Persistence of Patients Receiving Topical Glaucoma Monotherapy in an Asian Population

Desmond T. L. Quek, MRCSEd; Geok-Teng Ong, BSc; Shamira A. Perera, FRCOphth; Ecosse L. Lamoureux, PhD; Tin Aung, FRCOphth, PhD

Objective: To determine the persistence rates of patients who started taking topical intraocular pressure (IOP)-lowering monotherapy in a Singapore eye hospital.

Methods: This was a retrospective review of patients who started taking a single IOP-lowering medication between October 1, 2005, and September 30, 2006. Pharmacy dispensing records were traced for 3 years from the date of first prescription. A patient was defined as persistent if he or she was prescribed the same medication before or within 90 days after the previous prescription had lapsed during this period. Persistence was assessed after 1 and 3 years.

Results: A total of 2781 patients started taking topical IOP-lowering monotherapy during the 1-year study period. The mean (SD) age was 61.1 (15.7) years; 50.2% were male, and most were Chinese (81.1%) or Singaporean residents (85.4%). After 1 year, only 22.5% of patients (626 of 2781) persistently received the same therapy, which decreased to 11.5% (320 of 2781) after 3 years. Prostaglandin analogues had better persistence rates at 1 year compared with timolol maleate (29.6% vs 23.7%; \( P = .004 \)) and all other medications combined (29.6% vs 20.6%; \( P < .001 \)). Those who were not persistent at year 1 were younger (\( P < .001 \)) and more likely to not be Singaporean (\( P = .008 \)), not receiving government subsidies (\( P < .001 \)), and receiving unilateral therapy (\( P < .001 \)).

Conclusions: In this hospital-based study, the persistence rate of patients who started taking topical IOP-lowering monotherapy was low after 1 (22.5%) and 3 years (11.5%). These rates are lower than in previous studies in Western countries and may have implications for glaucoma care in Singapore and other parts of Asia.


Glaucoma, the leading cause of irreversible blindness worldwide,1 frequently requires long-term medical treatment to lower intraocular pressure (IOP) and prevent progressive visual field loss.2-3 Patients, however, often do not use medications as prescribed4-10 and are prone to poor adherence and persistence,11 leading to suboptimal treatment outcomes and increased health care costs.12,13 Persistence measures the duration of time that a patient fills a prescription and continues a prescribed therapy,14 which is a prerequisite for adherence. Persistence rates of patients who started taking initial glaucoma medications in the United States have been reported to be as low as 25% at 1 year,5,10,16 with prostaglandin analogues reportedly having higher persistence rates than beta-blockers and other classes of ocular hypotensive therapies.5,8,10,16-22

It has been estimated that by 2020,1 47% of the estimated 79.6 million people with glaucoma will be Asian, but to date, there are no data on persistence rates of IOP-lowering medications in Asian persons with glaucoma. The aim of this study was to determine the persistence rates during 3 years after Asian patients started taking topical IOP-lowering monotherapy in a Singapore hospital.

METHODS

The study had the approval of the hospital’s institutional review board. We performed a retrospective review of the pharmacy database of patients at the Singapore National Eye Centre (SNEC) during a 4-year period from October 1, 2005, to September 30, 2009. Patients who started taking a single IOP-lowering medication between October 1, 2005, and September 30, 2006 (and who were never dispensed any IOP-lowering therapy in the year before) were identified to measure persistence. Pharmacy dis-
pensing records of this cohort were traced from the date of the first prescription to 3 years thereafter. The SNEC pharmacy database was created on October 1, 2004, and includes information on patients’ demographics, billing status (those receiving government subsidies vs those without), and the type, quantity, and laterality of medication(s) prescribed. At the SNEC, almost all patients fill their prescriptions at a single pharmacy located within the center. Patients who were not receiving government subvention paid approximately 7% more for all medications (except for Travoprost, which was made available to government subvention paid approximately 7% more for all medications, and 60 days) between successive prescriptions in the definition of persistence.

A total of 2781 patients started receiving IOP-lowering monotherapy between October 1, 2005, and September 30, 2006. There were similar numbers of men and women (50.3% men), with a mean (SD) age of 61.1 (15.7) years. Of these patients, 81% (n=2254) were Chinese, 85% (n=2374) were Singaporean residents, and 51% (n=1423) were receiving government subsidies for their medications (Table 1). Timolol maleate, 0.5%, was the most frequently prescribed medication (62.2%), followed by Travoprost, 0.004% (10.4%), Latanoprost, 0.005% (10.4%), Brimonidine, 0.15% (9.5%), Dorzolamide, 2% (4.1%), pilocarpine, 4% (1.9%), Bimatoprost, 0.03% (0.8%), and Brinzolamide, 1% (0.7%). A total of 62.5% of patients (n=1738) were prescribed unilateral therapy, and the remaining 37.5% (n=1043) started receiving bilateral therapy.

At the end of 1 year, only 626 of 2781 patients (22.5%) persistently took the same therapy. Of these, 62.1% (n=389) continued taking the same medication, while 37.9% (n=237) were prescribed additional IOP-lowering medication(s). Table 2 shows the persistence rates of various medications at 1 year. Of the 2155 patients (77.5%) who were not persistent at the end of 1 year, 66.3% (n=1428) terminated therapy and were never subsequently prescribed any IOP-lowering medication, 17.6% (n=380) started taking a different medication (without a lapse), 12.7% (n=273) restarted therapy with the same medication, while 0.3% (n=7) restarted therapy with other medication(s) in addition to the original one (Figure 1).

Of the 1428 subjects who terminated therapy at the end of 1 year and were never subsequently prescribed any IOP-lowering medication, only 30.4% (434 of 1428) defaulted follow-up and never subsequently attended SNEC. The remaining 69.9% were still attending SNEC after 1 year.

Compared with persistent patients, the nonpersistent group tended to be younger (mean age, 60.2 vs 64.1 years; P < .001) and more likely to not be Singaporean (16.3% vs 12.0%; P = .008), not be receiving government subsidies (51.7% vs 42.3%; P < .001), and be receiving unilateral therapy (68.6% vs 41.5%; P < .001). There were no significant differences in sex or race between the 2 groups (P = .51 and P = .23, respectively). When compared with all other medications combined, prostaglandin analogues as a group (travoprost, latanoprost, bima-
toprost) had a better persistence rate at 1 year (29.6% vs 20.6%; \( P < .001 \)). Similarly, the persistence rate of prostaglandin analogues as a group was better than that of timolol (29.6% vs 23.7%; \( P = .004 \)).

After 3 years, only 320 of 2781 patients (11.5%) persistently received the same therapy. Of these, 40.9% (n=131) continued taking only the same medication, while 59.1% (n=189) required additional IOP-lowering medication(s). Of the 2461 subjects (88.5%) who were not persistent at the end of 3 years, 56.3% (n=1386) terminated therapy and were never subsequently prescribed any IOP-lowering medication during the duration of the study period, 17.7% (n=436) began taking a different medication (without a lapse), 20.1% (n=494) restarted treatment with the same medication, 5.6% (n=137) restarted treatment with a different medication, and 0.3% (n=8) restarted treatment with other medication(s) in addition to the initial one (Figure 2). Timolol had a better persistence rate at 3 years (12.5% vs 9.8%; \( P = .03 \)) than all other medications combined. There was no significant difference in persistence rates (at 3 years) of prostaglandin analogues as a group (12.9%) compared with all other medications combined (11.1%) or prostaglandin analogues compared with timolol (12.5%; \( P > .05 \)).

We further computed the corresponding persistence rates using varying intervals between successive prescriptions as the definition of persistence. The overall persistence rates at 1 year using 14-, 28-, and 60-day maximal intervals in the definition of persistence were 8.6%, 12.8%, 19.0%, respectively (Table 3 and Table 4). As secondary analysis, we excluded patients who began taking a single IOP-lowering medication for a period of less than 30 days and never subsequently prescribed either the same or any other IOP-lowering medication thereafter. Such patients were presumably prescribed short-term IOP-lowering therapy for transient spikes in IOP. After excluding these patients, the persistence rates at the end of 1 and 3 years were 34.9% and 18.0%, respectively.

We performed a further analysis of the patients who began taking unilateral monotherapy for a period of more than 30 days. Of the 887 patients who belonged to this group, persistence rates were 29.8% (n=264) and 15.6% (n=138) at the end of 1 and 3 years, respectively. These rates remained statistically lower than those of patients who began receiving bilateral monotherapy for a period of greater than 30 days (40.2% and 20.5% at the end of 1 and 3 years, respectively; \( P < .001 \) and \( P = .008 \), respectively).

Using a 90-day interval between successive prescriptions as the definition of persistence, the persistence rates among Singaporean individuals at the end of 1 year was 23.4%. This is not significantly different from the overall persistence rate of 22.5% (\( P = .44 \)). Hence, although persons in the nonpersistent group were more likely to not be Singaporean (\( P = .008 \)), the persistence rate of Sin-

---

**Table 3**

<table>
<thead>
<tr>
<th>Medication Combination</th>
<th>Persistence Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same medication</td>
<td>62.1%</td>
</tr>
<tr>
<td>Additional medication</td>
<td>37.9%</td>
</tr>
<tr>
<td>Changed medication</td>
<td>39.1%</td>
</tr>
</tbody>
</table>

**Table 4**

<table>
<thead>
<tr>
<th>Medication Combination</th>
<th>Persistence Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same medication</td>
<td>78.7%</td>
</tr>
<tr>
<td>Additional medication</td>
<td>21.3%</td>
</tr>
<tr>
<td>Changed medication</td>
<td>65.7%</td>
</tr>
</tbody>
</table>

**Figure 1.** Persistence rates at the end of 1 year.

**Figure 2.** Persistence rates at the end of 3 years.
Patients fail to be persistent with glaucoma therapy for various reasons including cost, tolerability, difficulty with administration, denial, lack of education, forgetfulness, and physician’s satisfaction with IOP control. To our knowledge, this is the first study undertaken to assess the persistence rates of patients who began taking glaucoma medication in an Asian country, namely Singapore. We found persistence rates to be only 22.5% at 1 year and 11.5% at 3 years, figures that are notably lower than have been reported in white populations.9,17,21,24-26 The increased likelihood of angle-closure glaucoma diagnoses in this Asian population might skew the persistence data compared with the greater number of patients with open-angle glaucoma in the previously published Western studies. The findings are of concern and have implications for glaucoma care in Singapore and possibly other countries in Asia. The poor persistence shows that patients frequently change or discontinue their treatment regimen, with potential effects on therapeutic effectiveness. These results indicate that strategies are urgently needed to elucidate reasons for poor persistence and to improve persistence in this population.

Previous studies have reported prostaglandin analogues to be associated with better persistence than any other drug class. For example, latanoprost-treated patients have been found to have higher persistence and lower rates of therapy failure and discontinuation compared with patients treated with other IOP-lowering medications, including beta-blockers.6-10,16-19,21,22 Our study confirms that prostaglandin analogues, as a group, have better persistence rates at 1 year compared with all other medications combined. In a retrospective survey of pharmaceutical records of American patients recruited during a 6-month period and followed up for 12 months, 1-year persistence rates of 69.4% for latanoprost, 70.6% for travoprost, and 68.1% for bimatoprost were reported.24 This is in contrast to our 1-year persistence rates of 36.7% for travoprost, 23.6% for latanoprost, and 14.3% for bimatoprost. Possible reasons for the differences between the 2 studies could be differing inclusion criteria, socioeconomic backgrounds, and health care systems. However, at 3 years, we found the persistence rate of timolol to be higher than for all other medications combined. Various factors including the cheaper cost of timolol, low frequency of ocular adverse effects, and physician and/or patient preferences could account for this observation.
In conclusion, we found that persistence rates of patients in a Singapore hospital who began taking IOP-lowering monotherapy were very low after 1 and 3 years. We believe that these results are reflective of persistence of patients with glaucoma in this region and fear that persistence may be even worse in less developed countries in Asia. Prospective cohort studies investigating reasons for lack of persistence, including the effect of the type and severity of glaucoma on persistence, should be carried out to help characterize patients who tend to be nonpersistent. In the long term, there is a need to implement appropriate strategies to improve persistence in patients with glaucoma.

Submitted for Publication: August 3, 2010; final revision received October 10, 2010; accepted November 9, 2010. Published Online: January 10, 2011. doi:10.1001/archophthalmol.2010.345

Correspondence: Tin Aung, FRCOphth, PhD, Singapore National Eye Centre, 11 Third Hospital Ave, Singapore 168751 (aung.tin@snec.com.sg).

Financial Disclosure: Dr Aung reports receiving research support from Alcon and Allergan and travel support/honoraria from Alcon, Pfizer, Allergan, Santen, and Merck.

Funding/Sponsor: This study was supported by a grant from the National Medical Research Council, Singapore.

REFERENCES


168751 (aung.tin@snec.com.sg).
Thus while it will do no harm if the pianist sits blankly in front of his piano for five minutes, or the orator stares and stutters at his audience and halts at the beginning of his speech, it may imperil the success of a cataract operation if the operator attempts to operate when in a similar state of nervousness.