Correlation of Asymmetric Glaucomatous Visual Field Damage and Water-Drinking Test Response

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Purpose. To determine whether there is a correlation between asymmetric glaucomatous visual field (VF) damage and water-drinking test (WDT) response.

Methods. A retrospective analysis was conducted of VF and WDT data from 101 patients with glaucoma in clinical therapy, who were receiving treatment with the same topical medication in both eyes, and asymmetric VF defect. Eyes were classified according to mean deviation (MD) into "better" and contralateral "worse" eyes. Maximum mean difference in basal IOP was 2 mm Hg between both eyes. The peak IOP and fluctuation obtained with the WDT were compared between both groups. For the statistical analysis, the Tukey post hoc multiple comparison test and paired *t*-test were used.

Results. Better and contralateral worse eyes presented mean MDs of -4.6 ± 5.3 and -9.0 ± 7.4 dB, respectively ($P < 0.001$). Mean basal IOPs were 13.9 ± 3.3 and 13.9 ± 3.1 mm Hg, respectively ($P = 0.67$). Mean maximum IOPs after water ingestion were 16.5 ± 3.8 mm Hg in the group with less severe VF defect and 17.2 ± 4.1 mm Hg in the contralateral group with worse visual fields ($P < 0.001$). Mean fluctuation (maximum IOP − minimum IOP after water ingestion) was 3.6 ± 1.8 and 4.4 ± 2.2 mm Hg ($P < 0.001$), respectively.

Conclusion. Eyes with worse MDs presented higher IOP peaks and fluctuation after water ingestion. This study demonstrates a lower capacity of eyes with worse glaucomatous lesion to respond to a stimulus that leads to a transitory elevation of IOP. (*Invest Ophthalmol Vis Sci.* 2006;47:641–644) DOI:10.1167/iovs.04-0268

Glaucoma treatment is based mainly on intraocular pressure (IOP) reduction, to prevent optic disc damage. However, it has been reported that a significant group of patients still experience progression of glaucoma despite IOP measurements in the ophthalmologist's office within normal limits.[1–4] However, it has been suggested that this finding may be explained by the occurrence of pressure peaks not detected by single measurements in the clinic. Drance[5] demonstrated that almost one third of patients with single IOP measurements during office hours may present pressure peaks only detected during a 24-hour pressure curve. Also, IOP fluctuation has been identified as a risk factor for the progression of glaucoma.[6–8] Thus, the IOP profile would be better assessed by a 24-hour daily tension curve.

Despite its importance, monitoring the IOP through the 24 hours of the day is not always feasible in the clinical practice. As an alternative, a modified diurnal tension curve consisting of four to five measurements during working hours is routinely used. However, this test may miss up to 70% of IOP peaks, because most of the highest IOP levels occur at 6 AM with the individual in the supine position.[9,10] A provocative water-drinking test (WDT) may be a practical way to estimate diurnal IOP peaks (Susanna R, et al. *IOVS* 2001;42:ARVO Abstract 2295).[11–14] Previous reports have demonstrated that IOP elevation during a WDT is a risk factor for the development of glaucomatous visual field progression in normal-tension glaucoma[15] and in open-angle glaucoma.[16]

This study was conducted to compare the WDT response between eyes with asymmetric visual field (VF) damage in patients with primary open-angle glaucoma.

Materials and Methods

This was a retrospective study that included visual fields and WDT data from 101 primary open-angle glaucoma patients from the private office of one of the authors, where the WDT is part of the routine examination of glaucomatous patients.

All the patients were in clinical therapy with the same medication in both eyes with a maximum difference of 2 mm Hg between the right and left eyes. Patients with IOP levels equal to or less than 18 mm Hg were included in the study.

Both eyes of each included patient had to show equal visual acuity better than 20/40. Visual fields were performed with the Humphrey automated perimeter, with the Full-Threshold strategy and 24-2 program (model 750; Carl Zeiss Meditec, Inc., Dublin, CA) Asymmetric glaucomatous VF damage was classified by means of the mean deviation (MD) index (range, 0.5–10 dB). Both eyes of each patient were included in the study. The eyes were divided according to the MD index into two groups: eyes with better MDs and another group of contralateral eyes with worse MDs. All eyes in this study had glaucomatous visual field defects characterized by a Glaucoma Hemifield Test (GHT) result outside normal limits.

Exclusion criteria were history of filtering surgery, laser trabeculoplasty, and any other ocular disease that could influence visual field examination results.

Primary open-angle glaucoma was defined as having a history of IOP higher than 21 mm Hg in at least one eye before the treatment; presence of glaucomatous visual field damage and/or glaucomatous optic nerve lesion; open angles and normal findings on gonioscopy; no history of any other ocular disease that could cause an increase in IOP.

No fluid ingestion was allowed 3 hours before the WDT. A basal IOP measurement was taken with the Goldmann applanation tonometer. The patient was asked to drink 1 L of tap water in less than 5 minutes. IOP measurement was repeated four times with 15-minute intervals.

IOP peak and fluctuation were compared between both eyes. IOP fluctuation was defined as the difference between the IOP peak and

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Submitted for publication March 9, 2004; revised July 29, 2005; accepted December 20, 2005.

Disclosure: **R. Susanna**, None; **M. Hatanaka**, None; **R.M. Vessani**, None; **A. Pinheiro**, None; **C. Morita**, None

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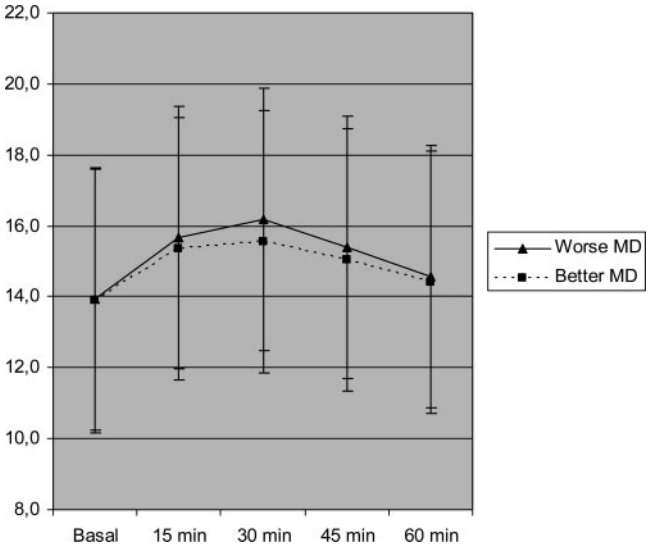

FIGURE 1. Water drinking test results.

IOP before water ingestion. Data were analyzed with the Tukey post hoc multiple-comparison test and the paired *t*-test.

RESULTS

One hundred one patients with primary open-angle glaucoma were included in this study. Mean ± SD MD was −4.6 ± 5.3 in eyes with better MDs and −9.0 ± 7.4 in the contralateral worse-eye group ($P < 0.001$).

WDT results are displayed in Figure 1. For statistical analysis of each curve, multiple comparisons between measurements at each time interval were made with the Tukey test (Tables 1, 2).

The paired *t*-test was used to compare IOPs. No significant difference was observed in mean basal IOP between the two groups (13.9 ± 3.3 mm Hg in eyes with worse MDs versus 13.9 ± 3.1 mm Hg in eyes with better MDs; $P = 0.67$).

A significant difference was observed in mean IOP between the two groups after 15 and 30 minutes of water ingestion ($P = 0.03$; Table 3). No significant difference was observed between groups at 45 and 60 minutes.

TABLE 3. IOP Comparison at Each Time Point

	Eyes with Worse MDs	Eyes with Better MDs	*P*
Basal	13.9 ± 3.1	13.9 ± 3.2	0.67
15 Minutes	15.7 ± 3.7	15.4 ± 3.6	0.03*
30 Minutes	16.2 ± 4.2	15.6 ± 4.0	0.003*
45 Minutes	15.4 ± 4.1	15.0 ± 3.8	0.10
60 Minutes	14.6 ± 4.0	14.4 ± 3.7	0.35

Data are IOP (mm Hg).
* Statistically significant; paired *t*-test.

Mean maximum IOP after water ingestion was 16.5 ± 3.8 mm Hg in the better eye group and 17.2 ± 4.1 mm Hg in eyes with worse MDs ($P < 0.001$). IOP fluctuation after water ingestion (maximum IOP minus basal IOP) was 3.6 ± 1.8 and 4.4 ± 2.2 mm Hg, respectively ($P < 0.01$; Table 4).

DISCUSSION

Glaucoma treatment is based mainly on IOP reduction. However, even in situations in which pressure levels are considered within adequate limits under clinical therapy, some patients continue to have progressive glaucoma.[1–4] One possible explanation was described by Drance,[5] who showed that almost one third of patients with single IOP measurements taken during doctor's office hours had pressure peaks detected only during a 24-hour pressure curve.

According to Zeimer et al.,[6] 29% of patients with progressive loss of visual field had IOP peaks. Cartwright and Anderson,[17] in one retrospective analysis of 14 cases of normal-tension glaucoma with asymmetric damage, showed that the eyes with worse glaucomatous damage presented higher levels of IOP. These data emphasize the need of IOP variability assessment in patients with glaucoma.

The WDT has been proposed initially by Schmidt[18] as a tool for the diagnosis of glaucoma. However, a poor correlation with the disease and its low prognostic value have been dem-

TABLE 1. Water-Drinking Test: Eyes with Higher MDs

	Basal	15 Minutes	30 Minutes	45 Minutes	60 Minutes
Basal	—	0.000017*	0.000017*	0.000017*	0.000121*
15 Minutes	0.000017*	—	0.998701 NS	0.867940 NS	0.000668*
30 Minutes	0.000017*	0.998701 NS	—	0.722149 NS	0.000213*
45 Minutes	0.000017*	0.867940 NS	0.722149 NS	—	0.022109*
60 Minutes	0.000121*	0.000668*	0.000213*	0.022109*	—

Repeated-measures ANOVA F = 26,48 ($P < 0.001$).
* Statistically significant; Tukey test.

TABLE 2. Water Drinking Test: Eyes with Lower MDs

	Basal	15 Minutes	30 Minutes	45 Minutes	60 Minutes
Basal	—	0.000030*	0.000017*	0.000423*	0.998030 NS
15 Minutes	0.000030*	—	0.27714*	0.948756 NS	0.000076*
30 Minutes	0.000017*	0.027714*	—	0.002307*	0.000017*
45 Minutes	0.000423*	0.948756 NS	0.002307*	—	0.001467*
60 Minutes	0.998030 NS	0.000076*	0.000017*	0.001467*	—

Repeated-measures ANOVA F = 21,31 ($P < 0.001$).
* Statistically significant.

TABLE 4. Maximum IOP and IOP Fluctuation after Water Ingestion

	Worse Eye Group (n = 101)	Better Eye Group (n = 101)	
Maximum WDT IOP	17.2 ± 4.1	16.5 ± 3.8	$P < 0.001$*
WDT IOP fluctuation	4.4 ± 2.2	3.6 ± 1.8	$P < 0.001$*

Data are IOP (mm Hg).
* Statistically significant; paired *t*-test.

onstrated.[19,20] Later, different studies demonstrated the correlation between IOP peaks detected during this provocative test and the pressure curve.[15–18] More recently, Malerbi et al.[21] demonstrated the usefulness of this test in the assessment of patients with POAG whose IOPs were equal to or less than the established target IOP during single measurements at the ophthalmologist's office.

In addition, the importance of this test has been shown by Armaly et al.[16] in a prospective study of 5000 patients with open-angle glaucoma. They studied 26 potential risk factors from which only five were significantly related to the development of glaucomatous visual field lesion: outflow facility, age, IOP, cup-to-disc ratio, and change in IOP after water ingestion. Yoshikawa et al.[15] evaluated of clinical tests that could predict the progression of visual field loss in normal tension glaucoma. The WDT was considered the main predictive test for glaucomatous progression in the studied group. Brubaker,[22] in a computer simulation, proposed that the WDT could be used as an indirect tool to measure outflow facility.

The WDT has also been used to compare the effect of different drugs on IOP and its fluctuation in eyes with elevated IOP.[23–26] The variability of IOP in patients with outflow controlled by filtering surgery was also evaluated with this test.[27,28]

The exact mechanism of the WDT over the IOP is uncertain. One hypothesis is that the change in blood osmolarity could be responsible for this elevation, due to the vitreous humor hydration. The change in the osmolarity could also lead to stimulus of the central nervous and endocrine systems.[29] In clinical practice, the WDT may be considered an indirect tool for evaluating the outflow system of the eye.

In our study, eyes with worse MDs had higher pressure peaks. We observed a difference of almost 1 mm Hg in IOP fluctuation during the WDT between the two groups. The data demonstrate that eyes with worse glaucomatous lesion present higher IOP fluctuations than the contralateral eyes, even when equally treated with topical medication. This relationship between asymmetric glaucomatous lesions and IOP elevation suggests that this fact can be important in the mechanism of glaucomatous damage. It is worth noting that in the management of glaucoma, each millimeter of mercury of IOP reduction accounts for the reduction of progression risk, as demonstrated by the Early Manifest Glaucoma Trial.[30]

It is possible that IOP variability after water ingestion could be even higher in patients without treatment, because some of the medications used by the studied patients can reduce IOP peaks by improving aqueous humor drainage.

In conclusion, this study demonstrates that eyes with worse glaucomatous damage have a greater variability in response to the WDT. This test could be useful in evaluating the efficacy of a treatment when its main objective is to reduce IOP as well as to lower its fluctuation. However, other studies are necessary to correlate the results of the WDT with glaucomatous progression, to confirm this hypothesis.

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