Aqueous Humor Outflow Facility by Tonography Does Not Change with Body Position

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PURPOSE. Intraocular pressure (IOP) varies with body position and previous research has indicated that most, but not all, of the variation in IOP is due to changes in episcleral venous pressure (EVP). Positional changes in other aqueous humor dynamic parameters may contribute to the change in IOP. The purpose of this study was to investigate the variation of aqueous humor outflow facility with body position changes.

METHODS. Healthy volunteers, aged 24 to 45 years old, were recruited for this study. Constant weight tonography was performed using a modified electronic Schiotz tonometer in two positions: seated position, 70° from horizontal with neck extended until the cornea was level with floor, and supine position. A minimum of 30 minutes was allowed between the two measurements. Tonography data were fitted to second order polynomials and values for the initial steady state IOP and the outflow facility were determined using standard tables and nomograms. IOP was measured using pneumatonometry.

RESULTS. Forty-two eyes from 21 subjects were studied. IOP in the sitting and supine positions were 17.8 ± 1.7 mm Hg and 19.9 ± 1.6 mm Hg, respectively, and were significantly different (P < 0.001). The mean outflow facility in the sitting and supine positions were 0.30 ± 0.31 μL/mL/mm Hg and 0.28 ± 0.09 μL/mL/mm Hg, respectively, and were not significantly different (P = 0.37).

CONCLUSIONS. Aqueous humor outflow facility measured with electronic Schiotz tonography does not vary significantly between the supine and sitting positions. (Invest Ophthalmol Vis Sci. 2010;51:1453–1457) DOI:10.1167/iovs.09-4058

Intraocular pressure (IOP) is a dynamic process influenced by various factors including body position, circadian rhythm, and conditions leading to elevated episcleral venous pressure.1 Aqueous humor dynamics involves the investigation of the physiologic factors that contribute to IOP. Characterization of aqueous humor dynamics is important to the understanding of glaucoma pathogenesis and the mechanisms of action of glaucoma therapies.

Our current model of steady state IOP is described by the modified Goldmann equation:

\[ IOP = \frac{Q - U}{c} + EVP \]

where \( Q \) is the rate of aqueous humor formation, \( IOP \) is the intraocular pressure, \( EVP \) is the episcleral venous pressure, \( U \) is the uveoscleral flow rate, and \( c \) is the tonographic outflow facility.2 Each of these factors, except uveoscleral flow rate, has been studied over a 24-hour diurnal period and in various body positions.3-9

Postural changes in IOP, notably between sitting and supine positions, have been described extensively.10-12 This change has also been noted to be more marked in subjects with ocular hypertension, primary open angle glaucoma, and normal tension glaucoma.13,14 This change is thought to be primarily related to changes in venous and arterial circulation16 but the relationship is unclear. Weinreb et al.8 demonstrated that a 1 mm Hg change in IOP resulting from postural changes was only associated with a 0.83 mm Hg change in EVP.15 They suggested that this may be due to a different inflow and outflow facility. Another possible explanation may be that other factors besides EVP are changing with body position. Previous work from Carlson et al.4 indicate that aqueous flow does not change significantly from the upright to supine positions. However, a thorough literature search indicates that to date there have been no published studies on the effect of body position on outflow facility. The purpose of our study was to investigate variations in outflow facility as a possible contributor to positional changes in IOP. We hypothesized that the increase in IOP in the supine position is due in part to a decrease in outflow facility in the supine position.

MATERIAL AND METHODS

The study was planned and conducted in accordance to the principles governing clinical research as set out by our Institutional Review Board and the Declaration of Helsinki (1989). A signed informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study. Twenty-one healthy young volunteers, male and female, ranging in age from 24 to 45, were recruited from Mayo Clinic employees and students, and local area residents. Subjects were given a complete dilated eye examination and an updated medical history was performed. Specific exclusion criteria for subject participation included: IOP greater than 22 mm Hg in the seated position, evidence of glaucomatous optic neuropathy, poor fixation, nystagmus, tropias, phorias, recent infection, corneal scarring prevent ing reliable tonometry, evidence of pigment dispersion, narrow angles, history of trauma or surgery, systemic use of beta blockers or steroids, diabetic eye disease, uveitis, high (>6 D) myopia, or high (>4 D) hyperopia. Subjects with chronic medical conditions (eg, hypertension) were allowed to participate as long as their medical condition had been under good control over the preceding 12 months. Subjects also needed to have good cervical neck malleability to be able to meet the physical demands of the protocol, which necessitated 4 minutes of neck extension.

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On the day of the experiment, subjects were asked to maintain a regular schedule and normal activities. This included avoiding excess caffeine intake, large deviations from normal sleep cycle, or exposure to systemic medications with IOP-modifying potential.

Subjects were seated in standard ophthalmologic examination chairs and reclined slightly to 70° from the horizontal in a quiet room with subdued lighting for approximately 5 to 7 minutes and the patient’s neck was extended until the anterior aspect of the cornea was level with the floor. Anesthesia was achieved by instilling 3 to 4 drops of proparacaine 0.5%. The contralateral eye was patched in a semi airtight fashion with an adhesive eye patch to reduce evaporative losses and drying of the cornea (Fig. 1). The patient was asked to keep their eyes closed before the start of measurements. When ready, the patient was asked to open their eyes and to observe a dim fixation target that was placed on the ceiling of the room, roughly 6 feet from the patient’s eyes. The right eye was always tested first, followed by the left.

Baseline IOP was measured using a pneumatometer (Model 30 Classic; Reichert, Inc., Depew, NY). Constant weight tonography (Fig. 2) was then performed using an electronic Schiotz tonographer designed by the Mayo Clinic Division of Engineering. The measurement head of an electronic Schiotz tonography consists primarily of a linear variable differential transformer (LVDT), which is a device that converts linear movement of the tonometer tip to an electrical signal. Our variable differential transformer (LVDT), which is a device that conditioned our study to detect a 20% change in facility between the sitting and supine (black) positions, with second order polynomial curve fits shown in black. The tracings are similar except for greater variability in the sitting position.

Data from the tonography tracing were collected electronically and was exported to a standard spreadsheet (Excel; Microsoft Corp., Redmond, WA) file. Data were fitted to a second order polynomial to help determine the adequacy of the collected sample. If tracings were erratic with multiple unusual spikes, rises, and falls, they were to be deemed inadequate for the study. Experience from previous studies using this method has shown that these tracings generally show little correlation to the derived curve of best fit. Tracings with a poorly fitted curve may occur for a variety of reasons including patient tenseness and anxiety, uncontrollable tendency to fall asleep, incidental interruptions such as a sudden wave of intestinal peristalsis, or technician error. Our protocol required poor tracings to be excluded from the final analysis. However, all tracings were adequate and none were excluded from the final data analysis. Values for the initial steady state IOP and the outflow facility were determined based on standard tables and normograms.

Based on our previous research from a similar subject population, outflow facility would need to decrease by 52% in the supine position to account for the measured IOP change, assuming sitting EVP of 9 mm Hg and constant uveoscleral outflow rate. However, outflow facility is unlikely to be the only cause of postural IOP change. Therefore, we designed our study to detect a 20% change in facility between the sitting and supine positions, which is the amount of change required to
account for non-EVP related IOP variations based on the results of Weinreb et al. Our study, based on 42 observations from 21 subjects, had a power of 82%, \( \alpha = 0.05 \), assuming a normal supine outflow facility to be \( 0.27 \pm 0.11 \) \( \mu L/mL/mm Hg \), based on our previous research. Since data from both eyes were included as individual measurements, statistical significance was determined using Generalized Estimating Equation (GEE) models. GEE models allow for analysis of paired data where a correlation may exist between the pairs without having to explicitly define a model for the origin of their dependency. Statistical significance was assumed for \( P < 0.05 \).

**RESULTS**

Twenty-one subjects were recruited with a mean age of 31.6 ± 6.9 years, ranging from 24 to 45 years of age (Table 1). There were slightly more males recruited into the study, with 12 males and 9 females. Sixteen subjects were Caucasian, with the remaining five being of Hawaiian, East Asian, and South Asian descent. All recruited subjects were healthy, with no known ocular conditions, no systemic medications use, and normal ophthalmic examinations.

IOP in the sitting and supine positions measured by pneumatomometry were 17.8 ± 1.7 mm Hg and 19.9 ± 1.6 mm Hg, respectively. This difference was statistically significant (\( P < 0.001 \)). IOP in the sitting position ranged from 15.0 to 21.0 mm Hg, and in the supine position from 16.5 to 21.5 mm Hg. Tonographic outflow facility in the sitting position ranged from 0.17 to 0.52 \( \mu L/mL/mm Hg \) with a mean of 0.30 ± 0.08 \( \mu L/mL/mm Hg \), while in the supine position facility ranged from 0.13 to 0.55 \( \mu L/mL/mm Hg \) with a mean of 0.28 ± 0.09 \( \mu L/mL/mm Hg \) (Table 2). The difference in outflow facility between the sitting and supine positions was not statistically significant (\( P = 0.37 \)).

Comparison of data between right and left eyes showed no significant differences (Table 3). Data were also compared between male and female patients for both IOP (\( P = 0.17 \)) and outflow facility (\( P = 0.90 \)) and showed no significant differences (Table 4). Comparison of subgroups of subjects aged 24 to 34 years versus 35 to 45 years showed no statistically significant difference in outflow facility (\( P = 0.38 \)) or IOP (\( P = 0.29 \)).

**DISCUSSION**

Elevation of IOP associated with a change from an upright to a recumbent position is the major contributor to nocturnal IOP elevations in normal subjects as well as glaucoma patients. This change is partially, but not completely, explained by hydrostatic changes in the eye, specifically an increase in EVP associated with the recumbent position. Since the average adult sleeps in a near recumbent position between 7 and 8.6 hours a day,25 with the amount of sleep decreasing in the elderly to around 6.5 hours,24 a clearer understanding of the mechanisms for positional changes in IOP is essential.

Weinreb et al. reported that changes in EVP accounted for a majority of the IOP change due to body position. They reported that EVP increased 0.83 ± 0.21 mm Hg for every 1 mm Hg rise in IOP during an inverted posture.15,25 They postulated that the lack of an exact 1:1 correlation between IOP and EVP changes, as predicted by the Goldmann equation, was due to the existence of a different facility of inflow caused by a decrease in aqueous production with elevated IOP. However, Brubaker et al. showed that aqueous flow did not change significantly between a 50° head up position or 50° head down position over 6 hours and thus is independent of body position. Given the two prior findings, it is reasonable to assume that there must be a change in either outflow facility and/or uveoscleral flow with changes in body position. However, as far as we are aware, no previous study has examined the positional changes in outflow facility. This is likely due to the difficulty associated with carrying out many of these experiments in non-conventional positions.

There are two commonly known methods of measuring outflow facility: weighted tonometer technique and aqueous suppression technique. However, given the restrictions of the latter technique, we chose to use the more commonly used weighted tonometer technique. These restrictions primarily include time, requiring 3 or more hours per eye per position, and the need to administer aqueous suppressants that may have an effect on the vascular column and thus potentially have a secondary effect on outflow facility calculations. The weighted tonometer technique used in this study involves electronic Schiotz tonography as originally described by Grant.20 The weight applies a constant force to the eye, elevating the IOP. As the IOP decays back to baseline over the course of the tracing, the rate of decay is recorded and calculated to determine facility. It requires the cornal surface of the patient to be parallel to the floor to exert a constant, reproducible gravitational force. As a result, published reports of outflow facility have only been measured in the supine position. Our protocol involved using neck extension to allow tonography in the near-sitting position, with comparisons to the traditional supine position.

**TABLE 1.** Characteristics of Study Population

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>31.6</td>
<td>± 6.9</td>
<td>24–45</td>
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<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
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<tr>
<td></td>
<td>12</td>
<td>9</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Race</th>
<th>Caucasian</th>
<th>Other (South Asian, East Asian)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16</td>
<td>5</td>
</tr>
</tbody>
</table>

| Concurrent systemic medication(s) | 0 |

* \( n = 42 \) eyes.

**TABLE 2.** IOP and Tonographic Outflow Facility

<table>
<thead>
<tr>
<th>Intraocular pressure, mmHg</th>
<th>Sitting (IOP ± SD)</th>
<th>Supine (IOP ± SD)</th>
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<tbody>
<tr>
<td></td>
<td>17.8 ± 1.7</td>
<td>19.9 ± 1.6</td>
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<table>
<thead>
<tr>
<th>Tonographic outflow facility, ( \mu L/mL/mm Hg )</th>
</tr>
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<tbody>
<tr>
<td>Sitting (c ± SD)</td>
</tr>
<tr>
<td>0.30 ± 0.08</td>
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<tr>
<td>Supine (c ± SD)</td>
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<tr>
<td>0.28 ± 0.09</td>
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</tbody>
</table>

**TABLE 3.** IOP and Tonographic Outflow Facility in Right versus Left Eyes

<table>
<thead>
<tr>
<th>Position</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outflow facility, ( \mu L/mL/mm Hg )</td>
<td>Sitting</td>
<td>0.29 ± 0.07</td>
</tr>
<tr>
<td>Supine</td>
<td>0.28 ± 0.07</td>
<td>0.28 ± 0.11</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>Sitting</td>
<td>17.81 ± 1.9</td>
</tr>
<tr>
<td>Supine</td>
<td>19.94 ± 1.7</td>
<td>19.83 ± 1.6</td>
</tr>
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</table>

**TABLE 4.** Male versus Female Patients

<table>
<thead>
<tr>
<th>Position</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outflow facility, ( \mu L/mL/mm Hg )</td>
<td>Sitting</td>
<td>0.296 ± 0.09</td>
</tr>
<tr>
<td>Supine</td>
<td>0.276 ± 0.09</td>
<td>0.278 ± 0.08</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>Sitting</td>
<td>17.87 ± 1.8</td>
</tr>
<tr>
<td>Supine</td>
<td>19.52 ± 1.6</td>
<td>20.38 ± 1.6</td>
</tr>
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</table>
Measurement of facility using constant-weight tonography also involves a number of assumptions. These include the assumptions of steady state conditions before the test, elastic expansion of the sclera, constant blood and tissue volumes, and constant EVP or consistent rise in EVP.\textsuperscript{28,29} Tonography also assumes that the duration is sufficient to assess pressure decay but not long enough to reach a new steady state. A number of ocular properties are assumed to be uniform across all eyes, including corneal radius of curvature and ocular rigidity.\textsuperscript{30} A final assumption is that outflow facility is constant during tonography measurement. This assumption is particularly controversial, as some studies have suggested that the IOP elevation created by the weighted tonometer causes a decrease in aqueous humor production, resulting in an apparent increase in facility known as “pseudofacility,” accounting for up to 20% of total facility.\textsuperscript{29} However, other studies have indicated that IOP has no significant effect on aqueous humor production\textsuperscript{31} and the measurement of pseudofacility may be due to inaccurate modeling of the exponential IOP decay curve.\textsuperscript{32}

In our study, there was a trend toward an increase in aqueous humor outflow facility in the sitting position, but the change was not statistically significant in our study population of young healthy subjects and the change was smaller than the detection threshold for our sample size. One possible reason for this result is that constant weight tonography requires the cornea to remain perpendicular to the direction of gravity so that the force applied by the weight remains constant. However, if subjects in the 70° seated, neck-extended position cannot hold their corneal surfaces parallel to the floor, the force applied by the weight will be reduced, resulting in a slower decay of IOP back to baseline. This would result in a falsely low outflow facility measurement. However, given current technical restrictions surrounding tonography, our protocol offers the best approximation of outflow facility that can be obtained with minimal risk in human patients.

Another possible factor is that the change in IOP from the sitting to supine position was less than we had anticipated. Based on a previous study that measured positional changes in IOP in young healthy subjects,\textsuperscript{19} we estimated that there would be an IOP difference of 5.1 mm Hg between the sitting and supine positions. However, we only detected a change of 2.0 mm Hg. One possible explanation for this difference is that neck extension may have led to an unanticipated rise in IOP, secondary to an increase in EVP. Additionally, tonography tracings showed greater variability while in the sitting position, despite every effort having been made to ensure that subjects were comfortable (Fig. 3). This may be an indication of patient discomfort which may have led to increased intra-abdominal pressure causing a further increase in EVP and subsequently a rise in IOP. An increasing EVP during tonography may have caused a decreased IOP decay rate producing an artificially low facility outflow measurement in the sitting position.

It is also possible that the 70° sitting position may be an inaccurate representation of sitting outflow facility. It is possible that outflow facility varies secondary to head position and changes induced by gravity on the lens-iris position may affect flow. Although previous research has indicated that anterior chamber depth changes minimally with body position,\textsuperscript{33} the effect on scleral spur tension and ciliary muscle tone is unknown. Significant changes may affect outflow facility as well as uveoscleral flow.\textsuperscript{34,35} Unfortunately, at this time facility cannot be measured horizontally in the head-up position using tonography.

Finally, it is possible that the entire positional change in IOP is due to change in EVP, and that previous measurements of EVP were inaccurate. However, there is currently no direct, reproducible measurement of EVP available for use in human subjects.

In summary, no difference in aqueous humor outflow facility, measured using electronic Schiotz tonography, was found between the supine and a 70° seated positions. Other factors, such as uveoscleral outflow changes, may be involved in the IOP change with body position. Further study will be needed to evaluate the validity and impact of our findings. Specifically, the development of a technology to allow measurement of outflow facility with the head in the upright position is required. As well, technology to allow accurate, direct measurement of EVP in both the sitting and supine positions is needed to better understand the changes in aqueous humor dynamics that occur with postural changes.

References