Correlation between osmolarity measurements using the TearLab™ and I-Pen® systems in subjects with a high body mass index

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Abstract

Background. Osmolarity is used to detect symptoms of dry eye disease (DED) and can be measured using TearLab™ and I-Pen® systems.

Objectives. To investigate the correlation between osmolarity measurements using the TearLab™ and I-Pen® systems in subjects with a high body mass index (BMI).

Materials and methods. Thirty male subjects with a high BMI (27–48 kg/m^2; 23.3 ±2.1 years old) participated in this study. The control group consisting of 30 healthy males (24.9 kg/m^2; 22.9 ±2.1 years old) was also enrolled. Osmolarity measurements were recorded from the right eye using the TearLab™ and I-Pen® systems, and interviews were conducted to determine ocular surface disease index (OSDI) scores.

Results. The OSDI ($p = 0.042$), TearLab™ ($p < 0.001$) and I-Pen® ($p < 0.001$) scores were significantly higher in the study group than in the control group. In the study group, OSDI scores ranged from 2 to 16 (median 8.0, interquartile range (IQR) 6.8), while it was from 0 to 10 (median 6.3, IQR 4.1) in the control group. The TearLab™ osmolarity scores were in the range of 278–309 mOsm/L in the study group, whereas the I-Pen® osmolarity measurements were in the range of 294–336 mOsm/L in the study group, compared with 263–304 mOsm/L and 278–317 mOsm/L in the control group, respectively. In the study group, there was a strong correlation between the TearLab™ and I-Pen® osmolarity scores ($r = 0.934$; $p = 0.001$). In addition, strong correlations were found between the BMI and both TearLab™ ($r = 0.736$; $p = 0.001$) and I-Pen® ($r = 0.707$; $p = 0.001$) scores, as well as between the OSDI scores and both TearLab™ ($r = 0.731$; $p = 0.001$) and I-Pen® measurements ($r = 0.666$; $p = 0.001$).

Conclusions. Osmolarity measurements using the I-Pen® system were significantly higher than those recorded using the TearLab™ system in subjects with a high BMI. The I-Pen® measurements showed large variations in osmolarity scores and were highly unreliable in correctly identifying normal eyes compared to the TearLab™ system. Also, a strong correlation was found between the osmolarity scores obtained from the TearLab™ and I-Pen® systems.

Key words: tear film, dry eye, tear osmolarity, high body mass index, TearLab™ system, I-Pen® system

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Background

The prevalence of obesity has been increasing in recent years and has become a challenge for society and a major public health concern globally.[1,2] The simplest measurement of obesity uses body mass index (BMI), and high BMI is a risk factor for many health problems and diseases.[3] For example, high BMI is associated with heart disease,[4] stroke,[5] hypertension,[6] diabetes,[7] and cancer.[8] In addition, it is a risk factor for glaucoma,[9] cataracts[10] and diabetic retinopathy.[11]

Dry eye disease (DED) is a common visual disorder that affects many people worldwide.[12] The prevalence of DED is increasing, and it has a negative effect on activities of daily life, quality of life, productivity, and on the economy.[13] This disease leads to discomfort, damage to the ocular surface, visual impairment, irritation, inflammation, light sensitivity, and increased osmolarity.[14] Dry eye disease occurs due to the loss of ocular surface homeostasis. It leads to tear film instability[15] and a decrease in wettability of the eye surface due dysfunction of goblet and epithelial cells.[16] Furthermore, the symptoms of DED can result from hyperosmolarity, lack of lubrication, and irregularities on the ocular surface.[16] Risk factors for DED include old age and female sex. They also include contact lenses wearing, cosmetics, medications, and systemic diseases such as diabetes, thyroid gland disorders and β thalassemia.[17] In addition, DED is associated with several environmental factors, including high temperature and humidity, sun exposure and wind.[17]

Diagnosis of DED should be based on quantifiable objective and subjective evaluations.[18] Multiple tools are available for such diagnosis, including the ocular surface disease index (OSDI), tear osmolarity, tear break-up time, and Schirmer tests, among others. The OSDI evaluates ocular symptoms, vision-related functions and environmental triggers, and has good validity, consistency and reliability.[18] Osmolarity testing provides useful information on the hyperosmolarity of the tear film,[19] and the in vivo tear osmolarity test has been commonly used since the introduction of new osmometers such as the TearLab™ system.[20] Tear osmolarity measurements using TearLab™ are accurate, precise and fast, and the system is easy to use to diagnose and classify DED based on severity.[21,22] However, other reports have raised questions over the ability of TearLab™ to diagnose DED.[23,24] The I-Pen® osmolarity system has also been used in recent years to measure tear osmolarity.[25] However, correlations between osmolarity scores based on the I-Pen® and other objective and subjective parameters of DED are poor.[25]

The prevalence of obesity in Saudi Arabia is high (24.7%).[26] Therefore, this comparative, nonrandomized, prospective study investigated the correlation between osmolarity scores in male subjects with a high BMI using 2 different devices. Data from these devices were then compared to scores obtained from the OSDI. In addition, OSDI and osmolarity scores were compared with the scores recorded for a healthy control group.

Objectives

To investigate the correlation between osmolarity measurements using the TearLab™ and I-Pen® systems in subjects with high BMI.

Materials and methods

Subjects

Thirty male subjects with a high BMI (27–48 kg/m^2; mean ± standard deviation (M ±SD) = 35.5 ±6.5 kg/m^2), aged 19–27 years (mean ±SD = 23.3 ±2.1 years), participated in the study. The benchmark for high BMI used in the study was 25 kg/m^2.[27] In addition, a control group of 30 healthy males (BMI < 24.9 kg/m^2; age range 20–28 years; mean age 22.9 ±2.1 years) was included in the study. The subjects were predominantly Saudi Arabians recruited from the population of Riyadh, the capital city of this country. Exclusion criteria included smoking, refractive errors, visual acuity less than 20/20, diabetes, anemia, wearing contact lenses, and a history of ocular surgery. In addition, subjects with high blood cholesterol (above 4 mmol/L), thyroid gland disorders, hypertension, and vitamin A or D deficiencies were excluded. Written informed consent was obtained from all participants. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of King Saud University (approval No. E-22-6803).

Participants were asked to complete the OSDI questionnaire, after which osmolarity measurements were performed. The TearLab™ system was used first; then, after a 5-minute rest period, the I-Pen® system was applied. Tests were performed once on the right eye of each participant by the same examiner in the same session, and all tests were conducted at the Department of Optometry, College of Applied Medical Sciences, Riyadh, Saudi Arabia. The measurements took place on the morning over several days. We previously demonstrated TearLab™ measurements to have a low average coefficient of variation (CV) of 0.80%.[20] Therefore, to minimize inaccuracies due to variable environmental conditions, the temperature, humidity and airflow were controlled in the room where the measurements were made.

Ocular surface disease index

The OSDI questionnaire was conducted in English in an interview format. All 12 questions included in the OSDI were answered by all subjects in the study and control groups. A score was assigned to each participant, with a score greater than 13 used to confirm the diagnosis.[28]

Table 1. Median (IQR) for the ocular surface disease index (OSDI) and osmolarity scores

Parameter	Study group (n = 30)	Control group (n = 30)	p-value
OSDI	8.0 (6.8)	6.3 (4.1)	0.042
TearLab™ [mOsm/L]	295.5 (13.3)	287.0 (12.5)	<0.001
I-Pen® [mOsm/L]	318.5 (18.8)	298.5 (12.3)	<0.001

TearLab™ osmolarity

The TearLab™ osmolarity system was obtained from the TearLab Corporation (San Diego, USA). Electronic cards were used to test the osmolarity system (the value of 334 ±4 mOsm/L means that the system is functioning well) at the beginning of each day to ensure its proper function. The system uses a very small volume of tear sample (50 nL), which was collected from the lateral lower tear meniscus without touching the lid margin or the globe. The countertop unit of the system analyzed the tear sample and displayed the osmolarity score on a digital screen. Based on the osmolarity measurements, the subject's eyes were classified as normal (<308 mOsm/L) or dry (>308 mOsm/L).[29]

I-Pen® osmolarity

The I-Pen® osmolarity system was obtained from I-MED Pharma (Dollard-des-Ormeaux, Canada) and was used in a distance of at least 2 m from any electronic devices to reduce the risk of interference leading to inaccurate readings. A single-use sensor was utilized for each participant; it was placed against the conjunctiva in the lower fornix to determine tear osmolarity. Dry eye disease was defined as a score of more than 308 mOsm/L.[29]

Statistical analyses

Microsoft Excel 2016 (Microsoft Corp., Redmond, USA) was used to record the data, which were then analyzed with IBM SPSS v. 22 (IBM Corp., Armonk, USA). The data were determined to be non-normally distributed using the Kolmogorov–Smirnov test ($p < 0.05$). Therefore, the Mann–Whitney U test was employed to analyze the data in both groups. Spearman's correlation coefficient (r) was used to test the association between different parameters.[30] Meanwhile, the Wilcoxon signed-rank test was employed to investigate the significance of any differences between the 2 osmolarity measurements within the same group. The mean scores were represented as the median and interquartile range (IQR).

Results

Tear osmolarity measurements were significantly different between the TearLab™ and I-Pen® systems, in both the study and control groups ($p < 0.001$). Also, median scores for the OSDI and osmolarity measurements were significantly higher in the study group than in the control group (Table 1). Indeed, OSDI scores ranged from 2 to 16 in the study group and from 0 to 10 in the control group. Six subjects (20%) in the study group had symptoms of DED according to the OSDI scores, whilst no DED symptoms were found in the control group. The same 6 subjects were also diagnosed with dry eyes using both the TearLab™ and I-Pen® osmolarity systems. Osmolarity scores in the study group using TearLab™ (278–309 mOsm/L) indicated that 33% (n = 10) of the participants had symptoms of DED, whilst the control group showed no symptoms (263–304 mOsm/L). Meanwhile, I-Pen® osmolarity measurements in the study group (294–336 mOsm/L) indicated that 70% (n = 21) of studied people had DED, while 30% (n = 9) of members of the control group (278–317 mOsm/L) has this disease.

Subjects in the study group were stratified into 4 categories based on their BMI: overweight (27–28 kg/m^2; n = 7); class 1 obesity (30–32 kg/m^2; n = 8); class 2 obesity (35–39 kg/m^2; n = 9); and class 3 obesity (40–48 kg/m^2; n = 6). In the class 1 obesity group, there was a strong correlation ($r = 0.976$; $p = 0.001$) between the TearLab™ and I-Pen® measurements. Also, there were strong correlations between the OSDI scores and the TearLab™ ($r = 0.892$; $p = 0.017$) and I-Pen® ($r = 0.926$; $p = 0.0081$) measurements in this group. There was also a strong correlation between the TearLab™ and I-Pen® measurements in the class 2 obesity group ($r = 0.962$; $p = 0.009$) and in the class 3 obesity group ($r = 0.965$; $p = 0.035$). No correlations were found among the OSDI or osmolarity systems in the overweight subjects.

Correlations between age, BMI, OSDI, TearLab™, and I-Pen® scores for the whole study group were investigated. Strong correlations were found between the scores obtained from the TearLab™ and I-Pen® osmolarity systems ($r = 0.934$; $p= 0.001$). The BMI strongly correlated with both the TearLab™ ($r = 0.736$; $p = 0.001$) and I-Pen® ($r = 0.707$; $p = 0.001$) scores. In addition, the OSDI had strong correlations with TearLab™ ($r = 0.731$; $p = 0.001$) and I-Pen® ($r = 0.666$; $p = 0.001$).

Bland–Altman plots (Fig. 1) show the mean differences in osmolarity for TearLab and I-Pen® measurements in the study and control groups. There was a strong correlation ($r = 0.697$; $p < 0.01$) between the TearLab™ and I-Pen® measurements in the study group, while a weak correlation ($r = 0.358$; $p < 0.01$) was found between the 2 measurements in the control group. The correlation between the TearLab™ and I-Pen® osmolarity scores

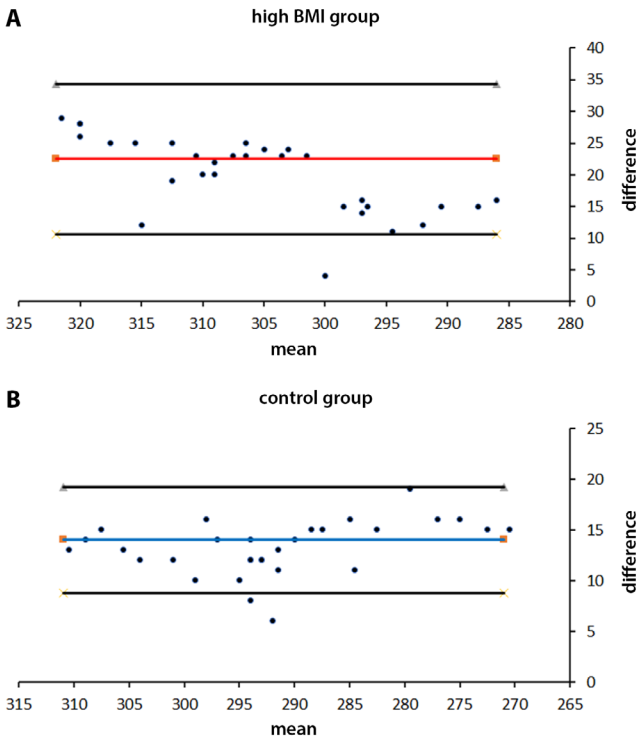

FIG. 1. Bland–Altman plots of the osmolarity mean differences for TearLab™ and I-Pen® measurements in (A) the study group (high body mass index) and (B) the control group

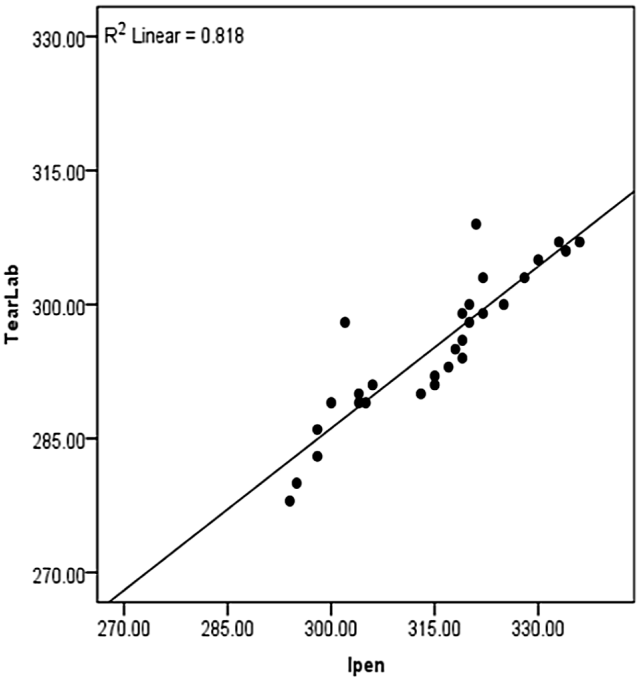

FIG. 2. Correlation between the TearLab™ and I-Pen® osmolarity scores in the study group

in the study group is shown in Fig. 2. Based on Spearman's correlation coefficient, a strong correlation was found between the TearLab™ and I-Pen® scores in both the study ($r = 0.904$; $p < 0.001$) and control ($r = 0.972$; $p < 0.001$) group.

Discussion

Obesity is associated with many disorders, such as neurological, behavioral and mental diseases.[31,32] Moreover, it is associated with high rates of mortality, bacterial infections, influenza, pneumonia, and many other illnesses.[33,34] An association between DED and body fat has been established.[35–37] As such, high BMI is a risk factor for DED and significantly affects tear film stability and the quality of tears.[35] Furthermore, an association between BMI and floppy eyelid syndrome has been reported.[38]

Osmolarity measurements using both I-Pen® and TearLab™ systems indicated that high BMI could induce DED. It should be noted that the median OSDI score for the control group (median 6.3 (IQR 4.1)) in the current study was comparable to those reported recently for healthy subjects by Fegahi et al. (median 8.3, IQR 8.8), Abusharha et al. (median 5.6, IQR 7.0) and Fagehi et al. (median 5.0, IQR 5.6).[39–41] For the study group, the median OSDI score (median 8.0 (IQR 6.8)) was comparable to smokers (median 8.3 (IQR 16.2))[39] and lower than for subjects with high BMI (median 10.2 (IQR 16.4)),[39] diabetes (median 12.0 (IQR 8.3)),[40] myopia (median 11.0 (IQR 7.5)),[41] and hyperopia (median 10.0 (IQR 33.5)).[41]

As reported in a study by Alanazi et al., in subjects with high BMI, there were strong correlations between age and OSDI scores ($r = 0.522$; $p = 0.018$), tear meniscus height (TMH) measurements ($r = -0.503$; $p = 0.024$) and tear ferning (TF) grades ($r = 0.579$; $p = 0.007$).[35] The noninvasive tear break-up time had strong negative correlations with the TMH ($r = -0.520$; $p = 0.008$) and phenol red thread (PRT) scores ($r = -0.498$; $p = 0.029$). In addition, the TF grades had strong negative correlations with the TMH ($r = -0.575$; $p = 0.008$) and PRT ($r = -0.773$; $p = 0.001$) scores.[35]

The hyperosmolarity of tears can be used as a marker of DED, as subjects with DED tend to have significantly greater hyperosmolarity than healthy subjects.[21] Hyperosmolarity is responsible for many DED symptoms, such as irritation, inflammation and ocular surface damage.[42] Also, osmolarity testing provides useful information on the tear film.[25] However, the correlations between osmolarity scores and those obtained from other DED tests are poor.[19] The current study suggests that osmolarity measurements using both the TearLab™ and I-Pen® systems are strongly correlated to each other in subjects with high BMI. However, the I-Pen® scores were significantly higher than the TearLab™ scores. Similar results were obtained in healthy subjects.[43] In addition, a correlation between tear film stability (tear break-up time) and tear volume (TMH and PRT) was reported.[44]

Rocha et al. measured osmolarity of 3 tear solutions of known osmolarity values (297 mOsm/L, 342 mOsm/L and 383 mOsm/L), containing mono- and divalent electrolytes along with albumin, were measured using the TearLab™, I-Pen® and Wescor 5520 osmometers. Mean osmolarity scores for the 3 tear solutions were 300.6 ±3.7 mOsm/L,

341.4 ±4.7 mOsm/L and 376.8 ±5.1 mOsm/L using TearLab™, 336.4 ±21.5 mOsm/L, 342.0 ±20.7 mOsm/L and 345.7 ±22.0 mOsm/L using I-Pen®, and 305.6 ±4.0 mOsm/L, 352.2 ±5.5 mOsm/L and 389.8 ±4.0 mOsm/L using the Wescor 5520 osmometer.[45] Meanwhile, the CV was in the range of 1.2–2.3%, 1.0–1.6% and 6.1–6.4% for TearLab™, I-Pen® and the Wescor 5520 osmometer, respectively.[45] Clearly, the TearLab™ and Wescor 5520 osmometers provided more accurate and precise measurements than the I-Pen® system.[45] Indeed, both the osmolarity scores and CV were high when using the I-Pen® system.

In a study by Nolfi et al., osmolarity was measured in 20 subjects (mean age: 27 ±8 years) with normal eyes (16 females and 4 males) using both the TearLab™ and I-Pen® systems. The mean osmolarity recorded was significantly ($p < 0.001$) lower for TearLab™ (295.4 ±8.6 mOsm/L) than for I-Pen® (319.4 ±20.3 mOsm/L).[46] In terms of diagnostic accuracy, I-Pen® identified normal eyes in only 15% of the subjects ($n = 3$), whereas TearLab™ indicated normal eyes in all subjects ($n = 20$).[47] The CV for the TearLab™ measurements was 1.3%, which agrees with that reported by the manufacturer (1.5%).[47] Clearly, I-Pen® showed large variations among osmolarity measurements and was highly unreliable in identifying normal eyes correctly. Calles et al. showed that I-Pen® is very sensitive to temperature and the measurements can vary by 2% for a 1°C change in temperature.[48] Motion is another factor that can affect the osmolarity measurements using the I-Pen® system. However, such a factor is not an issue with a highly skilled researcher.

Another study conducted among healthy subjects showed that the average osmolarity scores were 299.2 ±10.3 mOsm/L and 298.4 ±10.0 mOsm/L using the TearLab™ and Wescor 5520 osmometers, respectively, with a moderate correlation ($r = 0.500$, $p < 0.05$) between both scores.[49] The correlation ($r = 0.650$, $p < 0.05$) between TearLab™ and Wescor 5520 was better when using samples of collected tears (3 µL). Recently, the repeatability of the I-Pen® measurements has been tested in normal-eye subjects.[50] The main score was 308 ±4.8 mOsm/L, with a CV of 4.6%, which is much higher than that for the TearLab™ system.[50]

Limitations

Limitations of the study include the recruitment of a small sample size, only young males participating, a single osmolarity measurement, and single location (Riyadh). In addition, the effect of the order of use of the osmolarity systems was not tested.

Conclusions

Osmolarity measurements using the I-Pen® system were significantly higher than those using the TearLab™ system in subjects with a high BMI. The I-Pen® measurements showed large variations in osmolarity scores and were highly unreliable in identifying normal eyes correctly compared with the TearLab™ system. A strong correlation was found between the osmolarity scores obtained using TearLab™ and I-Pen®.

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