

Changes in medical and surgical treatments of glaucoma between 1997 and 2003 in France

P.-A. KENIGSBERG

PAK Santé, Paris - France

PURPOSE. *To analyze quantitative changes in glaucoma treatment strategies between 1997 and 2003 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. Numbers of patients treated per year were estimated from drug unit sales using defined daily doses for each drug.*

RESULTS. *New medical treatments of glaucoma and ocular hypertension, introduced in France between 1997 and 2003, allowed treatment of 557,000 patients. In 2003, 63% of patients treated with these new medicines were receiving prostaglandins (39% latanoprost, 9% travoprost, 8% the fixed combination of latanoprost + timolol, and 7% bimatoprost), 13% brinzolamide, 13% the fixed combination of dorzolamide + timolol, and 11% brimonidine. During the same period, trabeculectomies declined by 38% (-48% in public hospitals and -32% in private clinics), while the total number of glaucoma surgeries declined by 22% (-34% in public hospitals and -14% in private clinics). Hospital days related to open-angle glaucoma surgery declined by 51%. There is a strong correlation ($r^2 = -0.97$) between the reduction of glaucoma surgery and the increase in the number of patients treated with prostaglandins during the study period.*

CONCLUSIONS. *Between 1997 and 2003, new glaucoma drugs, primarily prostaglandins, improved intraocular pressure control and delayed surgery, reducing glaucoma surgery by 22%. (Eur J Ophthalmol 2007; 17: 521-7)*

KEY WORDS. *Glaucoma, Brimonidine, Brinzolamide, Bimatoprost, Dorzolamide, Latanoprost, Prostaglandins, Travoprost, Surgery, Trabeculectomy*

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INTRODUCTION

Elevated intraocular pressure (IOP) is a major risk factor for development of primary open-angle glaucoma (POAG) (1). Ocular instillation of a hypotensive agent has been shown to effectively delay or prevent the onset of POAG 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 POAG consists of reducing IOP either through medical therapies or surgery (1).

Historically, first-line medical therapy for POAG has consisted of treatment with a topical beta-blocker. If this approach fails, the patient is changed to an agent from another class of drugs such as the carbonic anhydrase inhibitors, sympathomimetics, or, more recently, the prostaglandin analogues, or combination therapy is instituted (1). When more than two topical treatments 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 (8-10). Other surgical treatments of glaucoma using lasers include trabeculoplasty and cyclophotocoagulation (7). Recent long-term outcomes studies have shown success rates of 60% at 6 years for trabeculectomy with mitomycin C (success defined as IOP \leq 15 mmHg) (11) and 41% at 14 years for initially successful trabeculectomy with 5-fluorouracil injections (success defined as IOP <21 mmHg or a reduction of 33% if preoperative pressure was less than 21 mmHg) (12). Non-penetrating deep sclerectomy showed a success rate of 66.4% at 5 years (success rate defined as IOP <21 mmHg) (13). Visual field defects may progress because of glaucoma in 41% of patients over 40 years of age at 3.5 years after trabeculectomy without antimetabolites (14). Up to one half of eyes within 5 years of argon laser trabeculoplasty (ALT) and two thirds of eyes within 10 years may require additional laser or surgical intervention for glaucoma control (15). ALT followed upon failure by second-line and third-line trabeculectomy showed a 10-year progression to blindness of 11.9% in eyes of black patients and 9.9% in eyes of white patients; trabeculectomy followed upon failure by second-line ALT and third-line trabeculectomy showed a 10-year progression to blindness of 18.5% in eyes of black patients and 7.3% in eyes of white patients (16). The magnitude of initial IOP reduction in trabeculoplasty has been shown to be a major factor influencing progression to glaucoma, progression risk decreasing by about 10% with each millimeter of mercury of IOP reduction from baseline to the first IOP visit at 3 months (17). Filtration surgery has been associated with a 54% probability of preservation of vision from progression to legal blindness at 10 years after surgery (18). Regardless of which approach is used, reintervention 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), the fixed combination of dorzolamide + timolol (available since November 1998, reimbursed since March 2001), brinzolamide (available since September 2001, reimbursed since April 2002), bimatoprost (available

since March 2002, reimbursed since April 2002), travoprost (available since November 2001, reimbursed since January 2002), and the fixed combination of latanoprost + timolol (available since November 2001, reimbursed since April 2002). The objective of the present study was to analyze quantitative changes in medical and surgical treatments of glaucoma in France during this period.

MATERIALS AND METHODS

Yearly estimates of numbers of patients treated between 1997 and 2003 with latanoprost, brimonidine, the fixed combination of dorzolamide + timolol, brinzolamide, bimatoprost, travoprost, and the fixed combination of latanoprost + timolol were based on unit sales of these drugs and on defined daily doses specified in market authorization summaries of product characteristics, assuming complete treatment compliance (19). In theory, a patient uses annually 13 flasks of 28 treatment days. In actual practice, however, the number of flasks must be multiplied by a coefficient of 1.2 in order to consider the rate of flask renewal. We therefore estimated an actual use of 15.6 flasks per patient per year.

The number of surgeries performed in either public or private hospitals in France between 1997 and 2003 was tabulated from information in the Programme de Médicalisation des Systèmes d'information (PMSI) database, a Diagnosis Related Group database managed by the French Ministry of Health (20). Trabeculectomy ab externo (PMSI procedure code H428) is the reference surgical treatment for open-angle glaucoma (7). Additional glaucoma interventions include trabeculotomy ab externo (H416), other fistulizing interventions to facilitate intraocular circulation (H426), other sclerotic-opening interventions (Krasnov, valves) (H431), postoperative reintervention of sclerotic opening (H430), goniotomy (H415), photocoagulation of irido-corneal angle (H418), treatment of ciliary body by other physical methods (H436), cyclophotocoagulation (H435), other glaucoma interventions (H438), other interventions to facilitate intraocular circulation (H419), cyclodialysis (H417), reduction of the ciliary body secretion, without other indications (H437), surgical transfixing iridotomy (H375), laser transfixing iridotomy (H379), other iridotomies (H376), iridectomy (H378), other iridoplasties (H400).

The relationships between the number of trabeculectomies and the numbers of patients treated with the new

medical treatments introduced in France between 1997 and 2003 (latanoprost, brimonidine, the fixed combination of dorzolamide + timolol, brinzolamide, bimatoprost, travoprost, and the fixed combination of latanoprost + timolol) were analyzed using a linear regression model. A determination coefficient of $r^2 > 0.8$ was considered to demonstrate a strong association between the variables.

RESULTS

Between 1997 and 2003, 557,000 patients with glaucoma were treated with new ocular hypotensives. In 2003, 39% of patients were treated with latanoprost, 13% with brinzolamide, 13% with the fixed combination of dorzolamide + timolol, 11% with brimonidine, 9% with travoprost, 8% with the fixed combination of latanoprost + timolol, and 7% with bimatoprost. Altogether, 2 patients under new drugs out of 3 (63%) were treated with prostaglandins (Fig. 1). The expansion of the therapeutic arsenal offered new medical alternatives whenever target IOP levels could not be obtained with traditional ocular hypotensives such as beta-blockers, pilocarpine, or dorzolamide. The

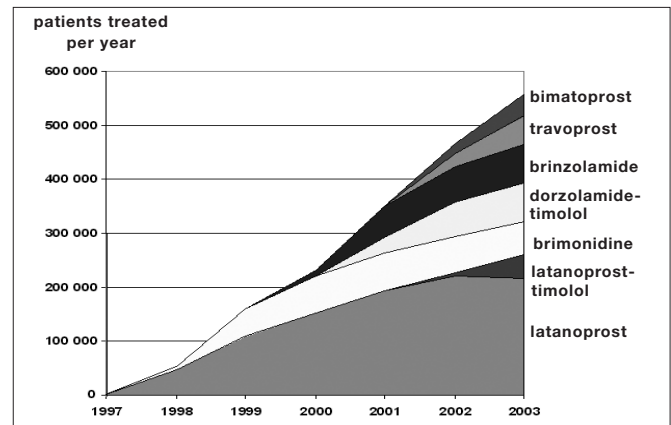


Fig. 1 - Number of glaucoma patients treated per year with new medical treatments in France: 1997-2003.

introduction of these alternatives apparently allowed medical treatment to be prolonged and surgery to be delayed for many patients with glaucoma.

During the 7-year study period, the total number of open-angle glaucoma-related surgical interventions declined from 30,480 to 23,851 interventions per year, a 22% reduction (-34% in public hospitals and -14% in private hospitals) (Tabs. I-III). Trabeculectomy (H428), the refer-

TABLE I - PUBLIC HOSPITALS

Procedure (PMSI code)	1997	1998	1999	2000	2001	2002	2003	2003/1997
Trabeculectomy ab externo (H428)	6,579	5,613	4,727	5,239	4,867	3,879	3,440	-48%
Other fistulizing interventions to facilitate intraocular circulation (H426)	828	885	829	911	945	874	671	-19%
Trabeculectomy ab externo (H416)	415	323	295	273	248	240	233	-44%
Treatment of the ciliary body by other physical methods (H436)	383	499	547	459	496	518	444	16%
Other sclerotic-opening interventions (Krasnov, valves) (H431)	336	357	367	385	363	298	272	-19%
Cyclophotocoagulation (H435)	293	299	379	443	523	518	475	62%
Photocoagulation of the irido-corneal angle (H418)	186	210	187	188	222	154	118	-37%
Other glaucoma interventions (H438)	184	244	310	201	160	96	91	-51%
Other interventions to facilitate intraocular circulation (H419)	132	168	194	215	247	201	223	69%
Postoperative reintervention on sclerotic opening (H430)	100	103	102	97	107	106	85	-15%
Goniotomy (H415)	98	10	22	24	23	26	12	-88%
Cyclodialysis (H417)	36	50	44	40	44	70	34	-6%
Surgical transfixing iridotomy (H375)	328	367	347	407	268	242	176	-46%
Laser transfixing iridotomy (H379)	485	514	548	520	505	463	417	-14%
Other iridotomies (H376)	27	34	24	22	29	13	22	-19%
Iridectomy (H378)	1,566	1,418	1,269	1,243	1,335	1,259	1,153	-26%
Other iridoplasties (H400)	65	51	43	26	54	37	40	-38%
Diminution of the ciliary body secretion, without other indication (H437)	29	29	12	18	12	32	30	3%
Total	12,070	11,174	10,246	10,711	10,448	9,026	7,936	-34%

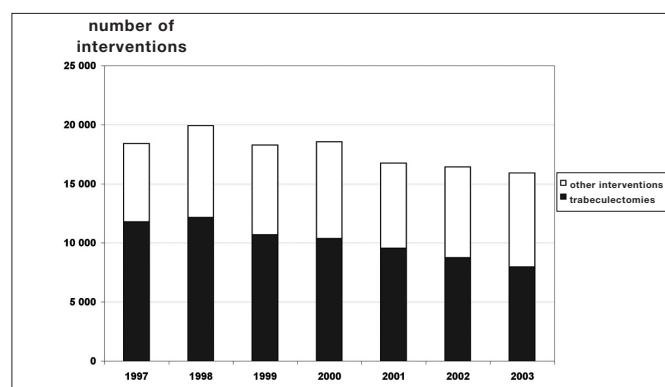


Fig. 2 - Frequency of glaucoma surgeries in French private clinics: 1997-2003.

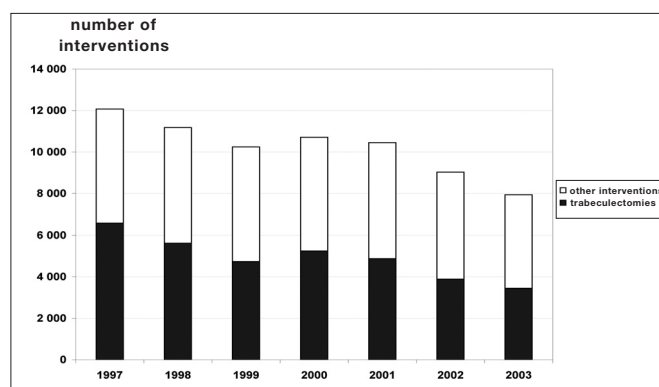


Fig. 3 - Frequency of glaucoma surgeries in French public hospitals: 1997-2003.

ence surgery for glaucoma, remained the most frequently performed glaucoma-related procedure in France, although the number of such procedures in both public and private hospitals decreased by 38%, from 18,349 to 11,387 interventions per year between 1997 and 2003. In 1997, trabeculectomies comprised 55% of all glaucoma-related surgeries in public hospitals but just 43% of the total in 2003. A comparable decrease was seen in private hospitals, from 64% to 50%, respectively. Alternatively,

new filtering procedures increased sharply during the study period. Procedures such as other fistulizing interventions to facilitate intraocular circulation (H426) and other sclerotic-opening procedures (Krasnov, valves) (H431) increased respectively by 91% and 157% in the private sector (Fig. 2); increases in such procedures partly offset the reduction in trabeculectomies, yielding however a 14% decrease in the total frequency of glaucoma-related surgeries performed in private hospitals between 1997

TABLE II - PRIVATE HOSPITALS

Procedure (PMSI code)	1997	1998	1999	2000	2001	2002	2003	2003/1997
Trabeculectomy ab externo (H428)	11,770	12,135	10,685	10,357	9,536	8,730	7,947	-32%
Other fistulizing interventions to facilitate intraocular circulation (H426)	691	1,083	1,371	1,382	1,174	1,156	1,321	91%
Trabeculotomy ab externo (H416)	570	824	812	1,052	1,329	1,407	1,464	157%
Treatment of the ciliary body by other physical methods (H436)	469	590	426	405	403	447	460	-2%
Other sclerotic-opening interventions (Krasnov, valves) (H431)	268	357	335	411	247	422	343	28%
Cyclophotocoagulation (H435)	123	137	118	82	112	72	70	-43%
Photocoagulation of the irido-corneal angle (H418)	115	124	182	236	241	309	207	80%
Other glaucoma interventions (H438)	115	108	158	170	186	213	218	90%
Other interventions to facilitate intraocular circulation (H419)	105	44	53	44	45	28	19	-82%
Postoperative reintervention on sclerotic opening (H430)	95	124	134	116	124	144	160	68%
Goniotomy (H415)	42	70	100	84	11	13	37	-12%
Cyclodialysis (H417)	27	24	32	52	28	22	18	-33%
Surgical transfixing iridotomy (H375)	523	370	331	306	246	219	161	-69%
Laser transfixing iridotomy (H379)	86	79	79	57	80	68	71	-17%
Other iridotomies (H376)	151	142	93	120	74	170	176	17%
Iridectomy (H378)	3,184	3,662	3,306	3,620	2,861	2,920	3,184	0%
Other iridoplasties (H400)	65	44	59	59	55	73	55	-15%
Diminution of the ciliary body secretion, without other indication (H437)	11	3	7	6	6	15	4	-64%
Total	18,410	19,920	18,281	18,559	16,758	16,428	15,915	-14%

and 2003. In public hospitals, the overall number of glaucoma-related surgeries was reduced by 34% (Fig. 3). In order to test for the existence of a connection between the reduction in glaucoma surgeries and the increase in the number of medical treatments between 1997 and 2003, a correlation analysis between these two variables was performed. The reduction in numbers of glaucoma surgeries was correlated with increases in the numbers of patients treated with new medical treatments introduced between 1997 and 2003 ($r^2=-0.97$). The existence of such a correlation does not establish causality between variables but demonstrates their joint evolution during the study period.

The share of the public sector in glaucoma surgery declined slightly over the study period, with public hospitals performing 33% of interventions in 2003 versus 40% in 1997.

DISCUSSION

Studies of shifts in surgical rates in patients with glaucoma have been performed recently in Scotland (21, 22), the United States (23), the Netherlands (24), and France (19).

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 (21, 22). 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 (23). 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 between 1997 and 2000 in France has been associated with a 47% reduction of glaucoma surgery rate (19). The present study in France confirms this trend, extending the study period to 2003. Medications introduced between 1997 and 2003 in

TABLE III - TOTAL PUBLIC AND PRIVATE HOSPITALS

Procedure (PMSI code)	1997	1998	1999	2000	2001	2002	2003	2003/1997
Trabeculectomy ab externo (H428)	18,349	17,748	15,412	15,596	14,403	12,609	11,387	-38%
Other fistulizing interventions to facilitate intraocular circulation (H426)	1,519	1,968	2,200	2,293	2,119	2,030	1,992	31%
Trabeculotomy ab externo (H416)	884	913	721	678	651	687	693	-22%
Treatment of the ciliary body by other physical methods (H436)	478	623	681	575	620	662	604	26%
Other sclerotic-opening interventions (Krasnov, valves) (H431)	906	1,181	1,179	1,437	1,692	1,705	1,736	92%
Cyclophotocoagulation (H435)	408	407	537	613	709	731	693	70%
Photocoagulation of the irido-corneal angle (H418)	291	254	240	232	267	182	137	-53%
Other glaucoma interventions (H438)	299	368	492	437	401	405	298	0%
Other interventions to facilitate intraocular circulation (H419)	400	525	529	626	494	623	566	42%
Postoperative reintervention on sclerotic opening (H430)	223	240	220	179	219	178	155	-30%
Goniotomy (H415)	140	80	122	108	34	39	49	-65%
Cyclodialysis (H417)	63	74	76	92	72	92	52	-17%
Surgical transfixing iridotomy (H375)	851	737	678	713	514	461	337	-60%
Laser transfixing iridotomy (H379)	571	593	627	577	585	531	488	-15%
Other iridotomies (H376)	178	176	117	142	103	183	198	11%
Iridectomy (H378)	4,750	5,080	4,575	4,863	4,196	4,179	4,337	-9%
Other iridoplasties (H400)	130	95	102	85	109	110	95	-27%
Diminution of the ciliary body secretion, without other indication (H437)	40	32	19	24	18	47	34	-15%
Total	30,480	31,094	28,527	29,270	27,206	25,454	23,851	-22%

France (latanoprost, brimonidine, the fixed combination of dorzolamide + timolol, brinzolamide, bimatoprost, travoprost, and the fixed combination of latanoprost + timolol) contributed to double the number of patients treated with an ocular hypotensive during the period. About half of the patients (47%) treated with one of these new therapies were receiving latanoprost in 2003. The use of these new medical treatments in such a large number of patients has substantially changed glaucoma management. Glaucoma surgery declined by 22% in 7 years (34% in public hospitals and 14% in private clinics).

By considering only trabeculectomies and/or laser argon 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 trabeculectomy surgeries. The present study clearly shows a steady, 7-year trend of reduction in the number of trabeculectomies, which has been only partly offset by the development of other surgical interventions, such as filtering surgeries. This trend, of very large magnitude, is observed in both public hospitals (-48%) and private settings (-32%). Furthermore, high rates of reduction in trabeculectomy surgery have been observed in other countries following the introduction of new medical treatments for glaucoma (45.9% decrease in trabeculectomy in Scotland between 1994 and 1999; 22.7% decrease in trabeculectomy and 36.7% in argon laser trabeculoplasty between 1995 and 1998 in the United States). With this converging evidence, 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. 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 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 patients with glaucoma 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 the new medical treatments.

CONCLUSIONS

Between 1997 and 2003, new glaucoma drugs, primarily prostaglandins, improved IOP control and delayed surgery, reducing glaucoma procedures by 22%.

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Reprint requests to:
Paul-Ariel Kenigsberg, PhD, MBA
PAK Santé
98 rue Barrault
75013 Paris, France
paul.kenigsberg@free.fr

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