

Efficacy and safety of prostaglandin analogues in primary open-angle glaucoma or ocular hypertension patients

A meta-analysis

Wenquan Tang, PhD^{a,b}, Feng Zhang, PhD^a, Ke Liu, PhD^a, Xuanchu Duan, PhD^{a,c,d,*}

Abstract

Background: To evaluate and compare the efficacy and safety of 3 prostaglandin analogues (0.005% latanoprost, 0.004% travoprost, and 0.03% bimatoprost) in treatment of primary open-angle glaucoma (POAG) or ocular hypertension (OHT).

Methods: PubMed, Embase, Cochrane library, Web of science, CNKI, Wanfang, and Vip database, published between January 1, 2000 and June 1, 2018, were systematically examined for randomized controlled trials (RCT) based on prostaglandin analogues for POAG or OHT treatment. Statistical analyses including weighted mean difference (WMD) calculation and odds ratio (OR) were performed using Review Manager Software version 5.3.

Result: The 17 studies were included in this analysis (N=2433 participants) with 1~12 months' follow-ups. The difference of intraocular pressure (IOP) reduction between latanoprost and travoprost group had not significant; there was significant difference of IOP reduction between latanoprost and bimatoprost group in the third month and sixth month; Travoprost was significantly different from bimatoprost in reducing IOP in the third month. Travoprost revealed an elevated risk of conjunctival hyperemia compared with latanoprost. An elevated risk of conjunctival hyperemia and growth of lashes compared with latanoprost. Bimatoprost shows lower ocular tolerability with higher incidence of side effects such as conjunctival hyperemia.

Conclusions: 0.03% bimatoprost appears more effective following long time use (3 and 6 month post-treatment) for IOP control compared to 0.005% latanoprost, and is more effective compared to 0.004% travoprost after being used for a certain period of time (3 months post-treatment); nevertheless, 0.005% latanoprost is better tolerated in patients with POAG or OHT.

Abbreviations: CIs = confidence intervals, IOP = intraocular pressure, OHT = ocular hypertension, OR = odds ratio, POAG = primary open-angle glaucoma, RCT = randomized controlled trial, WMD = weighted mean difference.

Keywords: bimatoprost, efficacy, glaucoma, latanoprost, meta-analysis, safety, travoprost

1. Introduction

Glaucoma is the leading cause of irreversible blindness in the world. Intraocular pressure (IOP) is considered a major risk factor for the development of glaucomatous optic neuropathy.^[1-3]

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Primary open-angle glaucoma (POAG) is the most common form of glaucoma in European and African populations.^[4] Currently, lowering IOP is the only approved approach used to prevent glaucoma formation in ocular hypertensive (OHT) patients and to prevent or delay glaucomatous progression in POAG patients.^[5] Management of elevated IOP is usually initiated with medical therapy, and the most popular drugs include — blockers, carbonic anhydrase inhibitors, α -agonists, miotics, and prostaglandin analogs (PGs). PGs are the most potent ocular hypotensive medications used in the treatment of POAG and OHT.^[6] Besides latanoprost (0.005%), travoprost (0.004%), and bimatoprost (0.03%), other popular PGs include tafluprost and unoprostone.

Several clinical trials have compared the efficacy and tolerance of different PGs.^[15-31] However, the results of these studies have not been consistent. Over the last decade, few meta-analyses have evaluated PGs for glaucoma treatment;^[7-9] nevertheless, they all have arrived to different conclusions. For example, Oghenowede Eyawo^[7] has revealed that PGs have similar efficacy effect, but differing hyperemia effects. Moreover, Florent Aptel^[8] has demonstrated that bimatoprost has a greater efficacy compared to latanoprost and travoprost; while according to Denis^[9] travoprost and bimatoprost might have greater efficacy in lowering IOP compared to latanoprost. Nonetheless, these studies have been published almost a decade ago, which means there is an urgent need for further research.

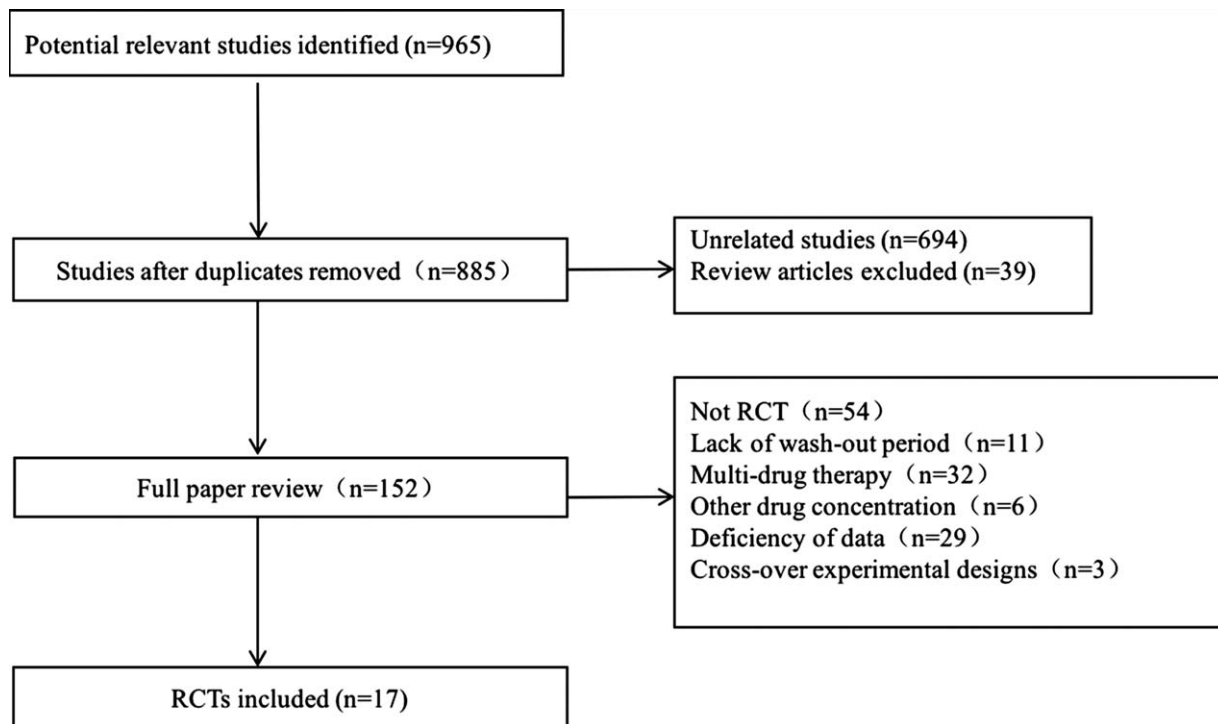


Figure 1. Flow diagram of included studies.

The aim of this study is to compare the efficacy and safety of 0.005% latanoprost, 0.004% travoprost and 0.03% bimatoprost in the treatment of patients with POAG or OHT. Meta-analysis of published clinical trials was conducted to compare the efficacy and/or safety of these 3 prostaglandin analogues.

2. Methods

2.1. Search strategy

This systematic review and meta-analysis were reported in accordance with the Preferred Reporting Items for Systematic

Reviews and Meta-Analyses (PRISMA) Statement.^[10,11] Ethics approval is not applicable. This study is a research on research study.

We selected relevant studies published between January 1st, 2000 and June 1st, 2018 by searching PubMed, Embase, Cochrane library, Web of science, CNKI, Wanfang, and Vip databases. We applied no language restrictions and used the following Medical Subject Headings (MeSH) terms: “Glaucoma, Open-Angle”, “Ocular Hypertension”, “Latanoprost”, “Travoprost”, “Bimatoprost”, “Intraocular Pressure”, “Randomized Controlled Trial”. The commercial name of

Table 1
Characteristics of the studies included in the meta-analysis.

Study	Region	Design	Comparison	No. of patients	Glaucoma types (POAG/OHT/other)	Mean age (yrs)	Sex (M/F%)	Duration
Arcieri ^[15] 2005	Brazil	RCT SB	LAT vs TRA vs BIM	15/17/16	34/0/30	67	34/30	6 mo
Birt ^[16] 2010	Europe	RCT SB	LAT vs TRA vs BIM	30/26/27	/	62	45/38	24 wk
Cantor ^[17] 2006	America	RCT SB	TRA vs BIM	81/76	108/48/1	65	81/76	6 mo
Cardascia ^[18] 2003	Italy	RCT DB	LAT vs TRA	9/9	18/0/0	52	9/9	6 mo
Cellini ^[19] 2004	Italy	RCT DB	LAT vs TRA vs BIM	20/20/20	60/0/0	64	32/28	6 mo
Faridi ^[20] 2010	America	RCT SB	LAT vs TRA vs BIM	42/40/40	35/55/32	68	65/57	6 mo
Gandolfi ^[21] 2001	Italy + America	RCT DB	LAT vs BIM	113/119	132/81/13	62	87/145	3 mo
Haili Huang ^[22] 2011	China	RCT NB	LAT vs TRA vs BIM	21/22/20	63/0/0	54	31/32	4 wk
Koz ^[23] 2007	Turkey	RCT DB	LAT vs TRA vs BIM	20/20/20	36/24/0	53	35/25	6 mo
Mishra ^[24] 2014	India	RCT SB	LAT vs TRA vs BIM	35/35/35	105/0/0	54	54/51	12 wk
Nettland ^[25] 2001	America	RCT DB	LAT vs TRA	193/197	259/126/5	64	189/201	12 mo
Noecker ^[26] 2004	America	RCT SB	TRA vs BIM	15/16	28/3/0	65	11/20	3 mo
Noecker ^[27] 2006	America	RCT SB	TRA vs BIM	45/49	67/27/0	63	37/57	3 mo
Parrish ^[28] 2003	America	RCT SB	LAT vs TRA vs BIM	136/138/136	309/95/6	65	172/238	12 mo
Varma ^[29] 2008	America	RCT SB	LAT vs TRA vs BIM	136/138/136	509/95/6	65	172/238	12 wk
Xiangmei Kong ^[30] 2006	China	RCT SB	LAT vs TRA vs BIM	51/24/27	91/11/0	52	65/37	4 wk
Yildirim ^[31] 2008	Turkey	RCT SB	LAT vs TRA vs BIM	17/15/16	48/0/0	/	/	8 wk

BIM = bimatoprost, DB = double-blind, LAT = latanoprost, NB = non-blind, SB = single-blind, TRA = travoprost.

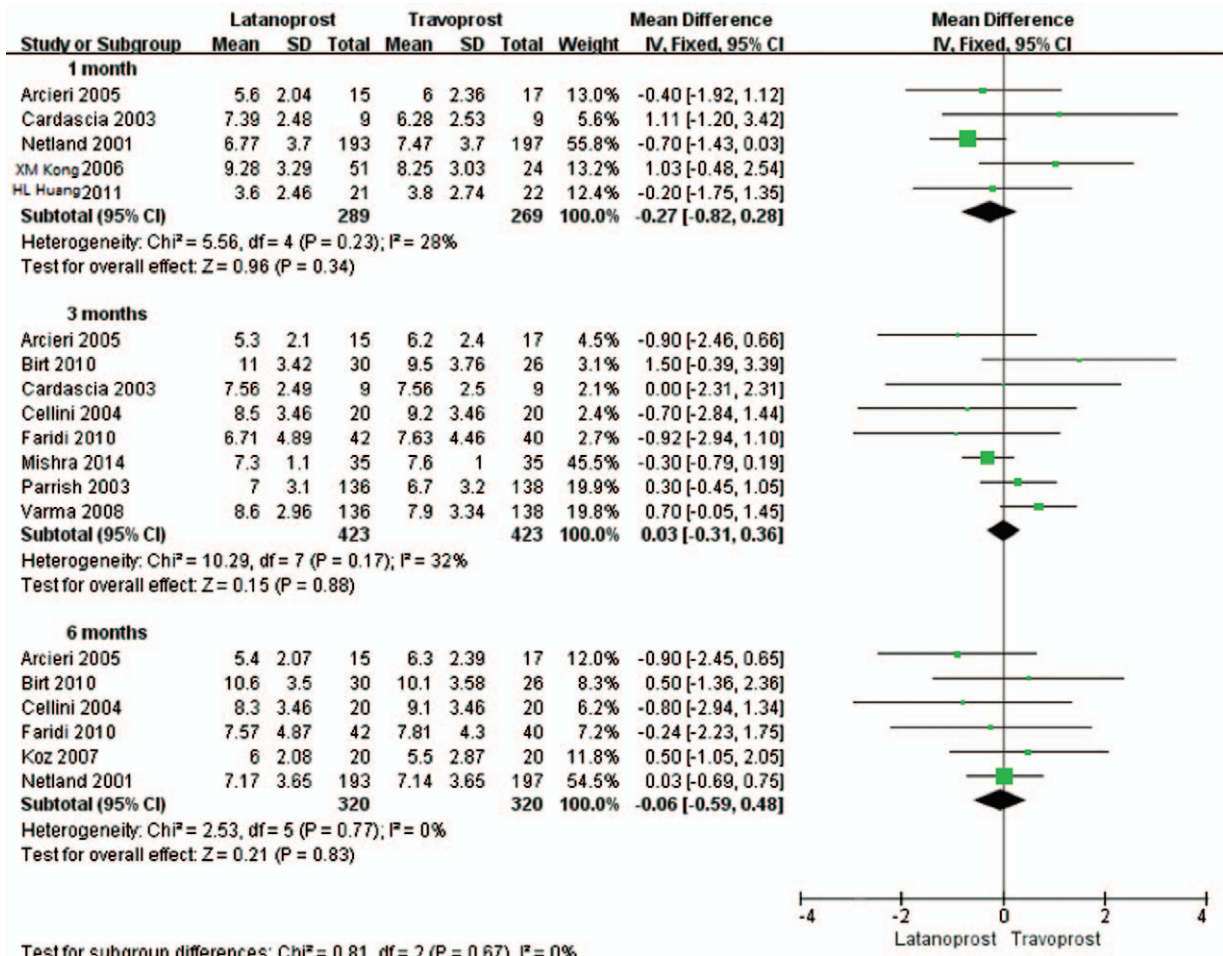


Figure 2. Meta-analysis, forest graph of latanoprost versus travoprost for IOP-lowering effects (Trials subgrouped based on duration analyses). CI=confidence interval, SD=standard deviation.

the medication and the other text terms were also investigated. The complete search used for PubMed was: (((Glaucoma, Open-Angle [MeSH] OR Glaucomas, Open-Angle [Title/Abstract] OR Open-Angle Glaucoma [Title/Abstract] OR Open-Angle Glaucomas [Title/Abstract] OR Glaucoma, Open Angle [Title/Abstract] OR Glaucomas, Open Angle [Title/Abstract] OR Open Angle Glaucoma [Title/Abstract] OR Open Angle Glaucomas [Title/Abstract] AND (Ocular Hypertension [MeSH] OR Hypertension, Ocular [Title/Abstract] OR Hypertensions, Ocular [Title/Abstract] OR Ocular Hypertensions [Title/Abstract]) AND (Latanoprost [Supplementary Concept] OR Xalatan [Title/Abstract] OR Pfizer brand of latanoprost [Title/Abstract] OR Travoprost [Mesh] OR Travatan ([Title/Abstract] OR Bimatoprost [Mesh] OR Latisse [Title/Abstract] OR Lumigan [Title/Abstract]) AND (Intraocular Pressure [MeSH] OR Intraocular Pressures [Title/Abstract] OR Pressures intraocular [Title/Abstract] OR Ocular Tension [Title/Abstract] OR Ocular Tensions [Title/Abstract] OR Tension Ocular [Title/Abstract] OR Tensions Ocular [Title/Abstract]) AND (Randomized Controlled Trial[Publication Type] OR Randomized [Title/Abstract] OR Placebo [Title/Abstract])))). In addition, we performed a manual search from reference list of retrieved papers and review articles.

2.2. Eligibility criteria and data collection

According to PICOS (Population, Intervention, Comparison, Outcome, Study design) principle, articles were selected based on the following criteria:

- (1) Population: patients with POAG or OHT, age >18, without sex, region, or race restriction;
- (2) Intervention and Comparison: latanoprost, bimatoprost, and travoprost;
- (3) Outcome: at least 1 of the interested outcome variables discussed later was included;
- (4) Study design: randomized controlled trials (RCTs). Exclusion criteria were: cross-over experimental designs, multi-drug therapy, short duration of follow-up, lack of wash-out period before the trial started, reviews, and duplicate publications.

Trial eligibility and data extraction were performed by 2 investigators working independently; data were extracted using standardized forms. The following information was recorded from each study: authors of the trial, publication year, location of the study, study design (double-blind, single-blind), interventions, participants' characteristics (number, mean age, sex), length of follow-up, IOP value from baseline to endpoint, and adverse events. Disagreements were resolved by discussion or consensus involving a third investigator.

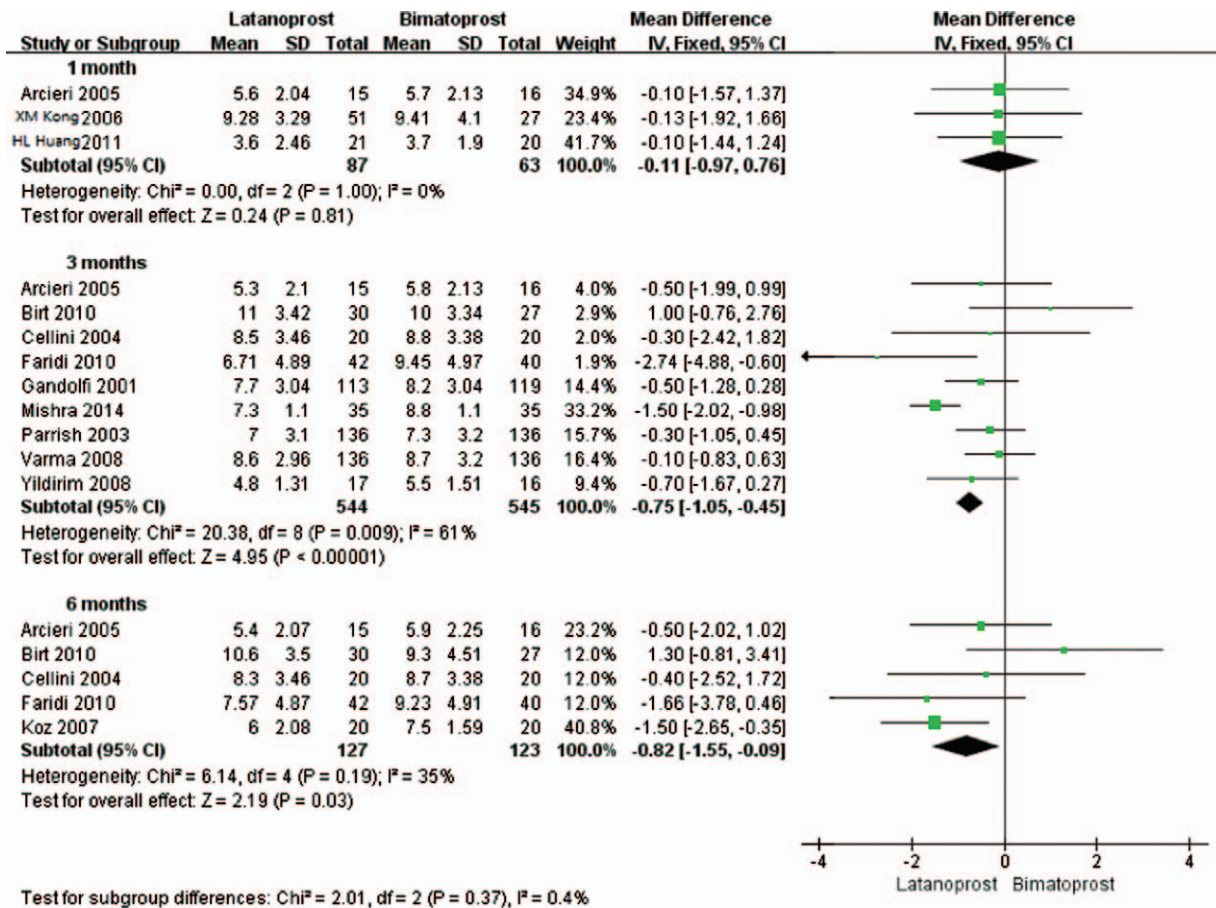


Figure 3. Meta-analysis, forest graph of latanoprost versus bimatoprost for IOP-lowering effects (Trials subgrouped based on duration analyses). CI = confidence interval, SD = standard deviation.

2.3. Quality assessment

We performed quality assessment of trials with Cochrane bias risk assessment tool (The Cochrane Collaboration) for RCTs.^[12] The risk of bias tool covers 6 domains of bias and 7 items: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), other bias. The tool involves assigning a judgment of high, low, or unclear risk of bias for each item. Discrepancies in ratings were solved by discussion between 2 authors.

2.4. Statistical analyses

The analysis was conducted by Review Manager version 5.3 software (The Cochrane Collaboration).

For efficacy, the mean IOP reduction (IOPR) from baseline to endpoint was determined. For tolerability, adverse events were analyzed based on the following conditions: conjunctiva hyperemia, discomfort (itching, eye irritation, foreign body sensation), and growth of lashes. IOPR is continuous variables and side effects are dichotomous variables. Continuous outcomes were expressed as weighted mean difference (WMD), with values >0 favoring left prostaglandin analogue, and dichotomous

outcomes as odds ratio (OR), with values <1 favoring left prostaglandin analogue. Both outcomes were reported with 95% confidence intervals (CIs).

For studies that only reported IOP at baseline and end-point, the IOPR and standard deviation (SD) of the IOPR (SD_{IOPR}) were calculated according the following formula:^[8]

$$IOPR = IOP_{baseline} - IOP_{endpoint} \tag{1}$$

$$SD_{IOPR} = (SD_{baseline}^2 + SD_{endpoint}^2 - SD_{baseline} + SD_{endpoint})^{1/2} \tag{2}$$

Heterogeneity of effective size across studies was tested using Cochran Q test, which was considered significant if P < .1.^[13] This study also did I² testing to assess the magnitude of the heterogeneity between studies, with values that were greater than 50% being regarded as indicative of moderate-to-high heterogeneity.^[14] If there was heterogeneity within these RCTs, random-effect model was selected. Otherwise, the fixed-effect model was used. And the subgroup analyses for each PG comparison were used. Additionally, this paper conducted a sensitivity analysis to evaluate the stability of meta-analysis.

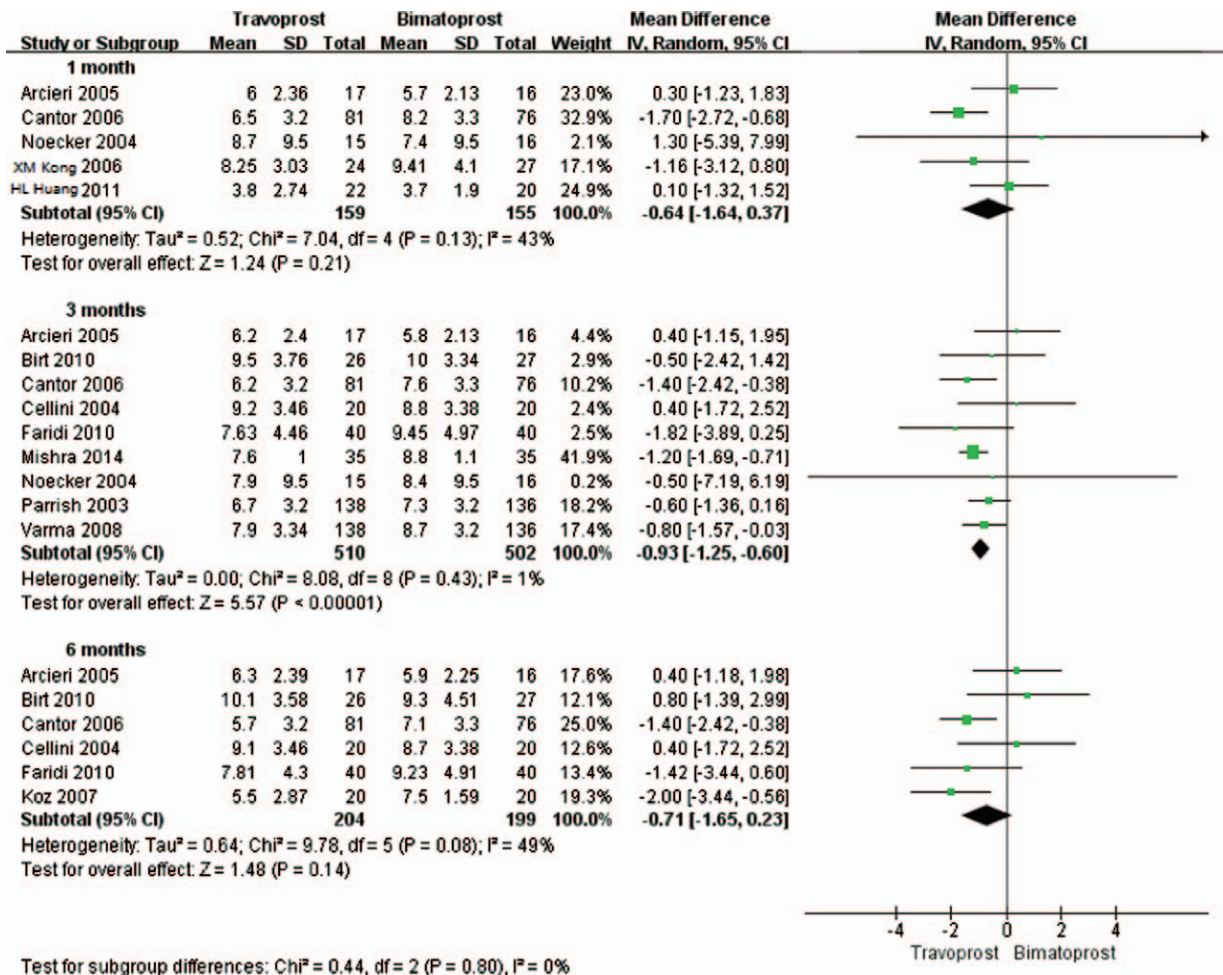


Figure 4. Meta-analysis, forest graph of travoprost versus bimatoprost for IOP-lowering effects (Trials subgrouped based on duration analyses). CI=confidence interval, SD=standard deviation.

3. Results

We identified 965 studies, of which 17 (with data for 2433 participants) were included in this analysis (Fig. 1). Trial duration ranged between 4 weeks and 12 months. The average age of patients was 52 to 68 years. Details of every study, such as the authors of trial, publication year, location of the study, study design (double-blind, single-blind), interventions, participants' characteristics in each study, are presented in Table 1.

3.1. Quality results

The quality of each RCTs were assessed by Cochrane bias risk assessment tool (data not shown). Two trials (11.8%) were judged at low risk of bias in every item; 4 trials (23.5%) were judged at high risk of bias in only 1 item; while 11 trials (64.7%) were judged at high or unclear risk of bias in at least 2 items. All these studies were RCTs. Seven trials (41.2%) had elaborated the generation of random sequence, while 10 (58.8%) had explained allocation concealment. Most studies were double-blinded, nevertheless, only 10 trials (58.8%) reported that appropriate methods had been used for assessors and participant blinding. Blinding of outcome assessment was a potential risk of bias in

23.5% of trials. Overall, the major potential sources of bias in the trials were selection and performance bias.

3.2. Efficacy

To be able to more effectively compare the curative effect of these PGs, this study has adopted subgroup analysis according to the period drug was used. The result, expressed as absolute change in mmHg, showed that there was no significant difference between latanoprost and travoprost in reducing IOP at 1, 3, and 6 month post-treatment (WMD = -0.27, 95% CI -0.82 to 0.28, P = .34; WMD = 0.03, 95% CI -0.31 to 0.36, P = .88; and WMD = -0.06 95% CI -0.59 to 0.48, P = .83, respectively) (Fig. 2). In addition, no significant heterogeneity in the first month (heterogeneity P = .23 > .1, I² = 28% < 50%), third month (heterogeneity P = .17 > .1, I² = 32% < 50%) and the sixth-month post-treatment (heterogeneity P = .77 > .1, I² = 0% < 50%) between each RCTs was observed. Hence, the fixed model was adopted.

We respectively pooled 3, 9, and 5 trials assessing latanoprost to bimatoprost in the first, third, and sixth-month post-treatment (Fig. 3). The WMD across groups in the first month was -0.11 mmHg (95% CI, -0.97 to 0.76, P = .81, I² = 0%, heterogeneity

Table 2
Summary of ocular adverse events, n (%).

Adverse events	Latanoprost (n=572)	Travoprost (n=602)	Bimatoprost (n=508)
Conjunctival hyperemia	158 (27.62)	232 (38.54)	204 (40.16)
Discomfort (itching, eye irritation, foreign body sensation)	53 (9.27)	105 (17.44)	35 (6.89)
Growth of lashes	5 (0.87)	3 (0.50)	20 (3.94)
Total	216 (37.76)	340 (56.48)	259 (50.98)

$P=.1$), in the third month was -0.75 mmHg (95% CI, -1.05 to -0.45 , $P<.00001$, $I^2=61\%$, heterogeneity $P=.009$), and in the sixth month was -0.82 mmHg (95% CI, -1.55 to -0.09 , $P=.03$, $I^2=35\%$, heterogeneity $P=.19$). These data indicated that bimatoprost was more effective for IOP control in the third and sixth month for patients with POAG or OHT compared to travoprost. Moreover, the heterogeneity in the third month (heterogeneity $P=.009<.1$, $I^2=61\%>50\%$) could be explained by clinical heterogeneity. Therefore, the fixed model was used.

The efficacy pooled estimates of IOPR between travoprost and bimatoprost based on the results of the RCTs included in the analyses are shown in Figure 4. Bimatoprost showed

greater efficacy in lowering IOP in the third month (WMD = -0.93 , 95% CI -1.25 to -0.60 , $P<.00001$, $I^2=1\%$, heterogeneity $P=.43$) for patients with POAG or OHT. Similar effect was observed in the first month (WMD = -0.64 , 95% CI -1.64 to 0.37 , $P=.21$, $I^2=43\%$, heterogeneity $P=.13$), and the sixth month (WMD = -0.71 , 95% CI -1.65 to 0.23 , $P=.14$, $I^2=49\%$, heterogeneity $P=.08$) for patients treated with travoprost and bimatoprost. Moreover, a mild heterogeneity was found in the sixth month (heterogeneity $P=.08<0.1$, $I^2=49\%$), which in turn couldn't be explained by clinical or methodological heterogeneity. Thus, the random model was adopted.

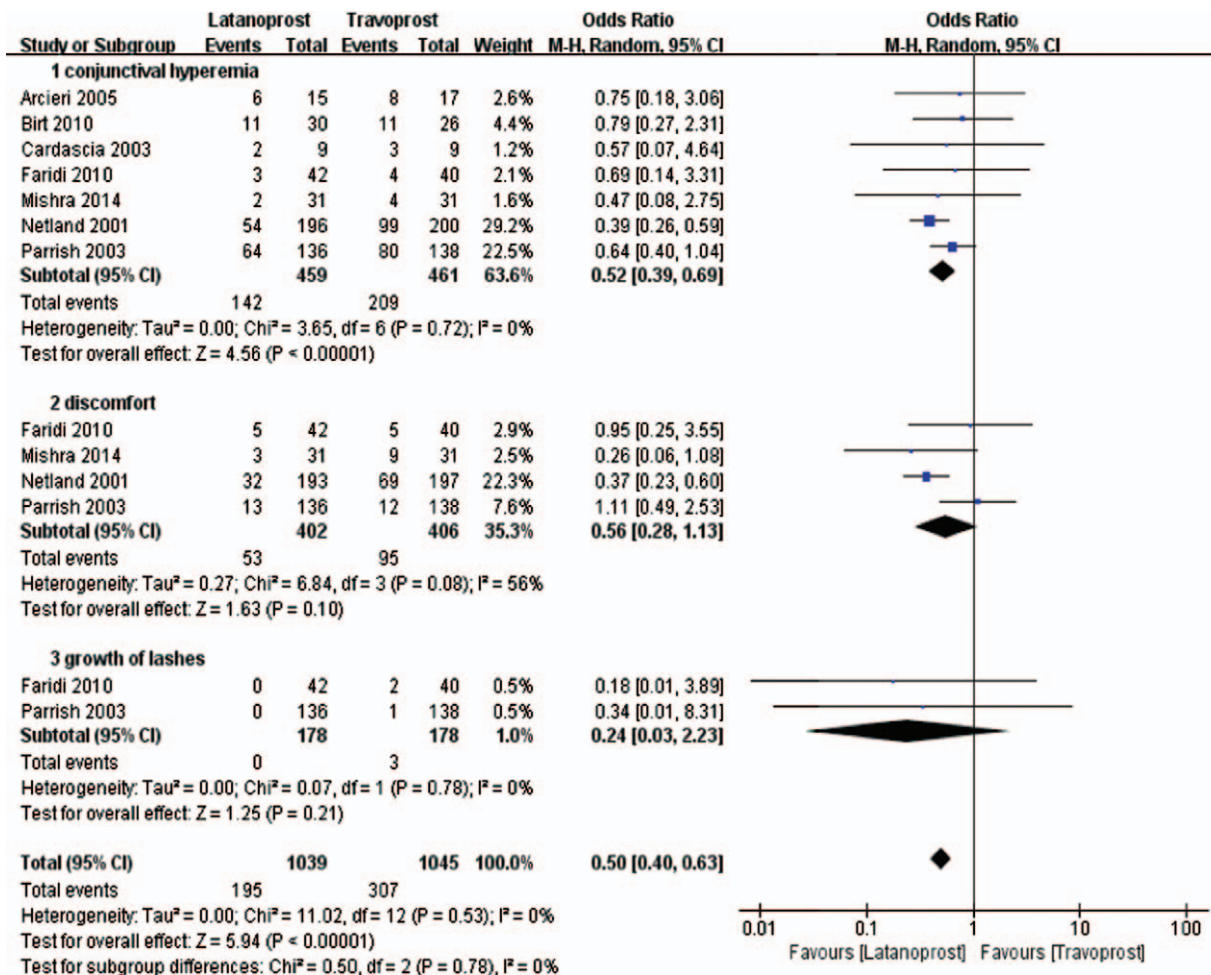


Figure 5. Meta-analysis, forest graph of latanoprost versus travoprost for ocular adverse effects (conjunctival hyperemia, discomfort and growth of lashes). CI = confidence interval.

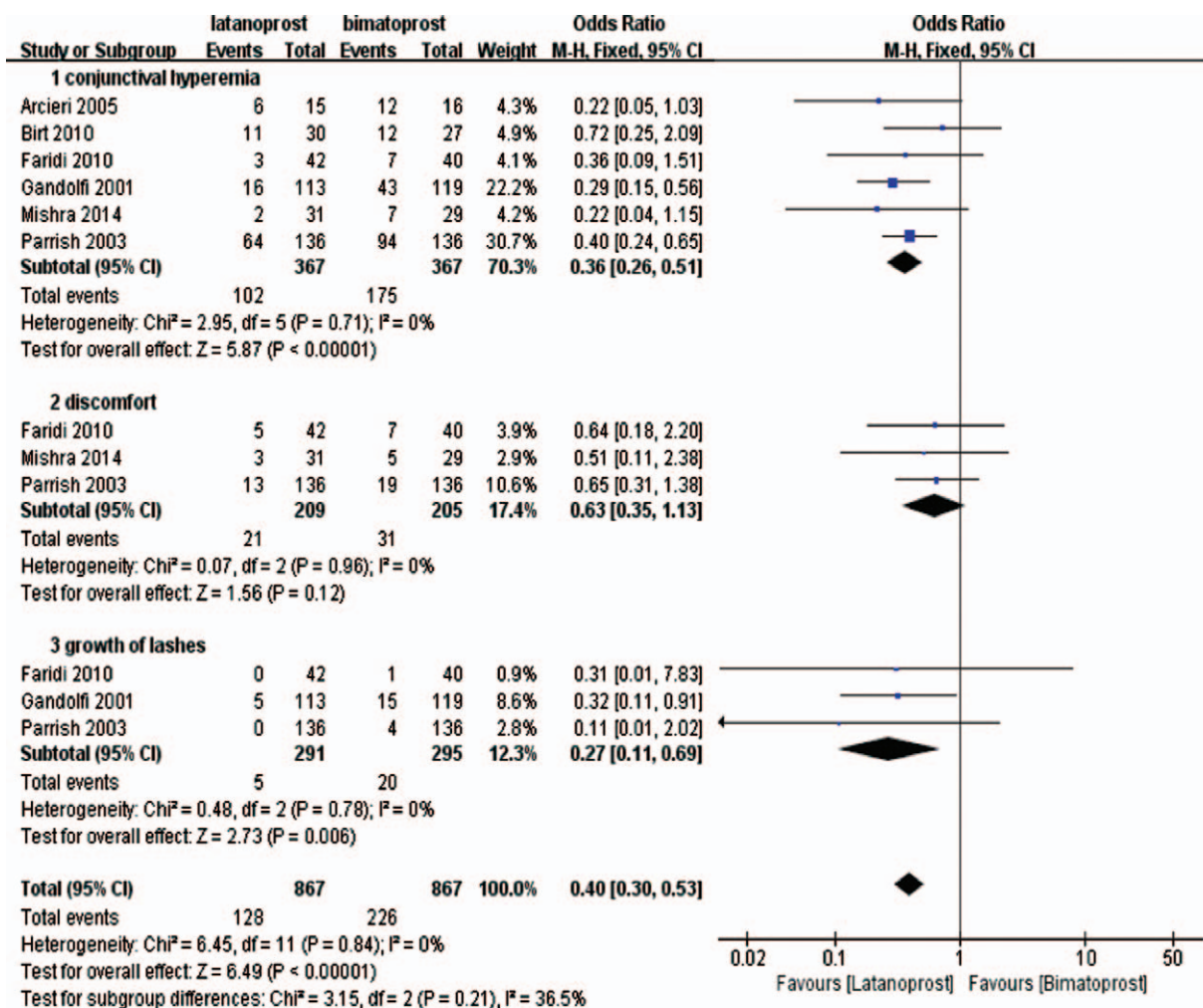


Figure 6. Meta-analysis, forest graph of latanoprost versus bimatoprost for ocular adverse effects (conjunctival hyperemia, discomfort and growth of lashes). CI = confidence interval.

3.3. Tolerability

Table 2 describes the overall ocular adverse events, including conjunctival hyperemia, discomfort (itching, eye irritation, foreign body sensation) and growth of lashes. Briefly, the data showed that travoprost led to a higher proportion than latanoprost in the conjunctival hyperemia (OR=0.52, 95% CI 0.39 to 0.69, $P < .00001$; $I^2 = 0\%$, heterogeneity $P = .72$, respectively) (Fig. 5). Furthermore, latanoprost and travoprost have similar incidence rate of discomfort (OR=0.56, 95% CI 0.28–1.13, $P = .10$, $I^2 = 56\%$, heterogeneity $P = .08$) and growth of lashes (OR=0.24, 95% CI 0.03 to 2.23, $P = .21$, $I^2 = 0\%$, heterogeneity $P = .78$). Moreover, moderate heterogeneity in the discomfort (heterogeneity $P = .08 < .1$, $I^2 = 56\%$) was observed. Thus, the random model was adopted. To sum up, travoprost revealed an elevated risk of adverse effects compared with latanoprost (OR=0.50, 95% CI 0.40–0.63, $P < .00001$, $I^2 = 0\%$, heterogeneity $P = .53$).

All of the adverse events showed a significant difference between latanoprost and bimatoprost, except for discomfort (OR=0.63, 95% CI 0.35–1.13, $P = .12$, $I^2 = 0\%$, heterogeneity $P = .96$) (Fig. 6). Moreover, no significant heterogeneity between each RCTs was found, thus the fixed model was used.

Bimatoprost shows lower ocular tolerability with higher incidence of conjunctival hyperemia (OR=0.64, 95% CI 0.46–0.88, $P = .007$, $I^2 = 0\%$, heterogeneity $P = .89$) compared with travoprost (Fig. 7). In terms of discomfort and growth of lashes, travoprost and bimatoprost have similar incidence rate (OR=1.01, 95% CI 0.62–1.65, $P = .97$, $I^2 = 16\%$, heterogeneity $P = .31$; OR=0.59, 95% CI 0.14–2.59, $P = .47$, $I^2 = 39\%$, heterogeneity $P = .20$). Moreover, no significant heterogeneity between each RCTs was found, therefore the fixed model was used.

3.4. Sensitivity analysis

To analyze the consistency and robustness of the results, a sensitivity examination was performed (data not shown). For assessing the influence of each individual clinical trial included in the meta-analysis, each study was excluded at a time and the analysis was performed again to determine the change in the WMD or OR. The punctual estimators for WMD varied between -0.47 and 0.27 in the latanoprost-travoprost efficacy analysis first-month post-treatment; between -0.14 and 0.3 third month after treatment, and between -0.16 and 0.06 6-months after

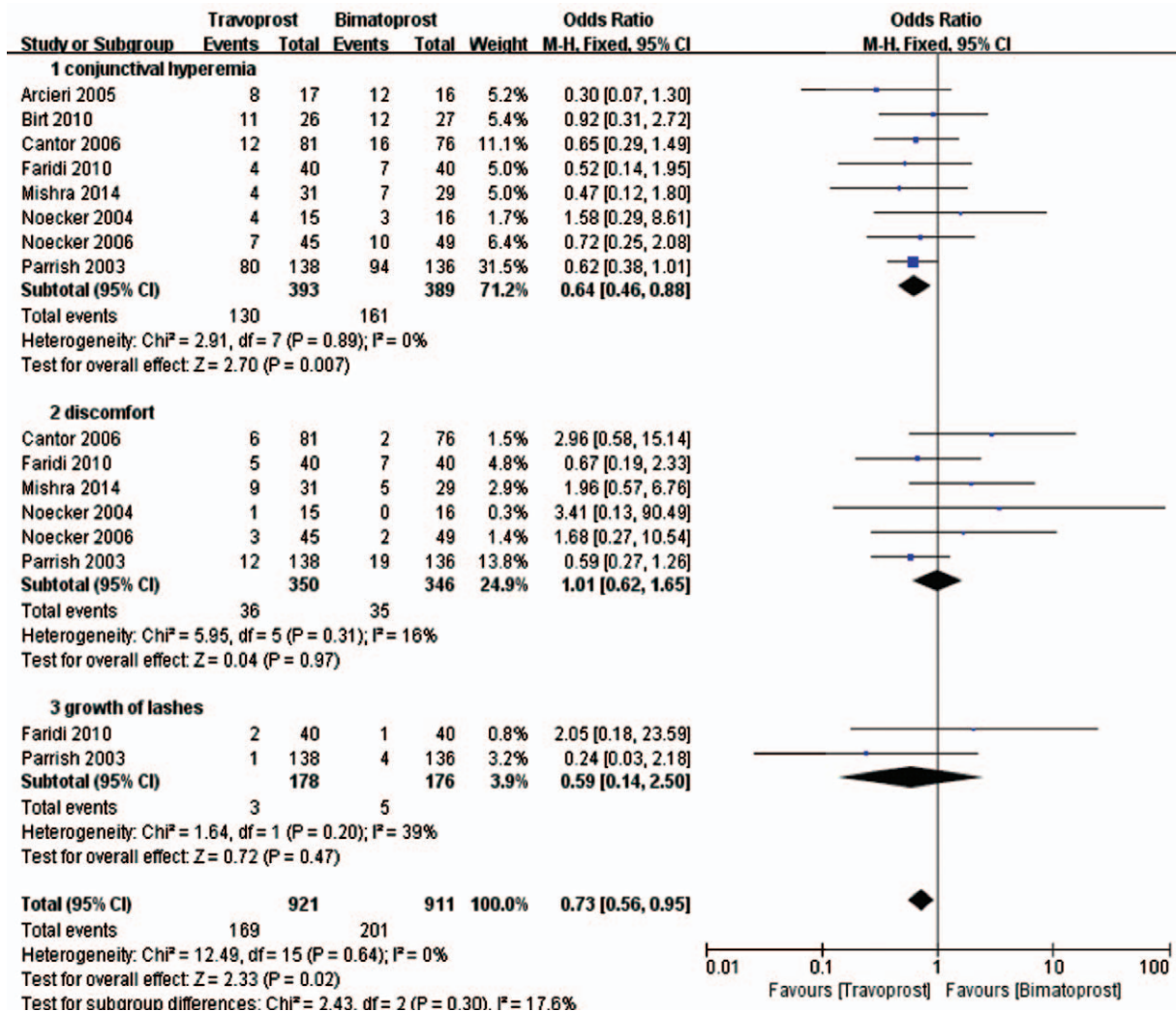


Figure 7. Meta-analysis, forest graph of travoprost versus bimatoprost for ocular adverse effects (conjunctival hyperemia, discomfort and growth of lashes). CI = confidence interval.

treatment, after excluding 1 by 1 each original clinical trial. During the sixth month of latanoprost-bimatoprost efficacy analysis, when excluding the Faridi's trial,^[20] the result of this meta-analysis changed from favoring bimatoprost to showing no significant difference between latanoprost and bimatoprost. In the travoprost- bimatoprost efficacy analysis, after excluding each RCTs, the results were the same. None of the clinical trials included in the meta-analysis had an important impact on the global estimation of the OR, except for the meta-analysis of discomfort in comparison between latanoprost and travoprost. When excluding Parrish's trial,^[28] the result of this meta-analysis changed. In general, the obtained results of meta-analysis were stable.

4. Discussion

Results of this meta-analysis suggested that bimatoprost is more effective in controlling IOP compared to latanoprost following longer treatment (3 and 6 months), and is more effective compared to travoprost when used for a certain period of time

(3-month post-treatment) in patients with POAG or OHT. Latanoprost and travoprost showed similar efficacy in lowering IOP, nevertheless, latanoprost was better tolerated in patients with POAG or OHT. These conclusions provide an effective theoretical basis for clinical medication.

As shown in Figures 2–4, this trial has produced robust and consistent findings which suggested that bimatoprost has the highest efficacy for patients with POAG or OHT. Furthermore, the comparison of adverse effects including conjunctival hyperemia, discomfort (itching, eye irritation, foreign body sensation) and growth of lashes between 3 PGs are shown in Figures 5–7. Briefly, the data suggested that conjunctival hyperemia occurs more frequently in patients treated with bimatoprost and travoprost compared to those treated with latanoprost. Besides, bimatoprost has shown to be associated with a higher incidence of growth of lashes compared to latanoprost.

Several studies have proved that prostaglandin analogues are more effective compared to brimonidine or timolol^[32,33] in lowering IOP. Nonetheless, the comparisons of these PGs, have

generated different conclusions. Some clinical trials^[22,28,30] have revealed that these 3 PGs, that is, travoprost, bimatoprost and latanoprost have the same efficacy. Contrary, other trials^[17,25,26] have proved that bimatoprost is more effective in lowering the IOP compared to latanoprost and travoprost. Travoprost has high selectivity and affinity for FP receptor, and it has been shown to be more effective for black patients.^[34] The differences in characteristics of population, region and methodological issues may account for these results.

A comparison between 3 PGs, that is, travoprost, Bimatoprost, and latanoprost have been previously published.^[7-9] However, these meta-analysis have reported different conclusions and had certain limitations. For example, none of these studies included subgroup analysis. Moreover, in some studies, significant heterogeneity and publication bias was observed, which in turn might have affected the outcome. By contrast, this study used the strict methods to investigate the comparison between latanoprost, travoprost, and bimatoprost in terms of efficacy and safety. Therefore, this study provides more useful advice to ophthalmologists.

To sum up, the findings suggested that different complex factors, that is, difference in corneal permeability and intraocular drug metabolism,^[35-37] have influenced the treatment outcome in patients with POAG or OHT. This might be mainly because the 3 drugs have different affinity for different types of FP receptors;^[38] latanoprost and travoprost have shown strong affinity for prostaglandin E1 (EP1), EP3, and prostaglandin FP (PGFP) receptor, while bimatoprost for PGFPR, but also certain affinity for EP1 and EP3 receptor.^[39] Different affinity causes different efficacy. Because of the different affinity for FP receptor between these 3 PGs, bimatoprost has shown to be more effective in controlling IOP compared to latanoprost and travoprost, even if, fewer side effects were observed in patients treated with latanoprost. Also, the different drug concentration (0.005% latanoprost, 0.004% travoprost, 0.03% bimatoprost) contributed to the terminal results, that is, higher concentration is positively correlated with drug efficacy, but also with higher side effects. According to these findings, bimatoprost was used at the highest concentrations, which in turn caused better efficacy and worse adverse effects compared to latanoprost and travoprost. Besides, the observed effects could also be attributed to different formula. In fact, bimatoprost is a prostamide analogue which has been synthesized,^[40] while latanoprost and travoprost are both prostaglandin analogues.

The prediction of individual medicine and their susceptibility is extremely difficult. Currently, there are no screening methods which could identify the optimum PG for individual cases. Therefore, according to our findings, it would be better to use bimatoprost for patients with POAG or OHT as they can tolerate the local side effects like conjunctival congestion.

Limitation of this meta-analysis is the unknown long-term durability of this treatment; included trials lasted more than 6 months. What's more, only 4 studies had a large sample size, while all other RCTs were based on a small sample size. Lastly, the publication bias cannot be excluded from the subgroup analysis.

5. Conclusion

The results of this meta-analysis suggested that 0.03% bimatoprost might be more effective compared to 0.005% latanoprost and 0.004% travoprost for lowering IOP in patients with POAG and OHT, even though latanoprost has low

incidence of ocular adverse effects. In clinical, the appropriate use of medicine is very important for patients. Lower the intraocular pressure of glaucoma patient to ideal level is essential to them. While there are no definite guides to direct ophthalmologists use prostaglandins (PAGs). These results may be useful for determining the optimal strategy for individual patients. Based on these findings, we recommend the use of bimatoprost for patients who can tolerate the side effects. In fact, everyone has a different response to PGs. Therefore, it is better for ophthalmologists considering all aspects for every patient. Personal treatment would be a trend in the future.

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Writing – original draft: Wenquan Tang.

Writing – review & editing: Ke Liu, Xuanchu Duan.

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