Published in final edited form as:

Ophthalmology. 2017 February ; 124(2): 257–262. doi:10.1016/j.ophtha.2016.10.006.

Diplopia in Medically and Surgically Treated Glaucoma Patients

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Abstract

Purpose—To report prevalence, type, and etiology of diplopia in medically and surgically treated glaucoma patients.

Design—Cohort study

Participants—195 adult glaucoma patients treated in a glaucoma referral practice.

Methods—195 adult glaucoma patients who had undergone surgical or medical management were prospectively enrolled. Forty-seven patients had undergone glaucoma drainage device (GDD) surgery (Baerveldt 350, Baerveldt 250, and/or Ahmed FP7), 61 had undergone trabeculectomy, and 87 were medically treated. All patients completed the Diplopia Questionnaire to assess diplopia. We defined presence of diplopia as “Sometimes,” “Often,” or “Always” in distance straight ahead and/or reading positions on the Diplopia Questionnaire. A chart review was performed jointly by a strabismus and glaucoma sub-specialist to characterize the type and etiology of the diplopia.

Main Outcome Measures—Frequency, type, and etiology of diplopia.

Results—Diplopia was reported in 41 (21%) of 195 medically and surgically treated glaucoma patients. Binocular diplopia attributable to the glaucoma procedure was present in 11 of 47 (23%) post-GDD patients (95% CI; 12%–38%), which was significantly greater than in post-trabeculectomy patients (2 of 61 (3%), 95% CI; 0.4% –11%; $P=0.002$). The most common type of strabismus associated with binocular diplopia attributable to glaucoma surgery was hypertropia (10 out of 11 GDD patients, 2 out of 2 trabeculectomy patients). Monocular diplopia was found in a similar proportion of medically treated, post-trabeculectomy, and post-GDD (4 of 87 (5%), 4 of 61 (7%), and 2 of 47 (4%) respectively) patients. Binocular diplopia not attributable to surgery was

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No authors have any financial/conflicting interests to disclose.

Presented in part at: The Association for Research in Vision and Ophthalmology meeting, Denver, CO, USA, May 5th 2015, and at the American Glaucoma Society, Coronado, California, USA, February 28th 2015.

found in similar proportions of GDD, trabeculectomy, and medically treated patients (3 of 47 (6%), 5 of 61 (8%), and 10 of 87 (11%) respectively).

Conclusions—Diplopia may be under-recognized in medically and surgically treated glaucoma patients and standardization of ascertaining patient symptoms using the Diplopia Questionnaire may be useful in these patients. Diplopia was more commonly seen after GDD than trabeculectomy, typically a non-comitant restrictive hypertropia. The prevalence of monocular diplopia and binocular diplopia unrelated to glaucoma surgery was similar among medical and surgical groups. It is important to counsel patients on the higher occurrence of diplopia associated with GDD surgery.

Précis

Diplopia was reported by 21% glaucoma patients undergoing medical or surgical treatment. Binocular diplopia attributable to the glaucoma procedure was more frequent post-glaucoma drainage device than post-trabeculectomy.

INTRODUCTION

Diplopia has been reported as a complication of glaucoma treatment,^{1–12} but has not been rigorously studied across the spectrum of medically and surgically treated glaucoma patients, nor has it been assessed prospectively with an instrument specifically designed to assess diplopia. The Diplopia Questionnaire¹³ was specifically designed as a patient-reported outcome measure (PROM) to assess symptoms of diplopia, in specific gaze positions, and has been used as an outcome measure for previous studies.^{14–16}

The purpose of our prospective study was to report the prevalence of diplopia and describe its causes following glaucoma drainage devices (GDD) surgery, trabeculectomy, and medically treated glaucoma patients, and to characterize the specific types and causes of diplopia.

METHODS

Approval was obtained from the Institutional Review Board, Mayo Clinic, Rochester MN, and each patient gave informed consent before participating. All procedures and data collection were conducted in a manner compliant with the Health Insurance Portability and Accountability Act.

Patients

Over an eight month period (August 2014 to April 2015), 108 surgical glaucoma patients were prospectively enrolled at their regularly scheduled follow-up glaucoma visits, which was their most recent follow-up examination. Eighty-seven medically treated patients were also consecutively enrolled during the same time period. Patients were classified as either, GDD (N=47), trabeculectomy (N=61), or medically treated patients (N=87). Surgical patients were only enrolled if they were at least one month after glaucoma surgery. In the surgical groups, patients with multiple tubes (N=10), previous cataract and/or failed glaucoma surgery, scleral buckle (N=4), penetrating keratoplasty (N=4), or Descemet's

stripping endothelial keratoplasty (N=4), were not excluded. Some of the surgically treated patients (N=108) had been treated by other and multiple ophthalmologists. Medically treated patients consisted of patients who received neither tube nor trabeculectomy for their glaucoma, but included patients who had undergone selective laser trabeculoplasty, trabectome, iStent, or cataract surgery. Patients were not recruited if they could not read or understand English or if they had severe cognitive impairment prohibiting completion of surveys.

Regarding the type and number of GDD, 35 patients had a Baerveldt (consisting of 29 Baerveldt 350, 3 Baerveldt 250, and 3 Baerveldt unspecified) and 16 patients had an Ahmed FP7. Regarding laterality of GDD, there were 23 patients with unilateral Baerveldt 350, 4 patients with bilateral Baerveldt 350, 2 patients with bilateral Ahmed/unilateral Baerveldt unspecified, 2 patients with unilateral Ahmed and unilateral Baerveldt unspecified, 3 patients with unilateral Baerveldt 250, 1 patient with unilateral Baerveldt unspecified, 10 patients with unilateral FP7 Ahmed, and 2 patients with bilateral Ahmed devices.

Regarding plate location of the GDD, 45 patients (45 out of 47) had GDD in the superior temporal quadrant. There were 2 patients that had GDD placed in other quadrants: 1 had a right inferior nasal GDD (with left superior temporal GDD), and 1 had an inferior temporal GDD.

Diplopia Assessment by Diplopia Questionnaire

The Diplopia Questionnaire assesses diplopia by asking whether the patient has experienced double vision during the past week in each position of gaze (reading, distance straight ahead, right, left, down and up), and asks the patient to indicate the frequency of diplopia in each position as "never," "rarely," "sometimes," "often", or "always". Because diplopia in distance and straight ahead and/or reading positions have the most profound effect on health-related quality of life,¹³ we defined diplopia as experiencing symptoms of diplopia within the past week with a frequency of "sometimes", "often", or "always" specifically in distance straight ahead and/or reading positions. Patients wearing prism at the time of Diplopia Questionnaire assessment (3 GDD, 4 trabeculectomy, and 7 medically treated) were counted as diplopic because without prism they would have had diplopia, and the cause of that diplopia was evaluated as described below.

Evaluation of Cause and Type of Diplopia

A glaucoma specialist (CLK) and a strabismus specialist (JMH) determined the type and etiology of diplopia by joint review of the entire medical record with specific attention to the characteristics and the time course of diplopia and strabismus. Measurements of strabismus (simultaneous prism and cover test and prism and alternate cover tests) had been recorded as part of routine care and these measurements along with all historical data were reviewed to assign the etiology of diplopia. Upon chart review, the location of the GDD was also noted. Additional data extracted from the medical record were: patient demographics (i.e., age, sex, race), comorbidities, operative characteristics (laterality, type of tube, pre-existing strabismus/diplopia etc.) Diplopia was classified as one of three primary types: binocular diplopia attributable to glaucoma surgery, binocular diplopia not attributed to glaucoma

surgery, and monocular diplopia. A judgement was made based on joint review of the entire medical record as to whether the diplopia was caused by or exacerbated by the glaucoma procedure, and/or was pre-existing.

Statistical Analysis

Patient demographics and clinical data (visual acuity, mean deviation, age, race, gender) were compared between medical, trabeculectomy, and GDD groups using ANOVA for continuous data or Fisher exact tests for dichotomous data. Frequency and type of diplopia were compared between groups using Fisher exact tests.

RESULTS

Patient Demographics

Patient demographics (age, gender, race/ethnicity) were similar across the three groups (Table 1), with the exception of the median time from surgery to evaluation of diplopia which was longer in trabeculectomy group (17 months, range 1 month to 19 years) compared with the GDD group (9 months, range 1 month to 9 years; $P=0.03$; Table 1).

Occurrence of Diplopia

Across the cohort of 195 medically and surgically treated patients, diplopia was reported in 41 (21%). Overall, diplopia was more common in the GDD group (16 of 47; 34%, $P=0.047$ Fisher exact), compared with the trabeculectomy group (11 of 61; 18%), and medical group (14 of 87; 16%, Figure 1). Binocular diplopia attributable to glaucoma surgery, was present in 11 of 47 (23%) post-GDD patients (95% CI; 12%–38%), which was significantly greater than among post-trabeculectomy patients (2 of 61 (3%); 95% CI; 0.4% –11%; $P=0.002$ Fisher exact) (Figure 1). Binocular diplopia not attributable to surgery was similar among GDD, trabeculectomy, and medically treated patients (3 of 47 (6%), 5 of 61 (8%), 10 of 87 (11%) respectively, $P=0.7$ Fisher exact) (Figure 1). The prevalence of monocular diplopia was also similar between GDD, trabeculectomy, and medically treated patients: (2 of 47 (4%), 4 of 61 (7%), 4 of 87 (5%) respectively, $P=0.8$ Fisher exact) (Figure 1).

Characteristics of Diplopia Attributable to GDD

The types of strabismus present in the 11 diplopic GDD patients with diplopia attributable to the surgery were: 4 exotropia with hypertropia, 3 hypertropia, 1 exotropia, 2 esotropia with hypertropia, and 1 esotropia with hypertropia and cyclotropia (Figure 2). Of the 11 patients with diplopia attributable to GDD surgery, 2(18%) had pre-existing diplopia that was exacerbated by the surgery, and the other 9 (82%) had new onset diplopia associated with surgery. Of the two diplopic GDD patients with pre-existing diplopia, the patient's history reflected a change in the characteristics of the diplopia following GDD placement, indicating contribution of the GDD to the diplopia. Of the two diplopic GDD patients with pre-existing diplopia, one patient had DSEK. Of the nine diplopic GDD patients with new onset diplopia, one patient had prior PK, two had previous SB, and two had prior DSEK.

Regarding the location of the GDD, 10 of 11 patients with diplopia attributable to GDD had a superior temporal GDD. Of the two patients who did not have a GDD in the superior

temporal quadrant, one patient with an inferior temporal GDD had diplopia. The patient with an inferior nasal GDD was not diplopic.

Characteristics of Diplopia Attributable to Trabeculectomy

Of the two patients in the trabeculectomy group who developed diplopia attributable to the surgery, 1 had pre-existing diplopia associated with pre-existing strabismus that was exacerbated by surgery, and the other had new onset diplopia associated with surgery. Both patients had a hypertropia (Figure 2). None of the patients with diplopia attributable to trabeculectomy had prior SB, DSEK, or PK.

Relationship of Type and Number of GDD to Diplopia

In the 11 diplopic post-GDD patients with diplopia attributable to surgery, 7 (64%) had a unilateral Baerveldt 350, 2 (18%) had multiple Baerveldt 350 valves, 1 (9%) had bilateral Ahmed valves with a unilateral unspecified Baerveldt, and 1 (9%) had a unilateral Ahmed FP7. Overall, in patients with Baerveldt 350 (N=29), 9 patients had diplopia attributable to GDD (31%). In patients with Baerveldt 250 (N=3), none had diplopia attributable to GDD whereas 2 (13%) of 16 patients with an Ahmed GDD had diplopia attributable to GDD.

Of the 23 patients who underwent unilateral Baerveldt 350, 7 (30%) experienced binocular diplopia attributable to GDD. Of the 4 patients who underwent bilateral Baerveldt 350, 2 (50%) experienced binocular diplopia attributable to GDD surgery. Of the 10 patients who underwent multiple tubes (unilateral and bilateral Baerveldt 350/unspecified Baerveldt and Ahmeds), 3 (30%) experienced binocular diplopia attributable to GDD surgery.

Characteristics of Binocular Diplopia Not Attributable to Surgery

All 3 patients in the GDD group who had binocular diplopia not attributable to surgery had convergence insufficiency-type exotropia. For the 5 patients in the trabeculectomy group who had binocular diplopia not attributable to surgery, 2 had adult onset distance esotropia, 1 had a small-angle adult-onset hypertropia, 1 had a new 6th nerve palsy, and 1 had mechanical strabismus associated with previous orbital trauma. For the 10 medically treated patients who had binocular diplopia, 4 had a small adult onset hypertropia, 2 had convergence insufficiency-type exotropia, 1 had an old left 4th nerve palsy, 1 had a small hypertropia associated with central peripheral rivalry, 1 had a mechanical strabismus associated with previous orbital trauma, and 1 had adult-onset distance esotropia.

DISCUSSION

In our prospective study of medically and surgically treated glaucoma patients using a standard diplopia questionnaire to collect data on symptoms of diplopia, we found the overall frequency of diplopia was 21%. Binocular diplopia attributable to surgery occurred in 23% of patients undergoing GDD, and 3% in patients undergoing trabeculectomy. Monocular diplopia and binocular diplopia not attributable to surgery were similar in medically treated patients and patients undergoing GDD or trabeculectomy.

Diplopia appears to be common in glaucoma patients, and we found the overall frequency of diplopia was 21% across medically and surgically treated patients. In our present study, we included a medically treated group to serve as a control, which allowed us to better evaluate binocular diplopia not attributable to the glaucoma surgery and monocular diplopia. In our study, diplopia occurred in 16% of medically treated glaucoma patients. Diplopia in glaucoma patients, not attributable to glaucoma surgery, has not been previously studied in detail, but we found that it reflected the occurrence of common strabismus conditions in this mostly elderly population, specifically convergence insufficiency, adult-onset distance esotropia, and small-angle hypertropia.¹⁷ We also found that binocular diplopia in glaucoma patients, not attributable to glaucoma surgery, may also be caused by mechanical strabismus, such as following orbital trauma, old or new cranial nerve palsies, or co-existent retinal conditions that may be associated with central peripheral rivalry.^{18, 19} In addition, other risk factors related to the glaucoma may further increase risk for diplopia, for example, visual field loss, and ocular surface compromise made exacerbated by topical ocular medications.

In the Tubes vs Trabeculectomy Study,¹ the authors also found a high prevalence of strabismus in glaucoma patients, reporting 28% of their patients had strabismus prior to surgery. Routine diplopia and strabismus evaluations are currently uncommon as standard of care in the glaucoma population, but may be a valuable addition to routine clinical care for these patients.

Previous prospective studies have reported diplopia in 5–12% of patients undergoing GDD. We found a higher frequency of diplopia in our GDD patients. We speculate that the use of a standardized tool to elicit the symptoms of diplopia may result in our higher prevalence of diplopia. Strabismus in the TVT study²⁰ was reported in 9.9% of patients undergoing Baerveldt 350, but the presence or absence of strabismus does not always predict diplopia. In addition, 30% of postoperative motility exams were not completed in the TVT study, which may underestimate the diplopia and strabismus reported. Diplopia resulting from a single Baerveldt 350 placement reported in the TVT and ABC studies may not be comparable to patients with multiple tubes, previous buckles, or various tube types, which may be an additional reason why our prevalence of diplopia is greater than in reported previous studies. Additional causes for increased prevalence of diplopia in our study in the GDD group compared to previous prospective studies may be that we included patients who had glaucoma surgery as recent as 1 month before questionnaire administration. Our data were based on the presence of diplopia 1 month or more after surgery. Among the post-GDD binocular diplopic group, diplopia resolved in 1 and improved in 2 patients by latest available follow-up visit. We noted that in these three (27%) GDD patients with diplopia attributable to surgery, the diplopia started immediately following tube opening and their diplopia improved over one month.

The most common type of strabismus associated with diplopia related to GDD or trabeculectomy reported in our study was a non-comitant hypertropia (with and without horizontal strabismus), suggestive of a restrictive mechanism caused by the plate size of the GDD, bleb, connective tissue surrounding the plate, or a combination of these mechanical factors inducing a hypertropia. GDDs with a larger plate area (Baerveldt 350) had a higher frequency of diplopia (31%) compared with GDDs of a smaller plate area (Baerveldt 250 or

Ahmed, 11%). In contrast, the prospective Ahmed Baerveldt Comparison (ABC) Study,² reported similar frequencies of diplopia following both smaller plate Ahmed FP7 (12%) and larger plate Baerveldt 350 (11%) placement.²¹ One reason why the ABC study may not have found a difference in frequency of diplopia between different types of GDD was that they did not perform baseline and postoperative motility examinations and they did not use a standardized diplopia assessment tool. In our study, diplopia was most often associated with the Baerveldt 350 rather than the Ahmed and Baerveldt 250, which is likely attributable to the size of the plate and size of the resultant bleb. Our finding of a difference in frequency of diplopia between types of GDD may influence providers in choosing the type of tube to minimize diplopia (i.e., Ahmed vs Baerveldt, Baerveldt 250 vs 350).

In contrast to the TVT and ABC studies, multiple types of GDD, including FP7 Ahmed, Baerveldt 250, and Baerveldt 350, were included in our study. Although only ten patients in our study had multiple tubes, 30% of these patients had diplopia attributable to the surgery. A possible increased risk of diplopia with multiple tubes may reflect both a more severe mechanical effect and worse underlying glaucoma with more severe visual loss and other factors, such as more severe surface disease. Similarly, our study suggests bilateral GDD may increase the frequency of diplopia, seen in 2 out of 4 (50%) bilateral Baerveldt 350 patients. GDD type and number may influence frequency of diplopia and preoperative counsel of complex surgical patients of this additional risk is warranted.

Our study found a higher incidence of diplopia post GDD (23%) compared with trabeculectomy (3%). Similarly, in the TVT study, diplopia developed more commonly in Baerveldt 350 compared to trabeculectomy, 5% versus 0%, respectively.

In two of our patients, diplopia following GDD had features of large variability of strabismus over seconds and was attributed primarily to advanced glaucomatous visual field loss, attributable to insufficient overlapping visual fields to maintain stable fusion. Strabismus found in these patients did not suggest a restrictive etiology and the extreme variability seen on strabismus testing was unlike strabismus seen in the other diplopic GDD patients. We have described this particular type of strabismus associated with advanced visual field loss in a separate manuscript.

Our study has multiple strengths, including the inclusion of a large number of glaucoma patients, the joint review of the medical record by both a strabismus specialist and a glaucoma specialist, and the standardization of data collection for symptoms of diplopia by administering a standardized instrument. Without a standard instrument, patients and providers may not broach the topic of diplopia in routine follow-up appointments and therefore diplopia may not be reported consistently in the medical record. Only relying on strabismus measurements is problematic. Worsening alignment by 4 PD was considered a significant change in motility in the TVT study.¹ Nevertheless, diplopia may be present when alignment changes less than 4 PD, which would be missed with such an approach used in the TVT study. A standardized tool to assess diplopia may be helpful in the routine care in glaucoma patients and should be used in studies reporting diplopia and strabismus.

Our data are limited by including only postoperative evaluations in surgical patients, and inclusion of a referral population treated by multiple and other surgeons, leading to variable types of GDD and treatment history for glaucoma. Our study is also limited by being one point in time, evaluating diplopia at the patient's last follow-up examination. An additional potential limitation is that our study was not designed to address strabismus that was not associated with diplopia.

Based on our study, diplopia appears to be under-recognized in glaucoma patients, managed both medically and surgically. Diplopia attributable to surgery appears to be more common in post-GDD patients, and specifically Baerveldt 350 patients, compared with post-trabeculectomy patients. Diplopia is more common in patients with multiple and bilateral GDD. We suggest that it is important to counsel patients on the occurrence of diplopia associated with GDD surgery. It may also be helpful for patients undergoing glaucoma surgery to have a standardized assessment of diplopia and strabismus, both before and after surgery.

Acknowledgments

Financial support: Supported by National Institutes of Health Grant EY024333 (JMH), Research to Prevent Blindness, New York, NY (an unrestricted grant to the Department of Ophthalmology, Mayo Clinic), and Mayo Foundation, Rochester, MN.

None of the funding organizations had any role in the design or conduct of this research.

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Figure 1.

Binocular diplopia attributable to the glaucoma procedure was present in 11 of 47 (23%) post-GDD patients (95% CI; 12%–38%), which was significantly greater than in post-trabeculectomy patients (2 of 61 (3%), 95% CI; 0.4% –11%; $P=0.002$). Monocular diplopia was found in a similar proportion of medically treated, post-trabeculectomy, and post-GDD (4 of 87 (5%), 4 of 61 (7%), and 2 of 47 (4%) respectively) patients. Binocular diplopia not attributable to surgery was found in similar proportions of GDD, trabeculectomy, and medically treated patients (3 of 47 (6%), 5 of 61 (8%), and 10 of 87 (11%) respectively).

Figure 2.

The most common type of strabismus associated with binocular diplopia attributable to glaucoma surgery was hypertropia (10 out of 11 GDD patients, 2 out of 2 trabeculectomy patients).

Table 1

Patient Demographics Based on Glaucoma Treatment

	Treatment Group		
	GDD (N=47)	Trabeculectomy (N=61)	Medically treated (N=87)
Age in years Mean $\pm$ SD	66 $\pm$ 17	74 $\pm$ 9	69 $\pm$ 13
Gender			
Male	20 (43%)	27 (44%)	28 (32%)
Female	27 (57%)	34 (56%)	59 (68%)
Race			
White	44 (94%)	59 (96%)	84 (97%)
African American	1 (2%)	1 (2%)	0
Asian	0	1 (2%)	2 (2%)
Native American	1 (2%)	0	0
Unknown	1 (2%)	0	1 (1%)
Months from surgery to completing questionnaires: Median (range)	9 (1 to 113)	17 (1 to 229)	N/A
Visual acuity: Median (range)			
Best eye	20/30 (20/20 to 20/400)	20/30 (20/20 to 20/63)	20/25 (20/15 to 20/63)
Worst eye	20/80 (20/25 to LP)	20/50 (20/20 to LP)	20/30 (20/20 to HM)
Deviation: Median (range)			
Best eye	−4dB (−29dB to 3dB)	−3dB (−24dB to 3dB)	−1dB (−29dB to 3dB)
Worst eye	−20dB (−32dB to −3dB)	−14dB (−32dB to 1dB)	−4dB (−31dB to 2dB)

dB = decibels; GDD = glaucoma drainage device; HM = hand motions; LP = light perception; N/A = not applicable