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Brimonidine .2% as a Replacement for Beta Blockers in Geriatric Patients With Glaucoma

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ABSTRACT

This 3-month multicenter, open-label study of 89 geriatric patients with glaucoma evaluated the substitution of brimonidine twice daily for topical beta blockers that had been used for at least 6 months. The primary outcome measures were reduction in intraocular pressure (IOP) from baseline at 2 hours postdose, change in cardiac and respiratory function, quality of life, and patient satisfaction. Patients were queried about adverse events at each visit and completed a quality-of-life questionnaire at the final evaluation. In this cohort with a mean age of 75.4 years, the average duration of topical beta-blocker therapy was 5 years. Brimonidine twice daily produced an additional mean reduction in IOP of 8.2% (1.4 mm Hg; $P<.001$). Eighty-eight percent of patients (60/68) reported being at least as satisfied with brimonidine as with their previous beta-blocker regimen, and 46% (31/68) reported greater satisfaction with brimonidine. Additionally, 40% of patients (27/68) noted increased energy after the switch, and 43% (29/68) described brimonidine as more soothing than topical beta blockers. In this elderly population, the replacement of topical beta blockers with brimonidine twice daily significantly decreased IOP, improved quality of life, and enhanced patient satisfaction.

Keywords: glaucoma; elderly; brimonidine; topical beta blockers

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INTRODUCTION

By the year 2015, 17% of the US population will be older than 65 years of age, and the number over 85 will more than double. By age 65, approximately one third of the population has some vision-reducing disease, with glaucoma among the leading causes of blindness in the elderly.[1]

Current therapy for glaucoma involves the use of topical ocular hypotensive agents to reduce intraocular pressure (IOP) below the level at which glaucomatous damage occurs. Beta blockers, among the most common medications for this purpose,[2] are often prescribed for patients of all ages. Elderly patients with glaucoma, however, often suffer from hypertension, chronic obstructive pulmonary disease, congestive heart failure, asthma, and arthritis, and some of these conditions may be adversely affected by topical beta-blocker therapy. Moreover, other side effects of topical beta blockers, such as depression, dizziness, fatigue, exercise intolerance, shortness of breath, and impotence,[3] affect quality of life. Brimonidine, a highly selective alpha$_2$ agonist, lowers IOP comparably to topical beta blockers,[4-6] but its use as replacement therapy in a geriatric population has not been evaluated. Hence, the purpose of this open-label study—to assess efficacy and quality of life in elderly patients who replaced topical beta blockers with brimonidine twice daily in their ongoing treatment of glaucoma.

PATIENTS AND METHODS

Eighty-nine patients with glaucoma were recruited at seven clinical sites, five university medical centers and two private practices. Six sites were in the United States; one site was in Canada. The patients were at least 65 years old and had been using topical nonselective beta blockers for at least 6 months prior to enrollment. Reasons for exclusion were use of systemic beta blockers, intraocular or laser surgery within the past 6 months, uveitic or inflammatory glaucoma, steroid glaucoma, or prior use of brimonidine.

After an initial screening visit, patients returned for a baseline evaluation (visit 2) between 8 and 10 AM (before their morning beta-blocker dose). Trough IOP was determined with Goldmann applanation tonometry prior to instillation of medication; peak IOP, 2 hours later. At peak and trough, pulse, blood pressure, and forced expiratory volume were measured. Patients then completed a five-point questionnaire to evaluate comfort and satisfaction with the current beta blocker. Completion of the baseline evaluation was followed by a 4-week washout from the topical beta blocker. Instillation of other topical ocular hypotensive agents was allowed to continue.

At visit 3 (conclusion of the 1-month washout), IOP, blood pressure, pulse, and respiratory function were measured again. Patients were given brimonidine with instructions to instill the drops at 8 AM and 8 PM.

After 1 month of brimonidine and before the morning instillation, patients returned for visit 4, at which baseline evaluations were repeated, including the questionnaire. Patients were queried about adverse events at each visit.

Conduct of this study complied with the Declaration of Helsinki. All investigators obtained institutional review board or ethics committee approval, and all patients provided written informed consent.

Statistical Analysis

Paired sample *t* tests were used for continuous data. All tests assumed the null hypothesis of no significant difference between beta-blocker treatment at baseline and after 1 month of brimonidine. The a priori α level was .05. StatView software (SAS Institute, Cary, North Carolina, USA) was used for all analyses.

RESULTS

The 89 patients ranged in age from 65 to 90 years and had been using topical beta blockers for between 6 months and 24 years (Table 1). Most patients were white and female.

Table 1. Patient Demographics

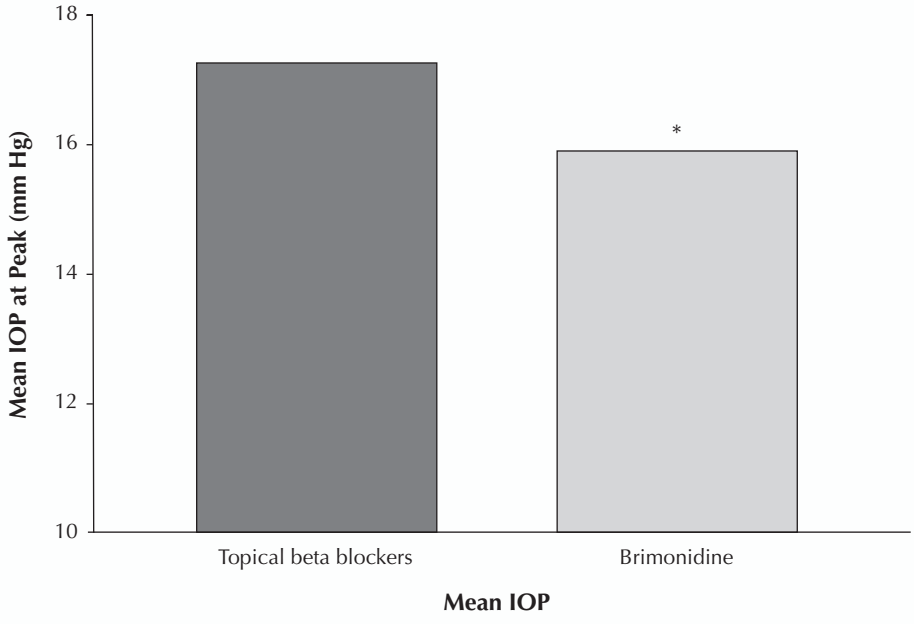
Age, y*	75.4±.7
Use of topical beta blockers, y*	5.0±.6
Sex, %	
Female	62.9 (56/89)
Male	37.1 (33/89)
Race, %	
White	83.1 (74/89)
Black	7.9 (7/89)
Hispanic	7.9 (7/89)
Asian	1.1 (1/89)
Concomitant topical medications, %	
Dorzolamide	7.9 (7/89)
Latanoprost	10.1 (9/89)
Pilocarpine	3.4 (3/89)
Dorzolamide + timolol	1.1 (1/89)

*Mean ± standard error.

Eighty of the enrolled patients completed all study visits (3 patients lost to follow-up; 2 left the study for personal reasons, 2 for adverse events unrelated to the study medication; 1 patient withdrew due to blurred vision; 1 patient was discontinued for a protocol violation).

Mean IOP at baseline was 17.3 ± .4 mm Hg; after 1 month of brimonidine replacement therapy, an additional 8.2% mean reduction occurred at peak (1.4 ± .4 mm Hg; $P<.001$; Figure). After the switch from topical beta blockers, mean increases were noted in forced expiratory volume (26.2 L/min at peak; $P = .227$ and 24.0 L/min at trough; $P = .253$) and in heart rate (2.3 bpm at peak; $P = .120$ and 1.8 bpm at trough; $P = .209$).

Mean IOP at the beta-blocker–treated baseline and after 1 month of brimonidine.



*P<.001.

Quality of life improved in this short-term study. The questionnaire administered at the final visit focused on comfort, vision, ability to function during daily activities, energy level, and overall satisfaction with brimonidine. Sixty-eight patients completed the questionnaire; 12 patients were not given the questionnaire because of administrative error; and the 9 patients who discontinued prematurely did not complete this instrument. Approximately 90% of responders reported either no change or improvement on all points evaluated (Table 2).

Many patients reported a diminution in ocular complaints after the switch. Table 3 shows the incidence of complaints (adverse events) at beta-blocker baseline and the rate of improvement with brimonidine.

The incidence of tachyphylaxis was determined in a post hoc analysis of IOP data for each patient. Patients were considered nonresponsive to beta-blocker therapy if the difference in IOP between visit 2 (beta-blocker–treated baseline) at trough and visit 3 (after 4-week beta-blocker washout) was 1 mm Hg or less. Topical beta-blocker "drift" occurred in 38 of these 80 patients (47.5%). The mean age of the nonresponders was comparable to that of the patients with a greater than 1-mm Hg increase in IOP (75.8 vs 75.33 years; P = .778). The mean duration of topical beta-blocker therapy was slightly longer for nonresponders than for responders (5.3 vs 4.6 years), but not significantly so (P = .598).

Table 2. Effect of Brimonidine on Quality of Life

	% of Patients (no.) (n = 68)
Brimonidine more soothing or comfortable than beta blockers	42.6 (29)
No difference between regimens	44.1 (30)
More energy after switch	39.7 (27)
No change	50 (34)
Greater overall satisfaction with brimonidine	45.6 (31)
No change	42.6 (29)
Improvement in vision	20.6 (14)
No change	70.6 (48)

Table 3. Adverse Events

Adverse Event	No. of Patients (%) Reporting Adverse Events With Beta Blockers	Improvement After Switch to Brimonidine
Dryness	8	4 (50)
Photophobia	9	3 (33)
Fatigue	8	3 (37.5)
Foreign-body sensation	8	3 (37.5)
Ocular itching	8	2 (25)

DISCUSSION

Topical nonselective beta antagonists (timolol, carteolol, and levobunolol) act at both $beta_1$ receptors (found predominantly in the heart) and $beta_2$ receptors (found predominantly in the lungs) and have been linked to heart failure, hypotension, and bronchospasm.[7,8] The number and density of beta-adrenergic receptors decrease with age.[9] Receptor sensitivity also changes with age and with exposure to adrenergic agonist and antagonist drugs.[10-12] These physiologic alterations may put elderly patients at increased risk for deteriorating respiratory function[13] and may help to explain why physicians in most medical specialties avoid using beta antagonists in

this group. Interestingly, ophthalmologists are the only specialists who routinely prescribe nonselective beta antagonists as first-line therapy for the elderly.[13]

The present study clearly demonstrates that brimonidine is an effective and well-tolerated replacement for topical beta blockers in geriatric patients. The additional mean reduction of 1.4 mm Hg in IOP was significant and was accompanied by a slight improvement in cardiac and respiratory function.

Although this was a short-term study, an improvement occurred in quality of life following the switch to brimonidine twice daily. For each evaluated variable, most patients were in the "no change" or "better" group. Fewer than 12% of patients expressed a preference for their previous beta-blocker regimen.

The rate of tachyphylaxis in this geriatric population was surprisingly high. Numerous studies have suggested that topical beta blockers often become less effective over time; in one report,[14] the rate of drift was estimated to be as high as 50%. The 47.5% incidence in the present study implies that many patients were exposed to the risk of beta-blocker side effects without receiving any therapeutic benefit. This finding underscores the importance of close monitoring of patients using topical beta blockers to ensure a favorable risk:benefit ratio and suggests that this drug class may not be the best option for long-term IOP control.

In many elderly patients, therefore, long-term use of topical nonselective beta blockers may not adequately lower IOP. Replacement therapy with brimonidine twice daily significantly reduced IOP and improved quality of life. Brimonidine was also safe and well tolerated in this large geriatric population.

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