S47.
23. Walters DR. development and use of Brimonidine in treating acute and chronic elevation of intra ocular pressure. A review of safety, efficacy and dosing studies. *Survey of Ophthalmology* 41: 1996: S19-S26.
24. Ziai N, Dolan JW, Kacere RD, Brubaker RF. The effects on aqueous dynamics of PhxA 41, a new prostaglandins F2a analogue, after topical application in normal and ocular hypertensive eyes. *Am J Ophthalmol* 1993;111:1351-58.
25. Asrani S, Zeimer R, Wilensky J, Gieser D, Vitale S, Lindenmuth K. Large diurnal fluctuations in intra ocular pressure are an independent risk factor in patients with glaucoma. *J Glaucoma* 2000;2:134-42.
26. Derick RJ, Robin AL, Walters TR, Barnebey HS, Choplin N, Schuman J, et al. Brimonidine tartrate: a one-month dose response study. *Ophthalmology* 1997;104:131-36.
27. Nordland JR, Pasquale LR, Robin AL, Rudikoff MT, Ordman J, Chen KS, et al. The cardiovascular, Pulmonary and ocular hypotensive effecys of 0.2 % Brimonidine: *Arch Ophthalmol* 1995;113:77- 83.
28. Walters DR. development and use of Brimonidine in treating acute and chronic elevation of intra ocular pressure. A review of safety, efficacy and dosing studies. *Survey of Ophthalmology* 41: 1996: S19-S26

Stories from stamps

Ibn-Al-Hiatham (Al Hazen) (965-1039 AD)

was born at Besra in Persian Gulf. He studied medicine, mathematics, physics and astronomy. He was the first to formulate the present-day concept of light and vision, although he was convinced that the lens was the central organ of vision. He showed that the corpuscular emission theory of vision was wrong and that vision was due to rays passing from the object to the eye. For the first time he established that the angle of incidence is equal to the angle of reflection. He was called to Egypt by Caliph Al Hakm to construct an apparatus to control the water of the Nile. But finding that he was unable to fulfill the Caliph's boast, he took refuge to feigned insanity till the death of Caliph. Then he promptly regained his reason and lived a life of quiet contentment until his death. He is considered the *'Father of Optics"*.

Courtesy: Samar K Basak, MD, DNB, Disha Eye Hospitals & Research Centre, Barrackpore, West Bengal-743 120, India.
E-mail: <disha@cal2.vsnl.net.in>