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Research Article

Correlation between Tear Osmolarity Measurements Using TearLab and I-Pen Osmolarity Systems in Normal Young Saudi Subjects

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Abstract

Background: Increases in tear osmolarity and instability of the tear film are core mechanisms of dry eye regardless of its etiology. Techniques for measuring tear osmolarity and detecting instability of the tear film should be reliable and accurate. TearLab and I-Pen are the most commonly used new techniques for measuring tear osmolarity. The purpose of this study was to determine the correlation between tear osmolarity measured using TearLab and I-Pen in normal young Saudi subjects.

Methods: Thirty-seven men aged from 20 to 28 years (mean, 23.0 ± 2.2 years) completed the study. The subjects were healthy with no symptoms of dry eye or ocular disease and did not wear contact lenses. The exclusion criteria were thyroid gland disorder, high cholesterol level (above 4 mmol/L), high body mass index (above 24.9 kg/m^2), vitamin A or D deficiency, hypertension, anemia, diabetes and smoking. The ocular surface disease index (OSDI) was completed first, followed by measurements of tear osmolarity in the right eye using TearLab and I-Pen.

Results: The average (mean ± SD) OSDI values and osmolarity readings from TearLab and I-Pen were normally distributed ($P > 0.05$, Kolmogorov-Smirnov test). The OSDI scores ranged from 0 to 10.4 and confirmed that none of the subjects had dry eye symptoms. The TearLab and I-Pen scores ranged from 263 to 304 mOsm/L and from 278 to 317 mOsm/L, respectively. I-Pen scores were higher than TearLab scores (300.5 ± 10.0 vs. 287.4 ± 10.7 mOsm/L). The TearLab and I-Pen scores were strongly correlated (Pearson correlation coefficient $r = 0.968$; $P < 0.001$).

Conclusion: Tear osmolarity scores with I-Pen were higher than those with TearLab in normal young Saudi subjects. The TearLab and I-Pen osmolarity scores were strongly correlated.

Keywords: *Tear Osmolarity; Normal Eye Subjects; Strong Correlation; Tear Film Stability; Dry Eye*

Introduction

Dry eye is an ocular disorder that is caused by a variety of factors. Dry eye is a complex disorder and finding a single gold standard diagnostic test for its detection and monitoring is a challenge [1]. It results from either a deficiency of tear production or excessive evaporation of tears. A number of techniques for early detection of dry eye are available. In most cases, there is a delay in the treatment and management of dry eye until the symptoms become apparent. Such delay, in particular in severe cases, has negative effects on quality of life and vision. However, a high proportion (43%) of individuals with no dry eye symptoms show clinical signs of dryness [2]. Dry eye symptoms include visual disturbance, light sensitivity, discomfort, inflammation, increase in tear osmolarity, and tear film instability [3]. Increased tear osmolarity and instability of the tear film are considered the core mechanisms by which dry eye occurs, regardless of its etiology [3]. Techniques for measuring tear osmolarity and detecting instability of the tear film should be reliable and accurate.

The osmolarity test is used to measure salt concentration in body fluids such blood, plasma, urine and tears. Measurement of tear osmolarity can be used as a quantitative test to detect dry eye [4]. Vapor pressure and Clifton osmometers have been used to measure tear osmolarity. These instruments have good accuracy, specificity, and sensitivity [5,6]. However, they have several disadvantages, such as the long period required for administration, involvement of several steps, high possibility of tear evaporation, and unsuitability for patients with low tear volume [5,6]. The I-Pen and TearLab osmolarity systems are the most recent electronic devices for measurement of tear osmolarity. Both techniques carry no risk of induction of reflux tears and involve collection of a small tear sample from the lid margin [7]. TearLab uses a microelectrode that does not contact the ocular surface and provides accurate measurements (± 2 mOsm/L) [6,8]. It requires a small sample of tears (0.2 µL) and provides instant results with good repeatability and sensitivity [9]. Recently, IPen, a portable, fast, and easy to use method of measuring tear osmolarity, became available [10]. The device is accurate and displays readings on a digital screen [1]. A reading of ≥ 316 mOsmol/L is considered a cutoff for hyperosmolarity (dry eye), 290 to 316 mOsmol/L indicates moderate dry eye, and ≤ 290 mOsmol/L is a cutoff for normal eye [11].

Aim of the Study

The present study investigated the correlation between measurements of tear osmolarity by TearLab and I-Pen in normal young Saudi men. It was expected that the correlation between measurements by these two systems would be strong and that the variation between them would be within the normal range for normal eyes.

Methods

Subjects

Thirty-seven men aged from 20 to 28 years (mean ± SD = 23.0 ± 2.2 years) completed the study. Each participant signed an informed consent prior to the measurements and the subjects were treated according to the Declaration of Helsinki. A single examiner performed all measurements in a controlled environment. The subjects were healthy with no symptoms of dry eye or ocular disease and did not wear contact lenses. Examination for abnormalities in the eyelids, lashes, and meibomian glands was performed using a slit lamp. The exclusion criteria were thyroid gland disorders, high cholesterol level (above 4 mmol/L), high body mass index (above 24.9 kg/m^2), vitamin A or D deficiency, hypertension, anemia, diabetes, and smoking. The ocular surface disease index (OSDI) was completed first, followed by measurements of tear osmolarity in the right eye using TearLab and I-Pen. The osmolarity measurements were carried out three times with a 5-minute gap between the tests, and the average was recorded for each subject [12].

OSDI

The OSDI was completed and a score was recorded for each subject. Normal eye was defined as a score less than [13].

TearLab™ osmolarity system

The TearLab™ osmolarity system (TearLab™ Corp., San Diego, CA, USA) was used to measure tear osmolarity. Electronic system check cards were used to test the osmolarity system (334 ± 4 mOsm/L) at the beginning of each day [14].

I-Pen osmolarity system

To ensure accuracy of the measurements, the I-Pen osmolarity system (I-MED Pharma Inc., Dollard-des-Ormeaux, Quebec, Canada) is not used near electronic devices. The subject closes his eyelids for 30 seconds, followed by gentle contact of the tip of the golden nodes of the disposable sensor with the palpebral conjunctiva of the lower eyelid at a 30-degree angle. After a few seconds, the I-Pen beeps and displays the osmolarity reading on its digital screen [15,16]. Based on the tear osmolarity measurements, the subjects were classified as having normal eye (< 300 mOsm/L) or mild dry eye (301 - 320 mOsm/L).

Statistical methods

Data were collected in Microsoft Excel 2016 (Microsoft Office, Microsoft Corp., Redmond, WA, USA). Statistical Package for the Social Sciences software (IBM Software, version 22, Armonk, NY, USA) was used to analyze the data. The Pearson correlation coefficient (r) was used to represent the strength of correlation between osmolarity measurements as strong (0.50 - 1.00) or medium (0.30 - 0.49) [17]. The OSDI scores and the osmolarity measurements obtained using TearLab and I-Pen were normally distributed (P > 0.05, Kolmogorov-Smirnov test) and the mean ± SD was used to represent the average.

Results

Average values for age (years), OSDI, and tear osmolarity (mOsm/L) obtained from TearLab and I-Pen are shown in table 1. The Scores for the OSDI and osmolarity readings from TearLab and I-Pen were normally distributed (P > 0.05, Kolmogorov-Smirnov test). The OSDI scores ranged from 0 to 10.4 and confirmed that none of the subjects had dry eye symptoms. TearLab and I-Pen scores ranged from 263 to 304 mOsm/L and from 278 to 317 mOsm/L, respectively. I-Pen scores were higher than TearLab scores (300.5 ± 10.0 vs. 287.4 ± 10.7 mOsm/L). Based on osmolarity measurements using TearLab, 94.6% of subjects (N = 35) had normal eyes and only 5.4% (N = 2) had mild dry eye. According to I-Pen measurements, 56.8% of subjects (N = 21) had normal eyes and 43.2% (N = 16) had mild dry eye.

Parameter	Mean ± SD
Age (years)	23.0 ± 2.2
OSDI	6.3 ± 3.0
TearLab osmolarity (mOsm/L)	287.4 ± 10.7
I-Pen osmolarity (mOsm/L)	300.5 ± 10.0

Table 1: *Age, ocular surface disease index (OSDI), and TearLab and I-Pen osmolarity scores in subjects with normal eyes (N = 37).*

Side-by-side box plots for tear osmolarity scores from TearLab and I-Pen in the study group (N = 37) are shown in figure 1. A strong correlation (Pearson correlation coefficient; r) was found between the scores obtained from TearLab and I-Pen (r = 0.968; P < 0.001). Figure 2 shows the correlation between TearLab and I-Pen tear osmolality scores in the study group (N = 37).

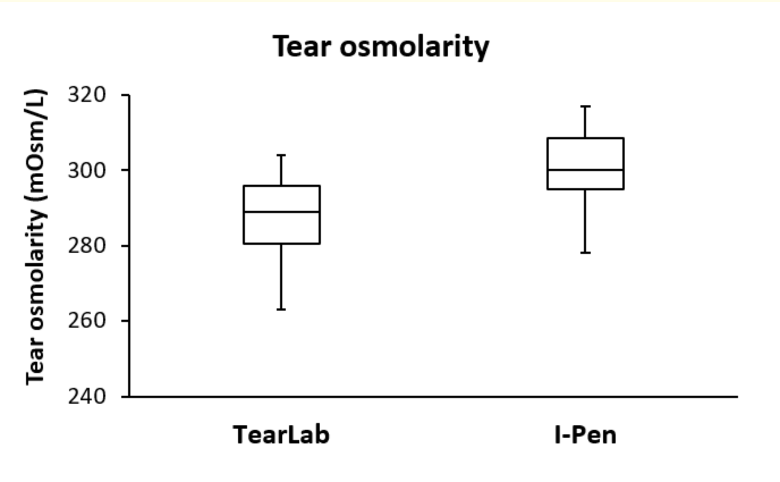

Figure 1: *Side-by-side boxplots of TearLab and I-Pen tear osmolarity measurements.*

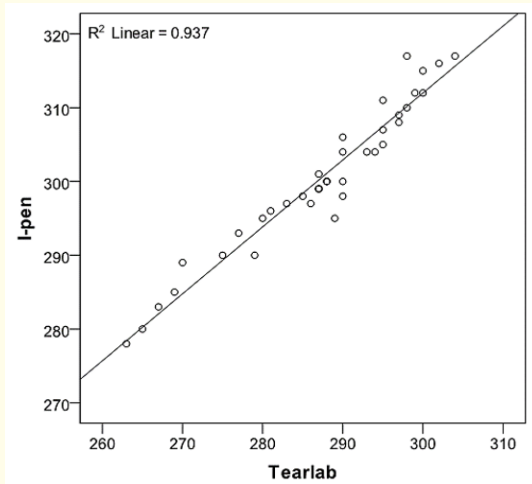

Figure 2: *Correlation between TearLab and I-Pen tear osmolarity measurements.*

Discussion

Dry eye is a very common ocular disorder that has a negative effect on quality of life and the economy. It can lead to ocular tear film damage if not treated. Symptomatology is not adequate on its own for the detection and diagnosis of dry eye [18]. Elevated tear osmolarity is one of the main pathogenic causes of ocular surface damage [3]. Tear osmolarity is among the common tests used to detect dry eye, since eye inflammation is mainly caused by tear hyperosmolarity [19,20]. Measurement of ear osmolarity provides useful information to evaluate the severity of dry eye and the status of the ocular surface [21]. The TearLab and I-Pen techniques use a nanoliter volume of tears and require the use of high-precision meters due to the relatively compressed dynamic range and low volume of tear fluid. TearLab and I-Pen have been used as accurate tools to measure tear osmolarity [22].

The current study found a strong correlation between tear osmolarity measured by TearLab and I-Pen. There were statistically significant differences between the osmolarity readings of the two systems. Both I-Pen and TearLab found that the majority of subjects (58.6% and 94.6%, respectively) had normal eyes. The measurements obtained using I-Pen were higher than those obtained using TearLab, which is consistent with reported results in subjects with normal eyes [16,23]. Clearly, TearLab is a more accurate tool than I-Pen for measurement of tear osmolarity. However, the variation between measurements using I-Pen in the current study was much smaller than reported values [23]. Clearly, the precision of TearLab was better, but nevertheless, the correlation between the results of the two systems was high. Indeed, the mean coefficient of variance (CV) for the osmolarity measurements using both TearLab and I-Pen systems were 1.1 and 4.6%, respectively. These values are consistent with those reported since the mean CV for the I-Pen osmolarity measurements was four-times higher than that for the TearLab score [14,15,23].

Measurements of tear osmolarity in subjects with normal eyes by TearLab or I-Pen are variable. For example, the average tear osmolarity recorded using TearLab in a large group of subjects with normal eyes (N = 299; 18 - 82 years) was 300.8 ± 7.8 mOsm/L [22]. The average osmolarity in 95 normal eyes of older subjects (48 - 61 years; 40 men and 55 women) using TearLab ranged from 298 to 304 mOsm/L (mean, 301 mOsm/L) [24]. The average tear osmolarity recorded in 20 subjects with normal eyes (27 ± 8 years) was 295.4 ± 8.6 mOsm/L [23]. Similarly, the average tear osmolarity was 298.0 ± 14.2 mOsm/L in a group composed of low number of subjects with normal eyes (N = 10) [25]. These tear osmolarity averages are higher than those obtained in the current study (287.4 ± 10.7 mOsm/L). However, the subjects in the current study were much younger (23.0 ± 2.2 years) than those in reported studies. A report showed that the average tear osmolarity measured in healthy subjects (N = 20) using I-Pen was 319.4 ± 20.3 mOsm/L, which is much higher than the value obtained in the current study (300.5 ± 10.0 mOsm/L) [23]. The effect of tear collection using either TearLab or a glass capillary tube (*in vivo* or *in vitro*) on measurements of tear osmolarity was investigated [26]. There was no difference between the osmolarity scores of tears collected by these two methods (301.2 ± 7.2 and 301.9 ± 16.0 mOsm/L, respectively) in subjects with normal eyes [26].

It is believed that I-Pen is more sensitive than TearLab to variations in temperature and motion artifacts, and therefore, its readings were higher [27-30]. The temperature of a tear sample can be affected by impedance measurements [29,30]. The change in impedance measurement could be 20% for each degree of temperature change [30]. The two osmolarity systems used in the current study provide results that are not directly comparable, but no significant difference is expected in practical applications.

Conclusion

Tear osmolarity measurements obtained using I-Pen were higher than those obtained using TearLab. A strong correlation was found between osmolarity measurements obtained from TearLab and I-Pen in normal young Saudi subjects.

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Disclosure

The authors report no conflicts of interest in this work.

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