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Intraocular pressure values during the water drinking test in a Colombian population

Comportamiento de la presión intraocular durante la prueba de sobrecarga hídrica en población colombiana

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Abstract

Background: *Intraocular pressure (IOP) peaks are key factors on the onset and progression of glaucoma. The water drinking test (WDT) detects IOP fluctuations and estimates the maximum IOP.* **Objective:** *To assess the IOP variations during the WDT in patients diagnosed or suspected of glaucoma treated at an ophthalmology clinic.* **Methods:** *This is an observational, descriptive, and retrospective study, using clinical records of patients whom underwent the WDT between January 2017 and August 2019.* **Results:** *The study included 300 eyes. The WDT was positive in 23.3% of the eyes. Basal IOP at 15, 30, and 45 min, as well as the maximum pressure, presented a similar mean, median, and mode, as well as a varying coefficient without much variability. The negative test group had a maximum IOP of 18.9 mmHg, compared with 20.3 mmHg in the positive test group.* **Conclusion:** *In a Colombian cohort of patients with diagnosed or suspected glaucoma whom underwent a WDT, 23.3% had positive result. 90% of the tests were positive at the 30-min interval. This test is a complementary tool in the follow-up of patients with glaucoma.*

Keywords: *Glaucoma. Intraocular pressure. Ophthalmopathy. Ocular hypertension. Diagnosis.*

Resumen

Introducción: *Los picos de presión intraocular son factores importantes para la aparición y progresión del glaucoma. La prueba de sobrecarga hídrica permite detectar fluctuaciones de presión intraocular y estimar la presión máxima.* **Objetivo:** *Evaluar las variaciones en la presión intraocular durante la prueba de sobrecarga hídrica en pacientes de una clínica oftalmológica.* **Métodos:** *Estudio observacional, descriptivo, retrospectivo de revisión de historias clínicas de pacientes sometidos a la prueba de sobrecarga hídrica entre enero de 2017 y agosto de 2019.* **Resultados:** *Se incluyeron 300 ojos. La prueba de sobrecarga hídrica fue positiva en el 23,3% de los ojos. La presión intraocular basal, a los 15, 30 y 45 min, al igual que la presión máxima, tuvieron una media, mediana y moda similares, con un coeficiente de variación sin mucha variabilidad. El grupo con resultados negativos tuvo una presión intraocular máxima de 18,9 mmHg comparado con 20,3 mmHg del grupo con resultados positivos.* **Conclusión:** *En una cohorte colombiana de pacientes con diagnóstico o sospecha de glaucoma quienes se les realizó la prueba de sobrecarga hídrica, el 23,3% tuvo resultados positivos. El 90%*

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de las pruebas fueron positivas en el intervalo de 30 min. Esta prueba es una herramienta complementaria en el seguimiento de pacientes con glaucoma.

Palabras clave: *Glaucoma. Presión intraocular. Oftalmopatías. Hipertensión ocular. Diagnóstico.*

Introduction

Glaucoma is an ocular disease characterized by impaired vision as a result of progressive damage to the optic nerve, potentially leading to eventual vision loss, decreased visual fields, and in severe cases, blindness[1].

Global prevalence has been reported at 3.54%, with almost 6.6 million people with glaucoma-induced blindness, making it the principal cause of irreversible blindness. It has been projected that the number of people worldwide (between 40 and 80 years old) with glaucoma will rise from 64.3 million in 2013 to 111.8 million in 2040[2]. Based on recent Health Ministry analysis in Colombia, glaucoma consults have been on the rise. In 2009, the prevalence was 0.08% (35097 cases), increasing to 0.14% (66229 cases) in 2014, almost doubling the previous report[3].

The primary risk factor for glaucoma is ocular hypertension producing irreversible damage to the optic nerve, which can be asymptomatic in its initial phases[4]. The normal intraocular pressure (IOP) is considered between 10 and 21 mmHg[5]. The IOP peaks have been considered important for the onset and progression of glaucoma[6]. Measuring the IOP in the outpatient consult can provide us with isolated data of the pressure; however it does not take into account the possible oscillations during day or night[7]. It has been shown that despite having the IOP in its normal range, the disease still progresses in a lot of patients, due to pressure peaks and fluctuations in the IOP that is not detected in a routine visit[8]. In a normal and healthy individual, the IOP can vary between 2 and 4 mmHg during a 24-h period. However, any variation >6 mmHg is highly indicative of an abnormality and has been associated with glaucoma onset or progression[9].

Circadian variations of the IOP were described for the first time in 1898 by Sidler-Huguenin using digital measurement; later, in 1904, Maslenikowy quantified these measurements using the Maklakov tonometer proving the importance of pressure fluctuations[9]. In an ideal setting, IOP monitorization should be made during a 24-h period to ensure an accurate mean IOP, accounting for day and night oscillations as well as the maximum peak. However, this is an invasive, complex, and impractical approach in our context given the high cost and required trained staff during the 24-h period[10].

As an alternative to the 24-h period measurement, the water-drinking test (WDT) arises as a practical and useful method to induce IOP peak changes in patients. This test measures the capability of the eye to recover from acute aqueous elevations, maintaining normal IOP values[11-13]. This is a cost-efficient, non-invasive, and accurate method to unmask IOP fluctuations in a "stressful" setting for the patient such as drinking water, detecting instabilities in the IOP, and making an estimate of the maximum IOP[10,13].

This report aims to describe the IOP changes during the WDT and to detect the fluctuations in patients with suspected or confirmed glaucoma.

Methods

An observational, descriptive, retrospective study was completed with a medical record review in patients whom underwent the WDT between January 2017 and August 2019 and attended in the diagnostic department of an Ophthalmological Clinic in Medellin, Colombia.

Patients included were adults, remitted by their ophthalmologist to undergo the WDT with confirmed or suspected diagnosis of glaucoma. All tests were performed by the same ophthalmologist, with the same slit lamp and the same tonometer.

Excluded patients included incomplete clinical histories, ocular superficial diseases, suspected angle closure, and closed-angle glaucoma. Other exclusions included proliferative retinopathies and ocular inflammatory diseases.

Demographic variables were analyzed including age and gender. Patients were categorized based on confirmed or suspected diagnosis of glaucoma. Any of these procedures was recorded as a history of surgery for glaucoma: Trabeculectomy, laser trabeculoplasty, valve implant, or minimally invasive glaucoma surgery. In addition, it was written down if the patient used any type of ocular antihypertensive medication.

All the tests were carried out with the patient fasting for more than 8 h, between 7 and 9 am. The measurement of the basal IOP was recorded in both eyes before the WDT. The test began with drinking 800 mL of water in a period no >5 min, and the IOP measurement was repeated in both eyes on 3 occasions at 15-min intervals.

Positive tests were considered if any pressure values presented an increase of at least 8 mmHg or 30% with respect to the basal measurement; describing among positive patients, at what point in the time (15, 30, or

Table 1. Age and results of intraocular pressure (IOP) in 300 eyes

	Basal IOP	15′ IOP	30′ IOP	45′ IOP	Max IOP
Mean ± SD	16.1 ± 4.2	18 ± 4.4	18.3 ± 5	17.4 ± 4.8	19.28 ± 4.9
Mean ± SD Right Eye	16 ± 4.2	18 ± 4.3	18.3 ± 4.9	17.4 ± 4.8	19.3 ± 4.8
Mean ± SD Left Eye	16.1 ± 4.2	18 ± 4.6	18.3 ± 5.1	17.4 ± 4.8	19.1 ± 5
Median (ICR)	15.5 (13-18.25)	18 (15-25)	18 (15-21)	16 (14-21)	18.5 (16-22)
CV	0.26	0.24	0.27	0.27	0.25
Range	8-28	10-31	10-37	10-32	10-37

SD: standard deviation; ICR: interquartile range; CV: coefficient of variation; IOP: intraocular pressure in mmHg.

45 min) the test became abnormal or positive, and also reporting the variations of IOP in the subgroup of patients with glaucoma and in treatment with topical antihypertensives or surgical treatment.

Measured and collected data were tabulated on a sheet in Microsoft Excel. Qualitative variables were expressed in absolute and relative frequencies, while quantitative variables were analyzed as median and interquartile ranges (P_{25} – P_{75}) (ICR). The statistical values were calculated using Epidat version 4.2.

The study was classified as an investigation without risk according to the 1993 October 4th Resolution #8430 of the Health Ministry of Colombia and the 2013 Helsinki Declaration, therefore, informed consent from patients was not required. Ethical approval was granted by the Ethical Committee of the Health Science School of the University and the Ophthalmological Clinic to use the patient's clinical records.

Results

The study included 300 eyes, corresponding to 150 patients that complied with the eligibility criteria. 58% of patients were female, while 42% were male. However, in positive test results 51.4% were male while 48.5% were female, with a median age of 60 (interquartile range: 51-69) years old. Basal and maximum IOP as well as at the 15-, 30-, and 45-min intervals had similar mean, median and mode, with a variability coefficient not very different (Table 1).

Previous clinical history of glaucoma, use of antiglaucoma drugs, and glaucoma surgery showed no statistically significant differences in positive and negative results (Table 2).

The negative results group had a maximum IOP of 18.9 mmHg compared to the 20.3 mmHg of the positive test group, resulting in a statistically significant difference (p = 0.004), and a difference of 1.3 mmHg (IC 95%; 2.7 mmHg; 0.006 mmHg).

Regarding the positive results, 23.3% of results were positive, representing a total of 70 eyes (47 patients). Variable analysis of the minute intervals of positivity showed that at 15 min, more than half of the eyes (60%) showed positivity, at 30 min, almost 90%, and at 45 min, the resulting 10% were positive (Fig. 1).

Discussion

The WDT is considered a useful marker for reserve drainage capacity and an important tool in measuring IOP peaks[4]. It is vital to analyze IOP fluctuations given the proven causal relation between pressure variations and the progression of glaucoma, independent to the basal IOP[14-16]. Previous studies have shown a correlation between diurnal pressure peaks and the WDT[17,18]. For example, Muñoz et al. showed a moderate correlation of established IOP peaks during the diurnal hours and the WDT, with a positive-correlation coefficient of 0.93 (pc = 0.99 almost perfect; pc = 0.95-0.99 substantial; pc = 0.90-0.94 moderate; pc < 0.90 poor)[10].

In the present study, results were similar in basal IOP at the 15, 30, and 45-min intervals, as well as the maximum IOP; compared to the previously reported WDT on glaucoma patients review by Razeghinejad et al.[19]. With regard to the positive test result, 23.3% of eyes had positive results, similar to Salcedo et al. descriptions with a positivity of 19.6%[9,19,20].

The precise mechanism of elevated IOP post-water intake is not known, however, hypotheses include elevated episcleral venous pressure (EVP) and stimulated autonomic nervous system. It has been demonstrated previously that water intake can increase EVP due to an "inverted" transient aqueous humor drainage[19]. Using swept-source optical coherence tomography,

Table 2. Previous ocular history, before measurement of the WDT

Previous history	n (%) 300 (100)	Positive result, n (%) 70/300 (23.3)	Negative result, n (%) 230/300 (76.7)	Proportion difference (IC 95%)	p-value
Glaucoma	100/300 (33)	18/70 (25.7)	82/230 (35.6)	0.09 (–0.02 to 0.21)	0.21
Use of antiglaucoma drugs	86/300 (28.6)	18/70 (25.7)	68/230 (29.56)	0.04 (–0.08 to 0.15)	0.53
Glaucoma surgery	22/300 (7.3)	4/70 (5.71)	18/230 (7.82)	0.021 (–0.043 to 0.086)	0.08

n(%): total number of eyes/percentage; positive result: eyes with positive water drinking test result; negative result: eyes with negative water drinking test result

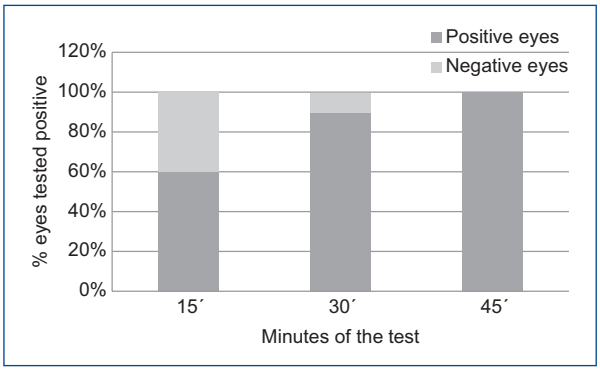

Figure 1. Accumulated frequency (in minutes) of positivity.

there was an increase of 4.3% and 5.7% of the macular choroidal and peripapillary thickness post-water intake, respectively. It is believed that this increase in choroidal volume causes a pressure gradient that transmits intraocularly[21,22].

Consistent with Susanna et al.'s descriptions, IOP differences can be found between both eyes if the ocular damage is asymmetric[23]. The maximum IOP in patients with similar basal IOP and asymmetric glaucomatous damage in our results was 0.7 mmHg, being highest on the worse eye.

In Razeghinejad et al.'s study, with participation of 113 males and 90 females, females had a greater variability of IOP, explained possibly due to greater uveal thickness compared to the males; meanwhile, in our study, there were no differences in positive results between females (48.5%) and males (51.4%)[24].

Muñoz et al., in their WDT reproducibility study, found 32 of 38 eyes with glaucoma diagnosis (84.21%); a percentage much larger than found in our study in which only 100 eyes (33%) had a previous history of glaucoma[10]. Meanwhile, in the Razeghinejad et al. study, the glaucoma antecedent was an inclusion criterion resulting in 100% of the subjects with this diagnosis[24].

Similar to Muñoz et al., previous eyes treated with antiglaucoma drugs were 39.5% (15 eyes), compared to our study of 28% (86 eyes), of these, 18 had a positive result. Alternatively, in the Martinez et al. study, there were no differences found in antiglaucoma drug patients 40% (16 eyes) compared to those without treatment[10,25].

Razeghinejad et al. described 24 patients (12.8%) without use of antiglaucoma drugs compared to 179 patients (87.2%) that used between 1 and 5 drugs. In addition, 84 patients (41.4%) had a surgical antecedent of trabeculectomy or valve surgery. Meanwhile, in our study, only 7.3% of patients had undergone a surgical procedure, of which only 18% had positive result in the WDT[22,24].

In regard to the time to positivity intervals, our results were similar to those in Hatanaka et al. where the maximum IOP peak appeared at the 30-min interval in 88 eyes with ocular hypertension or open-angle glaucoma without treatment. Contrarily, there was a difference comparing our results to the Tran et al. study which reported maximum IOP peak at 45-min, similarly to Hatanaka et al. with a higher degree of positivity also at the 45-min interval[26,27].

Our study's strengths include the sample size, which is greater than some of the previous studies. In addition, the use of the same Goldmann's tonometer and the same ophthalmologist was confirmed using each patient's clinical history. Alternatively, limitations include that the study was a retrospective one potentially generating selection bias; however, these were addressed using the inclusion and exclusion criteria. We hope that a prospective study can be made in the future to better understand the WDT concepts in relation to its utility in glaucoma.

Conclusion

In a Colombian cohort of patients with diagnosis or suspected glaucoma who underwent the WDT, 23.3%

had positive test results. In this group, 90% of the positivity results were at the 30-min measurement interval. The peak maximum pressure recorded in the positive group was 20.3 mmHg.

There were no differences detected in the positivity of the results in either subgroups of glaucoma diagnosis, use of antiglaucoma drugs, or previous surgical treatment. The WDT is an important complement in glaucoma patient follow-up, taking into account its use as a risk analysis tool in the disease progression, becoming a trustful, accessible, and cheap method.

Author contributions

All the authors contributed equally in the design of the study, recollection, and analysis of data, as well as writing and editing the final manuscript. All authors read and approved the final manuscript.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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