A comparison of the effects on intraocular pressure of latanoprost 0.005% and the fixed combination of dorzolamide 2% and timolol 0.5% in patients with open-angle glaucoma

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ABSTRACT.

Purpose: To compare the effects on intraocular pressure (IOP) of latanoprost 0.005% and the fixed combination of dorzolamide 2% and timolol 0.5%.

Methods: Overall, 226 patients whose IOP was insufficiently controlled by timolol alone were randomized to receive either latanoprost once daily or the fixed combination of dorzolamide plus timolol twice daily. Intraocular pressure was measured at 10:00 pm and 5:00 pm at baseline and after 3 months of treatment.

Results: Mean IOP was reduced from baseline in both groups ($p < 0.001$), with a mean $\pm$ SEM reduction of $-4.3 \pm 0.3$ mmHg (19%) for the latanoprost treatment group and $-4.0 \pm 0.3$ mmHg (17%) for the dorzolamide plus timolol treatment group. The two therapies were similarly effective in lowering IOP levels (mean difference in reduction: $-0.4 \pm 0.4$; 95% confidence interval: $-1.1, 0.4$).

Conclusions: Monotherapy with latanoprost once daily was as effective in reducing mean IOP as the fixed combination of dorzolamide plus timolol twice daily in patients with IOP insufficiently controlled by timolol alone.

Key words: intraocular pressure – open-angle glaucoma – treatment – latanoprost – dorzolamide – timolol

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At present, medical therapy is the first line of treatment for reducing intraocular pressure (IOP) in glaucoma. In some patients, the development of the glaucomatous disease or the diminishing effect of an ocular hypotensive drug makes the addition of another medication an obvious choice when IOP levels are no longer adequately controlled. Several ocular hypotensive agents, including the topical carbonic anhydrase inhibitor dorzolamide, have been shown to have an additive IOP-lowering effect when used in patients already on timolol (Hartenbaum 1996; Strahlman et al. 1996). Combined therapy, however, often requires more complex, sometimes inconvenient, treatment schedules involving an increased frequency of instillations of eye drops (Weinreb 1992; Patel & Spaeth 1995). Because such regimens can reduce medication compliance (Patel & Spaeth 1995), long-term management of glaucoma with monotherapy could be advantageous for patients.

Latanoprost is a prostaglandin $F_{2\alpha}$-analogue that effectively lowers IOP (Alm et al. 1995a; Alm et al. 1995b; Camras & the US Latanoprost Study Group 1996a; Camras et al. 1996b; Mishima et al. 1996; Watson et al. 1996; Watson & the Latanoprost Study Group 1998). Latanoprost acts to increase aqueous humour outflow with little or no effect on aqueous humour production (Toris et al. 1993; Ziai et al. 1993). Studies performed in monkey eyes show that latanoprost increases the uveoscleral outflow (Stjernschantz et al. 1995), and a corresponding effect has indirectly been demonstrated in humans (Toris et al. 1993). In three out of four clinical trials (Alm et al. 1995b; Camras et al. 1996a; Mishima et al. 1996; Watson et al. 1996), latanoprost monotherapy resulted in larger reductions in mean diurnal IOP levels than did treatment with timolol. Additional research (Bucci & the Italian Latanoprost Study Group 1999) has demonstrated that many patients whose IOP is no longer controlled on timolol
alone do as well on monotherapy with latanoprost as they do with timolol plus another drug.

An alternative to latanoprost monotherapy in patients with refractory disease might be the fixed combination of dorzolamide 2% and timolol 0.5% applied twice daily because the efficacy of this combination has been shown to be greater than that of either of the single components administered alone (Boyle et al. 1998; Clineschmidt et al. 1998). The purpose of the present study was to compare the effect on IOP of latanoprost administered once daily with that of the fixed combination of dorzolamide plus timolol instilled twice daily in patients with open-angle glaucoma or pseudoexfoliative glaucoma whose IOP is not adequately controlled on topical beta-adrenergic antagonists either alone or in combination with another ocular hypotensive drug. Ocular and systemic safety variables were also evaluated.

Methods

This 3-month, randomized, open-label study compared latanoprost (Xalatan®; Pharmacia Corporation, Peapack, New Jersey, USA) monotherapy with the fixed combination of dorzolamide plus timolol (Cosopt®; Merck Sharp & Dohme, Whitehouse Station, New Jersey, USA). The study was carried out in 30 eye clinics located in Finland, Germany, the Netherlands and Spain. Approvals were obtained from the appropriate regulatory authorities and ethics committees for each centre, and each patient provided written informed consent before study entry. The study adhered to the tenets of the Declaration of Helsinki.

After receiving timolol 0.5% as monotherapy twice daily for 3–6 weeks, consecutive patients were randomized alternately to two parallel study groups. One group switched from timolol to latanoprost 0.005% administered once daily in the evening and the other group switched from timolol to the fixed combination of dorzolamide 2% and timolol 0.5% administered twice daily. Patients were instructed to instil morning drops at approximately 8:00 am and evening drops at approximately 10:00 pm.

Patients aged 18 years or older with unilateral or bilateral primary open-angle glaucoma or pseudoexfoliative glaucoma were eligible. Glaucoma was defined as elevated IOP (≥21 mmHg) with glaucomatous visual field defects and/or glaucomatous changes of the optic nerve head. At the prestudy visit, eligible patients were being treated with either monotherapy in the form of a topical beta-adrenergic antagonist or dual therapy where one agent was a topical beta-adrenergic antagonist. Patients were included in the study if their IOP was ≥21 mmHg after the 3–6-week timolol run-in period. Patients requiring bilateral treatment had to fulfil all eligibility criteria for both eyes in order to have both eyes included. However, if only one eye fulfilled all inclusion criteria, only that eye was included as the study eye although the other (fellow) eye could be treated with allocated study therapy.

Exclusion criteria were: previous use of more than two ocular hypotensive medications; closed or barely open anterior chamber angle or a history of acute angle closure; ocular surgery or argon laser trabeculoplasty within the last 3 months; ocular filtering surgery at any time; ocular inflammation within the last 3 months, or any abnormal ocular condition that, in the investigator’s judgement, should exclude the patient from the study. In addition, histories of asthma or chronic obstructive pulmonary disease, cardiac failure, sinus bradycardia, or second and third degree atrioventricular block were considered criteria for exclusion, as were severe renal impairment and hyperchloremic acidosis. Women who were pregnant or breast-feeding and women of childbearing potential not using adequate contraception were excluded. Patients with a history of non-compliance or hypersensitivity to benzalkonium chloride or any other component of the study medications were also excluded.

Eligibility was determined at a prestudy visit that took place within the 6 weeks prior to the beginning of the study. At that visit, a medical and ocular history was taken, visual acuity (VA) and refraction were assessed, ophthalmoscopy and slit-lamp examinations were performed, and IOP was measured. Visual field testing was carried out unless it had been performed within the preceding year. Eligible patients were switched from their prescribed current therapy to timolol eye drops (Blocadren®, Merck Sharp & Dohme, Whitehouse Station, New Jersey, USA) at least 3 weeks before the start of the study. Three scheduled visits occurred during the 3-month treatment period: at baseline, at 2 weeks and at 3 months. A follow-up visit/telephone report was conducted within 2–4 weeks of the end of the treatment period. At the baseline visit, patients were assigned to treatment according to a computer-generated randomization code list (Biostatistics and Data Management, Pharmacia Corporation, Stockholm, Sweden), where groups were stratified according to previous ocular hypotensive therapy as well as to centre, and randomization was performed in blocks of consecutive patients within each centre. Envelopes with information concerning treatment assignment were sent to each centre. Once an investigator had confirmed that a patient was eligible for inclusion, the next consecutive envelope was opened, revealing the allocated treatment group for that patient.

Intraocular pressure was measured with calibrated Goldmann applanation tonometers. Three measurements were performed in each eye, starting with the right eye and alternating between eyes. Intraocular pressure levels were measured at 10:00 am and 5:00 pm at baseline, at any time before 12:00 pm at 2 weeks, and again at 10:00 am and 5:00 pm at 3 months. At each visit, best-corrected Snellen VA and refractive error were determined and a slit-lamp examination was performed. Cells and flare in the anterior chamber were looked for in the slit-lamp examination. Flare was graded as none, mild, moderate or severe, while cells present in a slit of 2 mm width were graded as none (1–2 cells), mild (3–5 cells), moderate (6–20 cells) or severe (>20 cells). At the prestudy and 3-month visits, ophthalmoscopy with examination of the vitreous body, retina and optic nerve head was performed through dilated pupils.

Adverse events were monitored carefully throughout the study. An adverse event was defined as any undesirable event occurring in a subject, whether or not the event was considered to be related to the investigational drugs. A serious adverse event was one that resulted in death, was life threatening or sight threatening, was disabling, required or prolonged hospitalization, or was associated with a congenital anomaly/birth defect.

The primary efficacy variable was the difference between groups in mean IOP reduction in study eye(s) from baseline to 3 months of treatment. Mean IOP was defined as the mean value of measurements at 10:00 am and 5:00 pm. If both eyes of a patient were studied, the mean
of both eyes was used in the calculations. Secondary efficacy variables were differences within and between groups in mean IOP reduction from baseline to 3 months of treatment stratified by measurement time (10:00 am and 5:00 pm), and differences in percentages of patients reaching target IOP levels.

Changes in the mean of IOP measurements from baseline to month 3 were analysed using the analysis of covariance model (ANCOVA), with baseline IOP as the covariate, and group and centre as factors. Reductions are reported as adjusted means ± standard errors of means. The 95% confidence interval (CI) of the difference in the mean change was calculated based on the ANCOVA model. Reductions in IOP from baseline to month 3 at 10:00 am and 5:00 pm were tested within and between treatment groups with ANCOVA using the model structure described for the primary analysis. The significance of differences between groups in the frequency of adverse events was evaluated using Fisher’s exact chi-square test. Intent-to-treat (ITT) efficacy analyses included all patients who received at least one drop of study medication; if data were missing, the last available IOP measurement was carried forward to month 3. Per-protocol (PP) efficacy analyses excluded patients who were withdrawn from therapy, who did not return for the month 3 follow-up evaluation, or who had protocol deviations (e.g. patients whose time from morning administration of the eye drop to the 10:00 am tonometry was < 1 hour). Prior to the study, a sample size of 86 patients per treatment group was calculated as sufficient to detect a difference of 0.5 mmHg in mean IOP reduction between treatment groups with a significance level of 0.05, a power of 0.80, and a standard deviation for IOP reduction of 3.5 mmHg. To allow for withdrawals, we set out to recruit a minimum of 100 patients for each treatment group.

Results

Of the 226 patients included in the study, 113 were randomized to receive latanoprost monotherapy and 113 were randomized to receive the fixed combination of dorzolamide plus timolol. (A diagram of patient flow is presented in Fig. 1) One patient from the dorzolamide plus timolol group received no study medication and was excluded from all analyses. Characteristics of the 225 patients in the ITT population are presented in Table 1. There were no significant differences between groups in terms of age, gender or diagnosis. Overall, 96% of patients (217/226) completed the study. Of the nine ITT patients withdrawn, five were from the latanoprost group and four were from the dorzolamide plus timolol group. Reasons for withdrawal are presented in Table 2.

Table 1. Patient characteristics in the two parallel treatment groups (intent-to-treat population).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Latanoprost (n=113)</th>
<th>Dorzolamide plus timolol (n=112)</th>
<th>Total (n=225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD (n=113)</td>
<td>Mean ± SD (n=112)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>65 ± 11</td>
<td>63 ± 12</td>
<td>64 ± 11</td>
</tr>
<tr>
<td>Range</td>
<td>36–87</td>
<td>19–85</td>
<td>19–87</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>79</td>
<td>75</td>
<td>154</td>
</tr>
<tr>
<td>Male</td>
<td>34</td>
<td>37</td>
<td>71</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary open-angle glaucoma</td>
<td>104</td>
<td>102</td>
<td>206</td>
</tr>
<tr>
<td>Pseudoxfoliatitive glaucoma</td>
<td>7</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Mixed diagnosis*</td>
<td>–</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pre-study medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blocker as monotherapy</td>
<td>87</td>
<td>90</td>
<td>177</td>
</tr>
<tr>
<td>Beta-blocker as dual therapy</td>
<td>24</td>
<td>19</td>
<td>43</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

* Mixed diagnosis: different glaucoma diagnosis in right eye and left eye. SD = standard deviation.
Allergic conjunctivitis 1 0
Increased intraocular pressure* 1 0
Ocular irritation 0 1
Rectal tenesmus 0 1
Retinal vein thrombosis* 1 0
Other† 0 1

Table 2. Reasons for patient withdrawals from the study (intent-to-treat population).

<table>
<thead>
<tr>
<th>Reasons</th>
<th>Latanoprost</th>
<th>Dorzolamide plus timolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=5)</td>
<td>(n=103)</td>
<td>(n=102)</td>
</tr>
<tr>
<td>Inclusion/exclusion criteria not fulfilled</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Increased intraocular pressure*</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ocular irritation</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Rectal tenesmus</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Retinal vein thrombosis*</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other†</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

* Reported as serious adverse event. See Results section for further explanation.
† Patients decided to withdraw without specifying a reason.

Table 2. Eleven additional patients were excluded due to protocol violations, giving 103 latanoprost-treated patients and 102 patients treated with dorzolamide plus timolol in PP analyses.

Results of PP analyses of changes from baseline in mean IOP levels in the two treatment groups after 3 months of treatment are presented in Fig. 2. Baseline mean IOP was similar between treatment groups (latanoprost, 23.2 ± 2.1 mmHg versus dorzolamide plus timolol, 23.1 ± 1.6 mmHg). Mean IOP changes after 3 months of therapy were −4.3 ± 0.3 mmHg for the latanoprost group and −4.0 ± 0.3 mmHg for the dorzolamide plus timolol group (p < 0.001 for both), representing reductions of 19% and 17%, respectively. The two therapies were similarly effective in lowering IOP levels (mean difference in IOP reduction: −0.4 ± 0.4 mmHg in favour of latanoprost; 95% CI: −1.1, 0.4). Comparable results were obtained in ITT analyses.

Per-protocol analyses were also performed for IOP reductions at specific time points. Baseline mean IOP levels at 10:00 am were 23.2 ± 2.1 mmHg in the latanoprost group and 23.2 ± 1.7 mmHg in the dorzolamide plus timolol group; after 3 months, reductions in mean IOP levels were −4.1 ± 0.3 mmHg and −4.2 ± 0.3 mmHg, respectively (p = 0.893 for difference between groups; see Fig. 2). Mean baseline IOP levels at 5:00 pm were 23.1 ± 2.5 mmHg in the latanoprost group and 22.9 ± 1.9 mmHg in patients receiving dorzolamide plus timolol; at month 3, reductions in mean IOP levels at 5:00 pm were −4.6 ± 0.3 mmHg and −3.8 ± 0.3 mmHg, respectively, giving a −0.7 ± 0.4 mmHg difference in favour of latanoprost (p = 0.045). At both time points, within treatment group reductions were statistically significant (p < 0.001).

Percentages of patients reaching specific reductions in mean IOP levels are shown in Table 3. A ≥20% reduction in mean IOP was achieved by 52% of patients in the latanoprost group and by 43% of patients in the dorzolamide plus timolol group.

Twenty-seven (24%) latanoprost patients reported 34 adverse events. This included 21 (19%) patients who reported 23 ocular-related signs or symptoms. In the dorzolamide plus timolol group, 40 (36%) patients experienced 58 adverse events, including 33 (30%) patients who reported 41 ocular-related signs or symptoms (Table 4). This reflects a trend where a higher proportion of patients treated with dorzolamide plus timolol was likely to report at least one adverse event and at least one ocular adverse event (p = 0.059 and p = 0.062, respectively), than were latanoprost-treated patients. Looking specifically at ocular adverse events, ocular discomfort was reported by nearly five times as many dorzolamide plus timolol-treated patients as latanoprost-treated patients. Similar proportions of patients in each group reported systemic adverse events (p = 0.483) (Table 5).

With few exceptions, adverse events in both groups were mild or moderate in severity. There were two serious adverse events: one subject reported IOP decompensation (increased IOP) and one reported retinal vein thrombosis. Both events involved patients receiving latanoprost and led to the discontinuation of the study treatment. The patient with IOP decompensation recovered completely and the individual with retinal vein thrombosis recovered with sequelae.

Table 3. Percentage of patients who reached a specific percentage reduction in mean intraocular pressure (IOP) at 3 months compared with baseline (per protocol population).

<table>
<thead>
<tr>
<th>IOP reduction from baseline (%)</th>
<th>Latanoprost (n=103)</th>
<th>Dorzolamide plus timolol (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>≥25</td>
<td>30</td>
<td>25</td>
</tr>
<tr>
<td>≥20</td>
<td>52</td>
<td>43</td>
</tr>
<tr>
<td>≥15</td>
<td>72</td>
<td>62</td>
</tr>
<tr>
<td>≥10</td>
<td>79</td>
<td>82</td>
</tr>
</tbody>
</table>

Fig. 2. Change in intraocular pressure (IOP) from baseline after 3 months of treatment with latanoprost monotherapy or the fixed combination of dorzolamide plus timolol (*p < 0.001 for differences within groups; †p < 0.045 for differences between groups).
One other latanoprost-treated patient withdrew from the study due to moderately severe allergic conjunctivitis. The only ocular adverse event-related withdrawal in the dorzolamide plus timolol group involved a patient with moderate irritative symptoms.

**Discussion**

In the medical treatment of glaucoma, a change of therapy is frequently warranted because the currently prescribed drug becomes ineffective or the disease itself progresses. Very often, a second drug is added to the first, making combination therapy common in clinical practice. The present study aimed to compare the effects of two alternative therapeutic changes in patients whose current treatment did not sufficiently control IOP. The changes involved either a change to once-daily monotherapy with latanoprost after using timolol as monotherapy for 3–6 weeks, or a change to twice-daily dual therapy with the fixed combination of dorzolamide plus timolol after using timolol as monotherapy for 3–6 weeks.

**Table 4.** Number of ocular adverse events reported during the study (intent-to-treat population).

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Latanoprost (n=113)</th>
<th>Dorzolamide plus timolol (n=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular discomfort*</td>
<td>7</td>
<td>33</td>
</tr>
<tr>
<td>Conjunctivitis/blepharitis</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Hypoaesthesia</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Blurred/decreased vision</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Other†</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>41</td>
</tr>
</tbody>
</table>

* Includes irritation, burning, and eye pain.
† Includes one report each of cataract, increased IOP, conjunctival discoloration, keratitis, eyelid oedema, retinopathy, retinal vein thrombosis, and vitreous disorder not otherwise specified in the latanoprost group and one report each of epiphora and meibomianitis in the dorzolamide plus timolol group.

Both treatments resulted in reductions in mean IOP levels compared with baseline: −19% for latanoprost and −17% for the fixed combination of dorzolamide plus timolol. These results are in agreement with a study by Emmerich (2000), where glaucoma patients switching from timolol to latanoprost and patients adding dorzolamide to timolol experienced IOP reductions of 20%. Another study (Garcia Sanchez & the Spanish Latanoprost Study Group 2000) demonstrated that glaucoma patients on timolol treatment who switched to latanoprost monotherapy had an additional 23% reduction in mean diurnal IOP after 3 months of treatment, while patients who added dorzolamide to their timolol treatment experienced an additional 17% reduction in mean IOP (p=0.005). The designs used by Emmerich (2000), Garcia Sanchez & the Spanish Latanoprost Study Group (2000) and the present research included initial timolol monotherapy, a factor that may have underestimated the effect of study treatments. Thus, a recent 3-month study (Fetchner et al. unpublished) of 246 patients with ocular hypertension or open-angle glaucoma randomly assigned to receive either latanoprost monotherapy or the fixed combination of dorzolamide plus timolol twice daily following washout of ocular hypotensive medications revealed reductions in mean diurnal IOP levels of 27% and 26%, respectively.

In the current study, the IOP measurement taken at 10:00 am may represent the peak effect of latanoprost and the combination of dorzolamide plus timolol, while the measurement taken at 5:00 pm may represent a reasonable estimate of the trough effect of the two treatments, although it probably comes before the true trough, at least for dorzolamide. At 10:00 am, both latanoprost monotherapy and the combination treatment of dorzolamide plus timolol reduced IOP by 18% to 19% compared with baseline. The same comparison at 5:00 pm resulted in a significantly larger percent reduction in IOP by latanoprost (21%) compared with the dorzolamide plus timolol fixed combination (17%). Latanoprost thus seems to result in a more stable reduction of IOP over the whole day. In fact, this long-lasting and steady IOP reduction was reported to last over the 24-hour period in a study by Larsson (2001), where latanoprost monotherapy provided a smooth diurnal and nocturnal IOP curve without any peaks, and IOP reduction was consistent over the 24-hour period. Maintaining stable IOP levels is important in management of glaucoma because IOP fluctuations have been found to represent a significant risk factor for disease progression (Asrani et al. 2000).

Complex treatment schedules can affect quality of life in glaucoma patients (Perfetti et al. 1998; Sherwood et al. 1998; Perfetti et al. 1998) reported that an increased number of medications negatively impact these patients’ daily lives. A simple treatment schedule also may maximize patient compliance (Weinreb 1992; Patel & Spaeth 1995). Therefore, the aim of medical glaucoma treatment may be to select the simplest treatment regimen that achieves the most effective IOP reduction in order to prevent or at least slow disease progression and to prevent the development of a visual handicap (Collaborative Normal-Tension Glaucoma Study Group 1998).

Switching to another drug rather than combining therapies is one way of achieving a simple treatment schedule.

In general, the two study drugs were well tolerated locally and systemically by the study patients, most of whom were elderly, with no major differences be-
tween the groups. Compared with latanoprost-treated patients, however, almost five times as many patients receiving dorzolamide plus timolol reported burning, stinging or eye pain, side-effects which may compromise compliance over time. Dorzolamide has been associated with ocular discomfort in other studies (Barneby & Kwok 2000; Silver & the Brinzolamide Comfort Study Group 2000) and may be the component of the combination drug responsible for these side-effects. Although fewer adverse events would generally be expected with the administration of one drug, compared with two drugs, conditions such as hypertrichosis (Johnstone 1997) and hyperpigmentation (Grierson et al. 2001) that are sometimes associated with long-term latanoprost use might not have developed during this 3-month study (Wistrand et al. 1997).

In conclusion, switching from timolol to latanoprost monotherapy resulted in similar reductions in IOP levels, as did changing to the fixed combination of dorzolamide plus timolol. In addition, latanoprost monotherapy resulted in a more stable IOP reduction over the course of the day, while the two therapies exhibited similar safety profiles. Thus, latanoprost monotherapy might be preferable to combined treatment with dorzolamide plus timolol in patients whose IOP is insufficiently controlled by timolol alone.

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