# Comparing method of Water Drinking Test in detecting peak Intraocular Pressure in primary open angle glaucoma

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## Abstract

**Introduction:** Intraocular pressure (IOP) rise detected during water drinking test (WDT) can predict peak IOP during a 24-hour diurnal tension curve and relate to glaucoma progression. Unfortunately, 1000-mL WDT is not practical for daily fluid intake habit and may increase the risks of some systemic diseases.

**Objective:** To compare intraocular pressure (IOP) rise between two drinking methods: 1) four ingestion of 250-mL (4*250 mL) WDT 2) a standard 1000-mL (1*1000 mL) WDT.

**Methods:** Twenty-three POAG patients were included in this prospective study. The WDT was performed, followed by taking 4 doses of 250 mL water every 15 minutes. A 1000 mL WDT was performed after a minimum washout period of 1 week. IOP were measured before WDT and at 15, 30, 45, 60 minutes after WDT. Statistical analysis was performed by paired T-test.

**Results:** There was no statistically significant difference of peak IOP between 4*250 and 1*1000 group. (mean 4.91±3.94 mmHg, 5.87 ±3.85 mmHg, respectively; p = 0.333). There was a statistically significant IOP rising from baseline at 15 minutes in both 4*250 (mean 4.26±3.79 mmHg; p = 0.000) and 1*1000 group (mean 5.35±3.94 mmHg; p = 0.000), at 30 minutes in both 4*250 (mean 2.52±3.58 mmHg; p = 0.003) and 1*1000 group (mean 4.17±3.87 mmHg; p = 0.000). At 45 minutes, there was a statistically significant IOP rising from baseline only in 1*1000 group (mean 2.48±3.17 mmHg; p = 0.001).

**Conclusion:** 4*250 mL WDT can be used to estimate the peak diurnal IOP and assess the risk for glaucoma progression as 1*1000 mL WDT.

**Key Words:** Water drinking test, intraocular pressure , glaucoma, fluid volume, IOP fluctuation

## Introduction:

Glaucoma is the second leading cause of blindness worldwide. In 2020, there will be 79.6 million people suffered from glaucoma, which is increasing from 60.5 million in 2010 and almost 75% will be open-angle glaucoma.[1] The results from The Early Manifest Glaucoma Trial (EMGT) and many studies confirmed that elevation of Intraocular Pressure (IOP) is a strong risk factor for glaucoma progression.[2]

In addition to IOP elevation, IOP fluctuation has been claimed as a risk factor for glaucoma progression in many studies. The Advanced Glaucoma Intervention Study (AGIS) found that long-term IOP fluctuation is a risk factor for glaucoma progression in low mean IOP. The *"long-term IOP fluctuation"* means IOP fluctuation which occurs between patient visits over months to years whereas *"Short-term IOP fluctuation"* means IOP fluctuation which occurs over hours or days.[3] Diurnal IOP fluctuation is short term IOP fluctuation which has been reported to associate with progression of open angle glaucoma in some studies.[4,5] Because peak IOP measurements are the most frequently highest in the early morning and single office measurement of IOP do not represent IOP fluctuation in many patients.[3,4,6] these reasons may explain mechanism of visual field progression in well-controlled IOP patients.

There are many ways to identify IOP fluctuation during the day such as home IOP assessment; however the instrument's reliability is still questionable. A 24-hours diurnal tension curve seems to be more reliable. Unfortunately, the inconvenience and unpractical procedure limited the usage and not yet a standard tool.[7]

The "water drinking test" (WDT) has been using as a diagnostic tool for open-angle glaucoma. After water ingestion, a 6 mmHg rise in IOP was considered a positive test for glaucoma diagnosis.[8] However it was found to be a low reliable test due to low sensitivity and specificity.[9,10] Mechanism of IOP elevation in WDT depends on a reduction in aqueous humor outflow, with variations caused by individual outflow facility.[8,9,18]

More recently, many studies have found the correlation between WDT and diurnal tension curve.[11,12] Some studies have shown the relationship between peak IOP in WDT and progression of glaucoma.[13,14] Thus, WDT may become an alternative method to access progression of glaucoma from IOP fluctuation.[15,16]

However, drinking 1000 mL of water is probably worsening some systemic diseases such as heart condition and also unpractical. There is still lack of data on how closely the peak circadian IOP simulated by other amounts of drinking water than the original 1000 mL.[11] Some studies suggested that 500 mL of water drinking could reveal the diurnal tension curve as 1000 mL.[8,17] Furthermore , in normal life we usually drink repeated small amount of fluid rather than a large bolus dose.

We would like to study the fluid ingestion pattern for WDT which simulate to our daily fluid intake habit. In this study, we compare IOP increasing in 4 consecutive 15-minute drinking of 250 mL water with original one-bolus 1000 mL WDT.

## Objectives:

To compare increasing IOP of in 4 consecutive 15-minute drinking of 250 mL water with original one-bolus 1000 mL WDT

## Methods:

Prospective randomized study involving right eye of 23 open angle glaucoma patients from ophthalmology outpatient clinic, Thammasat University hospital, Thailand between December 2010 and May 2011

**Inclusion criteria**

- Primary open angle glaucoma
- Last two-visit IOPs were less than 24 mmHg
- Age between 20-80 year old

**Exclusion criteria**

- Ocular pathologic condition other than POAG
- Intraocular pressure > 35 mmHg
- Previously undergone ophthalmic surgery or laser trabeculoplasty.
- Renal impairment
- Cardiac disease

**Discontinuation criteria**

- Intolerant to WDT such as nausea or vomiting

The protocol and consent form has been approved by an ethic committee of Thammasat University and informed consent was obtained from all participants.

Each type of WDT was performed in the different day at the same time interval; 7.00-9.00 AM. All Patients was recorded IOP with a Goldmann applanation tonometer by one examiner.

Four consecutive of 250 mL WDT was performed. The average IOP* were recorded by Goldmann applanation tonometer at baseline, 15, 30, 45, 60 minute (right after 250 Ml water ingestion)

After a minimum of 1-week washout period, 1000 mL WDT was performed between 7.00-9.00 am by drinking of 1000 mL water in less than 15 minutes and measure average IOP by the same technique.

Statistical analysis was performed by paired T-test

## Results:

Twenty-three right eyes from 23 POAG patients were included and completed the study. There were no significant difference between sex (Male and female; 56.52%, 43.48%, respectively) and mean baseline IOP (4*250 WDT and 1000 WDT; 17.52±3.42, 17.09±3.63, respectively), Figure 1. Mean age was 64.39 ±8.13 years.

There were no significant difference between baseline IOP, Peak IOP, mean IOP or maximal IOP fluctuation of 4*250 mL WDT and 1000 mL WDT at any time points. (Figure 1)

There were statistically significant IOP rising from baseline at 15 and 30 minutes in both groups. At 45 minutes, there was a statistically significant IOP rising from baseline only in 1000 mL WDT group.

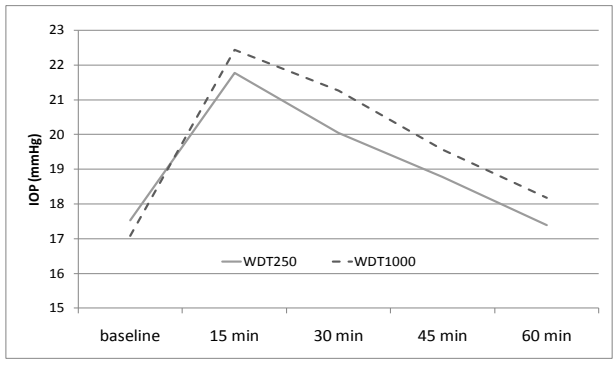


**Figure1** Mean IOP of 250 WDT and 1000 WDT

* Average from three IOP measurements

**Table 1** Comparison of mean IOP between 250 WDT and 1000 WDT using paired *t*-test

| | 250 WDT | 1000 WDT | P value (p≤ 0.05) |
|---|---|---|---|
| Baseline | 17.52±3.42 | 17.09±3.63 | 0.62 |
| 15 min after WDT | 21.78±5.02 | 22.43±4.77 | 0.39 |
| 30 min after WDT | 20.04±4.70 | 21.26±5.12 | 0.19 |
| 45 min after WDT | 18.78±4.28 | 19.57±4.19 | 0.30 |
| 60 min after WDT | 17.39±3.79 | 18.17±4.67 | 0.41 |
| Max IOP fluctuation from baseline | 4.91±3.94 | 5.87±3.85 | 0.33 |

**Table 2** Paired Differences of baseline IOP and 4*250 mL WDT IOP

| | **Mean Differences (95% CI)** | **Sig. (p≤ 0.05)** |
|---|---|---|
| Baseline – 15 min | 4.26±3.79 (2.62 to 5.90) | 0.000 * |
| Baseline – 30 min | 2.52±3.58 (0.97 to 4.07) | 0.003 * |
| Baseline – 45 min | 1.26±3.14 (-0.09 to 2.61) | 0.067 |
| Baseline – 60 min | -0.13±3.12 (-1.48 to 1.22) | 0.843 |

**Table 3** Paired Differences of baseline IOP and 1000 mL WDT IOP

| | **Mean Differences (95% CI)** | **Sig. (p≤ 0.05)** |
|---|---|---|
| Baseline – 15 min | 5.35±3.94 (3.64 to 7.05) | 0.000 * |
| Baseline – 30 min | 4.17±3.87 (2.50 to 5.85) | 0.000 * |
| Baseline – 45 min | 2.48±3.17 (1.10to 3.85) | 0.001 * |
| Baseline – 60 min | 1.09±2.89 (-0.16 to 2.34) | 0.085 |

## Discussion

From review of literatures and our knowledge the 1000 mL WDT can be used as a tool for glaucoma progression assessment by detecting short-term fluctuation of peak IOP after WDT.[11,12,13,14,15,16] Unfortunately, the standard 1000 mL WDT has limitation in some patients especially who cannot tolerate bolus of fluid drinking such as aging, cardiovascular compromise conditions. Our study try to compare between the standard 1000 mL WDT and new 4*250 mL WDT which may be more compatible, comfortable and similar to our daily drinking style. Some studies detected IOP elevation from 500 mL WDT.[8,17] Ker NM et al. reported a statistically significant rise in IOP from baseline at 15, 30 and 45 min after 500 mL WDT. However, 500 mL WDT cannot produced statistically significant maximal increase in IOP when compare to the standard 1000 mL WDT. [17]

From the result of Mehra KS study[19], there was no significant difference in result of WDT even when this test was carried out with a full stomach then our patients were allowed to take fluid or food prior to the WDT.

From the result of our study, the analysis of the maximal IOP fluctuation from baseline after 4*250 mL WDT and 1000 mL WDT revealed no statistically significant difference. The study showed 4*250 mL WDT could be used as an alternative for peak diurnal IOP detection. There was a statistically significant IOP rising from baseline at 15, 30 minutes after WDT in both groups. This result may imply that although in medically control POAG patient, drinking water in large amount (1000 mL) or frequently repeated small amount (250 mL or 1 cup every 15 minutes) may increase short-term IOP fluctuation and lead to glaucoma progression.

## Conclusion

Four consecutive 15-minute interval 250 mL WDT can be used to estimate the peak diurnal IOP and to assess the risk for glaucoma progression as 1000 mL WDT.

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# การเปรียบเทียบผลการเพิ่มขึ้นของความดันตาจากการทดสอบด้วยการดื่มน้ำปริมาณที่แตกต่างกันในผู้ป่วยโรคต้อหินมุมเปิด

**แพทย์หญิงปรียนันท์ อารีวิจิตร**
**นายแพทย์อนุวัฒน์ พฤทธิพงศ์สิทธิ์**
**รองศาสตราจารย์แพทย์หญิงมัญชิมา มะกรวัฒนะ**
ภาควิชาจักษุวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

**บทนำ :** ความดันในลูกตาที่เพิ่มสูงขึ้นภายหลังการทดสอบด้วยการดื่มน้ำ (water drinking test) สามารถใช้พยากรณ์ความดันตาที่สูงสุดในช่วง 24 ชั่วโมง (24-hour diurnal tension) และพบว่ามีความสัมพันธ์กับการแย่ลงของโรคต้อหิน แต่การทดสอบด้วยการดื่มน้ำปริมาณ 1000 มิลลิลิตรในคราวเดียวไม่เป็นที่นิยมเนื่องจากมีข้อจำกัดในโรคบางประเภท อีกทั้งไม่ใกล้เคียงกับพฤติกรรมการดื่มน้ำในชีวิตประจำวัน

**วัตถุประสงค์ :** เพื่อเปรียบเทียบความดันตาที่สูงขึ้นหลังจากการทดสอบด้วยการดื่มน้ำ 2 วิธี:

1) ดื่มน้ำปริมาณ 250 มิลลิลิตร 4 ครั้ง (4*250 มล.)

2) วิธีมาตรฐาน คือดื่มน้ำปริมาณ 1000 มิลลิลิตร 1 ครั้ง (1*1000 มล.)

**วิธีดำเนินการวิจัย :** การวิจัยแบบโพรสเปกทีป (prospective) นี้ทำในผู้ป่วยโรคต้อหินมุมเปิดจำนวน 23 คน ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ โดยทดสอบด้วยการดื่มน้ำปริมาณ 250 มิลลิลิตร ห่างกัน 15 นาที 4 ครั้ง หลังจากนั้น 1 สัปดาห์ จะทดสอบด้วยการดื่มน้ำปริมาณ 1000 มิลลิลิตร 1 ครั้ง ในเวลา 15 นาที และวัดความดันตาก่อนทำการดื่มน้ำ และที่เวลา 15, 30, 45, 60 นาทีภายหลังการดื่มน้ำจนครบปริมาณที่กำหนด ทำการวิเคราะห์ทางสถิติด้วยวิธี paired T-test.

**ผลการวิจัย :** ไม่พบความแตกต่างกันอย่างมีนัยสำคัญทางสถิติของความดันตาที่เพิ่มสูงขึ้นภายหลังการดื่มน้ำทั้งสองวิธี *(ค่าเฉลี่ย 4.91±3.94 มิลลิเมตรปรอท (4*250 มล.), 5.87±3.85 มิลลิเมตรปรอท (1*1000 มล.); p = 0.333).* พบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างค่าความดันตาก่อนดื่มน้ำและหลังจากดื่มน้ำที่ 15 นาที ทั้งกลุ่ม 4*250 มล. *(ค่าเฉลี่ย 4.26±3.79 มิลลิเมตรปรอท; p = 0.000)* และกลุ่ม 1*1000 มล. *(ค่าเฉลี่ย 5.35±3.94 มิลลิเมตรปรอท; p = 0.000)*, ที่ 30 นาทีทั้งกลุ่ม 4*250 มล. *(ค่าเฉลี่ย 2.52±3.58 มิลลิเมตรปรอท; p = 0.003)* และกลุ่ม 1*1000 มล. *(ค่าเฉลี่ย 4.17±3.87 มิลลิเมตรปรอท; p = 0.000)*, ที่ 45 นาทีเฉพาะกลุ่ม 1*1000 มล. *(ค่าเฉลี่ย 2.48±3.17 มิลลิเมตรปรอท; p = 0.001)*

**สรุป :** การดื่มน้ำปริมาณ 250 มิลลิลิตร 4 ครั้ง สามารถนำมาใช้พยากรณ์ความดันตาที่ขึ้นสูงสุดในช่วง 24 ชั่วโมง (24-hour diurnal tension) เพื่อติดตามการแย่ลงของโรคต้อหินมุมเปิดได้เช่นเดียวกับวิธีมาตรฐาน คือดื่มน้ำปริมาณ 1000 มิลลิลิตร 1 ครั้ง

**คำสำคัญ :** Water drinking test, intraocular pressure, glaucoma, fluid volume