A COMPARATIVE STUDY TO ASSESS THE EFFICACY AND TOLERABILITY OF LATANOPROST, BIMATOPROST AND TRAVOPROST IN PATIENTS WITH OPEN ANGLE GLAUCOMA

Prempal Kaur[1], Vishal Brar[2], Bhavkaran Singh Bal[3], Inderjit Kaur[4]

[1]Associate Professor, Department of Ophthalmology, Regional Institute of Ophthalmology, Government Medical College, Amritsar.
[2]Junior Resident, Department of Ophthalmology, Regional Institute of Ophthalmology, Government Medical College, Amritsar.
[3]Junior Resident, Department of Ophthalmology, Regional Institute of Ophthalmology, Government Medical College, Amritsar.
[4]Professor, Department of Ophthalmology, Regional Institute of Ophthalmology, Government Medical College, Amritsar.

ABSTRACT

Glaucoma is the leading cause of irreversible blindness in the world as it can remain asymptomatic until it causes severe visual loss. The target intraocular pressure with which progression is slowed sufficiently to avoid functional impairment should be achieved with the fewest medications and minimum adverse effects. The choice of medicine may be influenced by efficacy, cost, adverse effects, and dosing schedules. In general, prostaglandin analogues (PGA) are the first-line of medical therapy. These drugs are administered once at night and have few systemic adverse effects. The study was conducted to compare the efficacy and safety of available PGAs.

MATERIAL AND METHODS

The study was conducted on sixty diagnosed cases of primary open angle glaucoma visiting the Outpatient Department of Regional Institute of Ophthalmology, Government Medical College, Amritsar. They were divided into three groups of twenty each. Each group was put on either of these anti-glaucoma topical drug (PGA - latanoprost 0.005%, travoprost 0.004% and bimatoprost 0.03%) for three months duration. IOP at 9:00 AM ± 1 hr. and 4:00 PM ± 1 hr. were taken before and after 1 month and 3 months of treatment. The results of the reduction in mean IOP in each group were compared and analysed.

OBSERVATIONS

Mean baseline IOP at 8 AM in each group was similar (p value 0.772). Average decrease in IOP between the pretreatment (Baseline IOP) and post-treatment levels (i.e. at 3 months) was 31.90% in Group 1 (Bimatoprost Group), 32.97% in Group 2 (Latanoprost Group) and 34.75% in Group 3 (Travoprost Group). When we applied paired t test, in each group, p value was <0.001, showing a statistically significant change. Once the efficacy of drugs was seen, we compared the efficacy of 3 groups with each other by applying ANOVA, P value was 0.108 which is not statistically significant.

CONCLUSIONS

Individually Bimatoprost, Latanoprost and Travoprost significantly lowered the intraocular pressure but this reduction was not statistically significant when compared amongst themselves. All these three PGAs are quite safe drugs with no serious adverse events reported during our study. Conjunctival hyperaemia was the most common side effect followed by itching, burning and stinging sensation. Latanoprost exhibited the lowest incidence of adverse effects whereas Bimatoprost and Travoprost were similar in their tendency to cause these.

KEYWORDS

Glaucoma, Intraocular Pressure, Open Angle Glaucoma.

HOW TO CITE THIS ARTICLE: Kaur P, Brar V, Bal BS, et al. A comparative study to assess the efficacy and tolerability of latanoprost, bimatoprost and travoprost in patients with open angle glaucoma. J. Evid. Based Med. Healthc. 2016; 3(44), 2169-2175. DOI: 10.18410/jebmh/2016/482

INTRODUCTION: Glaucoma affects more than 70 million people worldwide with approximately 10% being bilaterally blind, making it the leading cause of irreversible blindness in the world.[1] Glaucoma can remain asymptomatic until it is severe, resulting in a high likelihood that the number of affected individuals is much higher than the number known to have it.[2,3]

Financial or Other, Competing Interest: None.
Submission 07-05-2016, Peer Review 21-05-2016,
Acceptance 27-05-2016, Published 31-05-2016.
Corresponding Author:
Dr. Prempal Kaur,
#333A, Medical Enclave, Amritsar-143001.
E-mail: ppkbal@gmail.com
DOI: 10.18410/jebmh/2016/482

Population level surveys suggest that only 10% to 50% of people with glaucoma are aware they have it.[2-6]

Although the pathogenesis of glaucoma is not fully understood, the level of intraocular pressure is related to retinal ganglion cell death. The balance between secretion of aqueous humor by the ciliary body and its drainage through two independent pathways—the trabecular meshwork and uveoscleral outflow pathway—determines the intraocular pressure (IOP). Inpatients with open-angle glaucoma (OAG), there is increased resistance to aqueous outflow through the trabecular meshwork. In contrast, the access to the drainage pathways is obstructed typically in patients with angle-closure glaucoma.

Current management guidelines from the American Academy of Ophthalmology Preferred Practice Pattern recommend lowering the IOP towards a target level, which is a value or range of values at which the clinician believes that the rate of disease progression will be slowed sufficiently to avoid functional impairment from the disease.[7] Target IOP levels for a particular eye are established from pretreatment pressure levels that were associated with retinal damage, the severity of damage, risk factors for progression, life expectancy, and potential for adverse effects from treatment. In general, the initial target aims for a 20% to 50% reduction in pressure; however, the target pressure needs to be continuously reassessed during patient follow-up, depending on the evolution of the disease.[7] The target IOP should be achieved with the fewest medications and minimum adverse effects. Several different classes of pressure-lowering medications are available. Medication choice may be influenced by cost, adverse effects, and dosing schedules. In general, prostaglandin analogues (PGA) are the first-line of medical therapy. These drugs reduce IOP by reducing outflow resistance resulting in increased aqueous flow through the uveoscleral pathway.[8] These drugs are administered once at night and have few systemic adverse effects. However, they can cause local adverse effects such as conjunctival hyperaemia, elongation and darkening of eyelashes, loss of orbital fat, induced iris darkening, and periocular skin pigmentation. Prostaglandins are known mediators of inflammation. At high doses, they can induce increased IOP. Conversely, at low doses prostaglandins have been shown to lower IOP.[9] Latanoprost, an ester prodrug analogue of a prostaglandin F2a is a selective prostanoid FP receptor agonist. It reduces IOP by increasing the aqueous outflow from the eye, through the uveoscleral pathway.[10] How this occurs is not known, but it is thought that they bind to the receptors of the ciliary body and upregulate metalloproteinases. These enzymes remodel the extracellular matrix and make the area more permeable to aqueous humor, thereby increasing outflow.[11] A single drop of latanoprost 0.005% solution (about 1.5 µg) once daily has been established as the most effective dosage regimen.[12]

Since its introduction in 1996 in the US, latanoprost has become the most popular drug for the treatment of glaucoma around the world. It was found to be effective in reducing IOP during the evening as well as during the day.[13] It exhibits greater ocular tolerability.[14]

It is available in 0.005% solution, administered in the evening and requiring refrigeration for longterm storage as well as protection from sunlight and stability.[15] Conjunctival hyperaemia occurs within the first two days after instillation of latanoprost treatment, which diminishes with time (after two to four weeks). Increased iris pigmentation has been reported in 5 to 25% of glaucoma patients treated with latanoprost. Iridial darkening may be a result of a prostaglandin-stimulated increase in melanin production.[16] Several effects on eyelid and lashes were seen, following treatment with latanoprost, including an increase in the length, number, colour and thickness.[17] previous surgery or a history of intraocular inflammation may predispose some glaucoma patients treated with latanoprost to cystoid macular oedema or uveitis. Systemic adverse effects are relatively not seen because the drug and its metabolites have rapid elimination half-life.

Bimatoprost is a synthetic prostamide analogue. Because of the unique structural presence of an amide ester group at the carboxy-terminal end of the α carbon chain Bimatoprost interacts with α prostamide receptor in the trabecular meshwork to increase outflow facility.[18] Bimatoprost enhances the pressure-sensitive outflow pathway and may also cause an increase in the rate of flow via the pressure-insensitive outflow pathway. Bimatoprost is available in 0.03% or 0.01% ophthalmic solution and is administered once daily in the evening. It does not require refrigeration to maintain stability.[19]

Travoprost is a synthetic prostaglandin F 2α analogue. Following absorption into the eye, the free acid form of travoprost interacts with the endogenous FP prostanoid receptor, to enhance aqueous humor outflow and lower IOP. It differs from other PGAs, which exhibit partial agonist activity, in that it is a full agonist at the PGF2α receptor. Travoprost provides robust lowering of IOP with little diurnal fluctuation and results in low target pressures in a large percentage of the patients. It is a very stable compound, to be applied once daily in the evening. It does not require refrigeration and protection from sunlight. Macular oedema, including cystoid macular oedema, is cited as a warning in the US product labelling for travoprost, as it is for other prostaglandin analogues.[20-22]

MATERIAL AND METHODS: The study was conducted on a total of sixty diagnosed cases of primary open angle glaucoma visiting the Outpatient Department of Regional Institute of Ophthalmology, Government Medical College, Amritsar. They were divided into three groups of twenty each. Each group was treated with either of these anti-glaucoma topical drug (PGA - latanoprost 0.005%, travoprost 0.004% and bimatoprost 0.03%) after explaining the nature of study and obtaining their written consent. A randomised prospective trial was conducted on the efficacy and tolerability of these drugs in the treatment of POAG. Patients with POAG of both sexes in the age group 21-70 years with IOP of ≥ 22 mm of Hg at least in one eye by Applanation Tonometer were included in the study. Patients with any acute ocular inflammation like conjunctivitis, uveitis, corneal ulcer or with conditions like macular oedema or any progressive retinal degeneration were excluded. Patients with angle closure glaucoma or secondary open angle glaucoma or with allergy to these drugs were also excluded from the study. IOP of the patients was measured with the Goldman's Applanation Tonometer and the patients fulfilling the criteria were enrolled. Patients with IOP ≥22 mm Hg in at least one eye were divided into three groups of twenty each and each group was administered one of the three different drugs. IOP measurement was done at 0(Baseline), 1 and 3 months.

Keeping in mind the diurnal variation in IOP, it was measured at 9:00 am and 4:00 pm ± 1 only and could not be measured at night. Patients who were not controlled with one drug were subjected to other drug and were considered as dropouts from the study. Patients were followed for 3 months and the IOP readings were tabulated and analysed.

OBSERVATIONS: 60 patients were divided into 3 groups of 20 patients each as follows:
Group 1: Twenty patients were treated with Bimatoprost 0.03% one drop at night time.

Group 2: Twenty patients were treated with Latanoprost 0.005% one drop at night time.

Group 3: Twenty patients were treated with Travoprost 0.004% one drop at night time.

Age Group Yrs.	Group-1	Group-2	Group-3	Total	% Age
21-30	-	-	1	1	1.7 %
31-40	-	2	3	5	8.3 %
41-50	6	3	2	11	18.3 %
51-60	8	5	5	18	30 %
61-70	6	10	9	25	41.7 %
	20	**20**	**20**	**60**	

Table 1: Age wise Distribution of POAG

Maximum no. of patients 25 (41.7%) were in age group of 61-70 yrs. followed by 18 (30%) in 51-60 yrs. There were 11 (18.3%) cases in the 41-50 yrs. bracket and 5 (8.3%) cases in 31-40 age group. Only 1 (1.7%) case was recorded in the 21-30 yrs.

Sex	Group-1	Group-2	Group-3	Total	% Age
Male	7	9	15	31	51.7%
Female	13	11	5	29	48.3%
	20	**20**	**20**	**60**	

Table 2: Sex wise Distribution of POAG

Area	Group-1	Group-2	Group-3	Total	% Age
Rural	9	8	7	24	40%
Urban	11	12	13	36	60%
	20	**20**	**20**	**60**	

Table 3: Number of Patients from Rural and Urban Areas

Visual Acuity	Group 1	Group 2	Group 3	Total
6/6	9	8	7	24
6/9	11	13	19	43
6/12	8	12	6	26
6/18	6	2	3	11
6/24	1	2	1	4
6/36	-	-	2	2
6/60	2	-	-	2
<6/60	3	3	2	8

Table 4: Pretreatment Visual Acuity (Best Corrected)

Modes of Presentation	Group 1	Group 2	Group 3	Total
Decreased Visual Acuity/Blurring of vision	10	10	10	30
Eye ache/Mild headache	4	3	5	12
Family History	2	2	1	5
Symptomless	4	5	4	13

Table 5: Various Modes of Presentation (Number of patients)

Findings	Group 1	Group 2	Group 3	Total
Circumcorneal congestion	-	-	-	-
Corneal Oedema	-	-	-	-
Ant Chamber Shallow Normal	- 40	- 40	- 40	- 120
Normal pupillary reaction	34	38	26	98
Sluggish pupillary reaction or RAPD	6	8	8	22
Immature senile cataract	10	8	10	28
Mature senile cataract	6	4	2	12
Iris atrophy	1	1	-	2

Table 6: Patient findings on Presentation (Number of eyes)

Fundus Findings	Group 1	Group 2	Group 3	Total
Nasal shift of vessels	6	8	6	20
Glaucomatous cupping with a cup disc ratio>0.5	28	26	28	82
Glaucomatous optic atrophy	1	1	1	3
Disc haemorrhages	2	-	1	3
Fundus details not clear due to hazy media	6	4	2	12

Table 7: Pretreatment Fundus Findings (Number of eyes)

DDLS stage	Group-1	Group-2	Group-3
1-4 (At risk)	29	25	28
5-7 (Glaucomatous damage)	10	14	11
8-10 (Glaucomatous disability)	1	1	1

Table 8: Disc Damage Likelihood Scale (DDLS)-Number of eyes

VFI	Group-1	Group-2	Group-3
>90	24	15	23
71-90	7	11	10
51-70	-	3	2
≤50	4	6	1
Unrecordable	5	5	4

Table 9: Visual Field Index (Humphrey Visual Field SAP 24-2 SITA Standard Strategy)-Number of Eyes

IOP range	Group 1	Group 2	Group 3
21-25	26	27	29
26-30	13	11	11
>30	1	2	-

Table 10: Pretreatment IOP level-Number of Eyes

Time	≤15	16-20	21-25	26-30	>30	Dropout
Day 0 (Baseline)	-	-	26	13	1	-
At 1 month visit	-	28	12	-	-	-
At 3 month visit	10	27	3	-	-	-

Table 11: Changes in IOP with Treatment in Group 1(Bimatoprost)

Time	≤15	16-20	21-25	26-30	>30	Dropout
Day 0 (Baseline)	-	-	27	11	2	-
At 1 month visit	4	27	8	1	-	-
At 3 month visit	11	27	1	1	-	-

Table 12: Changes in IOP with Treatment in Group 2 (Latanoprost)

Time	≤15	16-20	21-25	26-30	>30	Dropout
Day 0 (Baseline)	-	-	29	11	-	-
At 1 month visit	4	32	4	-	-	-
At 3 months visit	14	26	-	-	-	-

Table 13: Changes in IOP with Treatment in Group 3 (Travoprost)

Ocular Symptoms	Group 1	Group 2	Group 3	Total
Conjunctival Hyperaemia	9	7	9	25
FB sensation	2	1	1	4
Lengthening/ Darkening of eye lashes	-	-	-	-
Darkening of periocular skin	-	-	-	-
Increased Iris pigmentation	-	-	-	-
Burning/ stinging/itching	4	3	5	12
Any other	-	-	-	-

Table 14: Comparison of Ocular Side Effects (Number of patients)

STATISTICAL ANALYSIS: Mean baseline IOP at 8 AM were similar (p=.772) in all the groups. Average decrease in IOP between the pretreatment (Baseline IOP) and post-treatment levels (i.e. at 3 months) was 31.90% in Group 1 (Bimatoprost Group), 32.97% in Group 2 (Latanoprost Group) and 34.75% in Group 3 (Travoprost Group).

When we applied paired t test on each Group P value was <0.001, showing a statistically significant change in all the three groups. Likewise, when we applied test on Group 2 i.e. on Latanoprost Group, p value was <0.001 and on applying test on Group 3 i.e. on Travoprost Group, p value was <0.001 which again is statistically significant. Once the efficacy of drugs was seen, we compared the efficacy of 3 groups with each other by applying ANOVA, P value was 0.108 which is not statistically significant.

DISCUSSION: Present study was conducted on 60 patients of POAG. Maximum number of patients (41.7%) were in the age group of 61-70 yrs. followed by 30% of 51-60 yrs. In a study by Tuck MW, of the total cases, 7% were less than 55 years old, 44% were aged 55-74 years, and 49% were older. Rudnicka AR also showed the steepest increase in POAG prevalence with age.[23,24] Sia DI et al (2010), Xu L et al (2004) reported higher incidence of glaucoma in patients with increasing age. Age is a risk factor for the conversion from Ocular Hypertension to Primary Open Angle Glaucoma

as studied by Gordon M O et al (2002). In The Chennai Glaucoma Study conducted by Ronnie George et al, the prevalence of POAG in a ≥ 40 years old South Indian population increased with age, thus supporting our study.[25-28] In the present study, 51.7% patients were male and 48.3% female. Similarly, Naila Ali et al 2007 had reported that gender doesn't seem to have any significant influence on causation or occurrence of POAG. However, Dielemans et al,(1994), Xu L et al,(2004) Rudnicka AR et al (2006), Francis AW et al (2014) found higher prevalence in males than females. In another study, Al Mansouri F (2002) in Qatar found fewer males (41.6%) and more females (58.4%) to be suffering from POAG.[24,29-32]

In the present study, 40% patients were from rural area and 60% from the urban populace. In the Chennai Glaucoma Study by Lingam Vijaya et al (2008), the prevalence of POAG in a ≥ 40 years old South Indian urban population was 3.51% higher than the rural population.[33] Similar results were found by Francis AW et al in 2014.[31] in Andhra Pradesh.

Eye study by Chandrasekhar et al (2010), the prevalence of POAG was greater in urban than in rural population (4% vs. 1.6% p< 0.001), thus supporting our study.[34]

The patients with POAG were divided into three groups of 20 each and treated with Bimatoprost 0.03%, Latanoprost 0.005% and Travoprost 0.004% for three months duration. IOP at 9:00 AM ± 1 hr. and 4 PM ± 1 hr. were taken before and after 1 month and 3 months of treatment. The results of the reduction in mean IOP levels in each group were analysed.

In group 1 (Bimatoprost Group), there was a reduction of 19.46% in mean IOP at the end of first month and 31.90% at the end of the study i.e. at 3 months. In Group 2 (Latanoprost Group), the mean reduction in IOP at the end of first month was 27.07% and 32.97% at the end of study. In Group 3 (Travoprost Group), the mean reduction in IOP at the end of first month was 27.76% and 34.75% at the end of study. The findings of our study suggest that all the three PGAs i.e., Bimatoprost 0.03%, Latanoprost 0.005% and Travoprost 0.004% provide substantial lowering of IOP in POAG subjects. However, on comparing the IOP lowering efficacy between the three groups, the result was not statistically significant.

Gandolfi et al in year 2001 compared the efficacy of Latanoprost and Bimatoprost over 3 months and concluded that Bimatoprost was statistically superior in achieving low target pressures at every time throughout the study.[35]

This was contrary to our study. Richard K Parrish et al (2003), Luca Rossetti et al (2006) and Yildirim, Nilgun et al (2008) in their respective studies on POAG patients, compared the IOP lowering efficacy of PGAs and found no statistically significant difference in IOP lowering efficacy between Bimatoprost, Latanoprost and Travoprost which supports our study.[14,36,37] In 2005, Jin et al reported an average IOP reduction of 6.95±3.24 (29.9%) after 6 weeks of therapy with Bimatoprost while the IOP reduction reported with Latanoprost was 8.18±3.89 (34.3%). There was no statistically significant difference between the 2 groups. In 2006, Kong et al reported an IOP reduction from 24.57±3.6 to 15.29±2.67 with a reduction of 37.8% in the Latanoprost group, while IOP decrease from 24.54±2.95 to 16.29±3.11 a reduction of 33.6% in the Travoprost group and the IOP reduction was 25.41±3.63 to 16.00±4.45, a reduction of 37% in Bimatoprost group. They found no statistically significant difference in effectiveness among the three PGA mono therapies.[38,39]

Our study is supported by studies of Jin et al and Kong et al who observed no statistically significant difference in the IOP reduction efficacy of PGAs.[38,39] in months. Randomised clinical trial, Robert S. Noecker et al compared the IOP lowering efficacy of Bimatoprost and Latanoprost in patients with ocular hypertension and concluded that Bimatoprost is more effective than Latanoprost in lowering IOP.[40] In a study conducted by Dr Gursoy Alagoz et al (2008), comparing IOP lowering efficacy of Bimatoprost and Travoprost in patients with open angle glaucoma concluded that there was no significant difference between the two drugs on all followup visits over 6 months.[41] Similarly, Anne J Lee (2010) and Huang et al (2011) found a similar IOP lowering efficacy between Latanoprost, Travoprost and Bimatoprost, thus supporting our study.[42,43] There were no serious adverse effects that could be attributed to PGAs. Hyperaemia was the most common side effect of the drugs followed by itching/burning/stinging sensation. Of all the three, Latanoprost 0.005% exhibited the lowest incidence of adverse effects whereas Bimatoprost 0.03% and Travoprost 0.004% were almost similar in their tendency to cause adverse effects. Gandolfi et al (2001) performed a three month comparison of Bimatoprost and Latanoprost in patients with glaucoma. They concluded that both drugs are safe and well tolerated. Conjunctival hyperaemia was more common with Bimatoprost while headache was more frequent with Latanoprost. Richard K. Parish et al (2003) compared the three drugs Latanoprost, Travoprost and Bimatoprost in patients of open angle glaucoma over 12 weeks. Fewer Latanoprost treated patients reported ocular adverse events and fewer reported hyperaemia in accordance with our study.[35,14]

CONCLUSION: Individually Bimatoprost, Latanoprost and Travoprost significantly lowered the intraocular pressure but this reduction in intraocular pressure was not statistically significant when compared amongst themselves. All these three PGAs are quite safe drugs with no serious adverse events reported during our study. Conjunctival hyperaemia was the most common side effect followed by itching, burning and stinging sensation. Latanoprost exhibited the lowest incidence of adverse effects whereas Bimatoprost and Travoprost were similar in their tendency to cause these.

LIMITATIONS: The major limitation of our study was its short duration of treatment. In clinical practice, PGAs are prescribed for a long period. Another major limitation was small sample size of patients as only 20 patients were taken up in each group. Keeping in mind the diurnal variation of

IOP, it was measured 2 times in a day only i.e at 9:00 AM ± 1 hr. and 4:00 PM ± 1 hr. and no night time measurement could be taken. Adverse effects of PGAs generally don't show up within a short period of time of initiation of therapy, so a longterm study will be more apt to know the real adverse events that creep in with PGAs.

REFERENCES

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90(3):262–267.
2. Leite MT, Sakata LM, Medeiros FA. Managing glaucoma in developing countries. Arq Bras Oftalmol 2011;74(2):83–84.
3. Rotchford AP, Kirwan JF, Muller MA, et al. Temba glaucoma study: a Population - based cross-sectional survey in urban south Africa. Ophthalmology 2003;110(2):376–382.
4. Hennis A, Wu SY, Nemesure B, et al. Awareness of incident open-angle glaucoma in a population study: the Barbados eye studies. Ophthalmology 2007;114(10):1816–1821.
5. Sathyamangalam RV, Paul PG, George R, et al. Determinants of glaucoma awareness and knowledge in urban Chennai. Indian J Ophthalmol 2009;57(5):355–360.
6. Budenz DL, Barton K, Whiteside-de Vos J, et al. Prevalence of glaucoma in an urban West African population: the Tema eye survey. JAMA Ophthalmol 2013;131(5):651-658.
7. American Academy of Ophthalmology Preferred Practice Patterns Committee GP. Ophthalmology. Chicago, Illinois: American Academy of Ophthalmology; 2010. Preferred practice pattern: primary open-angle glaucoma.
8. Gaton DD, Sagara T, Lindsey JD, et al. Increased matrix metalloproteinases 1, 2, and 3 in the monkey uveoscleral outflow pathway after topical prostaglandin F(2 alpha)-isopropyl ester treatment. Arch Ophthalmol 2001;119(8):1165–1170.
9. Friström B, Nilsson SE. Interaction of PhXA41, a new prostaglandin analogue, with pilocarpine: a study on patients with elevated intraocular pressure. Arch Ophthalmol 1993;111(5):662–665.
10. Novack GD, O'Donnell MJ, Molloy DW. New glaucoma medications in the geriatric population: efficacy and safety. J Am Geriatr Soc 2002;50(5):956–962.
11. Marquis RE, Whitson JT. Management of glaucoma: focus on pharmacological therapy. Drugs Aging 2005;22(1):1–21.
12. Patel SS, Spencer CM. Latanoprost. A review of its pharmacological properties, and tolerability in the management of primary open-angle glaucoma and ocular hypertension. Drugs Aging 1996;9(5):363–378.
13. Orzalesi N, Rossetti L, Invernizzi T, et al. Effect of timolol, latanoprost, and dorzolamide on circadian IOP in glaucoma or ocular hypertension. Invest Ophthalmol Vis Sci 2000;41(9):2566–2573.
14. Parrish RK, Palmberg P, Sheu WP, et al. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. Am J Ophthalmol 2003;135(5):688–703.
15. Morgan PV, Proniuk S, Blanchard J, et al. Effect of temperature and light on the stability of latanoprost and its clinical relevance. J Glaucoma 2001;10(5):401–405.
16. Wistrand PJ, Stjernschantz J, Olsson K. The incidence and time-course of latanoprost induced iridial pigmentation as a function of eye color. Surv Ophthalmol 1997;41(Suppl 2):S129–138.
17. Johnstone MA. Hypertrichosis and increased pigmentation of eyelashes and adjacent hair in the region of the ipsilateral eyelids of patients treated with unilateral topical latanoprost. Am J Ophthalmol 1997;124(4):544–547.
18. Sherwood M, Brandt J. Six-month comparison of bimatoprost once-daily and twice-daily with timolol twice-daily in patients with elevated intraocular pressure. Surv Ophthalmol 2001;45(Suppl 4):S361–368.
19. Cantor LB. An update on bimatoprost in glaucoma therapy. Expert Opin Pharmacother 2002;3(12):1753–1762.
20. Suzuki ER, Franklin LM, da Silva LJ, et al. Comparison of the efficacy and safety of travoprost with a fixed-combination of dorzolamide and timolol in patients with open-angle glaucoma or ocular hypertension. Curr Med Res Opin 2006;22(9):1799–1805.
21. Dubiner HB, Sircy MD, Landry T, et al. Comparison of the diurnal ocular hypotensive efficacy of travoprost and latanoprost over a 44-hour period in patients with elevated intraocular pressure. Clin Ther 2004;26(1):84–91
22. Whitson JT. Travoprost: a new prostaglandin analogue for the treatment of glaucoma. Expert Opin Pharmacother 2002;3(7):965–977.
23. Tuck MW, Crick RP. The age distribution of primary open angle glaucoma. Ophthalmic Epidemiol 1998;5(4):173-183.
24. Rudnicka AR, Mt-Isa S, Owen CG, et al. Variations in primary open-angle glaucoma prevalence by age, gender, and race: a Bayesian meta-analysis. Invest Ophthalmol Vis Sci 2006;47(10):4254-4261.
25. Sia DI, Edussuriya K, Sennanayake S, et al. Prevalence of and risk factors for primary open-angle glaucoma in central Sri Lanka: the Kandy eye study. Ophthalmic Epidemiol 2010;17(4):211-216.
26. Gordon MQ, Beiser JA, Brandt JD, et al. The ocular hypertension treatment study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120(6):714-720.

27. Xu L, Chen JH, Li JJ, et al. The prevalence and its screening methods of primary open angle glaucoma in defined population -based study of rural and urban in Bejing. Zhonghua Yan Ke Za Zhi 2004;40(11):726-732.
28. George R, Hemamalini Arvind, Baskaran M, et al. The Chennai glaucoma study: prevalence and risk factors for glaucoma in cataract operated eyes in urban Chennai. Indian J Ophthalmol 2010;58(3):243-245.
29. Nalia Ali, Syed Ali Wajid, Nasir Saeed, et al. The relative frequency and risk factors of primary open angle glaucoma and angle closure glaucoma. Pak J Ophthalmol 2007;23(3):117-121.
30. Dielemans I, Vingerling JR, Wolfs RC, et al. The prevalence of primary open-angle glaucoma in a population-based study in the Netherlands. The Rotterdam study. Ophthalmology 1994;101(11):1851-1855.
31. Francis AW, Michael E Gyasi, Martin Adjuik, et al. Comparison of primary open angle glaucoma patients in rural and urban Ghana. Afr Health Sci 2014;14(3):729-735. doi: 10.4314/ahs.v14i3.32.
32. Al-Mansouri FA, Kanaan A, Gamra H, et al. Prevalence and determinants of glaucoma in citizens of Qatar aged 40 years or older: a community-based survey. Middle East J Ophthalmol 2011;18(2):141–149.
33. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai glaucoma study. Ophthalmology 2008;115(4):648-654.e1.
34. Chandershekhar G, Sirisha Senthil, Rohit C Khanna, et al. Prevalence and risk factors for primary glaucomas in adult urban and rural populations in the Andhra Pradesh eye disease study. Ophthalmology 2010;117(7):1352–1359.
35. Gandolfi S, Simmons ST, Sturm R, et al. Three-month comparison of bimatoprost and latanoprost in patients with glaucoma and ocular hypertension. Adv Ther 2001;18(3):110-121.
36. Nicola Orzalesi, Luca Rossetti, Andrea Bottoli, et al. Comparison of the effects of latanoprost, travoprost, and bimatoprost on circadian intraocular pressure in patients with glaucoma or ocular hypertension. Ophthalmology 2006;113(2):239-246.
37. Yildirim Nilgun, Sahin Afsun, Gultekin Saadet. The effect of latanoprost, bimatoprost, and travoprost on circadian variation of intraocular pressure in patients with open-angle. Journal of Glaucoma 2008;17(1):36-39.
38. Jin XH, Quin SH, Sun XH. 0.03% bimatoprost ophthalmic solution with 0.005% latanoprost eye drops IOP lowering efficacy and safety comparison. Chinese Journal of Practical Ophthalmology 2005;23(7):712-714.
39. Kong XM, Sun XH, Meng FR, et al. A comparison of the ocular hypotensive efficacy of three prostaglandin analogues. Chinese J Opt and Ophthalmology 2006;8(4):228-230.
40. Robert S Noecker, Monte S Dirks, Neil T Choplin, et al. A six-month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. Am J Ophthal 2004;137(1):210-211.
41. Alagöz G, Gürel K, Bayer A, et al. A comparative study of bimatoprost and travoprost: effect on intraocular pressure and ocular circulation in newly diagnosed glaucoma patients. Ophthalmologica 2008;222(2):88–95
42. Anne J Lee, Peter McCluskey. Clinical utility and differential effects of prostaglandin analogues in the management of raised intraocular pressure and ocular hypertension Clin Ophthalmol 2010;4:741–764.
43. Huang HL, Sun XH, Xiao M. Comparison of intraocular pressure reducing effects of three prostaglandin eye drops in open angle glaucoma. Zhonghua Yan Ke Za Zhi 2011;47(2):109-113.