Glaucoma Update

Issue 3

Latanoprost is associated with lower incidence of conjunctival hyperaemia compared to tafluprost in a meta-analysis

Glaucoma, an optic neuropathy, is characterized by the progressive degeneration and functional deterioration of the optic nerve, which advances to the reduction in visual sensitivity and blindness in some patients. It is the main cause of irreversible blindness worldwide, and remains asymptomatic until very severe.[1]

A GROWING ISSUE

Currently, >80 million people are affected by glaucoma, worldwide.[2]

About ~10% of glaucoma patients show loss of vision despite the treatment, with >120,000 cases of blindness attributable to the disease.[2]

Global prevalence estimates[3]

2010

- Glaucoma: 60.5 million people
- Bilateral blindness: 4.5 million people with open angle glaucoma

2020

- Glaucoma: 79.6 million people
- Bilateral blindness: 5.9 million people with open angle glaucoma

Primary open-angle glaucoma (POAG) is the most common form of open-angle glaucoma.[1]

Progression[1]

About 6 million people with POAG are likely to exhibit blindness in 2020

Risk factors[1]

High intraocular pressure (IOP), older age, and a thin central cornea are the known risk factors of POAG

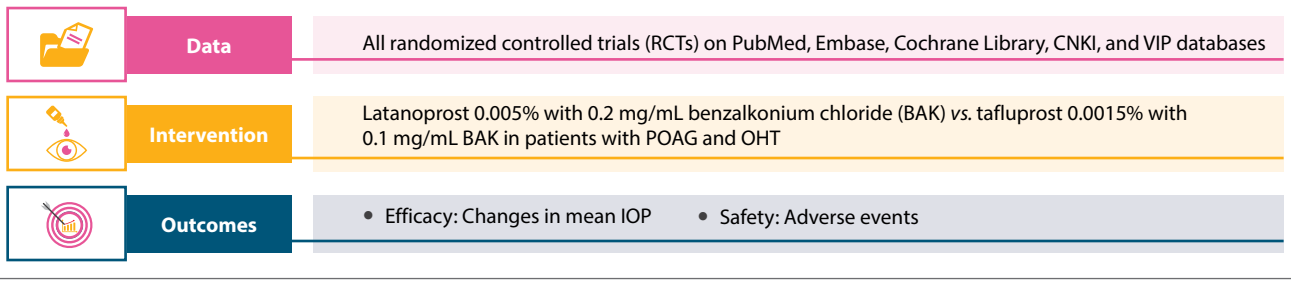
Treatment goal[1]

Lowering IOP to prevent further damage and delay disease progression is the main treatment goal

Latanoprost, a prostaglandin analog (first-line treatment), in randomized trials have proven its efficacy in lowering IOP for the management of POAG which is similar to travoprost and bimatoprost but the tolerability may be better.[4]

Tafluprost shows less ocular tolerability because of more incidence of conjunctival hyperaemia

A meta-analysis was conducted to assess safety and efficacy of latanoprost *vs.* tafluprost for the management of POAG and ocular hypertension (OHT).[5]



Characteristics of the studies included in the meta-analysis

A total of 5 RCTs including 888 glaucoma patients were selected. The follow-up period ranged from 1 to 24 months. The mean age of patients was 57 years, and 56% were females (Table 1).[5]

Table 1: Studies included in the meta-analysis[5]

First author	Year	No. of eyes (taf/lat)	Males (%)	Mean age (years)	Diagnosis (n)			Follow-up (months)	Loss to follow-up
					OAG	OHT	NTG		
Uusitalo	2010	269/264	221 (41.5)	62.5	533		0	24	131/533
Traverso	2010	19/19	12 (31.6)	NA	26	12	0	1.5	2/38
Park	2015	20/21	18 (43.9)	55.1	14	0	27	3	0/41
Ge	2015	122/124	125 (63.8)	44.1	144	52	0	1	21/246
Ikeda	2016	15/15	15 (50)	66.3	0	0	30	3	0/30

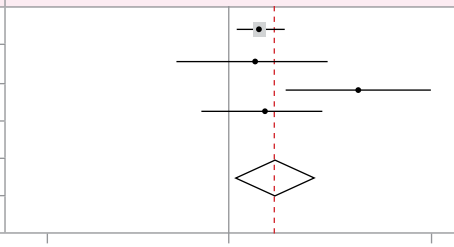
lat: Latanoprost; taf: Tafluprost; OAG: Open angle glaucoma; OHT: Ocular hypertension; NTG: Normal tension glaucoma; NA: Not available.

Efficacy outcomes: IOP reduction

IOP-lowering effect was assessed in 4 RCTs. There were no statistically significant differences between latanoprost and tafluprost in IOP reduction [standard mean difference (SMD) = 0.48, 95% confidence interval (CI) 0.07 to 0.88, $p = 0.085$; Figure 1].[5]

Figure 1: Forest plots (random-effect model) for IOP-lowering effect[5]

Studies	SMD (95% CI)	Weight
GE.J 2015	0.30 (0.05, 0.55)	39.65
Traverso 2010	0.23 (–0.40, 0.87)	21.41
Park 2015	1.22 (0.55, 1.89)	20.31
Ikeda 2016	0.32 (–0.41, 1.04)	18.63
Overall (I-squared = 54.7%, $p = 0.085$)	0.48 (0.07, 0.88)	100.00
NOTE: Weights are from random effects analysis		

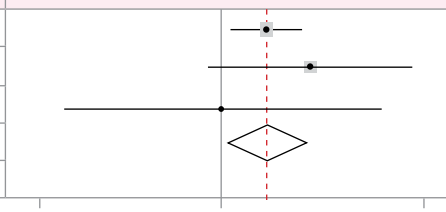


IOP: Intraocular pressure; SMD: Standard mean difference; CI: Confidence interval.

Safety outcomes: Conjunctival hyperaemia

Tafluprost was significantly associated with more incidence of conjunctival hyperaemia than latanoprost [relative risk (RR) = 2.11, 95% CI 1.24 to 3.59, $p = 0.006$, Z = 2.76; Figure 2].[5]

Figure 2: Forest plots (random-effect model) for incidence of conjunctival hyperaemia[5]

Studies		RR (95% CI)	Weight
GE.J 2015		2.08 (1.10, 3.95)	66.67
Uusitalo 2010		2.75 (0.89, 8.53)	22.22
Traverso 2010		1.00 (0.16, 6.38)	11.11
Overall (I-squared = 0.0%, $p = 0.659$)		2.11 (1.24, 3.59)	100.00
	0.117 1 8.53		

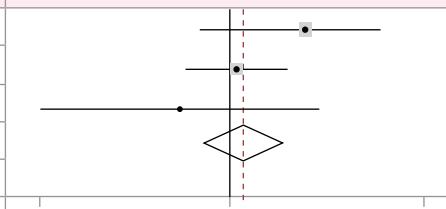
RR: Relative risk; CI: Confidence interval.

Safety outcomes: Eye irritation and foreign-body sensation

There were no statistically significant differences between latanoprost and tafluprost pertaining to eye irritation and foreign-body sensation:[5]

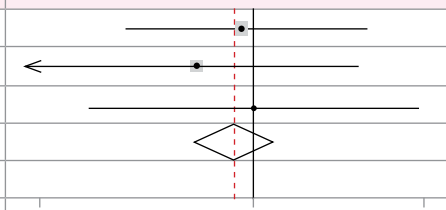
- Eye irritation: RR = 1.16, 95% CI 0.49 to 2.75, $p = 0.744$, Z = 2.76; (Figure 3)
- Foreign-body sensation: RR = 0.62, 95% CI 0.26 to 1.46, $p = 0.269$, Z = 1.10; (Figure 4)

Figure 3: Forest plots (random-effect model) for eye irritation rate[5]

Studies		RR (95% CI)	Weight
GE.J 2015		2.67 (0.72, 9.81)	29.97
Uusitalo 2010		1.00 (0.49, 2.06)	56.43
Traverso 2010		0.33 (0.04, 2.93)	13.60
Overall (I-squared = 33.2%, $p = 0.224$)		1.16 (0.49, 2.75)	100.00
NOTE: Weights are from random effects analysis			
	0.038 1 26.3		

RR: Relative risk; CI: Confidence interval.

Figure 4: Forest plots (random-effect model) for foreign-body sensation[5]

Studies		RR (95% CI)	Weight
GE.J 2015		0.67 (0.19, 2.30)	46.15
Uusitalo 2010		0.40 (0.08, 2.04)	38.46
Traverso 2010		1.00 (0.16, 6.38)	15.38
Overall (I-squared = 0.0%, $p = 0.761$)		0.62 (0.26, 1.46)	100.00
	0.783 1 12.8		

RR: Relative risk; CI: Confidence interval.

Safety outcomes: Eye pain, hyperpigmentation, dry eye, and eye pruritus

No statistically significant differences were observed between latanoprost and tafluprost with respect to eye pain, hyperpigmentation, dry eye, and eye pruritus (Table 2).[5]

Table 2: Results for eye pain, hyperpigmentation, dry eye, and eye pruritus[5]

Adverse reaction	Studies	RR	95% CI	I^2 (%)	P	Z
Hyperpigmentation	Uusitalo 2010 and Ikeda 2016	0.741	(0.235, 2.334)	0	0.61	0.51
Dry eye	Taverso 2010 and Uusitalo 2010	1.154	(0.409, 3.256)	0	0.79	0.27
Eye pain	Ge 2015 and Uusitalo 2010	2.000	(0.949, 4.216)	0	0.07	1.82
Eye pruritus	Taverso 2010 and Uusitalo 2010	1.600	(0.536, 4.774)	0	0.40	0.84

RR: Relative risk; CI: Confidence interval.

Clinical implications

- Latanoprost and tafluprost were comparable in IOP reduction for open angle glaucoma and OHT.
- Also, there were no significant differences between the incidence of foreign-body sensation, eye irritation, eye pain, iris hyperpigmentation, dry eye, and eye pruritus.
- However, tafluprost showed less ocular tolerability because of more incidence of conjunctival hyperaemia than latanoprost.
- The authors attributed it to the higher pro-inflammatory activity of tafluprost than latanoprost, independent of the preservative product.
- A poor drug tolerance and safety can lead to invalidity of treatment.

References

1. *Weinreb RN, Leung CK, Crowston JG, et al. Primary open-angle glaucoma. Nat Rev Dis Primers. 2016;2:1-19.*
2. *Sheybani A, Scott R, Samuelson TW, et al. Open-angle glaucoma: Burden of illness, current therapies, and the management of nocturnal IOP variation. Ophthalmol Ther. 2020;9(1):1-14.*
3. *Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006;90(3):262-67.*
4. *Tripathy K, Geetha R. Latanoprost. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. [cited 2020 Jun 7]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540978/*
5. *Yang XT, Zhao L, Wang LJ, et al. Efficacy and safety of 0.0015% tafluprost versus 0.005% latanoprost in primary open angle glaucoma, ocular hypertension: A meta-analysis. Int J Ophthalmol. 2020;13(3):474-80.*

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