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ASSESSING THE EFFECTS OF WATER CONSUMPTION ON DRY EYE SIGNS AND SYMPTOMS USING OCT-A RETINAL VASCULATURE AS A POTENTIAL MARKER OF HYDRATION STATUS

Judy Hoang
Pacific University, hoan1032@pacificu.edu

Amiee Ho
Pacific University, amieeho@pacificu.edu

John Hayes
Pacific University, JRHayes@pacificu.edu

Patrick Caroline
Pacific University, patpacific@aol.com

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Abstract

Purpose: To identify the effects of increased water intake on dry eye signs and symptoms and their association to retinal vessel diameter changes in healthy optometry students using the OCT-A.

Methods: Candidates were screened for their hydration status and only dehydrated candidates (those who drink less than what is required for their weight) were eligible to participate. All individuals self-reported having no systemic conditions or ocular conditions linked with dry eyes. Thirty-six qualified subjects were evaluated for dry eye signs by assessing tear break-up time, tear volume, lipid layer thickness, blink rate, and Meibomian gland health. The Standardized Patient Evaluation of Eye Dryness (SPEED) Questionnaire was used to screen subjects for severity of dryness as well as evaluate dry eye symptoms during the study. OCT-A was used to evaluate blood vessel changes pre- and post-water consumption. Qualifying subjects were asked to drink a specified amount of water within 24 hours. Signs and symptoms of dry eye were re-evaluated the next day.

Results: ANCOVA analysis compared each subject's post-treatment results to their pre-treatment (baseline) results. There was a significant difference between the control group and the experimental group for the SPEED score ($p < 0.05$). There was no significant difference for tear break-up time, tear volume, lipid layer thickness, blink rate and Meibomian gland health between the control group and experimental group. Retinal vessel diameter changes were compared between the two groups using a simple scatterplot. Retinal vessel diameter changes showed mixed results for water intake and retinal diameter correlations. Overall, there was no significance in vessel diameters between groups.

Conclusions: Increased water intake does not improve signs of dry eye. However, subjects in the experimental group of this study experienced improved symptoms after increased water intake. This effect must be further investigated. The study also showed inconclusive data on the effect of retinal vessel diameter changes after increased water intake. This also requires further investigation.

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Committee Chair

Amiee Ho, OD

Second Advisor

John Hayes, PhD

Third Advisor

Patrick Caroline, COT

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by

JUDY HOANG

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This thesis of *Judy Hoang titled "*Assessing the Effects of Water Consumption on Dry Eye Signs and Symptoms Using OCT-A Retinal Vasculature as a Potential Marker of Hydration Status*",* is approved for acceptance in partial fulfillment of the requirements of the degree of Master of Science.

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Accepted Date

Signatures of the Thesis Committee:

____
Thesis Advisor: Amiee Ho, OD.
Pacific University College of Optometry

____
Thesis Committee: John Hayes, PhD.
Pacific University College of Optometry

____
Thesis Committee: Patrick Caroline, COT.
Pacific University College of Optometry

____
*Date:*________________________
Director of the Vision Science Graduate Program: Yu-Chi Tai, PhD

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JUDY HOANG

MASTER OF SCIENCE IN VISION SCIENCE
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ABSTRACT

Purpose: To identify the effects of increased water intake on dry eye signs and symptoms and their association to retinal vessel diameter changes in healthy optometry students using the OCT-A.

Methods: Candidates were screened for their hydration status and only dehydrated candidates (those who drink less than what is required for their weight) were eligible to participate. All individuals self-reported having no systemic conditions or ocular conditions linked with dry eyes. Thirty-six qualified subjects were evaluated for dry eye signs by assessing tear break-up time, tear volume, lipid layer thickness, blink rate, and Meibomian gland health. The Standardized Patient Evaluation of Eye Dryness (SPEED) Questionnaire was used to screen subjects for severity of dryness as well as evaluate dry eye symptoms during the study. OCT-A was used to evaluate blood vessel changes pre- and post-water consumption. Qualifying subjects were asked to drink a specified amount of water within 24 hours. Signs and symptoms of dry eye were re-evaluated the next day.

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INTRODUCTION

Dry eye syndrome is an inflammatory process occurring on the ocular surface resulting in irritation, discomfort, and redness of the eyes. About 16.4 million adults in the US population suffer from dry eye syndrome.[1] There are many factors associated with dry eye syndrome, including systemic disease. Interestingly, healthy populations also suffer from dry eyes. This may be due to decreased blink rate, contact lens use, diet, and environmental factors. The study at hand will investigate the diet factor in dry eye syndrome – particularly that of water intake and its effect on dry eye syndrome. The study includes healthy optometry students, who all share similar work environments, including prolonged computer usage which is linked to decreased blink rates. One factor that is not entirely consistent among optometry students is the diet factor. One aspect of diet that can be easily manipulated is water consumption.

The primary hypothesis for this study is an increase in water intake will result in improved dry eye signs and symptoms. There are few published papers studying the effects of water intake on dry eye. One study evaluating blood plasma osmolality and dry eye found that those who have dry eye syndrome also had higher blood plasma osmolality, indicating dehydration. Conversely, the study found that those with less symptoms of dry eye or no dry eyes at all had lower blood plasma osmolality. The study concluded that hydration of the body is an important consideration in dry eye.[2] An unpublished pilot study conducted at Pacific University in 2011 showed that one week of increased water intake improved dry eye symptoms significantly.[3] Another unpublished study conducted at Pacific University found that increased water intake did not have a significant effect on dry eye signs or symptoms.[4] However, it is currently hypothesized that there may have been a ceiling effect in that particular study due to the fact that the study included well hydrated subjects. Therefore, in the current study, well hydrated subjects were excluded and only dehydrated subjects were included to participate in the study.

The secondary hypothesis for the study is that increased water intake increases retinal vasculature diameter which can be observed with OCT-A. This may allow insight for a non-invasive method of assessing a subject's hydration status, with the caveat that a baseline measurement is taken pre-hydration. Furthermore, since the retinal vasculature and lacrimal gland vasculature are branches of the ophthalmic artery, an increase of overall water intake may increase blood flow to the lacrimal gland and stimulate increased tear production to the lacrimal gland, increasing the tear volume and thereby reducing dry eye symptoms.[5] Assessing the retinal vasculature may reflect changes in all blood vessels supplying the ocular structures.

METHODS

Subjects

Thirty-six adults (28 females and 8 males, average 24.89 years old) were recruited from Pacific University College of Optometry. The study was approved through the Internal Review Board at Pacific University in Forest Grove, Oregon. All prospective subjects (total of 40) were screened for systemic and ocular health conditions, medications, refractive surgery status, height and weight, and average daily water intake. Three prospective subjects did not qualify for the study due to excessive amount of water intake based off of their weight. One qualified subject dropped out of the study.

Materials

Screening Form. A screening form with questions regarding water intake, caffeine and sugar consumption, ocular and systemic health conditions, medications, refractive surgery status, contact lens use, and height and weight were assembled. This form was used to identify qualifying candidates. See Appendix A for a copy of this screening form.

SPEED Questionnaire. The Standardized Patient Evaluation of Eye Dryness questionnaire was used as a screening tool to evaluate the level of dry eye symptoms in subjects. SPEED scores can be categorized into three groups: Mild (0-4), Moderate (5-7), and severe (8+). The SPEED questionnaire was also used during the study for baseline dry eye symptoms and post-treatment symptoms. The SPEED questionnaire was used because of its high specificity (0.80) and sensitivity (0.90) in diagnosing dry eye syndrome.[6]

Medmont Topographer. The "Tear Film Analysis" mode of the Medmont topographer was used to analyze the tear break-up time (TBUT) of each subject's eye separately. The default recording time of 15 seconds was used for all subjects. This method of measuring tear break up time was preferred over the traditional method of staining with fluorescein due to the benefit of being non-invasive and therefore unlikely to disrupt the tear film that may be induced by the fluorescein strip test. The traditional TBUT test may alter natural tear production as the fluorescein strip may induce reflex tearing.[46]

Electronic Blood Pressure Monitor. The Omron BP742 5 series electric blood pressure monitor was used to measure systolic pressure, diastolic pressure, and pulse for baseline and post-treatment sessions,

OptoVue OCT-A. Optovue AngioVue AngioAnalytics software was used to evaluate the optic nerve head and blood vessels emerging from it with a 3.0 mm cube.

OptoVue OCT. OptoVue anterior segment lens was attached to the OptoVue in order to obtain a cross section of the tear meniscus located at the junction of the middle inferior eyelid and the eyeball. The drawing tools accompanying the software were used to measure tear meniscus height (TMH) as well as tear meniscus area (TMA). These were used to calculate tear volume.

Lipiview II. The Lipiview II Ocular Surface Interferometer was used measure lipid layer thickness of each subject's eye as well as the superior and inferior Meibomian glands. It also calculates the blink rate and number of incomplete blinks over a twenty second period.

Statistics Software. SPSS was used to analyze the data. ANCOVA was used to test the differences between means of groups and ultimately to see if water improves dry eye signs and symptoms. Simple scatterplot was used to assess if there was a relationship between blood vessel diameter and water intake.

Retinal diameter measurement software. The Automatic Retinal Image Analysis (ARIA) software was used to measure vessel diameters of OCT-A images. This software is an open-source MATLAB operated program.

Procedures

There was one screening session for all interested participants in which the goal was to recruit qualifying participants. Once all qualified participants were officially recruited, all candidates were asked to schedule two sessions 24 hours apart. The first session was to measure baseline SPEED score, TBUT, tear volume, retinal vasculature, blood pressure, lipid layer, blink rate, and Meibomian glands. Following the first session, the subjects were then instructed to begin tracking their water intake and to begin their "treatment" as instructed by the faculty investigator of this study. The second session was scheduled 24 hours later at the same time of day as the first session in order to reduce variability in tear film changes throughout the day.[7] The same measurements were taken post treatment during the second session. The purpose of conducting a 24 hour study is to improve compliance of subjects while also reducing as many confounding factors as possible. Furthermore, a study conducted by Bhatti et. al. showed that ocular blood flow changes can be seen with laser speckle flowgraphy within 20 to 40 minutes of drinking water [8], thereby reducing the need for an extended study. Unfortunately, the article did not note the quantity of water the subjects consumed before seeing changes in ocular blood flow. In this study, subjects in the experimental group were asked to drink the daily recommended amount of water per day for the average person (about ten 8 oz. cups per day) or more if the subject feels comfortable enough to do so. This was also the average amount of water that optometry students in a previous pilot study from 2011 could comfortably drink daily.[3]

Randomization was accomplished by having the faculty investigator randomly assign "treatments" to students. There were two groups in the study – a control group who made no changes in water intake and an experimental group who were asked to drink 80 fluid oz or more of water. These groups were labeled A or B, however the principal investigator was blind to the labeling during the sessions. The subjects were also tasked to not provide any details as to which group they were in to the principal investigator. Labels were later revealed once the study was completed for statistical analysis.

In order to best control for confounding factors, subjects were asked to avoid the following activities: wearing contact lenses during the 24 hour period, drinking anything other than water if possible (including coffee, tea, soda, etc.), exercising one hour before each session, and using artificial tears during the 24 hour period. Subjects were asked to document any moments of non-compliance in detail (i.e. if they drank coffee, they should document what kind of coffee, how much of it was consumed in the 24 hour period, etc). Medications and supplements that are linked to improving or worsening dry eye were excluded, such as fish oil or omega-3 and acne medications such as Accutane. Subjects who have had refractive surgery such as LASIK or PRK were excluded from the study, as their dry eye symptoms are likely a result of their procedures.[9]

Retinal vasculature diameters were measured using the ARIA software, an open-source program that detects edges of vessels and calculates average diameter of the vessels. Only the four largest portions of the superior and inferior veins and arteries were measured, as the edges of these vessels were easiest to see and maintain consistent measurements between baseline photos and post-treatment photos. The same points from each vessel were chosen for the baseline and post-treatment to obtain an accurate measurement of blood vessel diameter change.

Data Analysis

Once all the data were gathered, they were compiled into the SPSS software. A mixed model ANCOVA analysis was used to calculate the results of the data. ANCOVA was used to compare differences in means between the two groups for the following dependent variables: SPEED score, tear break up time (TBUT), lipid layer thickness, tear meniscus height, tear meniscus area, and retinal diameters. Simple scatterplot was also used to analyze relationships between each group pre- and post-treatment. Excel was used to create bar graphs showing individual trends pre-treatment and post-treatment between the two groups. Excel was also used to create bar graphs showing frequency of dry eye severity. Scatterplots were also used in excel to show any relationships between increased water intake and vessel diameter growth.

RESULTS

Dry Eye Signs and Symptoms

Severity of dry eye symptoms were measured using the SPEED questionnaire. Twenty-nine subjects (twenty-three females, six males) had a SPEED score of 8 or above, indicating severe dry eyes. Only four subjects (three females, one male) had a SPEED score between 5 and 7, indicating moderate dry eyes, and only three subjects (two females, one male) had a SPEED score between 0 and 4, indicating mild dry eyes. Figure 1 shows that the majority of subjects were female and had severe dry eyes.

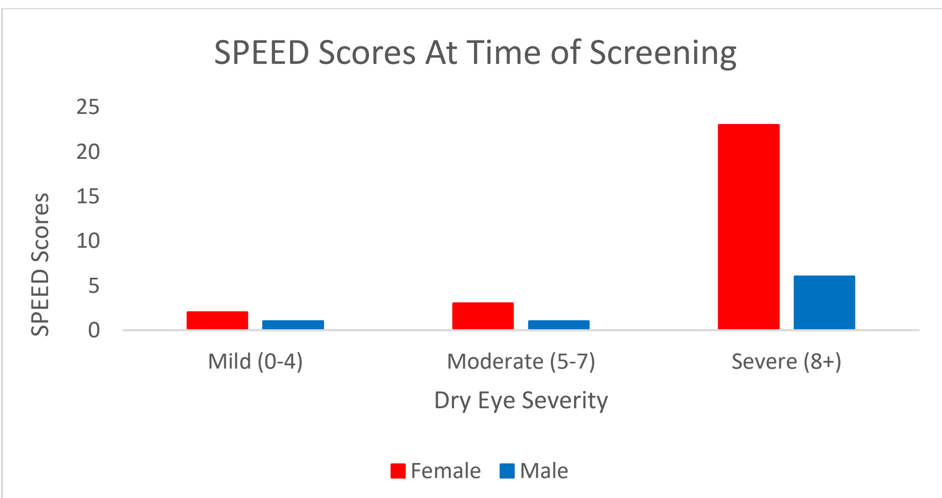


Figure 1. Number of subjects in three severity levels of dry eye based off of the SPEED scores. The majority of subjects have severe dry eyes. The participants in the study were mostly females.

ANCOVA analysis was used to assess signs of dry eye: TBUT, tear meniscus height, tear meniscus area, and lipid layer thickness. A higher measurement of all of these variables indicate improvement, or less dry eyes. Based off of estimated marginal means results, water intake had no effect on improving dry eye signs as the means for each variable post-treatment for the control group were higher than or equal to the means of the experimental group (Table 1). ANCOVA analysis was also used to assess symptoms of dry eye: SPEED scores. A lower SPEED score indicates less dry eye symptoms. Based off of estimated marginal means results, water intake did have an effect on improving dry eye symptoms since the mean for the experimental group was lower than the mean for the control group. Pairwise comparison and univariate testing show that the effects were significant ($p < 0.05$) between groups.

Variable	Control Mean	Experimental Mean
TBUT	7.340	4.249
TMH	230.771	230.841
TMA	0.018	0.018
LLT	55.955	50.307
SPEED Score	10.354	7.813

Table 1. For TBUT, TMH, TMA, and LLT, higher numbers indicate improved dry eye signs. The control group had the higher means for all signs, indicating that increased water intake has no effect on improving dry eye signs. For SPEED score, a lower number indicates improved dry eye symptoms. The experimental group had the lower mean for dry eye symptoms, indicating that increased water intake does have an effect on improving dry eye symptoms.

A comparison of each individual subject's SPEED score at baseline and post-treatment using a bar graph shows general trends for the control and experimental groups (Figure 2). Fifty percent of the control group rated their dry eye symptoms as the same or worse post-treatment (no treatment) compared to their baseline scores. Interestingly, the other fifty percent of the control group rated their dry eye symptoms as improved (lower score) post-treatment. The average difference between baseline and post-treatment scores for the control group was -0.167 points, a minor improvement in symptoms. Conversely, only seven subjects in the experimental group rated their dry eye symptoms as the same or worse post-treatment (drank more water) compared to their baseline scores. The majority of subjects in the experimental group rated their dry eye symptoms as improved post-treatment. The average difference between baseline and post-treatment scores for the experimental group was -2.194 points, an improvement in symptoms. Three subjects in the experimental group improved from the severe dry eye category to the moderate dry eye category and one subject from the experimental group improved from the severe dry eye category to the mild dry eye category. Only one subject from the experimental group improved from moderate to mild dry eye category.

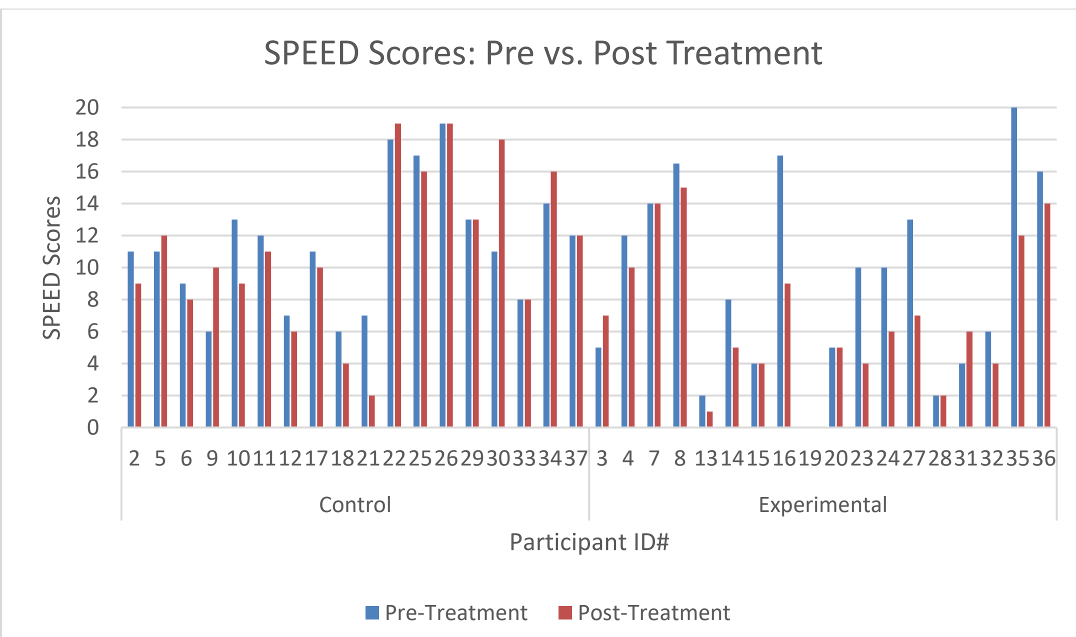


Figure 2. Difference in SPEED scores between baseline and post-treatment scores in the control and the experimental groups.

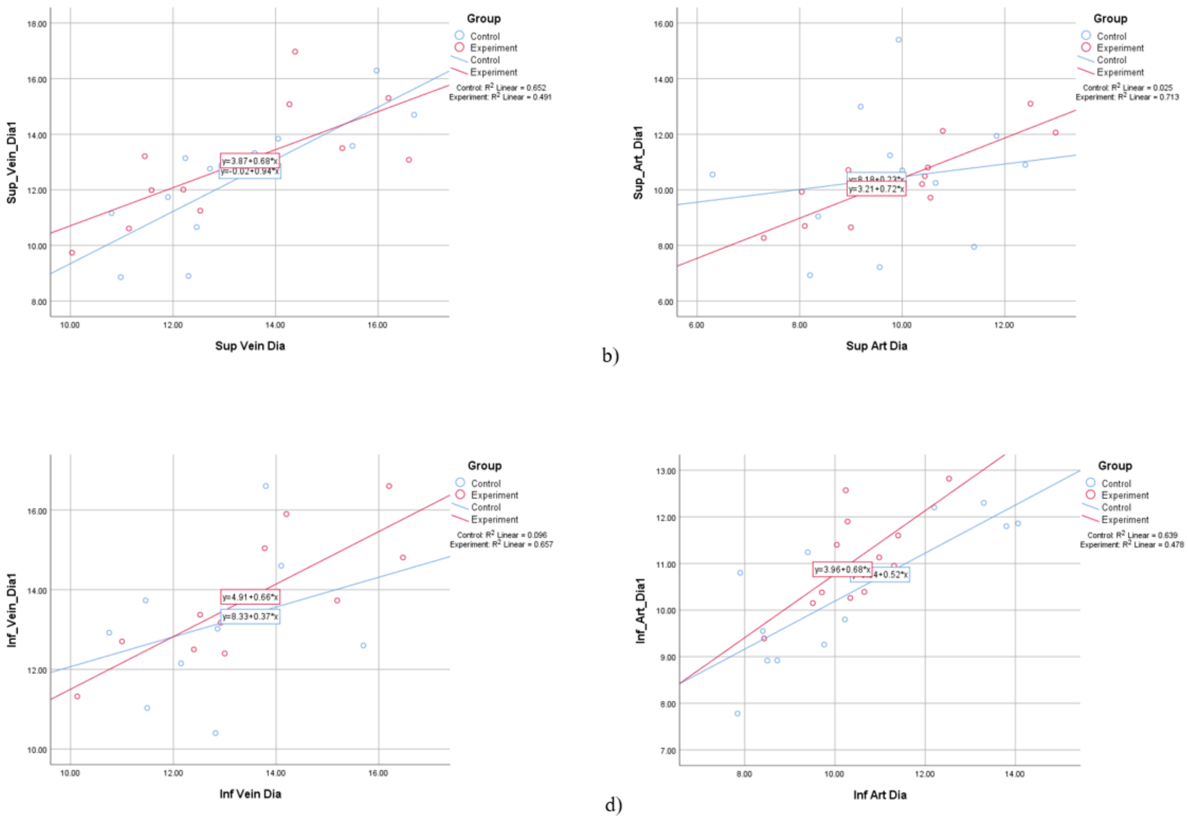
Retinal Vessel Diameters

Retinal vessel diameters were measured using the ARIA program. The vessels of interest are the superior vein, superior artery, inferior vein, and inferior artery. Measurements were taken at the widest part of these vessels, just outside of the optic disc margins. ANCOVA analysis was used to assess differences in vessel diameter means between the control group and the experimental group. Table 2 shows the mean differences between groups, with a higher number indicating a larger vessel diameter. The vessels were measured in units of pixels. The vessel diameters between the two groups were higher for the experimental group for the superior and inferior arteries only, and the diameters were slightly higher for the superior and inferior veins in the control group. However, pairwise comparisons and univariate tests reveal that there is no significance between any of the vessel diameters in both groups ($p > 0.05$).

Vessel	Control Mean	Experimental Mean
Superior Vein	12.864	12.856
Superior Artery	9.945	10.253
Inferior Vein	13.159	13.093
Inferior Artery	10.419	10.609

Table 2. ANCOVA analysis of mean vessel diameters between the control and experimental groups.

When simple scatterplots were used to plot baseline vessel diameters against post-treatment diameters, all vessels except the superior vein diameter had higher slopes when a trend line was added. Furthermore, only superior artery diameter and inferior vein diameter had a strong, positive correlation for the experimental group (Figure 3). This further confirms that there is no significant difference in vessel diameters between the two groups.



a) b) c) d)

Figure 3. Simple scatterplots plotting baseline vessel diameters against post-treatment vessel diameters between the control and experimental groups. Trend lines and R^2 values indicate mixed results.

When the difference between water intake (difference between baseline and post-treatment water intake) was plotted against difference between vessel diameters (difference between baseline and post-treatment vessel diameters), there was no strong correlation between the amount of water intake and vessel diameter changes for any vessel (Figure 4). Interestingly, correlations were not similar between eyes for all subjects, indicating that there may be an error in vessel diameter measurements.

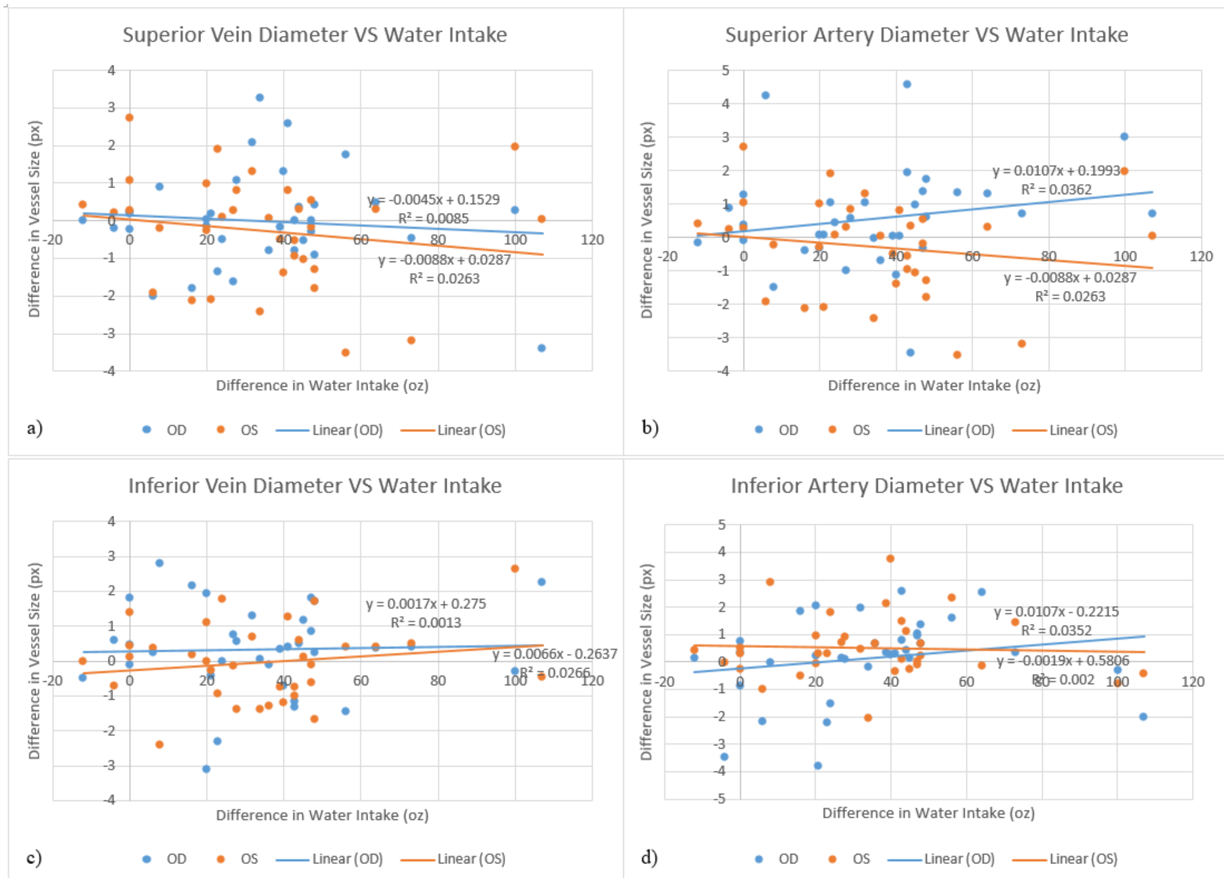


Figure 4. Scatterplots measuring difference in water intake against difference in vessel diameter size. The data is inconclusive that vessel diameter increases with increased water intake.

It should also be noted that an outlier may have skewed some of the results. Figure 5 plots baseline water intake against post-treatment water intake for both control and experimental groups. One subject from the control group had a baseline water intake of about 65 oz, but had a post-treatment water intake of about 175 oz.

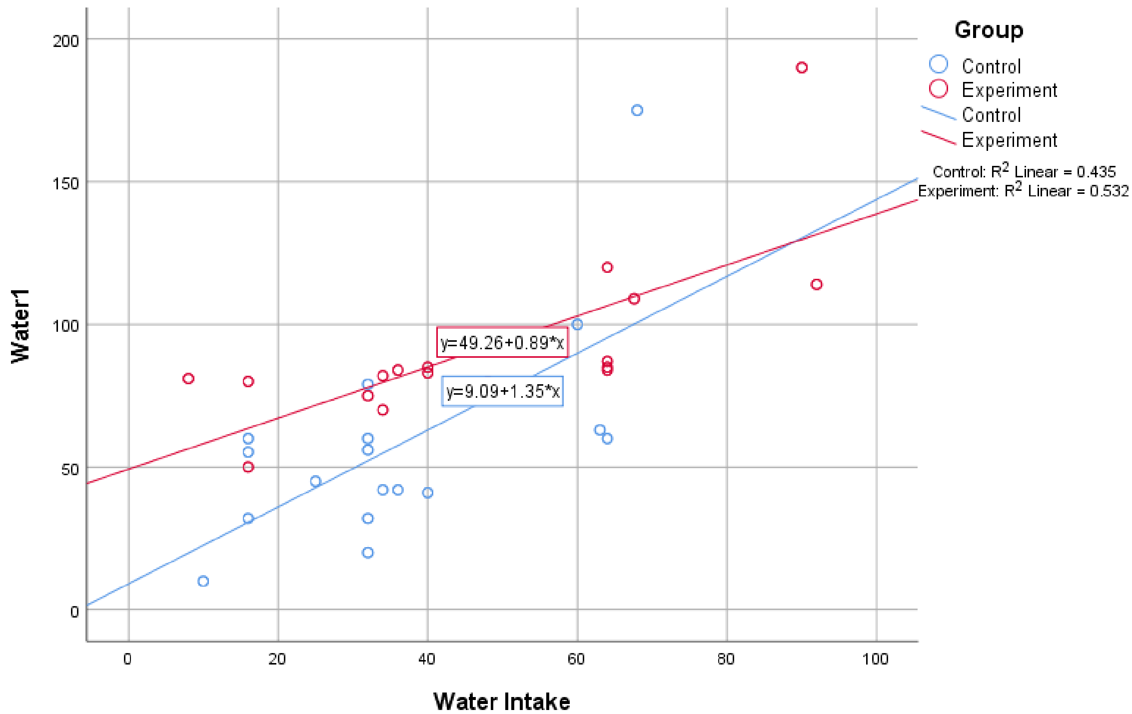


Figure 5. Baseline water intake plotted against post-treatment water intake. Note the outlier in the control group.

DISCUSSION

Dry eye syndrome affects many individuals in the US, including a generally healthy adult population. As evidenced by this study, dry eye syndrome is more common in women than in men.[1] This study investigates the probability of increased water intake on relieving dry eye syndrome. It also investigates the mechanisms by which increased water intake can improve dry eye signs.

Dry Eye Signs and Increased Water Intake

The results of the study showed that increasing water intake does not improve dry eye signs. There can be many explanations for this result, as dry eye syndrome is a multifactorial disorder of the ocular surface. Other factors influencing dry eyes include blink rate, completeness of blinks, quality of the lipid layer, and health of the Meibomian glands may influence the findings.[7] While it is important to control as many factors as possible, it may be impossible and even unreasonable to do so. The population in this study is a small representation of the general population and therefore it is important to not control for the factors mentioned above because it will reduce the ability to represent the general population. In general, studies that explore dietary changes and their effect on any health issue is difficult due to the fact that not all individuals' characteristics can be controlled perfectly.

Another theory that may explain the findings is that dry eye syndrome is an inflammatory disorder of the ocular surface.[10] There is little evidence to support whether or not water can reduce inflammatory responses. While this study attempted to limit beverage consumption to only water, a few subjects reported that they consumed other beverages such as alcohol and tea during the 24 hour period. One subject also reported having a large bowl of soup for dinner during the study. The study also did not control for food, which would be variable between subjects. Some subjects may have had a higher sodium or sugar intake than others, which can influence the amount of inflammation occurring in the body.[11]

Dry Eye Symptoms and Water Intake

Interestingly, the study showed that increased water intake improved dry eye symptoms. This proves that dry eye symptoms may not be directly related to dry eye signs and vice versa. It is possible for an individual to experience dry eye symptoms without having signs of dry eyes, and as seen in some individuals of this study, it is also possible to have dry eye signs but exhibit no dry eye symptoms. The findings of improved dry eye symptoms in this study may be attributed to a psychological phenomenon likened to a placebo effect in which subjects believed that drinking more water helps with their dry eye and therefore reported having less dry eye symptoms. However, this does not explain why some subjects who were in the experimental group felt their dry eye symptoms were the same or worsened after drinking more water.

Retinal Vasculature Diameters and Water Intake

Increased water intake is expected to increase blood flow and increase blood vessel diameter in the body. This can also be observed in retinal blood vessels.[8,12] However, this study demonstrated that there were mixed results in retinal blood vessel diameters. This can be attributed to user error in the blood vessel measurement program, or the program itself may not be accurate or sensitive enough for measuring blood vessel diameters. The purpose of investigating retinal vasculature diameter in this study was to possibly explore a mechanism in which improved dry eye signs can be explained, particularly increased tear meniscus height and tear meniscus area. Since the lacrimal gland is responsible for tear volume, observing the blood vessels for changes in diameters would provide insight as to whether or not there was increased stimulation to the lacrimal gland, therefore increasing tear volume and decreasing dry eye signs and symptoms.[5] However, since increased water intake had no effect on tear volume (tear meniscus area and tear meniscus height), it is irrelevant to observe retinal vessel diameters when studying dry eye syndrome and water intake.

One theory that may explain these findings is that the blood vessels have undergone homeostasis following increased water intake.[13]

Clinical relevance of the findings

While dry eye signs may not improve with increased water intake, this study showed that dry eye symptoms improve with increased water intake in the healthy adult population.

Therefore, it may be worthwhile to promote increasing water intake in a healthy adult with dry eye symptoms. This does not mean that increasing water intake can benefit adults who have systemic conditions, such as diabetes or Sjogren disease, which can also cause dry eye syndrome. Further investigation is required before any clinical conclusions can be made.

Limitations of the Study

Technological limitations.

One limitation of the study is the equipment and programs used for the study. While the OCT-A is a useful tool in diagnosing ocular disease, it may not have been a reliable or valid method of assessing retinal vasculature for the purpose of this study. A more appropriate tool would directly calculate blood flow in real time, however such equipment may be costly for the purpose of this study. Furthermore, the OCT-A can only assess vasculature of the retina. It was assumed that blood flow to the retinal vessels and lacrimal gland vessels were equal since the vessels were all branches of the ophthalmic artery, however it cannot be assumed that blood flow to these areas are proportionate. A tool that can directly measure lacrimal gland blood vessel diameter may be more appropriate for the purpose of this study.

The ARIA program was another limitation of the study, as vessel diameters measured from this program were not consistent and highly variable. This was made obvious in figure 4, in which subjects who had no changes in their water intake had a large change in vessel diameters. This could also be explained by other factors influencing blood vessel diameters, but it is more likely that the ARIA program is not as accurate. The program works by using edge detection and results are best when using colored fundus photos.[14] Unfortunately, the OCT-A only provides grayscale photos for downloading, which may have reduced the ability for the ARIA software to be accurate. The program also requires high quality photos in order to accurately detect edges. The OCT-A images varied in quality from 5 (an average quality scan) to 10 (a high quality scan). In hindsight, it may have been much more simple to use fundus photos rather than an OCT-A when conducting this study.

Lastly, using the SPEED questionnaire for a 24 hour time period may not have been a valid method for this study as one of the main questions on the questionnaire asks about frequency of symptoms. It is obvious the SPEED questionnaire would be more valid if used for more than one day. Subjects were asked to report their dry eye symptoms within the past week, including the baseline measurement day as well as the post-treatment measurement day.

Demographic limitations.

The study had a small sample size and only included optometry students and vision science students at Pacific University College of Optometry. The total student population is approximately under 300 students. The timing of this study was the greatest limitation of all, as most of the second and third year optometry students were very busy at the time this study was conducted. There were also several other studies occurring around the same time, which also limited the number of participants due to limited availability of extra credit allowed per course. Finally, the number of participants may have been greatly reduced due to the requirements to participate in the study, most notably requesting that participants refrain from consuming caffeine during a 24 hour time period. This caused many students to exclude themselves from joining the study as many students claimed that they experience side effects, such as headaches, when they do not drink coffee for one day.

Modality Limitations

The study may have had variable results due to not knowing when the subjects drank water throughout the study. It is unknown whether each subject drank the required amount of water throughout the day or all in one sitting. It is also unknown if the subjects drank water right before coming in for the second session. Subjects who did not have any water right before coming in may have processed much of the water beforehand, while those who have had water right before coming in may have had detectable changes in blood vessel diameters.

Compliance

After carefully re-evaluating the data set, it was evident that some subjects were not compliant with the requests for the study. For instance, one subject in the control group drank more than twice the amount of water reported for baseline. This could have been due to misunderstanding of instructions. There were also a few subjects in the experimental group who did not reach the goal of drinking 80 ounces of water within the 24 hour time period. Some subjects also reported drinking caffeine or alcohol, which may have impacted the results. However, after adjusting the data to include only compliant subjects, there were no significant differences in the results.

Future Studies

This study requires further investigation on whether the findings can be duplicated or not. The future study should have a larger sample size if possible. The future study should also have valid and reliable methods of measuring the variables mentioned above. Lastly, the future study should consider a method of controlling for other confounding variables, which may be the greatest challenge of all. It would also be of interest to conduct a study on only the effects of water on blood vessels using OCT-A. A future study may include a shorter time period of testing with the OCT-A and require that the subjects drink water for 20-40 minutes to see any changes in blood vessel diameter. This information can then be used to determine if the OCT-A is a valid method for measuring hydration and blood vessel changes from increased water intake.

CONCLUSION

Increasing water intake does not improve dry eye signs, but does improve dry eye symptoms. Increasing water intake shows no conclusive results on increasing retinal vessel diameter. Since tear volume does not increase with increased water intake, it can also be concluded that increased retinal vessel diameters are not a sign that the lacrimal gland has been stimulated to produce a higher tear volume. However, further investigation using appropriate and accurate methods is required.

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APPENDIX A

Dry Eye: Pre-screening Questionnaire

Participant Name: ____________________ Participant #: ________ Date: ________________

1) Approximately how much water do you drink per day?

2) Do you normally carry a water bottle with you? If so, approximately how big is your water bottle and how many times a day do you refill your water bottle?

3) Do you drink coffee, tea, juice, soda, or alcohol? If so, how many per day?

4) Do you wear contact lenses? If so, do you have a pair of glasses to wear?

5) Do you use ANY eye drops, including artificial tears? How often?

6) Have you had any refractive surgery or corneal transplants (LASIK, PRK, etc.)?

7) Are you currently taking any oral or topical medications (includes vitamin supplements, Restasis, or Xiidra)?

8) Do you have any ocular or systemic conditions (i.e. diabetes, Sjogren's, blood disorders, etc.)?

9) Do you exercise? How often?

10) What is your height and weight?

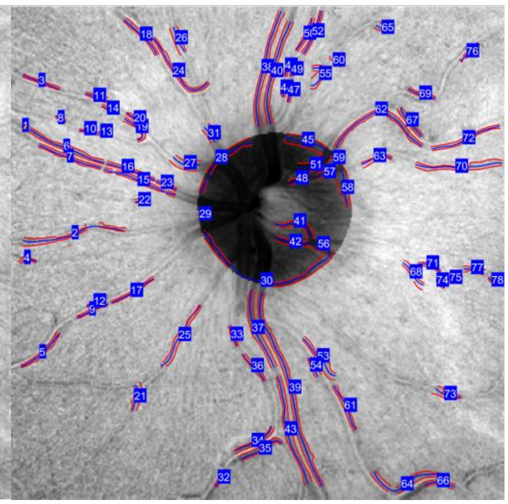
OD Year:
Extra credit course:
Randomly generated word code:

APPENDIX B

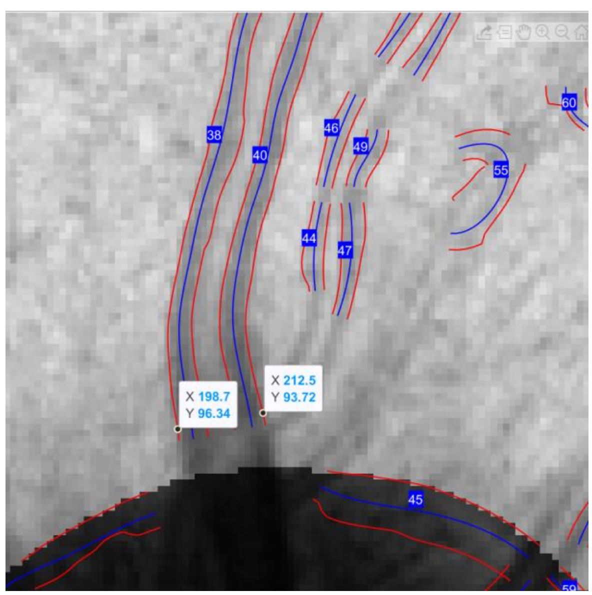
Automatic Retinal Image Assessment Program (ARIA)

ARIA is an open-source program that can be used with MATLAB. The following photos are examples of how the program was used:

a) Original Photo.



b) ARIA draws blood vessel edges.



c) Using the coordinates provided and Pythagorean's theorem, the diameter can be calculated.

APPENDIX C

Recommended Water Intake Per Day Based on Weight

Weight (pounds)	Weight (kg)	Ounces of Water Intake per Day	Millilitres (ml)
100	45.3	67 ounces	1981
110	49.8	74 ounces	2188
120	54.4	80 ounces	2366
130	58.9	87 ounces	2573
140	63.5	94 ounces	2780
150	68.0	100 ounces	2957
160	72.5	107 ounces	3164
170	77.1	114 ounces	3371
180	81.6	121 ounces	3578
190	86.1	127 ounces	3755
200	90.7	134 ounces	3963
210	95.2	141 ounces	4170
220	99.7	148 ounces	4377
230	104.3	154 ounces	4554
240	108.8	161 ounces	4761
250	113.3	168 ounces	4968

Source: https://hydrogenlivingwater.files.wordpress.com/2015/06/water-amount-vs-weight-table.jpg