European Journal of Ophthalmology / Vol. 13 / Suppl. 4, 2003 / pp. S53-S60

Changes in medical and surgical treatments of glaucoma between 1997 and 2000 in France

C. BAUDOUIN[1], J-.F ROULAND[2], C. LE PEN[3]

[1]National Hospital Center of Ophthalmology of Quinze-Vingts, Paris
[2]Ophthalmology Service, Regional and University Hospital Center, Claude Huriez Hospital, Lille
[3]Dauphine University of Paris, Paris - France

PURPOSE. *To analyze quantitative changes in glaucoma treatment strategies between 1997 and 2000 in France.*
METHODS. *Numbers of* ab externo *trabeculectomies and other glaucoma surgeries were extracted from the national database of the French Diagnosis Related Group system, which includes data for both public and private hospitals. Mean lengths of stay and hospital costs were estimated using national cost scales published by the French Ministry of Health. Numbers of patients treated per year with latanoprost, brimonidine, or the fixed combination of dorzolamide + timolol were estimated from drug unit sales using defined daily doses for each drug.*
RESULTS. *Between 1997 and 2000, the number of patients treated with a glaucoma drug increased from 410,000 to 734,000 patients per year. This increase was associated with the introduction of three new glaucoma drugs: 245,000 patients received latanoprost (71.0%), brimonidine (28.8%), or the fixed combination of dorzolamide + timolol (0.2%). During the same period, the surgery rate in patients receiving medical treatment declined by 47%, from 5.9% to 3.1% . The total number of glaucoma interventions declined by 4.6% (-12% in public hospitals and 0% in private hospitals). This relative stability resulted mostly from a shift from trabeculectomies to other procedures, mainly to new filtering procedures in private hospitals.*
CONCLUSIONS. *Between 1997 and 2000, new glaucoma drugs, primarily latanoprost and brimonidine, improved intraocular pressure control and delayed surgery, reducing the glaucoma procedure rate in patients receiving glaucoma-related medical treatment by 47%.* Eur J Ophthalmol 2003; 13 (Suppl. 4): S53-S60

KEY WORDS. *Brimonidine, Dorzolamide, Glaucoma, Latanoprost, Surgery, Timolol, Trabeculectomy*

Accepted: May 21, 2003

INTRODUCTION

Elevated intraocular pressure (IOP) is a major risk factor for development of primary open-angle glaucoma (1, 2). Ocular instillation of a hypotensive agent has been shown to effectively delay or prevent the onset of primary open-angle glaucoma in patients with ocular hypertension (2), and reductions in IOP have been associated with delayed progression of both optic nerve damage and visual field defects in patients with glaucoma (3-6). Given these findings, current treatment of glaucoma consists of reducing IOP either through medical therapies or surgery (1).

Historically, first-line medical therapy for glaucoma consisted of treatment with a topical beta-blocker. If this approach fails, many patients are changed to an

The study was presented at the 108th Congress of the French Society of Ophthalmology, 11-15 May 2002, Paris, France

1120-6721/S53-08$04.00/0

agent from another class of drugs, such as the carbonic anhydrase inhibitors or sympathomimetics. More recently, the prostaglandin analogues or combination therapy may be instituted (1), and when more than two topical agents are required to control IOP, surgical treatments may be needed (7).

Potential postoperative complications associated with trabeculectomy, such as excessive filtration and hypotension, which may alter vision, result in great part from the opening of the anterior chamber leading to a rapid ocular decompression (8-10). In order to reduce the incidence of such complications, alternative nonperforating surgical techniques have been developed. These procedures include trabeculotomy, sinusotomy, deep sclerectomy, and viscocanalostomy; long-term outcomes are not known (8-10). Other surgical treatments of glaucoma using lasers include trabeculoplasty and cyclophotocoagulation (7); the long-term efficacy of these treatments is uncertain (8, 11). Regardless of which approach is used, reintervention and/or other treatments are needed if surgery fails.

Since 1997, glaucoma management has changed significantly in France with the introduction of several new ocular hypotensive medications, including latanoprost (available since September 1997; reimbursed since April 1998), brimonidine (available since May 1998; reimbursed since October 1998), and the fixed combination of dorzolamide + timolol (available since November 1998; reimbursed since March 2001). The objective of the present study was to analyze quantitative changes in medical and surgical treatments of glaucoma in France during the period.

MATERIALS AND METHODS

Yearly estimates of numbers of patients treated between 1997 and 2000 with latanoprost, brimonidine, or the fixed combination of dorzolamide + timolol were based on unit sales of these drugs and on defined

TABLE I - FREQUENCIES OF GLAUCOMA-RELATED SURGERIES IN PUBLIC HOSPITALS IN FRANCE: 1997-2000

	Number of procedures				
Procedure (PMSI code)	**1997**	**1998**	**1999**	**2000**	**Change 1997-2000**
Trabeculectomy *ab externo* (H428)	6579	5613	4727	5239	-20%
Other fistulising interventions to facilitate intraocular circulation (H426)	828	885	829	911	+10%
Trabeculotomy *ab externo* (H416)	415	323	295	273	-34%
Treatment of ciliary body by other physical methods (H436)	383	499	547	459	+20%
Other sclerotic-opening interventions (Krasnov, valves, etc.) (H431)	336	357	367	385	+15%
Cyclophotocoagulation (H435)	293	299	379	443	+51%
Photocoagulation of iridocorneal angle (H418)	186	210	187	188	+1%
Other glaucoma interventions (H438)	184	244	310	201	+9%
Other interventions to facilitate intraocular circulation (H419)	132	168	194	215	+63%
Postoperative reintervention of sclerotic opening (H430)	100	103	102	97	-3%
Goniotomy (H415)	98	10	22	24	-76%
Cyclodialysis (H417)	36	50	44	40	+11%
Reduction of the ciliary body secretion without other indications (H437)	29	29	12	18	-38%
Totals	9599	8790	8015	8493	-12%

PMSI=Programme de Médicalisation des Systèmes d'Information

daily doses specified in market authorization summaries of product characteristics, assuming complete treatment compliance. The number of patients treated by combination therapy was estimated by considering the main treatment only: one of two treatments for two-drug combinations, one of three for three-drug combinations, one of four for four-drug combinations, and one of five for five-drug combinations. Thus, a patient was counted only once whether the prescription was for monotherapy or combination therapy. Prescription records revealed that 74.0% of glaucoma-related prescriptions were for a monotherapy, 20.9% were for two-drug combinations, 4.6% for three-drug combinations, 0.4% for four-drug combinations, and 0.1% for five-drug combinations. The annual number of patients receiving medical treatment for glaucoma was estimated by multiplying the number of annual prescriptions by a coefficient of 0.861, taking into account the relative proportions of patients treated with monotherapy and with combination therapy.

The number of surgeries performed in either public or private hospitals in France between 1997 and 2000 was tabulated from information in the Programme de Médicalisation des Systèmes d'Information (PMSI) database (12), a Diagnosis Related Group database managed by the French Ministry of Health. This time frame was chosen because data for the year 2000 were the most recently available when the study was undertaken (in 2002) and because data reported before 1997 by private hospitals were not sufficiently exhaustive to be useful. Trabeculectomy *ab externo* (PMSI procedure code H428) (Tabs. I and II) is the reference surgical treatment for open-angle glaucoma (7). Additional glaucoma interventions include other fistulising interventions to facilitate intraocular circulation (H426), trabeculotomy *ab externo* (H416), other sclerotic-opening interventions (Krasnov, valves, etc.) (H431), postoperative reintervention of sclerotic opening (H430), and goniotomy (H415). Treatments using laser or other physical methods include photocoagulation of irido-corneal angle (H418),

TABLE II - FREQUENCIES OF GLAUCOMA-RELATED SURGERIES IN PRIVATE HOSPITALS IN FRANCE: 1997-2000

	Number of procedures				
Procedure (PMSI code)	**1997**	**1998**	**1999**	**2000**	**Change 1997-2000**
Trabeculectomy *ab externo* (H428)	11.770	12.135	10.685	10.357	-12%
Other fistulising interventions to facilitate intraocular circulation (H426)	691	1083	1371	1382	+100%
Other sclerotic-opening interventions (Krasnov, valves, etc.) (H431)	570	824	812	1052	+85%
Trabeculotomy *ab externo* (H416)	469	590	426	405	-14%
Other interventions to facilitate intraocular circulation (H419)	268	357	335	411	+53%
Postoperative reintervention of sclerotic opening (H430)	123	137	118	82	-33%
Other glaucoma interventions (H438)	115	124	182	236	+105%
Cyclophotocoagulation (H435)	115	108	158	170	+48%
Photocoagulation of iridocorneal angle (H418)	105	44	53	44	-58%
Treatment of ciliary body by other physical methods (H436)	95	124	134	116	+22%
Goniotomy (H415)	42	70	100	84	+100%
Cyclodialysis (H417)	27	24	32	52	+93%
Reduction of the ciliary body secretion without other indications (H437)	11	3	7	6	-45%
Totals	14.401	15.623	14.413	14.397	0%

PMSI=Programme de Médicalisation des Systèmes d'Information

treatment of ciliary body by other physical methods (H436), cyclophotocoagulation (H435), other glaucoma interventions (H438), other interventions to facilitate intraocular circulation (H419), cyclodialysis (H417), and the reduction of the ciliary body secretion without other indications (H437). The surgery rate was obtained by dividing the total number of glaucoma procedures by the total number of glaucoma patients receiving medical treatment (potential surgical candidates).

Mean lengths of stay and hospital costs were estimated using national cost scales published by the French Ministry of Health (12), which assigns a number of resource points to each stay in a Diagnosis Related Group based on its relative index of care intensity; numbers of points are adjusted yearly. The cost per patient in a given Diagnosis Related Group is calculated by multiplying the number of points by the value assigned to points by the French Ministry of Health. Ninety-nine percent of trabeculectomies are classified as other intraocular interventions (PMSI Diagnosis Related Group 054), ambulatory interventions with other surgery (702), or ambulatory interventions on the crystalline (762). In this study, resource utilization and costs for glaucoma surgery were estimated based on data for Diagnosis Related Group 054, although that group does include other procedures.

The relationships between the number of trabeculectomies and the number of patients treated with latanoprost, brimonidine, or the fixed combination of dorzolamide + timolol between 1997 and 2000 were analyzed using a linear regression model. A coefficient of $r^2>0.8$ was considered to be significant.

RESULTS

Between 1997 and 2000, the number of glaucoma patients treated with ocular hypotensives increased by 79.0%, from 410,000 to 734,000 patients per year, respectively, a difference of 324,000 patients. In all, 245,000 of these patients were treated with latanoprost (71.0%), brimonidine (28.8%), or the fixed combination of dorzolamide + timolol (0.2%). As the fixed combination of dorzolamide + timolol was not reimbursed until March 2001, few patients received prescriptions for this medication during the study period. Changes in numbers of glaucoma patients treated per year with latanoprost or brimonidine are shown in Figure 1. The expansion of the therapeutic arsenal offered new medical alternatives when target IOP levels could not be obtained with traditional ocular hypotensives such as beta-blockers, pilocarpine, or dorzolamide. The introduction of these alternatives apparently allowed medical treatment to be prolonged and surgery to be delayed for many patients, and the surgical rate decreased between 1997 and 2000 by 47% in patients receiving glaucoma-related medical treatment, from 5.9% to 3.1% (Fig. 2).

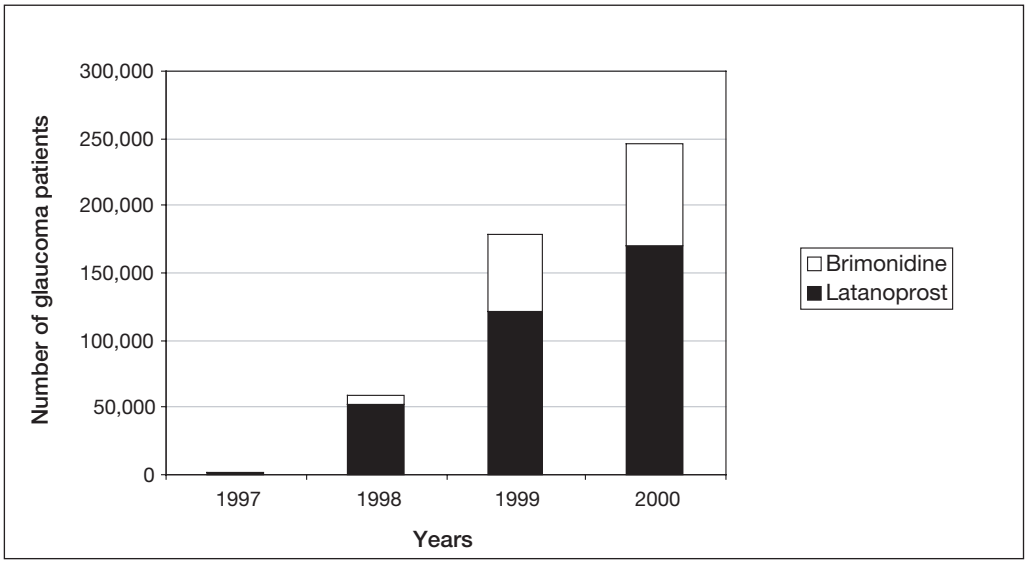

Fig. 1 - *Number of glaucoma patients treated per year with latanoprost or brimonidine in France: 1997-2000.*

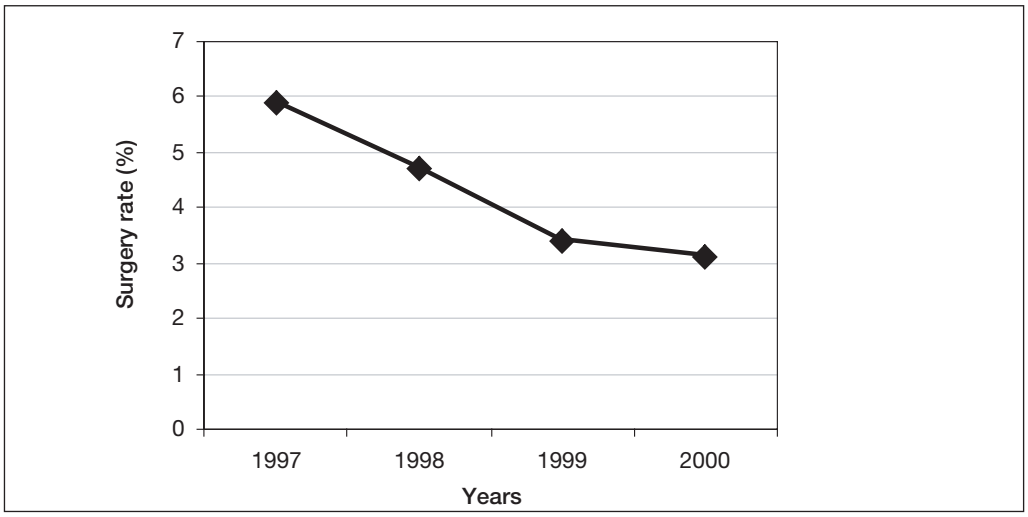

Fig. 2 - *Surgery rates in patients receiving glaucoma-related medical treatment in France: 1997-2000.*

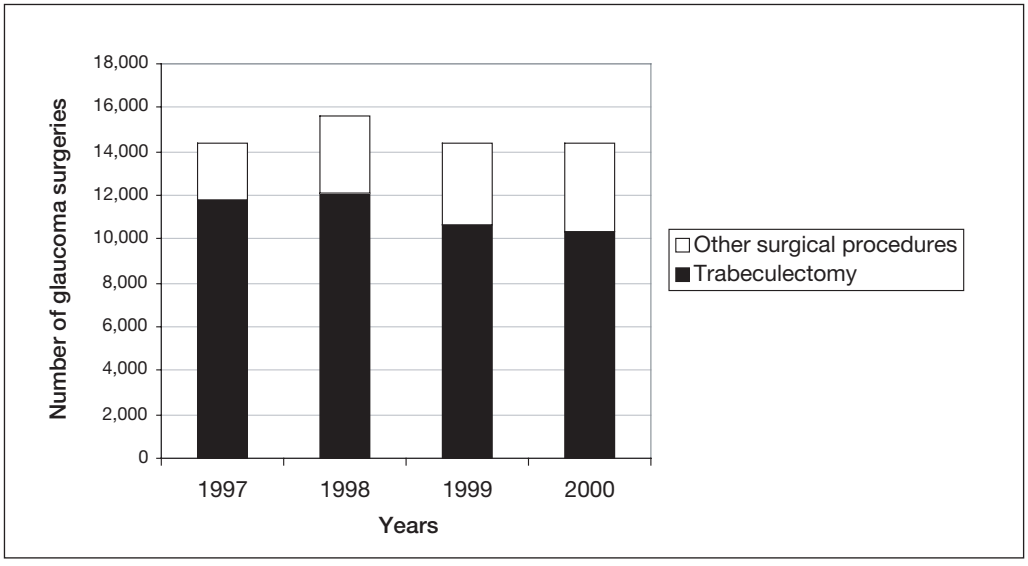

Fig. 3 - *Frequency of glaucoma surgeries in private hospitals in France: 1997-2000.*

Across the 4-year study period, the total number of glaucoma-related surgical interventions declined from 24,000 to 22,890 interventions per year, a 4.6% reduction (-12% in public hospitals and 0% in private hospitals) (Tabs. I and II). This relative stability reflected primarily a shift from trabeculectomies towards other procedures, especially in private hospitals. As the reference surgery for glaucoma, trabeculectomy remained the most frequently performed glaucoma-related procedure in France, although the number of such procedures decreased by 15%, from 18,349 to 15,596 interventions per year between 1997 and 2000. The percentage decline was greater in public than in private hospitals (-20% versus -12%, respectively), but the relative frequency of trabeculectomies in relation to the total number of procedures decreased over time in both public and private facilities. Thus, in 1997, trabeculectomy comprised 68.5% of all glaucoma-related surgeries in public hospitals but just 61.7% of the total in 2000. A comparable decrease was seen in private hospitals, from 81.7% and 71.9%, respectively. Sharp increases in new filtering procedures, such as "other fistulising interventions to facilitate intraocular circulation" (H426) and "other sclerotic-opening interventions (Krasnov, valves, etc.)" (H431), were seen in the private sector (Fig. 3); increases in such

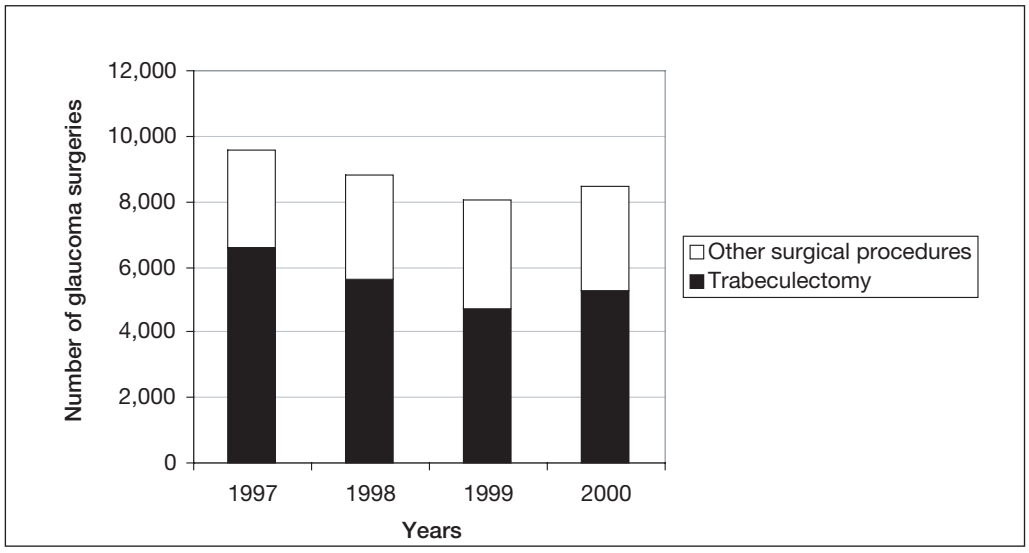

Fig. 4 - *Frequency of glaucoma surgeries in public hospitals in France: 1997-2000.*

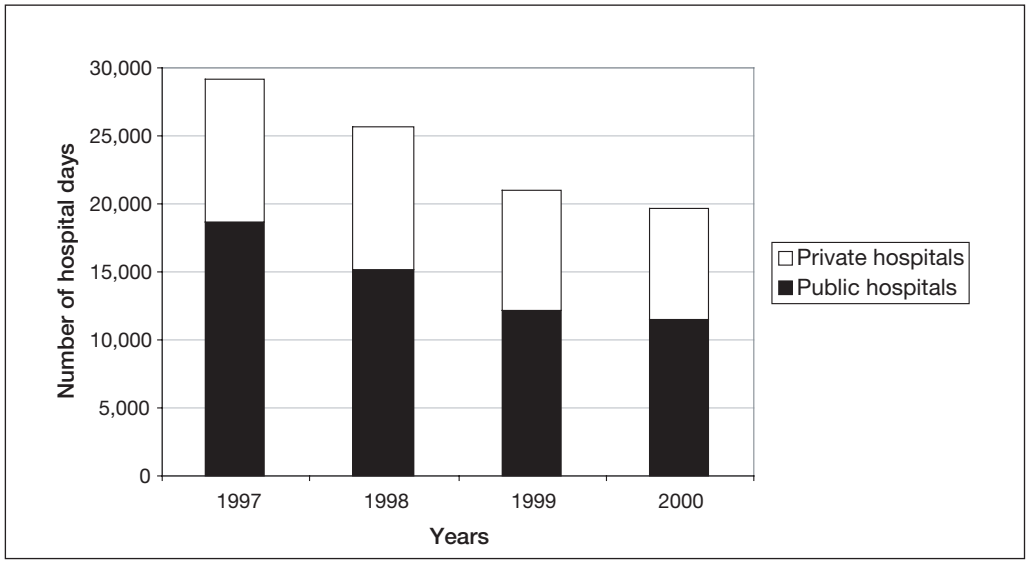

Fig. 5 - *Number of hospital days related to open-angle glaucoma procedures in France: 1997-2000.*

procedures offset the reduction in trabeculectomies, yielding no appreciable net difference in the total frequency of glaucoma-related surgeries performed in private hospitals between 1997 and 2000. In public hospitals, however, such reductions were not offset by increases in alternative glaucoma surgeries, and the overall number of glaucoma-related surgeries was reduced by 12% (Fig. 4). Thus, the residual reduction of trabeculectomies in public hospitals cannot be explained by shifts to other surgical procedures.

In order to test for the existence of a connection between the reduction in trabeculectomies and the increase in the number of medical treatments between 1997 and 2000, a correlation analysis between these two variables was performed. The reduction in number of trabeculectomies was strongly correlated with increases in the numbers of patients treated with latanoprost (r^2=0.88), brimonidine (r^2=0.93), and the fixed combination of dorzolamide + timolol (r^2=0.92). The existence of such a correlation does not establish causality between variables but simply demonstrates their joint evolution during the study period.

The share of the private sector in glaucoma surgery increased slightly over the study period with private

hospitals performing 57.8% of interventions in 2000 versus 55.4% in 1997. Glaucoma surgery was performed primarily as an inpatient procedure, although the proportion of trabeculectomies performed on an outpatient basis increased from 4.5% to 13.9% of such procedures in public hospitals and from 15.7% to 22.8% in private hospitals.

The total number of hospital days related to open-angle glaucoma procedures decreased in both public and private hospitals (Fig. 5). As a result, patients required approximately 9500 fewer hospital days in 2000 than in 1997 (-38.7% in public hospitals and -22.2% in private hospitals), yielding an estimated savings of € 9.4 million (euros).

DISCUSSION

Studies of shifts in surgical rates in glaucoma patients have been performed recently in Scotland (13, 14) and the United States (15). In Scotland, researchers evaluated changes in prescribing and in trabeculectomies (including nonpenetrating trabeculectomy) per 1000 population likely to have glaucoma and found that a 24.9% increase in prescriptions and a 45.9% decrease in number of surgeries occurred between 1994 and 1999, the period during which latanoprost, brimonidine, and topical carbonic anhydrase inhibitors were introduced in the United Kingdom (13, 14). A study of surgical trends in Medicare patients in the United States found that the volumes of trabeculectomy and of argon laser trabeculoplasty declined by 22.0% and 36.7%, respectively, between 1995 and 1998 (15). Because this change seemed unrelated to reimbursement rates, the authors hypothesized that the shifts were associated instead with new developments in glaucoma management and at least in part with the introduction of latanoprost and brimonidine.

The impact of new, effective ocular hypotensive drug therapies on glaucoma management is confirmed by results of the present study in France. Three medications introduced between 1997 and 2000, latanoprost, brimonidine, and the fixed combination of dorzolamide + timolol, greatly contributed to the nearly 80% increase in the number of patients treated with an ocular hypotensive during the period. More than 7 out of 10 patients treated with one of these new therapies received latanoprost. The use of these new medical treatments in such a large number of patients has substantially changed glaucoma management. The surgery rate in patients receiving medical treatment declined almost by half in 4 years, from 5.9% to 3.1%. Future research should investigate whether this represents a limit in the effectiveness of current medical treatments and whether surgical intervention will remain the last option for approximately 3% of patients receiving medical treatment. Long-term studies also are needed to determine if the increased use of these new ocular hypotensive medications actually prevents or merely delays trabeculectomies. Thus, if IOP levels are reduced and visual fields are stabilized over long periods of time, rates should remain at a lower level than those observed prior to the introduction of these drugs. Conversely, if a substantial proportion of patients experiences disease progression over time, surgeries that were delayed eventually will be required, and surgery rates will rise again.

By considering only trabeculectomies and/or argon laser trabeculoplasty as tracking surgeries, previous studies of changes in patterns of glaucoma-related surgeries could not examine possible shifts between surgical procedures as a possible explanatory factor for the reduction in trabeculectomies. The present study shows that in France the reduction in the number of trabeculectomies was in fact largely offset by the use of other surgical interventions and that the development of filtering surgeries differed in public and private hospitals. Nonperforating, deep sclerectomy was first performed in public hospitals where the procedure was well established by 1997; the shift from trabeculectomies towards this alternative was largely achieved by that time. Given this fact, the development of new filtering surgeries cannot completely explain the 12% net reduction in glaucoma interventions observed in public hospitals during the study period. We therefore hypothesize that the new medical treatments helped to stabilize glaucoma progression in many patients, allowing surgery to be delayed. This hypothesis is supported by the strong negative correlation between the number of trabeculectomies and the number of patients receiving a new medical treatment. In private clinics, however, new filtering surgeries developed rapidly during the study period, and the utilization of alternative techniques offset the reduction of trabeculectomies between 1997 and 2000.

The findings of the present study require confirmation as the correlations between increases in numbers of patients treated with one of the new ocular hypotensives and decreases in numbers of trabeculectomies may be due to coincidence or to confounders. In particular, the research was not designed to assess how many prescriptions dispensed were for newly diagnosed patients versus for existing patients who were changing therapies. In addition, potential explanatory variables not examined in the present study include changes in numbers of ophthalmology surgeons and shifts in numbers of potential glaucoma patients tested. We assumed that such factors remained stable and that the only notable influences on glaucoma management during the study period in France were the development of new filtering surgeries and the initiation of reimbursement for latanoprost and brimonidine.

CONCLUSIONS

Between 1997 and 2000, new topical ocular hypotensive agents, primarily latanoprost and brimonidine, improved IOP control and delayed surgery, reducing the glaucoma procedure rate in patients receiving glaucoma-related medical treatment by 47%.

ACKNOWLEDGMENTS

We thank Paul-Ariel Kenigsberg and François Pelen from Pharmacia S.A.S. as well as Eric Piriou from CLP-Santé, for their continuous support of this study.

This study was sponsored by Pharmacia Corporation, Peapack, NJ, USA.

Reprint requests to:
Christophe Baudouin, MD, PhD
Centre Hospitalier National d'Ophtalmologie
des Quinze-Vingts
28 rue de Charenton
75571 Paris Cedex 12, France
baudouin@quinze-vingts.fr

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Notes

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