The influence of lubricating eye drops on tear film osmolarity: a comparison between preserved and non-preserved products.

This report outlines the research carried out by Matthew Carter, 3rd year Optometry student at City University under the supervision of Ms Judith Morris during summer 2009.

Introduction

An elevated tear film osmolarity or ‘hyperosmolarity’ appears to be the common end consequence of the variations in tear dynamics seen in dry eye disease (DED) \(^{(1)}\). Both aqueous deficiency and evaporative dry eye patients show tear osmolarity recordings well above those of the normal population \(^{(2,3)}\). Hyperosmolarity has been shown to cause epithelial damage and is likely to result in the stimulation of the inflammatory reaction seen in DED \(^{(4,5)}\). Normal osmolarity has been reported as 304 ±1.4mOsm/L, compared to a mean of 343 ±32.3mOsm/L in DED \(^{(6)}\). The same study also suggested a cut-off of 312mOsm/L to separate the normal from the dry eye. More recently tear osmolarity has been reported as the most effective stand-alone test in DED diagnosis \(^{(7)}\) and as a result of this and similar studies tear osmolarity testing is now considered the gold standard in the diagnosis of DED. However, until recently tear osmolarity testing has not been clinically viable due to the complex procedure involved in its measurement. The arrival of the TearLab Osmolarity System allows in-practice tear osmolarity assessment and could therefore become integral to the diagnosis and management of dry eye patients. The TearLab Osmolarity System requires nanolitres of tear film to obtain a recording and boasts a collection time of less than one second. This allows for the collection of data quickly and with minimal discomfort to the subject, without the risk of evaporation that is observed with previous glass-capillary tube collection methods.

Since hyperosmolarity is the hallmark of the dry eye it is important to consider the impact that lubricating drops, the mainstay of dry eye treatment, have upon the tear film. This study has been designed to
assess how a brand of lubricating eye drops affects tear film osmolarity in patients with dry eye symptoms. Multi-dose ophthalmic preparations, including those used by DED patients, contain a preservative to limit microbial contamination to within a safe level. However, prolonged use of some preservatives has been shown to cause irritation in some patients \(^{(8)}\). This is a particularly important consideration in the treatment of dry eye as preservatives can disrupt the tear film, cause ocular surface damage and therefore exasperate the problem \(^{(9)}\). This has led to an array of ocular lubricants available as both preserved multi-dose and non-preserved single dose preparations. One such product was used in this study.

**Aims**
To investigate the influence of eye lubricants upon tear film osmolarity and the role preservatives have in this interaction.

**Subjects**
All subjects were required to meet the following selection criteria: 1. Significant dry eye symptoms identified using the McMonnies Dry Eye Questionnaire (MDEQ) and associated scoring system \(^{(10,11)}\). 2. No contact lens wear or eye drop use on the day of study. Eight suitable, consenting, adult female subjects were recruited with an age range of 29 to 73 (mean 47 years).

**Materials and Methods**
A score of 14 and above was used to identify subjects with dry eye symptoms as this value has been shown show to give 87% sensitivity and specificity for dry eye diagnosis \(^{(12)}\). The Tearlab Osmolarity System was used throughout to take osmolarity recordings from the inferior tear meniscus. Systane® lubricating eye drops from Alcon® were tested in this study. Tear osmolarity was recorded from the right and then the left eye. Following these baseline recordings a single drop (quantity grossly controlled by the experimenter) of the preserved test product (Systane® Multi Dose containing polyguaternium-1 as a preservative) was placed into the lower fornix of the right eye and a stopwatch started. 30 seconds later one drop of the unpreserved test product (Systane® Single Dose) was placed into the left eye and a second stopwatch started. At 5 and 30 minutes past instillation tear osmolarity was recorded again for both eyes. This experimental design is based upon Tearlab’s claim that the non-invasive nature of the
Tearlab Osmolarity System and quick collection time (<1 second) that make reflex tearing in the second eye a non-issue\(^\text{13}\). 

**Results**

Figure 1 illustrates the mean osmolarity values obtained at each stage of the investigation for both versions of the test product. Paired t-tests were used to compare tear osmolarity recorded at 5 and 30 minutes post drop instillation with the baseline measurement taken from the appropriate eye. Neither product caused a significant change in tear osmolarity at 5 nor 30 minutes post instillation (p>0.05). However, there was a large range in osmolarity responses at 5 minutes post instillation (e.g. change in osmolarity ranged from -56mOsm/L in the right eye in one subject to +10mOsm/L in another). 

The baseline osmolarity recordings taken from the left eye (mean 316.6mOsm/L, sd 12.8) were significantly (paired t-test p<0.005) lower than those recorded from the right eye (mean 334.1mOsm/L sd 12.5). However, there was no difference in osmolarity between the two eyes at 5 or 30 minutes post instillation (paired t-test p>0.05). This disparity between baseline recordings was not expected and suggests tear sampling caused reflex tearing thus lowering the osmolarity in the left eye. This result means that only the right baseline measurement can be taken to represent the true pre-drop state of the eyes.

All subjects had a right eye baseline measurement above the 312mOsm/L cut-off suggested by Gilbard et al. (1978) to diagnose dry eye. This suggests the MDEQ correlates well with tear osmolarity as a diagnostic test. Each subject was questioned on the experience after the protocol was complete and all subjects responded well to the device. No discomfort during data collection was reported or evidence of epiphora observed.
**Discussion**

The data shows recording osmolarity causes a subsequent reduction in osmolarity in the contralateral eye. This is most likely caused by reflex tearing and if it occurs in the contralateral eye it is safe to assume the same occurs in eye being tested. This has made a comparison between the two preparations impossible. Looking solely at the right eye (preserved drop) the mean osmolarity fell by 15.6 mOsm/L after 5 minutes post instillation, however this was not statistically significant. It would be worthwhile repeating the investigation on a larger scale and including a control group (tested with no drop) for comparison, which would show more clearly any impact tear sampling with the Tearlab device may have upon osmolarity. If the instrument is shown to affect tear osmolarity its usefulness in tracking changes over a short time scale could be thrown into question.

Interestingly the observed discrepancy between the two eyes was restricted to the initial recordings. An un-quantified observation was made by the investigator during the study; in the majority of cases the device took longer to collect a tear sample during the baseline measurement of the right eye compared with the left eye, and all subsequent recordings. The very first measurement often took longer than one second whereas subsequent recordings were collected almost instantaneously upon contact with the tear meniscus. An initial small tear meniscus would make it harder for the device to collect the sample and inevitably lead to a longer collection time. This may result in more lid contact and perhaps reflex tearing, explaining why the investigator noticed a reduced collection time for the left eye. Presumably the tear meniscus is larger following instillation of the eye drops making all subsequent measures of osmolarity quick, with little risk of further reflex tearing.

In conclusion, further study is necessary to investigate the influence Systane® and preservative content have upon tear osmolarity. This study has however suggested that reflex tearing is an important consideration when using the Tearlab Osmolarity System in scientific research and further investigation is required. This may be of interest to clinicians using the device in practice; the results suggest limiting osmolarity measurements to one eye per visit. Any subsequent readings are likely to be inaccurate and lower than the habitual level due to reflex tearing.
References

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