Efficacy of superior versus inferior punctal occlusion with Dissolvable Opaque Herrick Lacrimal Plugs

Skye Petty, O.D., Jeffery Miller, O.D., Richard Hoenes, Statistician
September 22, 2004

Purpose. The purpose of this study is to compare the efficacy of superior versus inferior punctal occlusion. **Method.** Twenty-seven subjects were randomized for superior occlusion in one eye and inferior occlusion in the opposite eye. Baseline measurements were taken and the subject's puncta were occluded with Synthetic Dissolvable Opaque Herrick Lacrimal Plug[®] (Lacrimedics, Inc., Eastsound, WA). Baseline data included subjective dryness, tear thinning time, tear break up time, NaFl staining, lissamine green staining, and the phenol red thread test. The subjects were seen at one week and three weeks following the initial visit. The same baseline measurements were taken. **Results.** At week one and three the only tests that showed statistical significance between the two eyes were the phenol red thread test and the NaFl staining, respectively. Inferiorly plugged eyes showed more improvement ($p<0.05$). For other tests at week one and week three, the difference between the right and left eyes was not significant. **Discussion.** These findings suggest that an inferior punctal plug is slightly more beneficial than a superior plug as shown by objective testing. Our study supports results from previous studies that support punctal occlusion as a treatment for dry eye.

INTRODUCTION

The term "dry eye" is a general expression used by patients and doctors to describe an extremely complex, yet common, condition. In order to understand the causes and associated symptoms, one must first understand the anatomy and physiology of the ocular tissues. Research has revealed many etiologies of dry eye syndrome.

The task of diagnosing dry eye syndrome is a challenge to researchers and clinicians alike. There are many clinical tests used to assess the ocular surface and the efficiency of the lacrimal system. By choosing the appropriate test and diagnostic criteria, the proper treatment plan can be administered.

Ocular lubrication is essential for the eye's health and refractive properties. The eye's main source of moisture is from the tear film.[1] The tear film has several functions including: lubricating and hydrating the surface of the globe; trapping debris; providing oxygen to the cornea; creating a smooth refractive surface; and providing antibacterial protection.[1]

The precorneal tear film is composed of three layers that originate from three different sources: 1) the thin, superficial oily layer is produced predominantly by the meibomian glands and to a slight

extent by the sebaceous glands (Zeis) and sweat glands (Moll); 2) the thick, watery layer is secreted by the accessory lacrimal glands; and 3) the thin mucin layer is secreted primarily by the conjunctival goblet cells.[2] Collectively these layers make up the tear film, with each having a separate individual function.

The function of the superficial lipid layer is important in retarding evaporation of the aqueous layer below.[3] The underlying aqueous layer provides the bulk of the tear film and contains most of the antimicrobial properties. The mucin layer is adsorbed by the glycocalyx of the corneal surface and acts as an interface that aids in the adhesion of the aqueous layer to the corneal surface.[1] The glycocalyx is instrumental in adhering the hydrophilic tear film to the hydrophobic corneal epithelium. The epithelium also has many projections located on the apical surface of the outermost cells, which increase the surface area, thus enhancing the stability of the tear film.[1]

The tear drainage system begins with the punctum lacrimale, which are small, medial openings in the superior and inferior lid. The puncta connect to the lacrimal canaliculi, a 10mm long tube that penetrates the lacrimal sac. The lacrimal sac, measuring about 12mm long, is situated in the lacrimal fossa formed by the lacrimal bone and the frontal process of the maxilla.[2] Tears, leaving the lacrimal sac, drain into the nasolacrimal duct. The nasolacrimal duct is an 18mm tube that terminates into the inferior meatus.

The terms keratoconjunctivitis sicca and dry eye syndrome are thought of and used as synonymous labels. There is, however, a distinction between the two. KCS was first noted by Sjӧgren as a way to specifically describe the ocular surface disorders associated with Sjӧgren's syndrome, an autoimmune disorder.[4] Dry eye syndrome, on the other hand, results from aqueous tear deficiency, lipid abnormalities, mucin deficiency, lid abnormalities and epitheliopathies.[5] Regardless of etiology, an estimated one million Americans between the ages of 65 and 84 have physiologic dry eye. An estimated three million elderly Americans use nonprescription ocular lubricants.[6]

Dry eye syndrome encapsulates a group of changes within ocular tissues. There can be many different causes of dry eye, most of which involve the tear film. Lipid layer deficiencies arise primarily from meibomian gland dysfunction. An occlusion of the meibomian gland openings results in a reduced outpouring of secretion or a qualitative change in the secretion.[2]

Any anomalies with the aqueous layer stems from defects in the lacrimal gland. Inflammation, loss of innervation, scarring or obstruction results in a loss of tear film volume.

The mucin layer is dependent on the conjunctival goblet cells. A loss of goblet cells causing an absence of mucin expression will result in an aqueous tear deficiency. This will aggravate the severity of dry eye syndrome by further destabilizing the tear film.[7] Abnormal binding properties of the surface of corneal epithelial cells coupled with anomalies of lipid and/or mucus production would contribute to the poor stability of the tear film.[8]

Blinking is an autonomic reflex affected by local ocular surface conditions as well as psychological and environmental factors.[9] The spontaneous blink rate in normal human adults is approximately 15 per minute.[10] Patients with dry eye syndrome have more frequent and/or erratic blinks.[11] Throughout the day dry eye patients have their eyelids closed three times more than normal individuals, reflecting the need to maintain a moist ocular surface.[11] The blink rate may also be affected by corneal sensitivity.

A recent study found that corneal sensitivity correlates significantly with a loss in corneal sensation in patients with positive dry eye syndrome clinical tests.[12] A chronically traumatized ocular surface results in sensory adaptation to the desiccation, which leads to corneal hypoesthesia. Corneal hypoesthesia can lead to an increased risk for infection, a decrease in functional visual acuity, and/or an increased risk of visual impairment.

The cornea receives most of the oxygen required from the tear film at the external surface.[12] The oxygen dissolves in the tear film and diffuses into the epithelium. Other sources of oxygen are the aqueous humor, conjunctiva, and episcleral capillary networks.[1] Oxygen deprivation can occur if there are disturbances in the tear film.

Tear film instabilities can be due to anatomical anomalies (i.e. a large palpebral aperture), glandular problems, or mechanical problems at the ocular surface. Any structure that could physically interrupt the tear film at any layer will cause instabilities (i.e. contact lenses).
The correct diagnosis and classification of each type of dry eye is critical in the proper therapy of dry eye. Once an accurate diagnosis is made, the treatment plan can be individualized.[13] There are a plethora of tests for diagnosing dry eye, and these tests are modified with new advancements added each year. Each test operates by measuring different properties of the ocular surface or the tear quality, which includes tear flow, volume, stability, concentration, lysozyme concentration, or meniscus.[14]

The techniques used in dry eye diagnosis can be grouped into seven categories according to which aspect of the tear film is evaluated. These include: symptoms and history, slit lamp biomicroscopy, tear secretion tests, tear stability test, tear solute tests, ocular surface evaluation, and lid surface assessment.[13]

Symptom evaluation is a key component of clinical dry eye diagnosis. Symptoms of dry eye syndrome include eyes feeling dry or gritty, eyes appear red, crust forms on the lashes, eyelids matted in the morning, foreign body sensation, excessive tears, intolerance to smoke or light, and eyes burn or itch.[14,15] The presentation of dry eye symptoms or history of dry eye warrants objective confirmation of the diagnosis. Although a doctor should always pay close attention to the patient history, objective tests are essential in confirming the diagnosis.

Slit lamp biomicroscopy should include an assessment of any excess debris in the tear film and measuring of the tear meniscus parameters.[13] Debris in the tear film can originate from the external environment or the sloughing of corneal epithelial cells.[2] Measuring the tear meniscus properties are an indication of the tear quantity; therefore, these measurements are an extremely crucial part of the diagnosis of aqueous deficient dry eye. Decreased tear secretion is pathognomonic of aqueous tear deficiencies.[13]

Clinical tests to evaluate the tear secretion or quantity include the Schirmer and phenol red thread tests.[13,14] The Schirmer test I is performed with topical anesthetic and filter paper. After the anesthetic drop is applied, a strip of filter paper is placed in the lateral one-third of the lower lid for five minutes. Dry eye is diagnosed if the strip wets less than 10 mm down the strip over a 5 minute period.[16] The phenol red thread test is another test to assess the tear secretion by the lacrimal gland. This test is superior to the Schirmer test I because the problems of comfort and excess time are overcome.

Tear stability tests used most often in clinical settings are the fluorescein tear breakup time and the tear thinning time. Tear breakup time is assessed with insertion of sodium fluorescein and a cobalt blue filter on a slit lamp biomicroscope. The fluorescein sodium is applied to the eye by touching a fluorescein strip to the inferior or superior bulbar conjunctiva. Tear thinning time evaluates the tear stability with a keratometer.[13]

Clinical tests for ocular surface evaluation include sodium fluorescein staining, rose bengal staining and impression cytology.[13] Fluorescein sodium stains damaged epithelial cells of the

cornea and conjunctiva. Rose Bengal and lissamine green dye both stain epithelial cells that have been deprived of mucin protein protection.

Rose bengal staining is performed with a rose bengal strip applied to the bulbar conjunctiva. The eye is then viewed with a white light behind a slit lamp biomicroscope. Although rose bengal is a reliable test for the integrity of the corneal and conjunctival epithelia, the dye can be uncomfortable when applied to the eye.[18]

Lissamine green staining is a relatively new dye for ocular surface staining. The dye is applied to the conjunctiva in the same way as rose bengal. This newer dye stains the conjunctival and corneal epithelial cells similar to rose bengal; however, patient tolerance of lissamine green is better than with rose bengal.

Impression cytology is a test which evaluates the ocular surface by removing the superficial layers of the conjunctival epithelium with a cellulose acetate filter. This testing procedure is noninvasive, easy to perform, and causes minimal discomfort to the patient. Impression cytology is used to follow changes in the morphology and the degree of squamous metaplasia of the conjunctival cells.[19]

Lid surfacing assessment is the evaluation of the blink rate and completeness of the blink.[13] Complete and frequent blinks are critical in maintaining the health of the eye by spreading the tears evenly over the ocular surface.[9] Partial or infrequent blinks cause an uneven tear surface and excessive evaporation, leading to an unprotected epithelium.[18]

The conservation of the tears produced is performed naturally by proper and frequent blinking or artificially with punctal occlusion.[18,22] Appropriate blinking spreads the tears across the ocular surface to prevent infection and keep the surface moist.[9,18]

Management of dry eye symptoms includes insuring lubrication of the eye and retaining tears produced by the ocular tissues.[20] There are a plethora of artificial tears produced to soothe dry eye. The primary goal of using artificial tears is to temporarily decrease the symptoms associated with dry eye. At this time, there are no artificial tears available that contain the same concentrations and components as natural human tears.[21] Restasis® ophthalmic solution (Allergan, Irvine, CA) is a prescription ophthalmic drop which contains cyclosporine, an anti-inflammatory agent.[18]

Punctal plugs are dry eye management devices used to prevent the tears from draining through the punctum lacrimale from the lacrimal lake and eye.[23] Either or both the inferior and/or superior lacrimal canaliculi can be plugged. Temporary or medium-term occlusion with dissolvable Collagen Plugs or synthetic Dissolvable Opaque Herrick Lacrimal Plugs is initially used to determine if long-term occlusion will be beneficial. If successful, medical-grade silicone plugs such as the Opaque Herrick® Lacrimal Plug (Lacrimedics, Eastsound, WA) are then used.[22]

METHODS AND MATERIALS

The purpose of this study is to compare the efficacy of superior versus inferior punctal occlusion. Superior punctal occlusion involves inserting a Dissolvable Opaque Herrick Lacrimal Plug® into the superior punctum of an eyelid. Inferior punctal occlusion involves inserting a Dissolvable Opaque Herrick Lacrimal Plug® in the inferior punctum of the opposite eyelid.

Approval for this study was given by the Northeastern State University (NSU) Human Experimentation Committee. Subjects were selected from student and faculty volunteers at NSU as well as personal acquaintances of the examiners. Each subject was given a copy of the informed consent document that listed risks of the study as well as contact information. A total of 27 subjects participated in this study, 18 males and 9 females. The subjects' ages ranged from 24 years of age to 42 years of age. At the beginning of the study, none were found to have any signs of blepharitis, keratitis, or conjunctivitis. At the completion of the study, two subjects requested to have their plugs removed due to ocular itching.

At the initial visit, the baseline measurements of the tear film of each eye were assessed. Based on symptoms, each subject was asked to assess their perceived dryness of each eye separately. A scale of one to five was used with one being no dryness and five being always dry. Procedures used included tear break up time, phenol red thread test, tear thinning time, sodium fluorescein staining, and lissamine green staining. Two subjects were withdrawn from the study due to absence of superior puncta and/or puncta which were too small for plug insertion.

Tear thinning time is measured using a keratometer to assess the quality of the tear film. The time is measured between a complete blink and the onset of the mires becoming distorted. Diagnosis of dry eye is confirmed with a time less than 10 seconds.[7]

The phenol red thread test was chosen for this study due to its ease of use and reliability. The thread used for the phenol red thread test is a cotton thread dyed with phenol red dye. The color of the thread changes from yellow to red in response to the pH of the tear fluid. While some researchers believe that the phenol red thread test measures the tear flow rate, recent research suggests that this test really estimates the magnitude of tear volume in the lower conjunctival sac.[14] The phenol red thread test is performed by placing a 3 mm hook of the thread over the lid margin into the lower conjunctival sac. The thread is placed toward the temporal side of the eye to avoid the cornea. The subject is then instructed to look ahead and blink normally. After fifteen seconds the thread is removed and quickly measured in millimeters.

The tear breakup time is an easy way to evaluate the quality of the tear film, as well as examining the cornea for other anomalies.[17] This value is the amount of time the tear film takes to lose coherence over the corneal surface. This is done routinely after fluorescein dye instillation and while viewing the tear film with a cobalt blue light filter at a slit lamp biomicroscope. A breakup time of less than 5 seconds is diagnostic of dry eye.[6]

Sodium fluorescein and lissamine green staining are both clinical tests to assess the quality of the ocular surface. A grading scale of zero to four was used for both tests. Zero represents no staining, one represents trace staining, two represents mild staining, three represents moderate staining, and four represents severe staining.

After the baseline data were collected, each subject had superior occlusion in one eye and inferior occlusion in the other eye. Punctal occlusion was performed with a 0.4mm Synthetic Dissolvable Opaque Herrick Lacrimal Plug® Lacrimedics, Inc. (Eastsound, WA). The six month dissolvable synthetic plug material is the same that is used in dissolvable sutures. The decision of which eyelid would be plugged in each was randomly assigned by the toss of a coin. This was a single blind study. The subject was not told which punctum was to be occluded. The examiner inserting the plugs falsely placed plugs in the opposing puncta.

Each subject was instructed not to use any artificial tears throughout the course of the study. Any other medications that a subject used were either discontinued or else used on a consistent basis over the course of the study. Subjects were allowed to continue the use of contact lenses as long as neither the lens nor the wearing regimen changed.

Punctal occlusion was performed after the application of topical 0.5% proparacaine HCl. The punctal occlusion was conducted by the first examiner. Due to time constraints the first examiner also ran the tear thinning time and phenol red test. The investigators believed that these two tests would lead to the least amount of subjective bias. The second examiner conducted the tear break-up time, sodium fluorescein staining, and lissamine green staining tests. When necessary, the second examiner dilated the appropriate puncta to aid in insertion of the punctal plug. The examiners found that superior punctal occlusion was more difficult than inferior punctal occlusion. The second visit took place one week after the initial data were collected. During this examination the baseline tests were repeated with each examiner running the same tests ran at the first visit. Each subject was asked again to note any changes in apparent dryness in either eye.

The last visit took place three weeks after the initial observations. The same follow up tests were conducted by the same examiners. At this visit, each subject was given the option of having the plugs removed by irrigation or allowing them to naturally dissolve.

The data collected at baseline, one week, and three weeks were analyzed to compare any differences found between the two eyes. The baseline data were compared to the data from one week and three week follow up visits. A t-test was applied to analyze the data and a p-value of <0.05 was considered statistically significant for this study.

RESULTS

Comparing Baseline to Week One

The overall dryness scale ranged from one to five, with five representing major dry eye symptoms. The subjective mean for inferiorly plugged eyes had a baseline value of 2.41 on this scale prior to punctal occlusion. At the week one follow up, there was a significant improvement in dryness with a mean change of 0.52, resulting in a new average of 1.89 ($p<0.05$) (see Table 1). Overall dryness mean for superiorly plugged eyes had a baseline value of 2.44 prior to punctal occlusion. At the week one follow up, there was a significant improvement in dryness with a mean change of 0.37, resulting in a new average of 2.07 ($p<0.05$). There was significant improvement in dryness for eyes plugged in either the superior and inferior puncta but the difference between the two eyes is not significant (see Table 2).

	Mean Day	Mean Week	Mean change	Significance (2-tailed)
Superior Overall Dryness (0-5)	2.44	2.07	0.37	0.150
Inferior Overall Dryness (0-5)	2.41	1.89	0.52	0.000
Superior Tear Thinning Time (sec.)	6.04	7.63	-1.59	0.089
Inferior Tear Thinning Time (sec.)	5.81	8.33	-2.52	0.002
Inferior Phenol Red Thread Length	19.11	21.67	-2.56	0.083

Table 1. Day One and Week One Values and Significance. Negative Change Indicates Day One Value is Less Than Week One Value.

	Mean Change	Significance (2-tailed)
Overall Dryness Superior vs. Inferior	0.1481	0.212
Tear Thinning Time Superior vs. Inferior	-0.9259	0.300
TBUT Superior vs. Inferior	-1.2222	0.327
Fluorescein Staining Superior vs. Inferior	0.1923	0.096
Lissamine Green Staining Superior vs. Inf	-0.0741	0.713
Phenol Red Thread Length Superior vs. I	-3.7778	0.029

Table 2. Day One and Week One Paired Samples Test. Negative Change Indicates Day One Value is Less Than Week One Value.

Inferiorly plugged eyes had an initial mean of 5.81 seconds on the tear thinning time prior to punctal occlusion. At the week one follow up, the average time was significantly increased by a mean of 2.52 seconds, resulting in a total mean of 8.33 seconds ($p<0.05$). Superiorly plugged eyes had an initial mean of 6.04 seconds prior to punctal occlusion. Following punctal occlusion for one week, the average thinning time approached significance ($p=0.089$), with a slight increase of 1.59 seconds. The difference in tear thinning time increase between the superiorly and inferiorly plugged eyes was not statistically significant.

Inferiorly plugged eyes had a baseline tear breakup time (TBUT) of 10.04 seconds on average prior to punctal occlusion. Superiorly plugged eyes had a baseline TBUT of 10.04 seconds on average prior to punctal occlusion. Following punctal occlusion for one week, the average change in time for both sets of eyes was not statistically significant. The difference in TBUT change between the superiorly and inferiorly plugged eyes was not statistically significant.

Sodium fluorescein (NaFl) staining was graded on a scale from zero to four, with four representing severe staining. Inferiorly plugged eyes had an initial grade of 1.56 with NaFl staining on average. At the one week follow up visit, the average change in staining grade was not statistically significant. Superiorly plugged eyes had an average baseline grade of 1.31 with NaFl staining. At

the one week follow up visit, the average change in staining was not statistically significant. The difference between the superiorly and inferiorly plugged eyes approached significance for the NaFl staining (p=0.096). Both inferiorly and superiorly plugged eyes had increased average staining from baseline to week one, but the inferiorly plugged eyes had less increase staining.

Lissamine green staining was graded on a scale of zero to four, with four representing severe staining. Inferiorly plugged eyes had a baseline lissamine green staining grade of 0.59 on average. Superiorly plugged eyes had an initial lissamine green staining grade of 0.56 on average. At the one week follow up visit, the change in lissamine green staining was not statistically significant for both sets of eyes. The difference in lissamine green staining between the superiorly and inferiorly plugged eyes was not statistically significant.

Inferiorly plugged eyes had an initial average length of 19.11mm with the phenol red thread test prior to punctal occlusion. After one week of punctal occlusion, the average increase in length was 2.56mm, which approached significance (p=0.083). Superiorly plugged eyes had an initial average length of 20.00mm with the phenol red thread test prior to punctal occlusion. At the one week follow up visit, the average change in length was not found to be statistically significant. Statistical significance was found (p<0.05) when comparing the increase in length with the phenol red thread test between the inferiorly and superiorly plugged eyes. The change in length on the phenol red thread test length was increased for the eyes plugged in the inferior puncta and decreased for the eyes plugged in the superior puncta.

Comparing Baseline to Week Three

Overall dryness for inferiorly plugged eyes had a baseline mean of 2.41 prior to punctal occlusion. At the three week follow up visit, there was a significant improvement in dryness with a mean change of 0.41 (p<0.05), resulting in a new average of 2.00 (see Table 3). Overall dryness for superiorly plugged eyes had a baseline mean of 2.44 prior to punctal occlusion. At the week three follow up, there was a significant improvement in dryness with a mean change of 0.48 (p<0.05), resulting in a new average of 1.96 (see Figure 1). Although there was significant improvement in dryness for eyes plugged in the superior and inferior puncta, the difference between the two eyes is not significant (see Table 4).
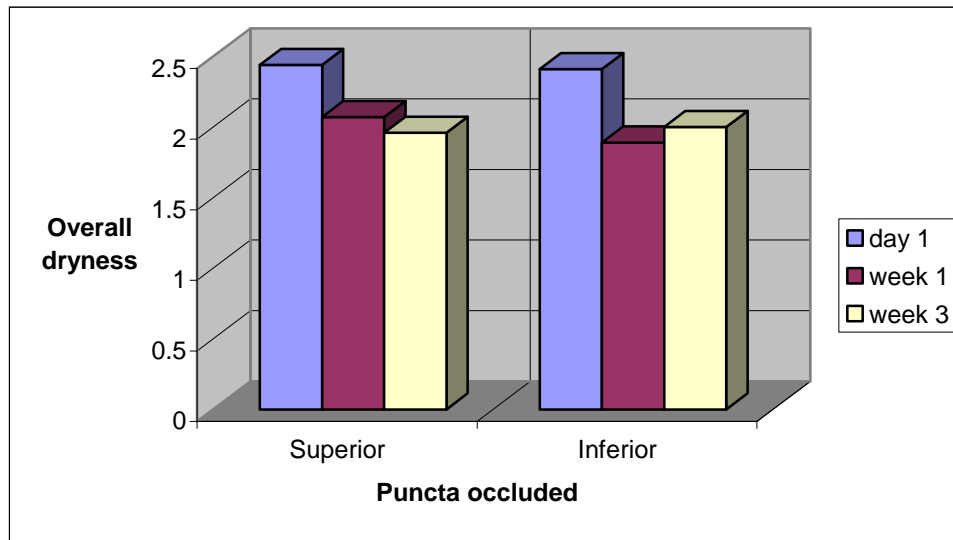
Figure 1. The Decrease in Overall Dryness from Day 1 to Week 3

Inferiorly plugged eyes had an initial mean of 5.81 seconds on the tear thinning time prior to punctal occlusion. At the week three follow up, the average time approached significance with an increase of 1.96 seconds (p=0.067) (see Figure 2). Superiorly plugged eyes had an initial mean of 6.04 seconds prior to punctal occlusion. Following punctal occlusion for three weeks, the average time and the difference between the two eyes was found not to be statistically significant.
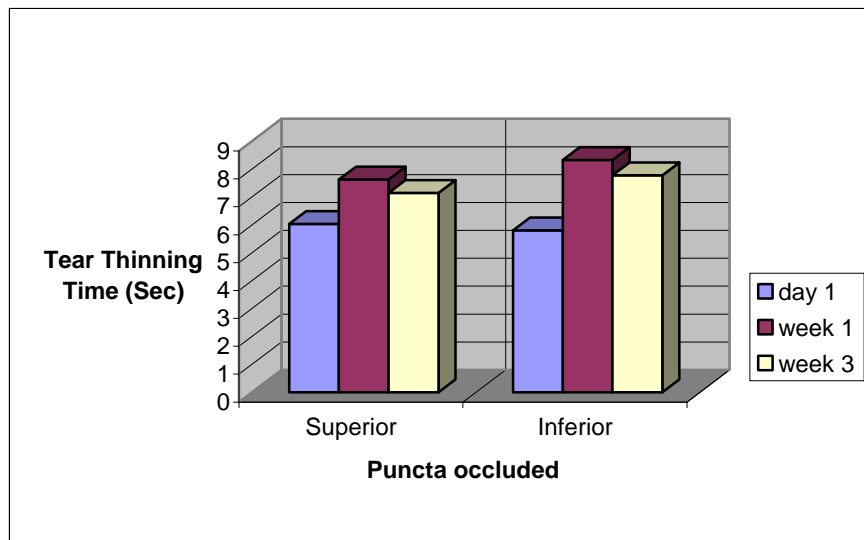

Figure 2. The Increase in Tear Thinning Time from Day 1 to Week 3

Inferiorly plugged eyes had a baseline TBUT of 10.04 seconds on average prior to punctal occlusion. At the week three follow up, the average change in time was not statistically significant. Superiorly plugged eyes had a baseline TBUT of 10.04 seconds on average prior to punctal

occlusion. Following punctal occlusion for three weeks, the average change in time was not statistically significant. The difference in TBUT change between the superiorly and inferiorly plugged eyes was not statistically significant.

	Mean Day 1	Mean Week 3	Mean change	Significa (2-tailed
Superior Overall Dryness (0-5)	2.44	1.96	0.48	0.030
Inferior Overall Dryness (0-5)	2.41	2.00	0.41	0.019
Inferior Tear Thinning Time (sec.)	5.81	7.78	-1.96	0.067
Superior Phenol Red Thread Length	20.00	24.22	-4.22	0.005
Inferior Phenol Red Thread Length (	19.11	24.37	-5.26	0.000

Table 3. Day One and Week Three Paired Samples Test. Negative Change Indicates Day One Value is Less Than Week Three Value.

Inferiorly plugged eyes had an initial grade of 1.56 with NaFl staining on average. Superiorly plugged eyes had an average baseline grade of 1.31 with NaFl staining. At the three week follow up visit, the average change in staining for either set of eyes was not statistically significant. The difference between the superiorly and inferiorly plugged eyes was significant for the NaFl staining ($p<0.05$). The eyes plugged in the inferior puncta had a small decrease in NaFl staining, while the eyes plugged in the superior puncta had a small increase in NaFl staining.

	Mean Change	Significance (2-tailed)
Overall Dryness Superior vs. Inferior	0.1481	0.212
Tear Thinning Time Superior vs. Inferior	-0.9259	0.300
TBUT Superior vs. Inferior	-1.2222	0.327
Fluorescein Staining Superior vs. Inferior	0.1923	0.096
Lissamine Green Staining Superior vs. In	-0.0741	0.713
Phenol Red Thread Length Superior vs.	-3.7778	0.029

Table 4. Day One and Week One Paired Samples Test. Negative Change Indicates Day One Value is Less Than Week Three Value.

Inferiorly plugged eyes had a baseline lissamine green staining grade of 0.59 on average. Superiorly plugged eyes had an initial lissamine green staining grade of 0.56 on average. At the three week follow up visit, the change in lissamine green staining for either set of eyes was not statistically significant. The difference in lissamine green staining between the superiorly and inferiorly plugged eyes was not statistically significant.

Inferiorly plugged eyes had an initial average length of 19.11mm with the phenol red thread test prior to punctal occlusion. After three weeks of punctal occlusion, the average length was statistically increased to 24.37mm, resulting in a 5.26mm change ($p<0.05$). Superiorly plugged eyes had an initial average length of 20.00mm with the phenol red thread test prior to punctal occlusion. At the three week follow up visit, the average change in length was found to be significant with an increase 4.22mm, resulting in an average of 24.22mm ($p<0.05$) (see Figure 3). Statistical significance was not found when comparing the increase in length with the phenol red thread test between the inferiorly and superiorly plugged eyes.
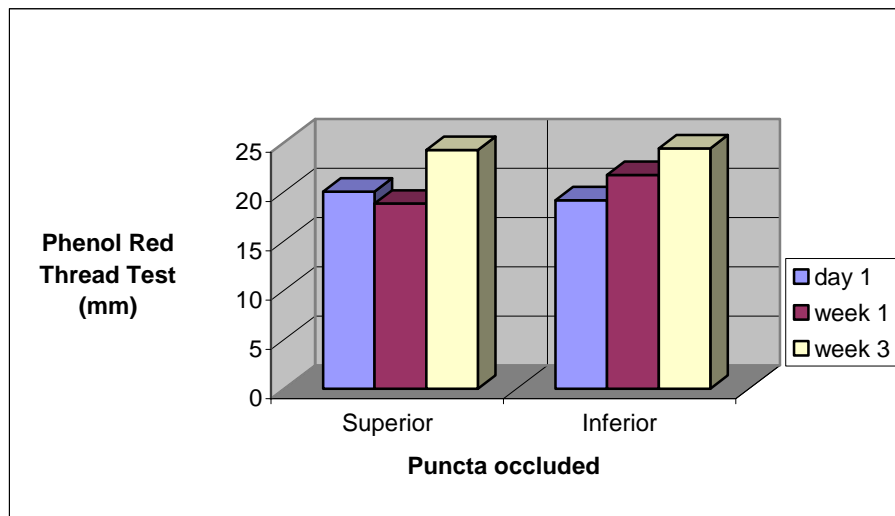

Figure 3. The Increase in Phenol Red Thread Test from Day1 to Week 3

DISCUSSION

Management of dry eye syndrome consists of treatment of the underlying condition and/or management of the symptoms. Treatment of dry eye with inflammation as the etiology is accomplished by inhibiting the inflammatory response at the cell level.[18] Current management of dry eye revolves around symptomatic relief. Two essential approaches used in managing symptoms include constant lubrication and conservation of existing tears with the use of punctal occlusion.[20] Punctal occlusion is not recommended for patients with inflammatory dry eye, due to the increase in time the inflammatory mediators spend on the ocular surface.

The current standard of care in dry eye treatment is to initially prescribe artificial tears. If the signs and symptoms of dry eye do not improve, then the next step is to plug the inferior puncta of both eyes. After another trial period, the superior puncta may be plugged if inferior occlusion is not

alleviating the complaints. A study conducted by Farrell, Patel, Grierson, et al. claims that double occlusion demonstrates no added benefit over single punctal occlusion. However, they do note that the double occlusion has prolonged effects on tear volume.[24]

Punctal occlusion is indicated in patients with moderate to severe dry eye, secondary to a low aqueous volume, to preserve the natural tears.[23] Current studies show dry eye signs and symptoms are calmed by punctal occlusion.[25]

This study was conducted to compare the efficacy of superior versus inferior punctal occlusion. The results suggest that both superior and inferior punctal occlusion significantly improve the subjects' comfort at one week and three weeks. There is not a significant amount of difference between the comfort of eyes plugged superiorly versus inferiorly at the week one and week three follow up visits. This correlates with a study conducted by Farrell, Patel, Grierson, et al., which found that subjective dryness improved five days after punctal occlusion. However, there was no increase in improvement at the day 12 follow up visit.[24] Therefore, with single punctal plugs, comfort improves from baseline up to three weeks time unless the plugs are lost or removed.

Of the 27 subjects in this study, 21 presented with subjective dry eye complaints. The six subjects without dry eye syndrome began the study with no initial dry eye symptoms and did not have an increase in complaints throughout the study. These subjects gave the overall dryness value one on a scale from one to five on the first and last visits. A value of one on the subjective scale represents no dry eye symptoms. Therefore, these six subjects could not report a decrease in subjective symptoms.

There were two sets of objective data, tear thinning time and phenol red thread test, which showed significant or near significant improvement from baseline to either follow up visit. The TBUT, NaFl staining, and lissamine green staining did not show significant improvements over time. This disagrees with a study conducted by Dursun, Ertan, and Bilezikci, et al., where TBUT and NaFl staining both significantly improved ($p<0.05$) over six weeks post plug insertion.[26]

At the week one and week three visits, the inferiorly and superiorly plugged eyes showed improvement in tear thinning time, with week one having the greater tear thinning time. The difference between the eyes was not statistically significant at either follow up visit. These results suggest that punctal occlusion of the superior or inferior puncta increases tear stability with no distinction between which punctum is occluded. Farrell, Patel, Grierson, et al. found a significant

increase (p<0.05) in tear thinning time with inferior and double punctal occlusion. The longest tear thinning time was found to be on the day five follow up visit with no difference between single and double occlusion.[24]

The inferiorly plugged eyes also showed more significance with the phenol red thread test. However, both superiorly and inferiorly plugged eyes were more significant at week three than at week one. These results suggest that the enhancement in tear volume found with the phenol red thread test continue to improve until three weeks after the puncta are occluded. The difference between the superiorly and inferiorly plugged eyes with this test was significant (p=0.029) at the week one follow up, but not at three weeks.

With the increase in tear characteristics found with the phenol red thread test and tear thinning time, the NaFl and lissamine green staining would be expected to decrease. However, in this study these findings were not consistent. One possible explanation for this could be due to the subjects discontinuing the use of artificial tears throughout the course of the study. In a study conducted by Dursun, Ertan, and Bilezikci, et al., where subjects were allowed to utilize artificial tears, significant improvements (p<0.05) in NaFl staining and rose bengal staining were found.[26]

Another possible explanation for the lack of improvement in fluorescein and lissamine green staining was the inconsistent use of contact lens wear between the subjects. Contact lenses have been shown to compromise the lipid layer of the tear film, resulting in subsequent aqueous desiccation.[27] Discontinued wear is usually adequate therapy, but this option is undesirable for most patients.[28] This creates the need for other treatments for contact lens related dry eye other than removal of contact lenses.

Eighteen of the twenty-seven subjects were contact lens wearers. Subjects were allowed to continue contact lens use throughout the study, but were asked to be consistent with their amount of wear time each day. However, some subjects were inevitably unable to maintain this strict requirement. Two subjects reported sleeping in their contact lenses the night before the week one follow up visit. Both subjects consequently presented with an increased amount of fluorescein and lissamine green staining.

Throughout the study, several subjects reported itching associated with the punctal plugs. Six subjects had itching complaints at the week one visit. Of the six subjects, four had itching in both eyes, one had superior itching only and the other had inferior itching only. For these six subjects,

the itching had subsided by the third week. Two subjects required plug removal at the conclusion of the study due to itching. Both subjects experienced complete relief following irrigation. Jones, Anklesaria, Gordon et al. found 2.2% of their plugged subjects complained of ocular irritation.[22] Therefore, patients must be advised of initial itching symptoms following insertion of punctal plugs.

CONCLUSION

At week one the only test that showed statistical significance between the two eyes was the phenol red thread test, with the inferiorly plugged eye showing more improvement ($p<0.05$). At week three the NaFl staining was the only test that showed statistical significance, with the inferiorly plugged eye showing less staining ($p<0.05$). For all the other test data taken, at week one and week three, the difference between the two eyes was not significant. These findings suggest that inferiorly plugged puncta is slightly more beneficial as shown by objective testing.

The results of this study agree with previous studies which conclude that dry eye patients benefit from punctal plugs. However, these plugs are not designed for every patient and may cause ocular itching. For patients with moderate to severe dry eye, punctal plugs may need to be supplemented with lubricating drops.

Dry eye syndrome is a multifaceted condition with significant implications for those involved with patient care and those who suffer with the symptoms. A basic knowledge of the ocular anatomy and its function will aid in diagnosis and treatment of this common yet complex disorder. The causes of dry eye symptoms are numerous, as well as the clinical presentations of this condition. Current research is constantly changing the etiology and management of dry eye syndrome in the medical community.

Knowledge gained over the course of time has led to vast improvements in the way dry eye is diagnosed and managed. Although this condition still affects a large proportion of the population, frequent advances will continue to increase the number of choices and effectiveness of treatments available.

BIBLIOGRAPHY

Bandeen-Roche K, Munoz B, Tielsch JM, West SK, Schein OD. Self-reported assessment of dry eye in a population-based setting. Invest Ophthalmol Vis Sci. 1997;38:2469-2475.

Bartlett JD, Jaanus SD. Clinical Ocular Pharmacology. MA: Butterworth-Heinemann, 2001.

Bawazeer, AM, Hodge WG. One minute Schirmer test with anesthesia. Cornea 2003;22(4):285-287.

Bjerrum KB. Test and symptoms in keratoconjunctivitis sicca and their correlation. Acta Ophthalmol Scand 1996;74:436-441.

Charlton JF, Schwab IR, Stuchell R. Tear hyperosmolarity in renal dialysis patients asymptomatic for dry eye. Cornea 1996; 15(4):335-339.

Cohen EJ, Holland EJ, Mannis MJ, Matoba AY, Meisler DM, Udell IJ, et al. Punctal occlusion for the dry eye. Ophthalmology 1997;104:1521-1523.

Craig JP, Tomlinson A. Importance of the lipid layer in human tear film stability and evaportation. Optom Vis Sci 1997;74:8-13.

Dursun D, Ertan A, Bilezikci B, Akova Y, Pelit A. Ocular Surface Changes in Keratoconjunctivitis sicca with silicone punctum plug occlusion. Curr Eye Res 2003;26:263-269.

Farrell J, Patel S, Grierson DG, Sturrock RD. A clinical procedure to predict the value of temporary occlusion therapy in keratoconjunctivitis sicca. Ophthalmol Physiol Opt 2003;23:1-8.

Floegel I, Horwath-Winter J, Muellner K, Haller-Schober E. A conservative blepharoplasty may be a means of alleviating dry eye symptoms. Acta Ophthalmol Scand 2003;81:230-232.

Fujishima H, Toda I, Shimazaki J, Tsubota K. Allergic conjunctivitis and dry eye. Br J Ophthalmol 1996;80:994-997.

Gilbard J. Dry eye: pharmacological approaches, effects, and progress. CLAO 1996;22:141-145.

Gilbard J, Farris R, Santamaria A. Osmolarity of tear microvolumes in keratoconjunctivitis sicca. Arch Ophthalmol 1978;96:677-81.

Gilbard JP, Rossi SR, Azar DT, Heyda KG. Effect of punctal occlusion by Freeman silicone plug insertion on tear osmolarity in dry eye disorders. CLAO 1989;15:216-218.

Goto D, Tseng S. Kinetic analysis of tear interference images in aqueous tear deficiency dry eye before and after punctal occlusion. Invest Ophthalmol and Vis Sci 2003;44(5):1897-1905.

Hom M. Hallway controversies in dry eye. Rev Optom 2003 Aug;1A-7A.

Huang, F, Tseng S, Shih M, Chen F. Effect of artificial tears on corneal surface regularity, contrast sensitivity, and glare disability in dry eyes. Ophthalomogy 2002;109:1934-1940.

Jones C, Anklesaria M, Gordon A, Prouty R, Rashid R, Singla R. Retrospective safety study of the Herrick Lacrimal Plug: a device used to occlude the lacrimal canaliculus. CLAO J 2003;28:206-210.

Kobayashi TK, Tsubota K, Takamura E, Sawa M, Ohashi Y, Usui M. Effect of retinal palmitate as a treatment for dry eye: a cytological evaluation. Ophthalmologica 1997;211:358-361.

Koh S, Watanabe H, Hosohata J, Hori Y, Hibino S, Nishida K, et al. Diagnosing dry eye using a blue-free barrier filter. Am J Ophthalmol 2003;136:513-519.

Korb D, Greiner J, Glonek T, Esbah R, Finnemor V, Whalen A. Effect of periocular humidity on the tear film lipid layer. Cornea 1996;15:129-134.

Lemp MA, Wolfley DE. The Lacrimal Apparatus. In: Hart WM, eds. Adler's Physiology of the Eye: Clinical Application. 9th ed. St. Louis: Mosby-Year Book, 1992:18-28.

Liu D, Sadhan Y. Surgical punctal occlusion: a prospective study. Br J Opthalmol 2002;86:1031-1034.

Mainstone JC, Bruce AS, Golding TR. Tear meniscus measurement in the diagnosis of dry eye. Curr. Eye Res. 1996;15:653-661.

Marcozzi G, Liberati V, Madia F, Centofanti M, de Feo G. Age and gender-related differences in human lacrimal fluid peroxidase activity. Ophthalmolgica 2003;217:294-297.

Marner K, Moller PM, Dillon M, Rask-Pedersen E. Viscous carbomer eye drops in patients with dry eyes. Acta Ophthalmol. Scand. 1996;74:249-252.

Mathers W. Ocular evaporation in meibomian gland dysfunction and dry dye. Ophthalmology 1993;100:347-51.

Mathers WD, Lane JA, Zimmerman MB. Assessment of the tear film with tandem scanning confocal microscopy. Cornea 1997;16(2):162-168.

Mori A, Oguchi Y, Okusawa Y, Ono M, Fujishima H, Tsubota K. Use of high-speed, high-resolution thermography to evaluate the tear film layer. Am J Ophthalmol 1997;124:729-735.

Murube J, Murube E. Treatment of dry eye by blocking the lacrimal canaliculi. Surv Ophthalmol 1996;40:463-480.

Nakamori K, Odawara M, Nakajima T, Mizutani T, Tsubota K. Blinking is controlled primarily by ocular surface conditions. Am J Ophthalmol 1997;124:24-30.

Nava-Castaneda A, Tovilla-Canales JL, Rodriguez L, Tovilla ya Pomar JL, Jones C. Effects of lacrimal occlusion with collagen and silicone plugs on patients with conjunctivitis associated with dry eye. Cornea 2003;22(1):10-14.

Nelson JD. Impression Cytology. Cornea 1988;7:71-81.

Ohashi Y, Ishida R, Kojima T, Goto E, Matsumoto Y, Watanabe K, et al. Abnormal protein
     profiles in tears with dry eye syndrome. Am J Ophthalmol 2003;136:291-299.

Patel S, Farrell J, Bevan R. Relation between precorneal tear film stability and tear production rate
     in normal eyes. Optom Vis Sci 1989;66:300-303.

Pfister R. The normal surface of corneal epithelium: a scanning electron microscopic study.
     Invest Ophthalmol 1973;12:654-68.

Remington, LA. Clinical Anatomy of the Visual System. MA: Butterworth-Heinemann, 1998.

Rumelt S, Remulla H, Rubin PA. Silicone punctal plug migration resulting in dacryocystitis and
     canaliculitis. Cornea 1997;16(3)377-379.

Schaumberg D, Sullivan D, Buring J, Dana R. Prevalence of dry eye syndrome among US
     women. Am J Ophthalmol 2003;136:318-327.

Schein O, Muñoz B, Tielsch J, Bandeen-Roche K, West S. Prevalence of dry eye among the
     elderly. Am J Ophthalmol 1997;124:723-728.

Shaker GJ, Ruffini J, Arora I, Aquavella JV. Soluble collagen disks for the treatment of dry eye
     syndrome. CLAO 1989;15:299-303.

Snell RS, Lemp MA. Clinical Anatomy of the Eye. MA: Blackwell Science, 1998.

Sullivan LJ, McCurrach F, Lee S, Taylor HR, Rolando M, Marechal-Courtois C, et al. Efficacy
     and safety of 0.3% carbomer gel compared to placebo in patients with moderate-to-severe
     dry eye syndrome. Ophthalmology 1997;104:1402-1408.

Toda I, Yagi Y, Hata S, Itoh S, Tsubota K. Excimer laser photorefractive keratectomy for patients
     with contact lens intolerance caused by dry eye. Br J Ophthalmol 1996;80:604-609.

Tomlinson A, Cedarstaff T. Tear evaporation from the human eye: the effects of contact lens
     wear. J Br CL Assoc 1982;5:141-50.

Tsubota K. The importance of the Schirmer test with nasal stimulation. Am J Ophthamol 1991;
     111:106-108.

Tsubota K, Fujuhara T, Kaido M, Mori A, Mimura M, Kato M. Dry eye and Meige's syndrome. Br
     J Ophthalmol 1997;81:439-442.

Tsubota K, Hata S, Yukio O, Egami F, Ohtsuki T, Nakamori K. Quantitative videographic
     analysis of blinking in normal subjects and patients with dry eye. Arch Ophthalmol
     1996;114:715-720.

Tsubota K, Toda I, Yagi Y, Ogawa Y, Ono M, Yoshino K. Three different types of dry eye
     syndromes. Cornea 1994;13:202-209.

Varnell RJ, Freeman JY, Maitchouk , Beuerman RW, Gebhardt BM. Detection of substance P in human tears by laser desorption mass spectrometry and immunoassay. Curr. Eye Res. 1997;16:960-963.

Virtanen T, Houtari K, Härkönen M, Tervo T. Lacrimal plugs as a therapy for contact lens intolerance. Eye 1996;10:727-731.

Wilson G. The effect of osmolality on the shedding rate of the corneal epithelium. Cornea 1996;15:240-244.

Xu K, Yagi Y, Tsubota K. Decrease in corneal sensitivity and change in tear function in dry eye. Cornea 1996;15:235-239.

Yeo AC, Carkett A, Carney LG, Yap MK. Relationship between goblet cell density and tear function tests. Ophthal. Physiol. Opt. 2003;23:87-94.

Yokoi N, Komur A, Nishida K, Kinoshita S. Effectiveness of hyaluronan on corneal epithelial barrier function in dry eye. Br J Ophthalmol 1997;81:533-536.

LITERATURE CITED

1. Remington LA. <u>Clinical Anatomy of the Visual System</u>. MA: Butterworth Heinemann, 1998.

2. Snell RS, Lemp MA. <u>Clinical Anatomy of the Eye</u>. MA: Blackwell Science, 1998.

3. Craig JP, Tomlinson A. Importance of the lipid layer in human tear film stability and evaportation. Optom Vis Sci 1997;74:8-13.

4. Bartlett JD, Jaanus SD. <u>Clinical Ocular Pharmacology</u>. MA: Butterworth-Heinemann, 2001.

5. Ohashi Y, Ishida R, Kojima T, Goto E, Matsumoto Y, Watanabe K, et al. Abnormal protein profiles in tears with dry eye syndrome. Am J Ophthalmol 2003;136:291-299.

6. Schein O, Muñoz B, Tielsch J, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. Am J Ophthalmol 1997;124:723-728.

7. Dursun D, Ertan A, Bilezikci B, Akova Y, Pelit A. Ocular surface changes in keratoconjunctivitis sicca with silicone punctum plug occlusion. Curr Eye Res 2003;26:263-269.

8. Patel S, Farrell J, Bevan R. Relation between precorneal tear film stability and tear production rate in normal eyes. Optom Vis Sci 1989;66:300-303.

9. Nakamori K, Odawara M, Nakajima T, Mizutani T, Tsubota K. Blinking is controlled primarily by ocular surface conditions. Am J Ophthalmol 1997;124:24-30.

10. Lemp MA, Wolfley DE. The lacrimal apparatus. In: Hart WM, eds. <u>Adler's Physiology of the Eye: Clinical Application</u>. 9th ed. St. Louis: Mosby-Year Book, 1992:18-28.

11. Tsubota K, Hata S, Yukio O, Egami F, Ohtsuki T, Nakamori K. Quantitative videographic analysis of blinking in normal subjects and patients with dry eye. Arch Ophthalmol 1996;114:715-720.

12. Xu K, Yagi Y, Tsubota K. Decrease in corneal sensitivity and change in tear function in dry eye. Cornea 1996;15:235-239.

13. Mainstone JC, Bruce AS, Golding TR. Tear meniscus measurement in the diagnosis of dry eye. Curr Eye Res 1996;15:653-661.

14. Bandeen-Roche K, Munoz B, Tielsch JM, West SK, Schein OD. Self-reported assessment of dry eye in a population-based setting. Invest Ophthalmol Vis Sci 1997;38:2469-2475.

15. Bjerrum KB. Test and symptoms in keratoconjunctivitis sicca and their correlation. Acta Ophthalmol Scand 1996;74:436-441.

16. Bawazeer, AM, Hodge WG. One minute Schirmer test with anesthesia. Cornea 2003;22 (4):285-287.

17. Goto D, Tseng S. Kinetic analysis of tear interference images in aqueous tear deficiency dry eye before and after punctal occlusion. Invest Ophthalmol and Vis Sci 2003;44(5):1897-1905.

18. Hom M. Hallway controversies in dry eye. Rev Optom 2003 Aug;1A-7A.

19. Nelson JD. Impression Cytology. Cornea 1988;7:71-81.

20. Liu D, Sadhan Y. Surgical punctal occlusion: a prospective study. Br J Opthalmol 2002;86:1031-1034.

21. Huang, F, Tseng S, Shih M, Chen F. Effect of artificial tears on corneal surface regularity, contrast sensitivity, and glare disability in dry eyes. Ophthalomogy 2002;109:1934-1940.

22. Jones C, Anklesaria M, Gordon A, Prouty R, Rashid R, Singla R. Retrospective safety study of the Herrick Lacrimal Plug: a device used to occlude the lacrimal canaliculus. CLAO J 2003;28:206-210.

23. Cohen EJ, Holland EJ, Mannis MJ, Matoba AY, Meisler DM, Udell IJ, et al. Punctal occlusion for the dry eye. Ophthalmology 1997;104:1521-1523.

24. Farrell J, Patel S, Grierson DG, Sturrock RD. A clinical procedure to predict the value of temporary occlusion therapy in keratoconjunctivitis sicca. Ophthalmol Physiol Opt 2003;23:1-8.

25. Nava-Castaneda A, Tovilla-Canales JL, Rodriguez L, Tovilla ya Pomar JL, Jones C.Effects of lacrimal occlusion with collagen and silicone plugs on patients with conjunctivitis associated with dry eye. Cornea 2003;22(1):10-14.

26. Dursun D, Ertan A, Bilezikci B, Akova Y, Pelit A. Ocular Surface Changes in Keratoconjunctivitis sicca with silicone punctum plug occlusion. Curr Eye Res 2003;26:263-269.

27. Tomlinson A, Cedarstaff T. Tear evaporation from the human eye: the effects of contact lens wear. J Br CL Assoc 1982;5:141-50.

28. Virtanen T, Houtari K, Härkönen M, Tervo T. Lacrimal plugs as a therapy for contact lens intolerance. Eye 1996;10:727-731.