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Switching Patients With Glaucoma or Ocular Hypertension From Dual Therapy to Monotherapy: Evaluation of Brimonidine as a Model

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ABSTRACT

A multicenter open-label study investigated the clinical effectiveness and economic feasibility of switching 142 patients from dual therapy to twice-daily monotherapy with brimonidine for glaucoma or ocular hypertension. Evaluations were performed at baseline and 2 (visit 2) and 8 (visit 3) weeks after the switch. Patients completed a questionnaire that rated medication-related visual function and satisfaction (comfort, convenience, vision, ease of remembering to use drops) at each visit. At visit 3, investigators, taking into account IOP measurements, safety, and responses on the questionnaire, recommended whether the patient should remain on brimonidine. A pharmacoeconomic analysis, including the number of visits, cost of medication, and success rates, compared the cost of dual therapy with that of switching to brimonidine monotherapy. Of the 131 patients who completed the study, 77 (59%) had no change or a decrease in IOP from baseline, and 53 (41%) had an increase. Investigators recommended that 77% of the study completers continue to take brimonidine monotherapy. Extending treatment with brimonidine for 12 months would achieve a significant cost savings of 16%. Brimonidine monotherapy is an efficacious and cost-effective alternative to dual

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therapy for glaucoma and ocular hypertension. Appropriate monotherapy may be as effective as dual therapy for many patients, and a clinically relevant trial such as this may be economically advantageous for testing a switch.

Keywords: glaucoma; ocular hypertension; intraocular pressure; pharmacoeconomics; brimonidine

INTRODUCTION

Many clinical studies have compared medications for glaucoma and ocular hypertension, but few have discussed how (or when) to change a treatment regimen. In particular, when a patient taking monotherapy needs further reduction in intraocular pressure (IOP), the general tendency is to add another medication rather than switch to a new regimen. The assumption that adding rather than replacing drugs would better reduce IOP and the number of office visits may not be correct, however. For example, adding medications may increase adverse events and costs, decrease compliance, and still not adequately control IOP.[1] The clinician must have a replacement and follow-up strategy with the most favorable risk:benefit profile.

Over time, patients taking two different IOP-lowering medications may not receive the full benefit of both drugs. For example, an often-overlooked issue is the so-called beta-blocker drift. After several months of beta-blocker therapy, some patients may experience an upward drift of IOP or loss of a beta-blocker effect.[2-4] This phenomenon was identified following 12 months of timolol.[5] The drift seems to be more severe when beta blockers are added to therapy than when they are the sole antiglaucoma medication. A switch to monotherapy with a new medication may produce comparable control.

Decreased IOP, improvements on visual-field and ophthalmoscopic testing, and reduced risk(s) have traditionally indicated successful treatment of glaucoma. Quality of life, visual function, and satisfaction, though frequently undervalued, are other important measures of clinical success. Dual therapy affects cost[6] and perhaps compliance. As the armamentarium for glaucoma and ocular hypertension increases, so does the number of potential candidates for a dual therapy to monotherapy switch.

Brimonidine decreases IOP as effectively as timolol[7-9] and has a favorable systemic adverse-event profile.[10] Drug-related adverse events are not serious and include allergic reactions, dry mouth, fatigue/drowsiness, and headache. In a large community-based study,[10] additional reductions in IOP occurred when brimonidine replaced beta blockers, apraclonidine, dipivefrin, latanoprost,[11] dorzolamide, and miotics.[12] These results made it a logical choice to model a switching strategy.

From the standpoint of efficacy, either increased compliance or loss of beta-blocker effect could drive a successful therapeutic switch. In a clinical setting, however, physicians must know what would happen to IOP, slit-lamp findings, and quality-of-life factors. The success rates and the pharmacoeconomic feasibility of a switch are other relevant considerations. This study evaluated efficacy, safety, satisfaction, and pharmacoeconomic value of a switch from two medications (beta blocker and other agent) to brimonidine twice-daily monotherapy. The study was designed to resemble the common pattern of how patients are evaluated and monitored in clinical practice when an antiglaucoma regimen is altered.

PATIENTS AND METHODS

Patients

Men or women, 18 years of age or older, with a history of either open-angle glaucoma or ocular hypertension were considered for inclusion. Stable bilateral dual therapy (one agent a beta blocker) for at least 3 months prior to enrollment was required, as was a Snellen-equivalent visual acuity of at least 20/100 in both eyes. Reasons for exclusion were ocular surgery or laser treatment within 3 months of enrollment, contraindications to use of alpha-adrenoceptor agonists (depression, cerebral/coronary insufficiency, or orthostatic hypotension), uncontrolled systemic disease, other active ocular disease that could interfere with the evaluation, and previous or current use of brimonidine. Use of contact lenses or topical ophthalmic medications, other than brimonidine and intermittent application of artificial tears, was not permitted during the study. All patients gave informed consent in writing, and the study protocol and consent form were approved by an institutional review board. Response to current dual therapy and IOP limitations were not required for entry.

Study Design

This multicenter open-label study involved three visits: baseline, week 2 (± 2 days), and week 8 (± 1 week).

Visit 1

Initial screening and baseline examinations were performed on dual therapy. Demographic data, medical and medication history, and informed consent were obtained; eligibility criteria, current treatment regimen, and compliance were reviewed. An ophthalmic examination included best-corrected Snellen visual acuity; slit-lamp evaluation of lids, conjunctiva, cornea, anterior chamber, and iris; and bilateral IOP measurement by means of Goldmann applanation tonometry (2 hours ± 30 minutes following instillation of dual therapy). From a list of adverse events common to glaucoma medications, patients noted which, if any, they experienced on therapy. A nonvalidated questionnaire rated visual function and satisfaction with current therapy (Table 1). Dual therapy was discontinued, and brimonidine was dispensed with instructions for twice-daily instillation.

Visit 2

Medical and medication histories were updated; ophthalmic and slit-lamp examinations were conducted (within ± 60 minutes of the time at visit 1 and 2 hours ± 30 minutes following instillation of brimonidine); and IOP measurements were recorded. Patients indicated which, if any, adverse events (dryness, fatigue, ocular ache, burning, hyperemia or allergic reaction, eyelid edema, dizziness, insomnia, and depression) they experienced while taking brimonidine. Compliance with monotherapy was assessed, and the questionnaire completed during visit 1 was repeated (see Table 1).

Table 1. Patient Questionnaire

QOL Factor	Visit 1 Questions*	Visits 2 and 3 Questions†
Comfort	When I put in my two different drops, overall they are comfortable	When you put your eye drops in, is the new medicine more comfortable than your previous two-drug therapy?
Convenience	It is convenient to use two different drops	Is the new medicine more convenient to use than your previous therapy?
Change in vision	In using the two drops, there is no overall change in my vision	With the new therapy, is there an improvement in your vision?
Remember	It is easier to remember to use both my drops at the times prescribed	With the new medicine, is it easier to remember to take your drops?
Satisfaction	Overall, I am satisfied with the two drops I am using	Overall, are you satisfied with the new therapy compared to your previous two-drug therapy?

*Assessment of current dual therapy on a scale of 1–5 (1 = strongly disagree; 2 = disagree; 3 = no opinion; 4 = agree; 5 = strongly agree).
†Comparison of previous dual therapy with brimonidine monotherapy on a scale of 1–5 (1 = definitely worse; 2 = somewhat worse; 3 = neutral; 4 = somewhat better; 5 = definitely better).

Visit 3

Historical and clinical information, as in visit 2, was recorded; adverse events were noted; the questionnaire was completed; and compliance with brimonidine therapy was assessed. Investigators evaluated IOP, adverse events, cost, and patient satisfaction with brimonidine to recommend either continuation of monotherapy or resumption of previous dual therapy.

Pharmacoeconomic Analysis

A cost-minimization model[13] was chosen that used average wholesale prices (AWPs) of all study drugs[14] and assumed that extending either brimonidine monotherapy or previous dual therapy for 12 months after the study would yield equal results. To calculate AWPs for drugs sold in generic form (eg, timolol, levobunolol), half of the patients were assumed to be using the generic and half the branded drug. The average cost of all generic forms of a specific drug was calculated to determine the AWP of generic timolol, levobunolol, and pilocarpine. To determine monthly drug cost, it was assumed that one 2.5-mL bottle would last 1 month when used once daily and a 5-mL bottle would last 1 month when used twice daily.

The cost per month of a three-times-daily drug was calculated by multiplying the AWP of a 5-mL bottle by 1.5. The cost of treating patients with the study regimen was included in the analysis.

Calculation of visit costs used the following assumptions: if treatment was judged a failure at any study visit, the patient would return to previous dual therapy and would have follow-up visits at 1, 6, and 12 months. At the 1- and 6-month visits, patients would undergo a standard eye examination with IOP measurement; at the 12-month visit, a standard eye examination (including dilated fundus and bilateral visual fields) and IOP measurement. Study completers who were recommended to remain on brimonidine monotherapy would have follow-up visits at 6 months (eye examination and IOP measurement) and 12 months (eye examination, IOP, dilated fundus, and visual fields). The 2000 HICFA CPT (Medicare billing) codes and Massachusetts Medicare reimbursements for the visits were as follows: #92012 ($56.11) for the cost of each eye examination and IOP measurement, #92226 ($59.69) for dilated fundus examination, and #92083 ($62.09) for bilateral visual-field testing.

A comparison was made between the hypothetical cost of treating 142 patients with dual therapy for 12 months, including two follow-up examinations, and switching 142 patients to brimonidine monotherapy under this study design. Switching costs included study and follow-up visits, brimonidine, and return to dual therapy for treatment failures.

Statistical Analysis

Demographic characteristics (age, sex, race, iris color, and duration of beta-blocker therapy) were tabulated; mean IOP for both eyes at each study visit was calculated; and a χ^2 analysis of each demographic variable was performed. A survivability analysis used the number and percentage of patients who had a decrease, no change, or an increase in IOP from baseline to visits 2 and 3. A decrease or increase in IOP of 1 mm Hg or less was considered no change. Means for each response to the questionnaire at each visit also were calculated, as was the percentage of visit 3 completers recommended to remain on brimonidine monotherapy. Responses to the questionnaire and mean change in IOP for patients successfully and unsuccessfully treated with brimonidine were tabulated. Data for patients on various prestudy dual-therapy regimens were tabulated with success rates. A paired *t* test was used to analyze changes in IOP (primary efficacy variable) and responses to the satisfaction questions. Data from the adverse-event profiles were tabulated. Significance was set at $<.05$.

RESULTS

Study Population

Nineteen US sites enrolled 142 eligible patients. One hundred thirty-four (94%) completed visit 2, and 131 (92%) completed the study (visit 3). Racial breakdown was as follows: 37% black (52/142), 55% white (78/142), 5% Hispanic (7/142), and 2% Asian (3/142) (data not available for 2 patients). At study entry the most common beta blockers were levobunolol (70/142; 49%), timolol (22/142; 16%), and betaxolol (12/142; 8%); the most common second drugs were latanoprost (76/142; 54%), dorzolamide (29/142; 20%), and pilocarpine (16/142; 11%).

Efficacy

Mean IOP (± SD) was 17.5 (± 3.6) mm Hg (range, 10–30 mm Hg), 17.4 (± 4.2) mm Hg (range, 8–40 mm Hg), and 18.2 (± 4.3) mm Hg (range, 10–37 mm Hg) at baseline and visits 2 and 3, respectively, and did not differ significantly. Mean change from baseline was –0.1 (± 4.2) mm Hg at visit 2 and –0.3 (± 7.7) mm Hg at visit 3.

Two of the 139 patients evaluated at visit 2 were discontinued owing to an unacceptable increase in IOP. Among the 131 study completers, IOP decreased in 47 (35.8%) (mean, 18.2 [±4.3] mm Hg), increased in 53 (40.5%) (mean, 18.1 [±4.2] mm Hg), and did not change in 30 (22.9%) (mean, 18.0 [±4.0] mm Hg) from baseline. One of the completers had an asymmetric response: IOP increased by 6 mm Hg in the right eye and decreased by 6 mm Hg in the left eye. Thus, 77 of the 131 completers (58.8%) had a decrease or no change in IOP from baseline. Of the 142 enrolled patients, 77 (54%) who completed the study while on brimonidine monotherapy showed a decrease or no change in IOP from baseline.

Table 2 summarizes IOP-lowering efficacy stratified by the specific components of the original dual therapy. Clinical success was not significantly influenced by duration of beta-blocker treatment or by the second agent used prior to study entry.

Table 2. IOP-Lowering Efficacy, by Specific Components of Original Dual Therapy and 8 Weeks After Switch to Brimonidine Monotherapy*

Drug	No Change in IOP	Clinically Successful	Discontinued
Beta blocker			
Levobunolol	56 (39/70)†	80 (56/70)	0 (0/70)
Timolol	35 (9/26)	77 (20/26)	23 (6/26)
Betaxolol	77 (17/22)	77 (17/22)	14 (3/22)
Timoptic XE®‡	50 (9/18)	67 (12/18)	11 (2/18)
Carteolol	50 (2/4)	75 (3/4)	0 (0/4)
Metipranolol	50 (1/2)	100 (2/2)	0 (0/2)
Second IOP-lowering agent			
Latanoprost	54 (41/76)	74 (56/76)	4 (3/76)
Dorzolamide	57 (16/28)	79 (22/28)	4 (1/28)
Pilocarpine	38 (6/16)	50 (8/16)	38 (6/16)
Dipivefrin	33 (3/9)	56 (5/9)	11 (1/9)
Methazolamide	50 (1/2)	100 (2/2)	0 (0/2)
Brinzolamide	100 (7/7)	71 (5/7)	0 (0/7)
Dichlorphenamide	100 (1/1)	100 (1/1)	0 (0/1)
Apraclonidine	100 (1/1)	100 (1/1)	0 (0/1)

*All values compared with baseline.
†One patient had an asymmetric IOP response at visit 3 (decreased in one eye, increased in the other eye). This patient was recommended to remain on brimonidine monotherapy.
‡Registered trademark of Merck & Co., Inc., Whitehouse Station, NJ, USA.

Effect on IOP and clinical success were stratified by eye color and race (Table 3). Clinical success was not significantly influenced by race, IOP at visit 1, sex, age, or iris color.

Table 3. Effect of Switch to Brimonidine Monotherapy on IOP, by Eye Color and Race

		Percentage of Patients (no.)		
	No. Enrolled	Decrease/No Change in IOP	Clinically Successful*	Discontinued
Eye color				
Brown	94	56 (53/94)	72 (68/94)	7 (7/94)
Blue	24	46 (11/24)	67 (16/24)	4 (1/24)
Hazel	14	64 (9/14)	86 (12/14)	14 (2/14)
Green	6	50 (3/6)	50 (3/6)	0 (0/6)
Race				
White	77	47 (36/77)	64 (49/77)	10 (8/77)
Black	52	62 (32/52)	77 (40/52)	6 (3/52)
Hispanic	7	71 (5/7)	86 (6/7)	0 (0/7)
Asian	2	100 (2/2)	100 (2/2)	0 (0/2)

*At visit 3 (week 8).

Safety

No unexpected adverse events occurred. Four of the 142 patients (3%) discontinued prior to visit 2: 2 for headaches and 1 patient for ocular itching; 1 withdrew consent. Between visits 2 and 3, 6 patients (4%) experienced treatment-related adverse events (dry mouth [2], headaches [1], blurring/itching [1], ocular itching [1], and hyperemia [1]) and were discontinued. Only 1 patient (<1%) was discontinued because of tinnitus, which was considered unrelated to brimonidine.

No clinically significant changes in visual acuity or biomicroscopic findings were noted between visits. Among the entire enrollment, one patient (<1%) reported a subconjunctival hemorrhage (considered unrelated to study medication), and two patients (1%) cited decreased vision (both not drug-related). Visual acuity remained unchanged from baseline in one patient (whose IOP decreased by 6 mm Hg in both eyes at visit 3) and decreased in another as a result of macular degeneration (IOP: 20 mm Hg, right eye; 24 mm Hg, left eye at baseline; 30 mm Hg, both eyes, at visit 3). Increased IOP prompted withdrawal of two patients at visit 2 (average increase, 16.8 ± 9.4 mm Hg).

Table 4 presents the percentage of patients reporting adverse events at the three study visits. Adverse events occurred in 67 patients at visit 2 and in 55 patients at visit 3; 8 (12%) and 7 (13%) events, respectively, were attributed to brimonidine. Approximately 1% of patients experienced brimonidine-related fatigue and ocular dryness, burning, aching, and allergic reaction.

Table 4. Percentage of Patients (Discontinued and Completers) Reporting Adverse Events

	Percentage of Patients (no.)		
	Dual Therapy	Brimonidine Monotherapy	
	Visit 1 (Baseline)	Visit 2	Visit 3
Patients with AEs	42 (60/142)	50 (67/134)	42 (55/131)
Treatment-related AEs	18 (11/60)	12 (8/67)	13 (7/55)
Ocular dryness			
Total	6 (9/142)	9 (12/134)	6 (8/131)
Treatment-related	1 (2/142)	1 (1/134)	1 (1/131)
Ocular burning			
Total	10 (14/142)	5 (16/134)	5 (7/131)
Treatment-related	2.8 (4/142)	1 (1/134)	2 (2/131)
Fatigue			
Total	4 (6/142)	6 (8/134)	6 (8/131)
Treatment-related	1 (1/142)	1 (1/134)	1 (1/131)
Dizziness			
Total	3 (4/142)	5 (6/134)	5 (4/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)
Ocular aching			
Total	4 (5/142)	6 (8/134)	2 (2/131)
Treatment-related	0 (0/142)	2 (2/134)	0 (0/131)
Ocular hyperemia			
Total	3 (4/142)	4 (5/134)	3 (4/131)
Treatment-related	1 (1/142)	2 (2/134)	2 (2/131)
Ocular allergic reaction			
Total	5 (7/142)	4 (5/134)	3 (4/131)
Treatment-related	2 (3/142)	0.7 (1/134)	1 (1/131)
Edema			
Total	1 (2/142)	3 (4/134)	3 (4/131)
Treatment-related	0 (0/142)	0 (0/134)	1 (0/131)
Insomnia			
Total	1 (2/142)	2 (2/134)	2 (2/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)
Depression			
Total	2 (3/142)	5 (6/134)	5 (4/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)
Itching			
Total	1 (2/142)	2 (2/134)	2 (2/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)
Headache			
Total	1 (1/142)	2 (3/134)	0 (0/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)
Stinging			
Total	1 (1/142)	0 (0/134)	0 (0/131)
Treatment-related	0 (0/142)	0 (0/134)	0 (0/131)

Questionnaire/Clinical Success

On the five-point questionnaire, the mean score for convenience of regimen was 3.0 ± 1.0 at baseline (neutral response); the scores of 4.1 ± 1.1 at visits 2 and 4.1 ± 1.3 at visit 3 reflected the patients' opinion that brimonidine monotherapy was more convenient than their previous dual therapy (Table 5). Respective mean scores for satisfaction with regimen were 3.4 ± 1.1, 4.1 ± 1.1, and 3.9 ± 1.3.

Table 5. Frequency of Responses to Questionnaire at Each Visit

Quality-of-Life Factor	Quality-of-Life Score	Frequency		
		Visit 1 (n = 142)	Visit 2 (n = 139)	Visit 3 (n = 131)
Comfort	5	21	30	34
	4	77	40	51
	3	12	62	41
	2	29	5	4
	1	3	1	0
	Mean±SD	3.6±1.0	3.6±1.1	3.7±1.2
Convenience	5	5	65	66
	4	43	45	39
	3	38	27	23
	2	53	1	2
	1	3	0	0
	Mean±SD	3.0±1.0	4.1±1.1	4.1±1.3
Change in vision	5	15	5	15
	4	65	31	29
	3	37	95	81
	2	22	7	4
	1	3	0	1
	Mean±SD	3.5±1.0	3.2±0.8	3.2±1.1
Ease of remembering	5	6	45	50
	4	66	50	43
	3	27	42	35
	2	40	1	2
	1	4	0	0
	Mean±SD	3.2±1.0	3.9±1.0	3.8±1.3
Satisfaction	5	14	58	58
	4	68	56	45
	3	24	18	18
	2	28	2	7
	1	8	4	2
	Mean±SD	3.4±1.1	4.1±1.1	3.9±1.3

Note: At visit 1, patients assessed their current dual therapy on a scale of 1–5 (1 = strongly disagree; 2 = disagree; 3 = no opinion; 4 = agree; 5 = strongly agree). At visits 2 and 3, patients compared previous dual therapy to brimonidine monotherapy on a scale of 1–5 (1 = definitely worse; 2 = somewhat worse; 3 = neutral; 4 = somewhat better; 5 = definitely better).

Table 6. Mean Wholesale Price (AWP)* of Brimonidine Monotherapy and Dual-Therapy Medications

	AWP/Month, $	No. of Patients
Monotherapy		
Brimonidine	25.94	142
Total per month		$3,683.48
Primary beta blocker		
Levobunolol	17.29	70
Timolol	17.04	26
Betaxolol	24.75	22
Timoptic XE	16.89	18
Carteolol	31.69	4
Metipranolol	15.68	2
Total per month		$2,660.34
Second agent		
Latanoprost	45.03	76
Dorzolamide	36.15	28
Pilocarpine	7.6	16
Dipivefrin	16.08	9
Brinzolamide	30.57	7
Methazolamide	42.23	2
Dichlorphenamide	33.39	1
Apraclonidine	42.50	1
Total per month		$5,075.14
Dual therapy		
Total cost per month for 142 patients		$7,735.48
Average per-patient cost per month		$54.48

*Listed AWP represents an average of the generic and branded products.

Investigators recommended that 101 of the 131 study completers (77%) remain on brimonidine monotherapy; this represents 71% of the entire enrollment. Mean response scores from all patients on four of the five questions (comfort, convenience, ease of remembering, and overall satisfaction) indicated that brimonidine monotherapy was rated somewhat better than previous dual therapy.

Investigators recommended that 77 patients (95%) with a decreased (mean, 3.9 mm Hg) or unchanged IOP at visit 3 continue to take brimonidine. Among patients with increased IOP at visit 3, a mean response higher than 4.0 on four of the five satisfaction questions (comfort, convenience, ease of remembering, and overall satisfaction) indicated that brimonidine was "somewhat better" than previous dual therapy (see Table 1). Investigators considered improved scores when recommending that 27 of these 53 patients (51%) remain on brimonidine. The mean IOP increase in

this group was 3.6 mm Hg, and the mean score for the five questions was 4.0 (± 0.7). The mean increase in IOP overall during the study was 4.3 mm Hg. The 30 patients not recommended to continue brimonidine had a mean questionnaire score of 2.7 (± 1.6) and a mean IOP increase from baseline of 3.85 mm Hg.

A total of 454 office visits occurred during the study; 417 were per protocol. Of the 37 additional visits, 8 were required for treatment of adverse events, and 29 were follow-up visits for patients switching back to dual therapy.

Pharmacoeconomics

Table 6 lists the monthly AWPs of the various antiglaucoma medications identified in this study. When the AWP of brimonidine monotherapy ($3,683/month) was compared with the AWP of dual therapy ($7,735/month) for the entire study population, a 52% cost savings was evident.

Table 7. Drug Costs After Switch to Brimonidine Monotherapy (Extended to 1 Year) and to Continue Dual Therapy

Patient Subset	Months on Dual Therapy	Months on Brimonidine	No. of Patients	Total Cost for Subset*
Failures (discontinuations)				
Following visit 1	12	0	3/142	$1,961
Following visit 2	11.5	0.5	8/139	$5,116
Following visit 3	10	2	30/131	$17,900
Successes				
Through visit 3	0	2	101/139	$2,620
Following visit 3	0	10	101/131	$26,199
Total drug cost for switching 142 patients to brimonidine considering success rates				$53,797
Versus				
Total drug cost for continuing 142 patients on dual therapy for 12 months				$92,834

*AWP/month multiplied by time on drug.

The cost of treating the 142 enrolled patients with their previous dual regimen for 12 months (ie, not enrolling them in this study) was $92,834 for the drug (Table 7) and $41,196 for three follow-up visits (day 0, month 6, month 12; Table 8), for a total treatment expenditure of $134,030.

Drug cost for the 142 patients enrolled in this switch study was $53,797; the three study visits and follow-up visits (months 6 and 12) cost $58,646 (Figure). The total treatment expenditure was $112,443. A 16.1% total cost savings was realized by enrolling patients in this trial and continuing the recommended treatment for 12 months.

Table 8. Cost Comparison of Dual Therapy for 12 Months Versus Switching to Brimonidine Monotherapy

Visit	CPT#	Procedures	Total Visit Cost	Visit Cost (× 142)
Day 0	92012	Slit-lamp, IOP	$56.11	$7,968
Month 6	92012	Slit-lamp, IOP	$56.11	$7,968
Month 12	92012	Slit-lamp, IOP	$177.89	$25,260
	92083	Fundus		
	92226	Visual field		
Total annual cost of visits				$41,196
Cost of dual therapy for 12 months (AWP/month × 12)				$92,834
Total annual cost for patients on dual therapy				$134,030
Total cost of visits for study group (switch to brimonidine)*				$58,646
Cost of brimonidine for study group*				$53,797
Total annual cost of switch to brimonidine				$112,443
Cost savings				16.1%

*Refer to Table 7 for drug costs and to Figure for calculation of visit costs.

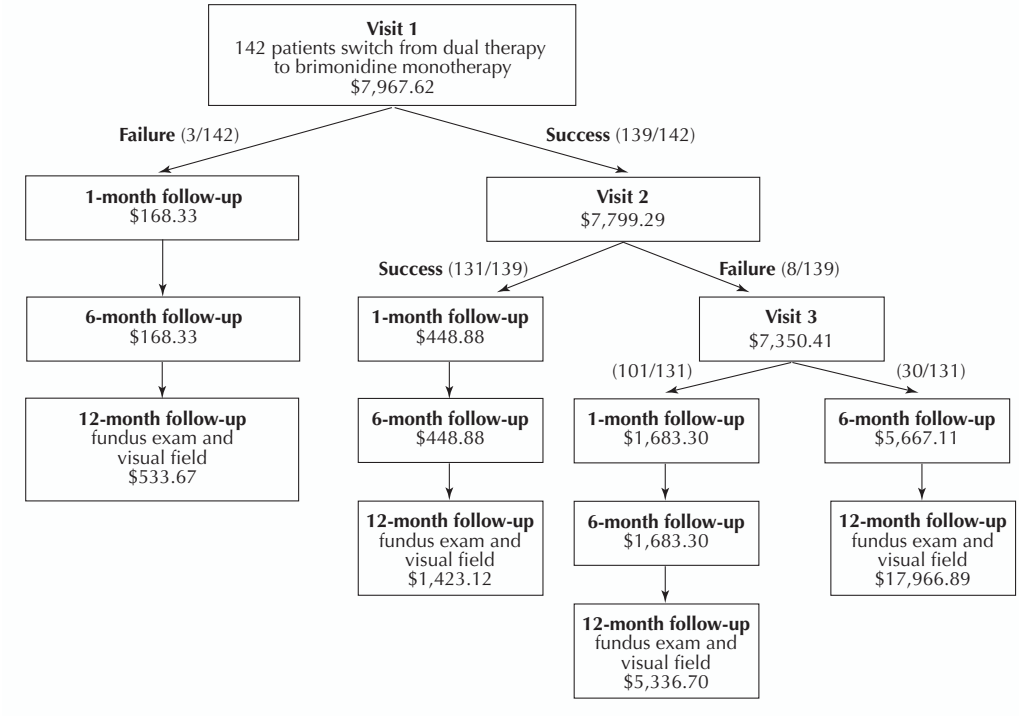
DISCUSSION

In clinical practice, ophthalmologists often encounter patients using two drugs who may be better or equally controlled with monotherapy. How and when to negotiate such a therapeutic switch requires both clinical and pharmacoeconomic information, however. The safety and efficacy of brimonidine provided an appropriate framework for construction of a model to make this evaluation.

This study investigated the clinical success rate, defined by physician's recommended continuation of brimonidine monotherapy, and the pharmacoeconomics of switching patients with glaucoma or ocular hypertension from dual therapy to monotherapy with brimonidine. Notably, 54% of all enrolled patients who were switched had a decrease or no change in IOP by visit 3 (8 weeks of treatment), and investigators recommended that 71% of the entire study enrollment remain on bri-

monidine. Fifty-two of the 142 patients (36.6%) were black, a population in whom glaucoma is typically difficult to control.[15] Of these black patients, 32 (62%) had a decrease or no change in IOP, and investigators recommended that 40 (77%) continue with brimonidine (P = NS).

Treatment algorithm for switching from dual therapy to brimonidine monotherapy for glaucoma (see *Pharmacoeconomic Analysis* in text for explanation of how costs were derived).



Total cost of all visits for study group = $58,646

Compared with the combined side effects of dual therapy, monotherapy may offer a better safety profile, although this study was too small to evaluate the reduced incidence of rare severe adverse events. Adverse events associated with beta-blocker treatment tend to be more serious than those with brimonidine monotherapy and include pulmonary effects as well as central nervous system events such as depression, mood alteration, fatigue, lethargy, confusion, and psychosis.[16,17] The incidence and treatment costs of adverse events, including visits to the primary care physician, lost days of work, and decreased productivity, were not evaluated. This study did demonstrate, however, that switching to brimonidine monotherapy may produce significant cost savings for the year, assuming that three

visits are required for the switch, success and failure rates are considered, and cost of extra office visits to the ophthalmologist and drug costs (AWP) are included. These results go further than a previous investigation of daily costs of glaucoma medications[18] that did not factor in costs for combining drugs or for additional visits to manage them.

Patients who are satisfied with their regimen can be assumed to be more compliant with it. At baseline, questionnaire ratings for convenience of dosing with dual therapy and ease of remembering to use it corresponded to a neutral opinion about this regimen. At visit 3, after 8 weeks of brimonidine monotherapy, ratings for those factors as well as for comfort of the drops and overall satisfaction with the regimen indicated greater satisfaction with brimonidine. These responses suggest that patients may be more compliant with brimonidine monotherapy than with dual therapy, thereby increasing the likelihood of effective IOP control.[1,19,20]

The investigators recommended that 95% of study patients with a decrease or no change in IOP from baseline to visit 3 and 51% with an IOP increase remain on brimonidine monotherapy. The higher satisfaction with brimonidine and the fact that IOP increases remained in the target range supported this decision. Overall, 71% of all study participants, including those who withdrew and those whose IOP increased at visit 3, were recommended to continue brimonidine. Therefore, ophthalmologists appear to base their treatment decisions not only on IOP measurements but also on cost and patient satisfaction. This open-label study mirrored the reality of clinical practice.

Diurnal IOP measurements were not performed during this study; rather, IOP was measured only at peak after administration in the morning (latanoprost was instilled the evening before for baseline measurements). Previous research has shown that twice-daily administration of brimonidine acceptably reduces IOP throughout the day,[11] and its peak and trough levels are established. Moreover, this study, designed to mimic "real world" clinical practice, allows the pharmacoeconomic analysis to correspond with the actual cost of a trial of brimonidine monotherapy.

The questionnaire employed in this study, though nonvalidated, did capture overall well-being and satisfaction with the study medication compared with previous dual therapy. The apparent increase in satisfaction with brimonidine may reflect enhanced efficacy as well as improved quality of life. In addition to the satisfaction factors measured in this study, the cost-effectiveness of a treatment can be assessed by missed work days, productivity, and mental, social (measured by withdrawal), and physical well-being.[13] A validated instrument that measures a wider range of factors may further clarify the link between quality of life and the pharmacoeconomic impact of monotherapy.

CONCLUSIONS

Brimonidine monotherapy is an efficacious and cost-effective alternative to dual therapy for glaucoma and ocular hypertension and, in many patients, may produce comparable therapeutic benefits. A simple trial similar to the one described is economically advantageous and can be performed in any clinical practice setting to evaluate a switch from dual therapy to monotherapy.

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