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Water drinking test in glaucoma management: a review of the literature

Khoo Phong Yue, **Cheng** Teck Chee, Norshamsiah **Md Din**

Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Kuala Lumpur, Malaysia

Abstract

Purpose: To describe the methods of performing the water drinking test (WDT) and its applications in glaucoma management.
Methods: This review is based on pertinent publications retrieved by a selective search in PubMed, supplemented by further articles chosen by the authors.
Results: Intraocular pressure (IOP) changes throughout the day. IOP peak has been identified as a risk factor in glaucoma onset and progression. WDT is a simple stress test used by many researchers to elicit IOP peaks in assessing response to glaucoma treatments.
Conclusions: Studies have shown the reproducibility and promising results of WDT in various pharmacological and surgical treatments of glaucoma. It is an important tool in glaucoma management.

Keywords: intraocular pressure, glaucoma, water drinking test

Correspondence: Associate Professor Dr. Norshamsiah Md Din, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia.
Email: shamsiahdr@hotmail.com

Ujian minum air dalam rawatan glaukoma: kajian tinjauan literatur

Abstrak

Tujuan: Untuk menerangkan kaedah menjalankan ujian minum air (WDT) dan aplikasinya dalam rawatan glaukoma.
Kaedah: Kajian ini adalah berdasarkan penerbitan jurnal berkaitan yang diperoleh melalui carian terpilih dalam PubMed, ditambah dengan artikel lanjut yang dipilih oleh pengarang.
Keputusan: Tekanan intraokular (IOP) berubah sepanjang hari. Puncak IOP telah dikenal pasti sebagai faktor risiko dalam pembentukan dan perkembangan penyakit glaukoma. WDT ialah ujian yang digunakan oleh ramai penyelidik untuk mendapatkan puncak IOP dalam menilai tindak balas terhadap rawatan glaukoma.
Kesimpulan: Berdasarkan tinjauan literatur, WDT menunjukkan kebolehulangan dan menunujukkan peranan WDT yang memberangsangkan dalam pelbagai rawatan farmakologi dan pembedahan glaukoma. WDT merupakan ujian yang penting dalam rawatan glaukoma.

Kata kunci: glaukoma, kesihatan dan kesejahteraan yang baik, tekanan intraokular, ujian minum air

Introduction

Intraocular pressure (IOP) is the main modifiable risk factor that contributes to glaucoma progression.[1] The Early Manifest Glaucoma Trial (EMGT) showed that the risk of glaucoma progression decreased by 10% with each 1 mmHg of IOP reduction from baseline.[2] However, IOP is not a fixed value, but varies throughout the circadian cycle. Twenty-four-hour IOP profile studies have shown that two-thirds of patients experienced peak IOP outside of the regular clinic hours.[3] Hence, some glaucoma patients still progress with IOP apparently within the target range during clinic visits.

Diurnal and 24-hour IOP curves have been useful to determine peak IOP. Methods to measure 24-hour IOP such as the modified diurnal tension curve (four to five IOP measurements during office hours from 8 AM to 6 PM), home tonometry, and contact lens sensor are time- and resource-intensive.

The water drinking test (WDT) has been suggested as a practical and easy test to estimate the diurnal IOP profile more feasibly. It was originally described as a diagnostic test for glaucoma but was eventually abandoned due to its low

sensitivity, low specificity, and low diagnostic value.[4] However, it has since been revamped into a stress test to detect IOP instability and predict IOP peaks.[5] This concept has led to a growing interest in the WDT. Many researchers have used the WDT to compare the effects of different clinical and surgical treatment modalities in glaucoma.

How to perform the WDT

Currently, the WDT is widely used to predict peak IOP and IOP fluctuation. It also serves as a reliable tool to assess the efficacy of different glaucoma treatments. Concomitant systemic diseases such as cardiac diseases, renal diseases, and urinary retention are the contraindications to this test. Prior to the test, participants are required to refrain from food and liquid intake for at least 2 hours. This is to avoid any possible influence of previous liquid ingestion on the results. This is particularly important for patients who are on special high-sugar or high-salt diets. Unfortunately, there is no recommendation on the washout period for patients who are on diuretics as of now. Most researchers performed WDT during office hours. However, it is advised to perform WDT within a fixed time of the day to minimise diurnal variation.

Essentially, IOP fluctuation is independent of the positioning during measurement. However, a study concluded that IOP values obtained in the supine position during practice hours were more appropriate for the estimation of nocturnal IOP peaks than measurements made in the sitting position.[6] Therefore, IOP measurements in both sitting and supine positions are recommended.

Firstly, the patient's baseline IOP is measured. Then the patient drinks a given volume of water within 5 minutes. Following water ingestion, patients are required to rest at a sitting or supine position. Subsequently, another four IOP measurements are taken at 15-minute intervals (15, 30, 45, and 60 minutes after water ingestion). One examiner measures the IOP. The average of three measurements is recorded and the measurement is repeated if the difference between the three measurements is greater than 3 mmHg. In a meta-analysis, of all available tonometers when compared with the Goldmann applanation tonometer, the least amount of variability in IOP measurement (mean difference of 0.2 mm Hg) was seen with non-contact tonometers.[7]

The volume used in WDT has not been standardized. Some authors use a fixed volume of water, whereas others use a volume adjusted to body weight. It is not yet clear whether the use of 1000 mL, 800 mL, or 10 mL/kg body weight improves the correlation or predictive value of the WDT.

A volume of 10 mL of water/kg of body weight has been used in an attempt to correct the effect of body mass and shift of fluid between intravascular, intracellular, and interstitial spaces.[8] It is presumed that a fixed volume, for example, 1000

mL, is likely to have a different physiological effect in a 100 kg patient compared to a 50 kg patient. WDT based on body weight-adjusted volume is known to induce a significant IOP response that correlates to diurnal IOP peak as well as the ingestion of 800 mL, but not 500 mL. A comparison between the ingestion of 1000 mL or 500 mL of water demonstrated that the latter failed to estimate the peak diurnal pressure.[9] Current preference is based on personal experience and scientific principles. Most recent studies use 800 mL or 10 mL/kg of body weight. Unfortunately, there is a lack of consensus regarding the maximum volume of water allowed to be consumed in this test.

Mechanism of action

The exact mechanism behind WDT has not been established. Studies have suggested that an increase in episcleral venous pressure, blood-aqueous osmotic pressure gradient, choroidal expansion, and autonomic nerve stimulation may lead to the IOP changes post-WDT.[10-13]

Previously, it was thought that the rapid ingestion of a relatively large amount of water affects blood and ocular osmotic gradients. Nongpiur *et al.* demonstrated that a significant decrease in serum osmolality occurred after water intake in WDT, and this was significantly correlated with changes in IOP.[10] This may be explained by the osmotic gradient causing water movement into the aqueous humour with a subsequent increase in IOP.

Water intake has also been shown to be associated with an increase in blood pressure and peripheral vascular resistance. Haemodynamic changes may be associated with increased episcleral venous pressure (EVP), which leads to decreased outflow facility. Aqueous fluorophotometry and estimation of the EVP using manometry following a 1000 mL WDT has been measured in young healthy volunteers.[11] Estimated EVP more than doubled within 10 minutes of the water load and was maintained at this level for 90 minutes, at which time measurement was stopped. At the same time, increased fluorescein concentration was detected in the aqueous at 10 minutes. It subsequently returned to baseline 60 minutes after the water load. The explanation for increased fluorescein concentration is unclear, but it may represent negative flow or reflux of fluorescein from Schlemm's canal. These findings suggest a role for increased EVP in the WDT response, hence explaining the rationale for performing the test over 60 minutes.

More recent studies focus on the role of choroidal expansion. The rapid water ingestion would lead to a transient increase in hydrostatic pressure and a decrease in osmotic pressure, which shifts fluid from the systemic circulation to the choroidal space due to the osmotic gradient. De Moraes *et al.* suggested that systemic fluids are transmitted into the choroidal space, causing the choroid to expand and increase the IOP.[12] This pressure gradient causes increased outflow

of aqueous humour from the anterior chamber into the trabecular meshwork. In a more recent study involving swept-source optical coherence tomography, Mansouri *et al.* found an increase of 5.7% in the peripapillary choroidal thickness and 4.3% in the macular choroidal thickness after water intake by healthy participants.[14]

The autonomic nervous system is also thought to be involved in IOP regulation. Yan *et al.* showed that aerobic exercise causes sympathetic nervous system stimulation, consequently causing the expansion of Schlemm's canal, which in turn causes IOP reduction.[13] Sasamoto *et al.* observed many unmyelinated nerves containing substance P in the inner wall of Schlemm's canal, which indicates that parasympathetic nerves may be involved in the regulation of Schlemm's canal.[15] It has been proven that water intake accelerates parasympathetic activation. Chen *et al.* later showed that the WDT could cause parasympathetic nervous system stimulation, which may cause the collapse of Schlemm's canal, leading to increased IOP post-WDT.[16]

Regardless of the mechanism that increases IOP following WDT, an intact outflow facility should be associated with rapid IOP recovery, whereas an impaired outflow facility is more likely to lead to sustained IOP elevations.

Interpreting the results

Following IOP measurement at baseline and four other measurements at 15, 30, 45, and 60 minutes, these parameters are assessed: trough IOP (lowest IOP after drinking water), peak IOP (highest IOP after drinking water), mean IOP (the mean of the four IOPs after drinking water), IOP fluctuation (difference between peak IOP and baseline), IOP range (difference between peak IOP and lowest IOP reading after drinking water), and end-pressure difference (IOP at 60 minutes *versus* baseline).

Several studies have shown that the peak IOP obtained with this test is strongly correlated and in agreement with the IOP peaks that occur during the day.[17,18] Eyes with higher IOP peaks after water ingestion take longer to return to baseline levels than eyes with lower IOP peaks, which may reflect the state of the drainage system in the eye. The factors influencing time to peak IOP following WDT are less certain, as reported findings are inconsistent. For example, Mansouri *et al.* reported that the highest mean peak IOP from 58 healthy eyes occurred at 15 minutes.[14] Similarly, Ulas *et al.* have shown that IOP elevation after WDT in healthy eyes occurs within the first 10 minutes and recovers quickly.[19] Tran *et al.* reported mean peak IOP was highest at 45 minutes after water ingestion in patients with primary open-angle glaucoma (POAG),[20] whereas Hatanaka *et al.* found that mean peak IOP was highest at 30 minutes in subjects with ocular hypertension and open-angle glaucoma.[21] It has been postulated that a more rapid return to baseline IOP following WDT may reflect an improved outflow facility.

Clinical and research applications

The WDT helps us to further understand how IOP-lowering treatments work and why glaucoma progresses. Researchers evaluated the WDT-IOP profile of glaucoma patients treated with medications and those who had undergone glaucoma procedures such as trabeculectomy, deep sclerectomy, peripheral laser iridotomy, and glaucoma drainage device (GDD) implantation.

In a comparison between latanoprost and the fixed combination of dorzolamide and timolol, patients who received latanoprost showed significantly smaller elevations in their IOP levels following the WDT.[22] The authors demonstrated that prostaglandin analogues that act on the outflow system of the eye are associated with better IOP stabilization during WDT compared to drugs that decrease aqueous humour production, such as β-blockers and carbonic anhydrase inhibitors.

Some drugs may demonstrate similar IOP reduction but different effects on blunting IOP spikes that occur during the day. Although timolol 0.5% showed similar IOP reduction to brimonidine 2.0%, IOP was more stable on brimonidine than with timolol. Eyes treated with timolol had an earlier IOP spike, higher mean IOP peak (3.5 mmHg), and longer return to baseline in WDT compared to brimonidine.[23]

Waisbourd *et al.* suggested a role for WDT in assessing response to peripheral laser iridotomy in primary angle-closure suspects.[24] Although no significant change in peak IOP was reported before and after laser peripheral iridotomy, a more rapid recovery in the IOP curve was seen after treatment. The authors postulate that this is due to the enhanced outflow facility that accompanies reduced iris-trabecular apposition.

In recent years, WDT was also performed on glaucoma patients who were treated surgically. Medeiros *et al.* reported that IOP change in 30 patients with one or two trabeculectomies was significantly lower than that of a group of patients with medicallycontrolled glaucoma.[25] Razeghinejad *et al.* studied the effects of WDT on patients with Ahmed glaucoma valve and those treated with trabeculectomy. They concluded that both groups had IOP increases, despite showing seemingly stable IOPs in a standard clinical setting. However, the WDT-IOP profile was lower in the trabeculectomy group.[26] Subsequently, Razeghinejad *et al.* also assessed primary congenital glaucoma patients who had undergone trabeculotomy and GDD implantation. Interestingly, the authors revealed a smoother WDT-IOP profile in their GDD group.[27] Martinez *et al.* revealed that subjects who had undergone either trabeculectomy or tube shunt surgery showed similar IOP responses to the WDT.[28] Studies have also shown that patients on glaucoma medications have a greater IOP increase following WDT when compared to patients who have undergone filtration surgery despite similar baseline IOP.[25,29]

A test must be reproducible to be considered clinically applicable. IOP peaks detected by WDT performed 24 hours apart in untreated patients with ocular

hypertension, showed excellent reproducibility.[21] Similarly, outstanding reproducibility was observed by the same research group in a cohort of treated POAG patients with a mean interval of 4.85 (range 3–6) months between tests. By performing WDT on 34 treated POAG patients in two consecutive visits without any change in the treatment regimen, Babic *et al.* demonstrated better reproducibility for IOP peaks than IOP fluctuation.[30]

There are certainly some limitations to the WDT. It cannot be used as a diagnostic test for glaucoma. IOP response to this test may be affected by prior topical antiglaucoma treatment, as some medications can reduce IOP peaks by improving aqueous humour drainage. Another study also demonstrated that eyes with worse glaucomatous lesions experienced higher IOP fluctuations than the contralateral eyes, even when equally treated with topical medication.[31] There are no reports of systemic complications related to WDT. However, some side effects such as corneal oedema, hyperaemia, and discomfort have been associated with its use.

Conclusion

There has been increased attention on IOP peaks being risk factors for glaucoma onset and progression. More studies are being carried out to establish a target IOP peak or target IOP peak range instead of a single target IOP level. Better methods to evaluate the IOP profile over 24 hours are warranted.

The practicability of current 24-hour IOP monitoring devices remains doubtful. Meanwhile, the WDT is reproducible and shows clinically relevant results validated several times by a series of peer-reviewed studies. It can be an important tool for IOP profile assessment in glaucoma management, particularly in treatments that aim to improve outflow facility. Further studies on the 24hour diurnal curve and WDT after glaucoma surgery, including microinvasive glaucoma surgery, will provide more insights into the IOP profile after filtration surgery.

Declarations

Ethics approval and consent to participate
Not required, as this is a literature review.

Competing interests
None to declare.

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