European Journal of Ophthalmology / Vol. 13 / Suppl. 4, 2003 / pp. S1-S4

Topical therapies for glaucoma and ocular hypertension: An update on current practice

Introduction

J-F. ROULAND

Ophthalmology Service, Regional and University Hospital Center, Claude Huriez Hospital, Lille - France

Glaucoma is a group of diseases of the eye that is characterized by progressive, irreversible optic nerve damage and visual field loss (1). Ocular hypertension, often a precursor to glaucoma, is considered to be present in patients with intraocular pressure (IOP) levels >21 mmHg and no optic nerve damage (1). Current treatment in patients with both conditions focuses on lowering IOP levels, usually with ocular hypotensive medications. This approach is supported by research demonstrating that reduced IOP levels in patients with ocular hypertension delay and prevent the onset of glaucoma (2). IOP reductions in glaucoma patients, for whom no direct treatment for optic neuropathy exists, have been associated with prevention of disease progression, protection of the optic nerve, and preservation of the visual field (3-6).

For more than a decade, first-line therapy in patients with glaucoma or ocular hypertension has consisted of a topical beta-adrenergic blocker. When beta-blocker therapy proved ineffective, patients were switched to monotherapy with an agent in an alternate drug class, eg, a systemic carbonic anhydrase inhibitor or cholinergic agent, or were treated with a combination of a beta-blocker and another ocular hypotensive. If IOP remained uncontrolled, surgery often was undertaken. The introduction of new medications that lower IOP has altered treatment strategies in recent years. Many ophthalmologists now prescribe drugs such as prostaglandin analogues as either first- or second-line therapies, and the increasing use of such medications has been associated with reductions in rates of trabecular surgery (7-9).

The standard method for evaluating the efficacy and safety of a newly developed drug is the double-blind, randomized, controlled clinical trial. The results of such trials may have limited applicability to actual medical practice, however. The patients included are selected from relatively homogeneous populations that are often quite different from the population of future users, and the conditions of clinical trials in which dose, duration of therapy, and follow-up regimens are dictated are rarely (if ever) duplicated in routine practice settings. Studies of drug use in naturalistic settings are needed, and this supplement to the *European Journal of Ophthalmology* provides results of naturalistic studies of persistency (time on therapy), effectiveness, cost, and utilization patterns of therapies for glaucoma and ocular hypertension.

The first article by Rouland et al (10) summarizes the results of a naturalistic, prospective study of the clinical outcomes and treatment costs of second-line treatment strategies in patients with primary open-angle glaucoma or ocular hypertension in France. The article reports an interim analysis of 1-year follow-up data for nearly 300 patients (more than 500 eyes) who had at least two contacts with a study ophthalmologist.

Diestelhorst et al (11) present results of a 2-year, observational, multicenter, retrospective medical chart review study conducted in four European countries. Patients with primary open-angle glaucoma or ocular hypertension whose first-line glaucoma treatment was latanoprost or a beta-blocker are compared with regard to time on therapy and several clinical outcomes, including IOP level, nerve head excavation, and visual field defect.

 1120-6721/S1-04$02.00/0

TABLE - SUMMARY OF KEY FINDINGS FROM FIVE STUDIES OF TOPICAL THERAPIES FOR GLAUCOMA OR OCULAR HYPERTENSION

Variable	Author	Methods	Key findings
Persistency	Rouland et al (10)	• Naturalistic, prospective study of second-line treatment strategies in patients with POAG or OH treated in 37 centers in France between 1998 and 2000 • n=549 eyes • Interim analysis of 1-year data	• Patients with eyes treated with latanoprost either alone or in combination with another drug stayed on therapy longer (p≤0.01) and were more likely to remain on treatment after 1 year (p<0.01) than those treated with beta-blocker monotherapy or a combination not including latanoprost
	Diestelhorst et al (11)	• Retrospective chart review conducted in four European countries • Patients with POAG or OH who began initial treatment with latanoprost (n=94) or a beta-blocker (n=166) between 1996 and 1998 • Two-year follow-up	• Patients receiving latanoprost initially stayed on therapy more than twice as long as those who received a beta-blocker (p<0.0001) • Those receiving a beta-blocker first were 3.8 times more likely to change therapy than those treated initially with latanoprost (p<0.0001)
	Bernard et al (12)	• Decision-analytic model compared costs and consequences of latanoprost or beta-blocker as first-line treatment • Hypothetical cohort of patients newly diagnosed with open-angle glaucoma and/or OH assessed over 2 and 3 years' duration • Analyses assumed 10,000 patients for each treatment strategy	• Latanoprost-treated patients remained on initial therapy for an average of 20.5 months compared to 13.4 months for those treated first with a beta-blocker (p<0.0001) • After 2 and 3 years, patients receiving first-line latanoprost treatment used fewer therapies than those treated initially with a beta-blocker (p<0.0001)
	Reardon et al (13)	• Population-based, retrospective cohort study in a US managed care plan • Patients treated initially with betaxolol, brimonidine, dorzolamide, latanoprost, or timolol between 1999 and 2001 • n=2850	• Patients first treated with latanoprost monotherapy were more persistent with therapy than those who began treatment with any alternate therapy (p<0.05)
Effectiveness	Rouland et al (10)	• See Persistency section (above)	• Mean IOP reductions were greater in eyes treated with latanoprost versus beta-blocker monotherapy (p=0.02) and in eyes treated with the latanoprost + timolol versus combination therapies that did not include latanoprost (p=0.01)
	Diestelhorst et al (11)	• See Persistency section (above) • Clinical outcomes were measured until the time of first therapy change or last study visit, whichever came first	• Patients first treated with latanoprost monotherapy had greater mean decreases in IOP (p<0.0001) and fewer had worsened optic nerve head excavation (p<0.05) than those receiving a beta-blocker
	Bernard et al (12)	• See Persistency section (above)	• Compared with patients receiving first-line beta-blocker therapy, those receiving latanoprost initially experienced 50 more days of IOP control over two years and 74 more days of IOP control over 3 years (p<0.0001 for both comparisons)

to be continued

TABLE - SUMMARY OF KEY FINDINGS FROM FIVE STUDIES OF TOPICAL THERAPIES FOR GLAUCOMA OR OCULAR HYPERTENSION (continued)

Variable	Author	Methods	Key findings
Costs	Rouland et al (10)	• See Persistency section (above) • Resource use was evaluated from the perspective of the National Health Insurance	• The average daily cost for latanoprost monotherapy was similar to that for patients who failed beta-blocker monotherapy • Latanoprost + timolol was less costly than therapeutic combinations without latanoprost
	Bernard et al (12)	• See Persistency section (above) • Resource use was evaluated from a third-party payer perspective	• Latanoprost's higher acquisition costs were largely offset by reductions in costs associated with surgical procedures, resulting in an additional cost of € 41 and € 27 over 2 and 3 years, respectively • Incremental cost per day of IOP control gained when using the first-line latanoprost strategy compared to the first-line beta-blocker strategy was € 0.82 and € 0.36 over 2 and 3 years, respectively
Utilization	Baudouin et al (14)	• Numbers of patients in France treated with latanoprost, brimonidine, or fixed combination dorzolamide + timolol were derived from sales and defined daily doses • Frequencies of trabecular surgeries between 1997 and 2000 in France were extracted from national data bases • Costs of surgeries were estimated using governmental cost scales	• Number of patients treated with these drugs increased from 410,000 to 734,000 patients per year • 245,000 were treated with latanoprost (71.0%), brimonidine (28.8%), or dorzolamide + timolol (0.2%) • The surgery rate in patients receiving medical therapy for glaucoma declined by 47%, from 5.9% to 3.1% • Reductions in surgeries were strongly correlated with increases in numbers of patients receiving new therapies

€=Euro; IOP=Intraocular pressure; OH=Ocular hypertension; POAG=Primary open-angle glaucoma; US=United States

Next, Bernard et al (12) use a decision-analytic model made up of data from a retrospective chart review conducted in four European countries. The cost-effectiveness of treatment strategies that utilize latanoprost as first-line therapy is compared with those based on initial beta-blocker therapy in patients with open-angle glaucoma or ocular hypertension in France. A hypothetical cohort including 10,000 newly diagnosed patients for each treatment strategy is assessed over 2 and 3 years.

Reardon et al (13) report findings of a population-based, retrospective cohort study of claim records from a large New England (United States) insurer. Survival analysis is used to compare rates of therapy discontinuation or discontinuation/change for patients who initiated monotherapy with betaxolol, brimonidine, dorzolamide, or timolol against rates for the reference therapy, latanoprost, a prostaglandin analogue that is becoming the new standard of pharmacologic ocular hypotensive care.

Finally, Baudouin et al (14) analyze quantitative changes that have occurred in glaucoma treatment strategies between 1997 and 2000 in France. In particular, these authors assess the relationship between changes in numbers of patients treated with three relatively new ocular hypotensives (latanoprost, brimonidine,

or the fixed combination of dorzolamide + timolol) and reductions in the frequency of trabecular surgery. Results are compared with those from recent studies showing shifts in surgical rates in Scotland (7, 8) and the United States (9).

Together these articles provide a compendium of studies based on data from routine practice settings that can be used by physicians as they assess and compare various topical ocular hypotensives.

Key findings regarding persistency, effectiveness, costs, and utilization are summarized in the Table.

ACKNOWLEDGMENTS

The author wishes to thank Lisa Cowan, PhD for editorial assistance.

Reprint requests to:
Prof. Jean-François Rouland, MD
Service d'Ophtalmologie
Centre Hospitalier Régional Universitaire de Lille
Hôpital Claude Huriez
12 avenue Oscar Lambret
59037 Lille, France
jfr3@wanadoo.fr

REFERENCES

1. Alward WLM. Medical management of glaucoma. N Engl J Med 1998; 339: 1298-307.
2. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study. A randomised trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002; 120: 701-13.
3. The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. Am J Ophthalmol 2000; 130: 429-40.
4. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Am J Ophthalmol 1998; 126: 487-97.
5. Collaborative Normal-Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. Am J Ophthalmol 1998; 126: 498-505.
6. Mao LK, Stewart WC, Shields MB. Correlation between intraocular pressure control and progressive glaucomatous damage in primary open-angle glaucoma. Am J Ophthalmol 1991; 111: 51-5.
7. Bateman DN, Clark R, Azuara-Blanco A, Bain M, Forrest J. The impact of new drugs on management of glaucoma in Scotland: observational study. BMJ 2001; 323: 1401-2.
8. Bateman DN, Clark R, Azuara-Blanco A, Bain M, Forrest J. The effects of new topical treatments on management of glaucoma in Scotland: an examination of ophthalmological health care. Br J Ophthalmol 2002; 86: 551-4.
9. Paikal D, Yu F, Coleman AL. Trends in glaucoma surgery incidence and reimbursement for physician services in the Medicare population from 1995 to 1998. Ophthalmology 2002; 109: 1372-6.
10. Rouland J-F, Le Pen C, and the Ophthalmologists of the GLAUCOMA Study. Naturalistic, prospective study of glaucoma and ocular hypertension treatment in France: strategies, clinical outcomes, and costs at 1 year. Eur J Ophthalmol 2003; 13 (Suppl 4): S5-20.
11. Diestelhorst M, Schaefer CP, Beusterien KM, et al. Persistency and clinical outcomes associated with latanoprost and beta-blocker monotherapy: evidence from a European retrospective cohort study. Eur J Ophthalmol 2003; 13 (Suppl 4): S21-9.
12. Bernard LM, Althin R, Dhawan R, Grima DT, Lam A, Aballéa S. Clinical and economic impacts of latanoprost 0.005% in the first-line treatment of open-angle glaucoma and ocular hypertension in France. Eur J Ophthalmol 2003; 13 (Suppl 4): S30-43.
13. Reardon G, Schwartz GF, Mozaffari E. Patient persistency with pharmacotherapy in the management of glaucoma. Eur J Ophthalmol 2003; 13 (Suppl 4): S44-52.
14. Baudouin C, Rouland J-F, Le Pen C. Changes in medical and surgical treatments of glaucoma between 1997 and 2000 in France. Eur J Ophthalmol 2003; 13 (Suppl 4): S53-60.