Evaluation of Sudden Visual Loss and Central 10-Degree Visual Field Change Following Glaucoma Surgery in Severe and End-Stage Eyes

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Abstract

Objectives: The purpose of the study was to evaluate the sudden visual loss and central 10-degree visual field (VF) change following glaucoma surgery in eyes with severe and end-stage glaucoma.

Methods: This was a single-center retrospective study. The charts of patients with severe and end-stage glaucoma who had undergone trabeculectomy and Ahmed glaucoma valve (AGV) implantation surgery were reviewed. Patients who had 10-2 Humphrey VF automated (HVFA) at follow-up were included and classified into two following groups: With split fixation on 10-2 HVFA before surgery split fixation group (SFG) and those without split fixation (WSFG).

Results: The data of 37 patients in SFG and 28 patients in WSFG were reviewed. The mean follow-up duration was 2.06±0.24 years in SFG and 2±0.3 years in WSFG. 10-2 HVFA revealed that SFG had a mean MD –25.8±5.2 dB preoperatively and –25.2±1.1 dB (p=0.18) at last visit, WSFG had a mean MD −9.8±4.8 dB preoperatively and −10.8±1.5 dB at last visit (p=0.10). In SFG, the mean intraocular pressure (IOP) decreased from 30.1±9.5 mmHg to 12.3±0.62 mmHg (p<0.001), and in WSFG, the mean IOP decreased from 30±6.9 mmHg to 12.3±0.90 mmHg at last visit (p<0.001). There was no statistical difference for visual acuity of both the groups at the follow-up (p=0.30 and p=0.70). In SFG, one patient had wipe-out phenomenon who had undergone AGV surgery.

Conclusion: Although wipe-out phenomenon was a rare complication, it can develop not only after trabeculectomy but also after AGV surgery, and patients with split fixation and severe and end-stage glaucoma were at risk for this phenomenon regardless of the type of surgery. Both trabeculectomy and AGV surgery appear to provide stability of the central 10° VF.

Keywords: Ahmed glaucoma valve, end-stage glaucoma, split fixation, trabeculectomy, wipe-out
Hypotonia, severe inflammation, cystoid macular edema, suprachoroidal hemorrhage, and decreased visual acuity (VA) due to cataract formation are common complications that can be seen after filtration surgery. The previous studies reported that filtration surgery for advanced glaucoma was associated with wipe-out phenomenon (sudden loss of vision in end-stage glaucoma after filtration surgery, despite no ocular pathology) (4-7). Discrepant incidence rates ranging from 0% to 13.6%. Some studies have reported that this phenomenon emerges in advanced glaucoma after filtration surgery, (4-8) while others have reported that this phenomenon has never seen in their surgical practice (9-12). The wipe-out phenomenon thought to be occurs suddenly and without any pathology. Its risk factor has been reported advanced age, a history of coronary artery disease, post-operative severe hypotonia, and split fixation on VF tests (7,11,13). Even though IOP decreases to normal after filtration surgery, VF loss may persist (14). To demonstrate progression in advanced glaucoma, 10-2 VF test offers better results than 24-2 VF test in assessing rates of mean deviation (MD) changes (15). The previous studies investigated wipe-out phenomenon after trabeculectomy and non-penetrating deep sclerectomy (NPDS) (9-13,16). To the best of our knowledge, this phenomenon has not been reported after Ahmed glaucoma valve (AGV) surgery in the literature yet. This study aimed to compare the occurrence of wipe-out phenomenon and 10/2 VF progression (MD, the mean sensitivity of four central points, the number of four central points with a sensitivity ≤5 dB) in severe and end-stage glaucoma patients with and without split fixation group (WSFG) who underwent to glaucoma surgery (trabeculectomy and AGV surgery).

Methods

The charts of patients who had undergone to trabeculectomy and AGV surgery at the Ophthalmology Department of Haydarpaşa Numune Training and Research Hospital between 2015 and 2020 were retrospectively reviewed. The patients with severe and end-stage glaucoma and who had 10-2 VF (Swedish Interactive Threshold Algorithm [SITA]-fast) on the pre-operative and post-operative Humphrey VF automated (HVFA) were selected. Patients with split fixation on 10-2 VF assessment before surgery comprised as split fixation group (SFG) and those WSFG comprised as WSFG. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee for local clinical trials.

Based on the Bascom Palmer Glaucoma Staging System, severe glaucoma was described as MD < −20 dB on 24–2 HVFA and at least 2 points within the central 5° with the sensitivity of <0 dB (17). End-stage glaucoma was defined as the best-corrected VA (BCVA) due to glaucoma of <20/200 (17). Split fixation was defined as a retinal sensitivity of 0 dB in all locations of at least one quadrant using 10-2 SITA-fast program, with a test stimulus size III on HVFA.

Wipe-out phenomenon was defined as a decrease of BCVA of less than 20/200 in the immediate post-operative period or a decrease of BCVA to counting fingers when VA was below 20/200 preoperatively.

The data of each patient before surgery were recorded regarding BCVA testing (Snellen chart was converted into log MAR [logarithm of the reciprocal of the minimal angle of resolution]), slit-lamp biomicroscopy, IOP measurement with Goldmann applanation tonometer (Haag-Streit, Bern, Switzerland), measurement of central corneal thickness using pachymeter (Haag-Streit AG, Koniz, Switzerland), gonioscopy, and optic disk evaluation with a Volk 90 D lens. SITA-fast 24-2 and 10-2 VF results on HVFA (Humphrey VF Analyzer [Carl Zeiss Inc., Dublin, CA]) with size III stimulus and OCT screening examining retinal nerve fiber layer (RNFL) thickness (Spectralis®, Heidelberg Engineering GmbH, Heidelberg, Germany) were recorded.

Patients with fixation loss rate of <20%, and false-positive response rate of <15%, and false-negative response rate of <15% in the HVFA were included in the study. Patients whose VA was too poor to perform VF testing, and those with retinal and neurological pathology causing split fixation and who had intraoperative complications during surgery were excluded from the study.

Surgical procedures were performed by the same team (three experienced surgeons) under local (subconjunctival) or general anesthesia. Trabeculectomy was performed singly or in combination with phacoemulsification (PHACO). Trabeculectomy involved preparing a limbus-based conjunctival flap, applying mitomycin C (0.2 mg/ml, Kyowa, Tokyo, Japan) subconjunctival for 3 min, preparing a scleral flap measuring 4 × 4 mm, sclerokeratectomy measuring 1 × 2 mm, peripheral iridectomy, and closure of the flap with 10/0 nylon sutures and conjunctiva. The AGV-FP7 model (New World Medical, Rancho Cucamonga, CA, USA) was used in the surgical procedure of AGV implantation and the plate was implanted at the superior temporal or superior nasal quadrant by the long scleral tunnel technique. A fornix-based conjunctival flap was prepared and three scleral incisions, 10–12 mm, 6–8 mm, and 1.5–2 mm away from the limbus, respectively, were performed. The incisions, which were 2.5 mm in length and one-half to two-thirds of the thickness of the sclera in depth, were made parallel to the limbus. Valve's plate was placed under the conjunctiva in the equatorial region of the globe and sutured to the sclera at a distance of 8–10 mm from the limbus. The tube was placed in the anterior chamber, with its tip obliquely cut to allow 2–3 mm insertion, in
phakic patients and in the sulco-phakic patients. The scleral flap was sutured with a 10/0 nylon, and the conjunctiva was closed. PHACO surgery included “divide-and-conquer” technique and monofocal intraocular lens implantation.

All patients were examined at day 1, week 1, and months 1, 3, 6, and 12 and at last visit, postoperatively. The BCVA, IOP, slit-lamp anterior segment assessment, and fundus biomicroscopy were recorded at each visit. The results on 10-2 HVFA (MD, the number of four central points with a sensitivity ≤5 dB, and the mean sensitivity of four central points) that was taken at pre-operative and post-operative (last visit) were also recorded. In addition, four central VF points were analyzed in two ways. First was the number of points among the four central VF points with a sensitivity ≤5 dB and the second was the mean sensitivity of the four central points. We decided to select a cut-off value of the sensitivity point to be very low and 5 dB was optionally selected (9).

Post-operative complications (shallow anterior chamber, hypotonia (defined as IOP <5 mmHg) and was considered temporary if it continued <2 weeks), choroidal detachment, hyphema, malignant glaucoma, etc.) were also recorded at each visit. Primary outcome measures of this study were BCVA, IOP, the occurrence of wipe-out phenomenon, number of anti-glaucomatous medications, and 10-2 HVFA results.

The study data were analyzed using SPSS (Statistical Package for the Social Sciences) 21.0 software Mac (IBM SPSS, Chicago, IL, USA). The Kolmogorov–Smirnov test was used for the normal distribution of data. The independent t-test was used for comparison of normally distributed continuous data. The Mann–Whitney U-test, the Wilcoxon test, and Spearman correlation test were used for non-normally distributed data. The Chi-square test was performed on the categorical data. P<0.05 was considered to be statistically significant.

**Results**

Thirty-seven patients (26 men and 11 women) in SFG and 28 patients (23 men and five women) in WSFG met the inclusion criteria and their data were reviewed. The mean age was 59.1±10.6 years in SFG and 64.8±13.4 years (p=0.59) in WSFG. There was no statistically significant difference between SFG and WSFG with mean pre-operative BCVA and IOP (0.6±0.42, 0.4±0.32 [p=0.08]; 30.1±9.5, 30.6±9 mmHg [p=0.91], respectively). The mean pre-operative MD of 24-2 HVFA was −29.3±3.6 dB in SFG and −22.8±4.8 dB in WSFG (p=0.004). The mean pre-operative MD of 10-2 HVFA was −25.8±5.2 dB in SFG and −9.7±4.8 dB in WSFG (p<0.001). The most common associated systematic comorbidities among patients in both groups were hypertension, diabetes, ischemic heart disease, renal diseases, hypothyroidism, and cerebrovascular disease. The most prevalent associated ocular comorbidity was cataract. The baseline clinical characteristics of the patients are presented in Table 1.

The mean time from the diagnosis of glaucoma to surgery was 6 years in SFG (1–20 years) and 5.3 years in WSFG (1–20 years), and the number of anti-glaucomatous medications was 3.86±0.34 in SFG and 3.78±0.49 in WSFG (p=0.83 and p=0.76).

At follow-up period, no statistical difference was observed in BCVA in both groups. In SFG, the mean BCVA was 0.6±0.42 preoperatively and was 0.72±0.62 at 3 months, 0.56±0.33 at 6 months, and 0.66±0.57 at last visit (mean duration 2.06±0.24 years) (p=0.15). In WSFG, the mean BCVA was 0.4±0.32 preoperatively and was 0.59±0.16 at 3 months, 0.3±0.06 at 6 months, and 0.41±0.52 at last visit (mean duration 2±0.3 years) (p=0.58) (Fig. 1).

The mean IOP significantly decreased at 3 months, 6 months, and last visit when compared with pre-operative values in both groups (Fig. 2). In SFG, the mean IOP was 30.1±9.5 mmHg preoperatively and was 12.9±4.5 mmHg at 3 months, 12.2±3.1 mmHg at 6 months, and 12.3±0.62 mmHg at last visit (p<0.001). In WSFG, the mean IOP was 30±6.9 mmHg preoperatively and was 12.6±5.2 at 3 months, 13.3±2.1 at 6 months, and 12.3±3.9 at last visit (p<0.001). The number of anti-glaucomatous medications decreased from 3.86 to 1.5 (p<0.001) in SFG and from 3.78 to 0.76 (p<0.001) in WSFG after the surgery.

Outcomes of HVFA and RNFL thickness showed no statistically significant difference at last visit according to pre-operative levels in both groups. 10-2 HVFA revealed that SFG had a mean MD −25.8±5.2 dB preoperatively and −25.2±1.1 dB at last visit (p=0.18), the sensitivity of four central points 11±1.4 preoperatively and 11.8±1.3 at last visit (p=0.22), and the number of four central points with sensitivity ≤5 dB 1.8±0.16 preoperatively and 1.7±0.15 at last visit (p=0.56) (Table 2). WSFG had mean MD −9.7±4.8 dB preoperatively and −10.8±1.5 dB at last visit (p=0.1), the sensitivity of four central points 26.2±1.6 preoperatively and 25.9±1.5 at last visit (p=0.5), and the number of four central points with sensitivity ≤5 dB 0.14±0.14 preoperatively and 0.14±0.14 at last visit (p=1) (Table 3). The mean of 10-2 HVFA post-operative slope was 1.1±1.75 dB/year in SFG and 1.3±0.98 dB/year in WSFG (p=0.19). RNFL thickness was 48.34±7.5 μm preoperatively and 48.10±6.62 μm at last visit in SFG (p=0.83), and it was 52.40±5.44 μm preoperatively and 51.45±5.63 μm at last visit in WSFG (p=0.92).

Spearman's rho did not show a statistically significant relationship between the mean BCVA and HVFA results and...
There were no intraoperative complications. Three patients in SFG and two patients in WSFG developed choroid detachment recovered completely within a period of 2 weeks after surgery. Transient hypotonia occurred in two patients and two patients had spontaneous resolution of hyphema within 1–2 weeks in each group. During the post-operative period, six patients in SFG and five patients in WSFG underwent bleb needling with 5-fluorouracil (5-FU) for encapsulated bleb. Six months after surgery, cataract formation was observed in four patients in the SFG and in two patients in the WSFG. Wipe-out phenomenon was seen in a 56-year-old man who had undergone AGV surgery. The patient had diabetes, hypertension, and chronic renal failure and history of vitrectomy due to vitreous hemorrhage (proliferative diabetic retinopathy) before AGV surgery. The operation was performed under general anesthesia and a viscoelastic agent was left in the anterior chamber. The patient’s IOP was 5 mmHg at 1 day, 7 mmHg at 1 week, and 13 mmHg at 1 month. One month after surgery, BCVA was counting fingers from 1 m distance. There was no post-operative change in fundus examination and optic coherence tomography (OCT) imaging of macula and optic nerve head. Sudden vision loss was evaluated as a wipe-out phenomenon.

| Table 1. Baseline clinical characteristics of split and without split fixation groups |
|-----------------------------------------------|-------------------|------------------|
|                                | SFG (n=37)       | WSFG (n=28)      | p     |
| Age (yr)                       | 59.1±10.6        | 64.8±13.4        | 0.06  |
| Gender (M/F)                   | 26:11            | 23:5             | 0.27  |
| Lens status (n, %)             | 28 (75)          | 19 (67)          | 0.48  |
| Phakic                         | 28 (75)          | 19 (67)          |       |
| Pseudophakic                   | 9 (25)           | 9 (33)           |       |
| SE (D±SD)                      | -0.009±2.2       | 0.64±2.4         | 0.35  |
| Type of glaucoma (n, %)        |                  |                  |       |
| Primary open angle             | 19 (51.3)        | 7 (25.0)         |       |
| Pseudoexfoliative              | 14 (37.8)        | 15 (53.5)        |       |
| Stickler syndrome              | 1 (2.7)          |                  |       |
| Glaucoma after vitrectomy      | 3 (8.1)          | 1 (3.57)         |       |
| Chronic angle closure          | 1 (3.57)         |                  |       |
| Traumatic                      | 2 (7.14)         |                  |       |
| Uveitic                        | 2 (7.14)         |                  |       |
| Type of surgery (n, %)         |                  |                  | 0.2   |
| Trab                           | 24 (64.8)        | 14 (50.0)        |       |
| Phaco + Trab                   | 4 (10.8)         | 3 (10.7)         |       |
| Avv                            | 9 (24.3%)        | 11 (39.8)        |       |
| BCVA (logMar)                  | 0.6±0.42         | 0.4±0.32         | 0.08  |
| IOP (mmHg±SD)                  | 30±9.5           | 30±6.9           | 0.9   |
| CCT (μm±SD)                    | 540±37.2         | 544±38.9         | 0.68  |
| C/D ratio                      | 0.96±0.05        | 0.93±0.09        | 0.07  |
| Number of antiglaucoma agents  | 3.8±0.34         | 3.7±0.49         | 0.45  |
| Systemic disorders             |                  |                  |       |
| DM                             | 10 (31.3)        | 6 (25)           | 0.6   |
| HT                             | 9 (28.1)         | 9 (37.5)         | 0.45  |
| Humphrey 24/2 MD (dB±SD)       | -29.3±3.6        | -22.8±4.8        | 0.004 |
| Humphrey 10/2 MD (dB±SD)       | -25.8±5.2        | -9.7±4.8         | 0     |

AGV: Ahmed glaucoma valve implantation, BCVA: Best-corrected visual acuity, CCT: Central corneal thickness, C/D: Cup-disk ratio, D: Dioptr, DM: Diabetes mellitus, HT: Hypertension, IOP: Intraocular pressure, PHACO: Phacoemulsification, SD: Standard deviation, SE: Spherical equivalent, SFG: Split fixation group, Trab: Trabeculectomy, WSFG: Without split fixation group.

patients’ age, gender, refractive errors, surgery type, glaucoma type, systemic diseases, and changes in the IOP (Spearman correlation, p>0.05).
Discussion

In this study, wipe-out phenomenon was seen after AGV implantation surgery in eyes with severe and end-stage glaucoma with split fixation, but not observed in eyes with similar properties who underwent trabeculectomy. In both groups, no signs of progression were observed in 10-2 HVFA.

There is some evidence verifying that reduced levels of IOP slow the progression of glaucomatous optic neuropathy (18-21). The advanced glaucoma intervention study showed that lower IOP caused little VF deterioration during follow-up in advanced glaucoma patients (18). The control of IOP is the most important achievable target in glaucoma treatment. When anti-glaucomatous agents fail, laser procedures or glaucoma surgeries are preferred. However, in advanced glaucoma, surgeons are afraid of surgery due to the possibility of wipe-out phenomenon.

Wipe-out phenomenon was defined as a sudden and irreversible loss of vision seen after filtration surgery in advanced glaucoma, and no ocular pathology was found to explain this loss of vision (4-7). Although the mechanism of wipe-out is not completely clear, it is thought to be associated with hypotonia during surgery, which can lead to hemorrhage in the optic nerve and reduction optic nerve head perfusion which has already low blood flow because of advanced glaucoma. A microembolic episode can also be seen in the remaining nerve fibers (10-11). Hypotonia, choroidal detachment developing at 1 week postoperatively, advanced age, coronary artery disease, and split fixation were reported to include important risk factors (7,22,23).

This phenomenon has been reported between 0% and 14% (4-11) in the literature. Several studies reported wipe-out phenomenon after filtration surgery in eyes with advanced glaucoma. Retrospectively, Kolker et al. reported sudden vision loss after trabeculectomy in 3 (13.6%) of 22 eyes (4). Costa et al. conducted in 580 eyes, reported wipe-out in 4 eyes (0.8%) and the study by Francis et al. performed with 301 eyes (sensitivity <10 dB in any of the main quadrants tested on HVFA), reported wipe-out in 6 eyes (2%) (7,18). In prospec-

Table 2. Post-operative data: Split fixation group

|                          | Pre-operative | Last visit | Mean difference (%95 CI) | p   |
|--------------------------|---------------|-----------|--------------------------|-----|
| Mean BCVA (logMar)       | 0.6±0.42      | 0.66±0.57 | -0.15±0.50 (-1.8, 0.4)   | 0.3 |
| Mean IOP (mmHg)          | 30.1±9.5      | 12.3±6.2  | 15.5±8.94 (3.48)         | 0.00|
| Glaucoma medications     | 3.86          | 1.5       | 2.28±1.42 (-1.4)         | <0.001|
| MD (dB)                  | -25.8±0.88    | -25.2±1.15| 0.84±2.76 (-2.71, 9.74)  | 0.18|
| Mean sensitivity of four central points (dB) | 11±1.4 | 11.8±1.3 | -0.80±2.70 (-8.5)        | 0.22|
| Number of central visual field points with sensitivity ≤5 dB | 1.83±0.16 | 1.77±0.15 | -0.06±0.42 (-1.1)        | 0.56|

BCVA: Best-corrected visual acuity, IOP: Intraocular pressure, MD: Mean deviation, CI: Confidence interval.
tive studies by Aggarwal et al. (2/26 eyes [pre-operative VF confined to a central island around 10°, 7.6%] and Fujishiro et al. (2/27 eyes [MD of two adjacent points <−20 dB within the four central points in the lower and upper hemifields and that of the other two points better than 10 dB], 7.4%) showed the risk of wipe-out phenomenon.

Despite this reported studies, some studies reported that wipe-out phenomenon was not observed in their filtration surgery series. In retrospective studies, Lichter et al., Levene et al., and Martinez et al. did not detect sudden loss of vision in their series (10,11,24). In prospective studies, Toupozis et al. reported that no wipe-out phenomenon was observed in 21 eyes with end-stage glaucoma (9). Balekudaru et al. also reported that they did not seen this phenomenon in 65 eyes (retinal sensitivity of 0 dB in all the locations in at least one of the quadrants in the macular threshold program on HVFA) with advanced glaucoma with split fixation (12). Due to conflicting data, even the reality of wipe-out has been questioned by some authors (13). Studies in which this phenomenon was reported at high rates are mostly earlier studies. Several years ago, the lack of technological instruments such as OCT may have caused easily missing subtle macular changes and some central vision loss due to these changes may have misdiagnosed as wipe-out. Since then, there have been advances in glaucoma surgery (working with smaller instruments and developing the Moorfields Safer Surgery System) and in intraoperative interventions (25,26).

Wipe-out was investigated not only after trabeculectomy but also after NPDS. Ateş et al. studied sudden loss of vision after NPDS in 54 eyes with advanced glaucoma (VF with MD <−12 dB) and they reported that the wipe-out phenomenon was not observed in their series (27). Leleu et al. reviewed the results for 73 eyes (constricted VF <0°) with severe or end-stage glaucoma that underwent NPDS and no patients experienced wipe-out (28).

No wipe-out has been reported among the complications of AGV surgery in the previous studies. In our study, one patient with advanced glaucoma and split fixation developed wipe-out phenomenon after AGV surgery. He had diabetes, hypertension, chronic renal failure, proliferative diabetic retinopathy, and history of vitrectomy. The risk factors for wipe-out phenomenon included impaired microvascularization and split fixation. Changes in IOP at surgery may have reduced the perfusion pressure of the optic nerve head, which was already compromised. If this patient underwent trabeculectomy instead of AGV surgery, the result could be the same. Central vision loss in glaucoma surgery should always be kept in mind in patients with very advanced glaucoma and severely reduction blood supply to optic nerve.

Successful glaucoma surgery (IOP <16 mmHg) prevents VF progression. However, sometimes progress may continue despite reduction in IOP to the target level (3,25) We also analyzed whether there was any progression in 10-2 HVFA. In advanced glaucoma, most of the VF points have 0 dB sensitivity at all, MD may be inadequate to detect smaller changes in the central island of vision. By the use of the four central points together with the MD value on HVFA provided more quantitative information about whether there was any progress in the post-operative VF. Both groups showed no improvement in the VF at post-operative follow-up.

The limitation of this study is related to its retrospective design. The patients who had 10-2 HVFA and severe and end-stage glaucoma at the pre-operative and post-operative follow-ups were included in the study, the number was limited, especially in the AGV group.

We believe that future studies addressing this problem should be performed to confirm our findings. Larger study populations must be obtained to evaluate this visual threatening condition.

Conclusion

Our case series includes patients who were not at very advanced age but had severe and end-stage glaucoma. We found only one patient who had developed wipe-out phenomenon, suggesting that this phenomenon can be seen, albeit rarely. Moreover, this phenomenon was shown to occur not only after trabeculectomy but also after AGV surgery and patients with split fixation and severe and end-stage glaucoma were shown to be at risk for wipe-out. In the medium term, both trabeculectomy and AGV implantation provide stability of the central 10° VF with a trend toward improvement and significant IOP decrease.

| Table 3. Post-operative data: Without split fixation group |
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