Performance of an *In Vivo* Tear Film Osmometer in Normal Ocular Surface Conditions

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Abstract

Purpose: **To assess the performance of an *in vivo* osmometer in a clinical setting using the i-Pen® (I-MED Pharma) osmometer in patients who scored within normal limits on the SPEED questionnaire.** ***Methods:*** **A total of 28 patients (ages 26-87) underwent comprehensive ocular surface assessment at an accredited dry eye center in Burnaby, BC, Canada. Patients were screened for ocular surface disease (OSD) with the SPEED questionnaire and the *in vivo* osmometer i-Pen, and included in the study if all eligibility criteria were met.** ***Results:*** **The mean tear osmolarity encountered in this study was 295 mOsm/L, with an average of 300.85 mOsm/L. Exam values ranged from 276 to 336 mOsm/L, with a statistically higher upper reference limit (URL) when compared to the URL published by the manufacturer. Because of this discrepancy, one might claim that most symptoms of OSD have no defined, sudden onset, leading to a proportionally small group of those patients being classified as normal. OSD symptoms might be initially masked or subclinical, leading to artificially low questionnaire scores in patients that would otherwise be classified as positive for ocular surface disease. The results of an analysis of the tear osmolarity in different ethnical groups revealed a statistically significant variance, with patients of African-American descent presenting with the lowest average value (287 mOsm/L), followed by Mixed (292 mOsm/L), Caucasians (298.36 mOsm/L), Hispanic (302.22 mOsm/L) and lastly Asians (312.8 mOsm/L). No statistical significance was observed when analyzing the distribution of tear osmolarity by age or time of testing. The i-Pen True Negative Rate (TNR), also known as Specificity (SPC), was calculated as 91.7%.** ***Conclusions:*** **The test has proved to have high specificity, allowing OSD to be excluded where osmolarity testing is negative. It is also important to consider the statistically significant correlation between ethnicity and ocular surface osmolarity, and be conscientious when analyzing dry eye questionnaires, as some patients might neglect to report symptoms in early stages of the condition.**

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Introduction

Ocular surface disease (OSD) has been objectively correlated to elevated tear osmolarity, and most progressive diagnostic algorithms currently include osmometers. Eye care practitioners must rely on objective testing to better evaluate patients with dry eye disease, whose gamut of symptoms covers a wide range of presentations from mild ocular pruritus to severe ocular pain.

A fundamental concern in OSD investigation is that the performance of osmometers could be influenced by a variety of factors. Among those that could lead to osmolarity underestimation are the administration of non-contact tonometry, retinal photography and topical medication up to two hours prior to OSD screening. Other factors lead to osmolarity overestimation, such as the use of eye makeup and/or contact lenses, or even the excessive use of handheld electronic devices on the day of the examination.

It is paramount to understand that a test with high specificity allows eye care practitioners to rule out a condition when encountering a negative result. Several studies have been conducted to assess the validity of osmolarity testing, but most study designs include patients with mild, moderate or severe disease, with emphasis in test sensitivity. Contrary to that approach, the authors intended to evaluate the true negative rate (TNR), also known as test specificity (SPC) of the commercially available *in vivo* osmometer, I-MED Pharma's i-Pen, in patients with normal ocular surface.

$$TNR = \frac{\sum TN}{\sum condition\ negative}$$

Methods

The study included 56 eyes, initially screened with the SPEED questionnaire. Patients who failed to meet eligibility criteria were excluded from the study. Inclusion criteria included: patient age greater than 18 years, negative history of makeup or topical ocular medication within 24 hours from the exam, negative history of ocular disease, and SPEED score equal or inferior to 8. Patients were then subcategorized by SPEED score, age, ethnicity and time of osmolarity measurement.

Osmolarity measurements with the i-Pen were acquired by CCOA (Canadian Certified Optometric Assistant) personnel strictly following the manufacturer's manual, with proper patient consent.

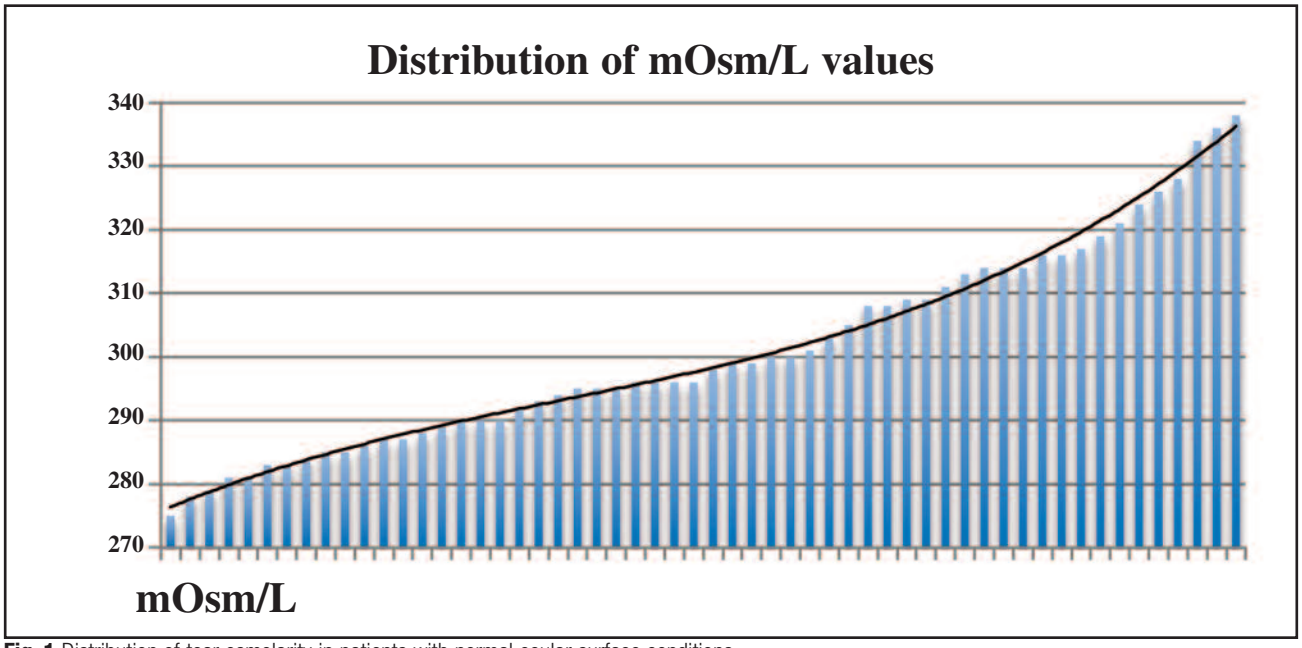

Fig. 1 Distribution of tear osmolarity in patients with normal ocular surface conditions

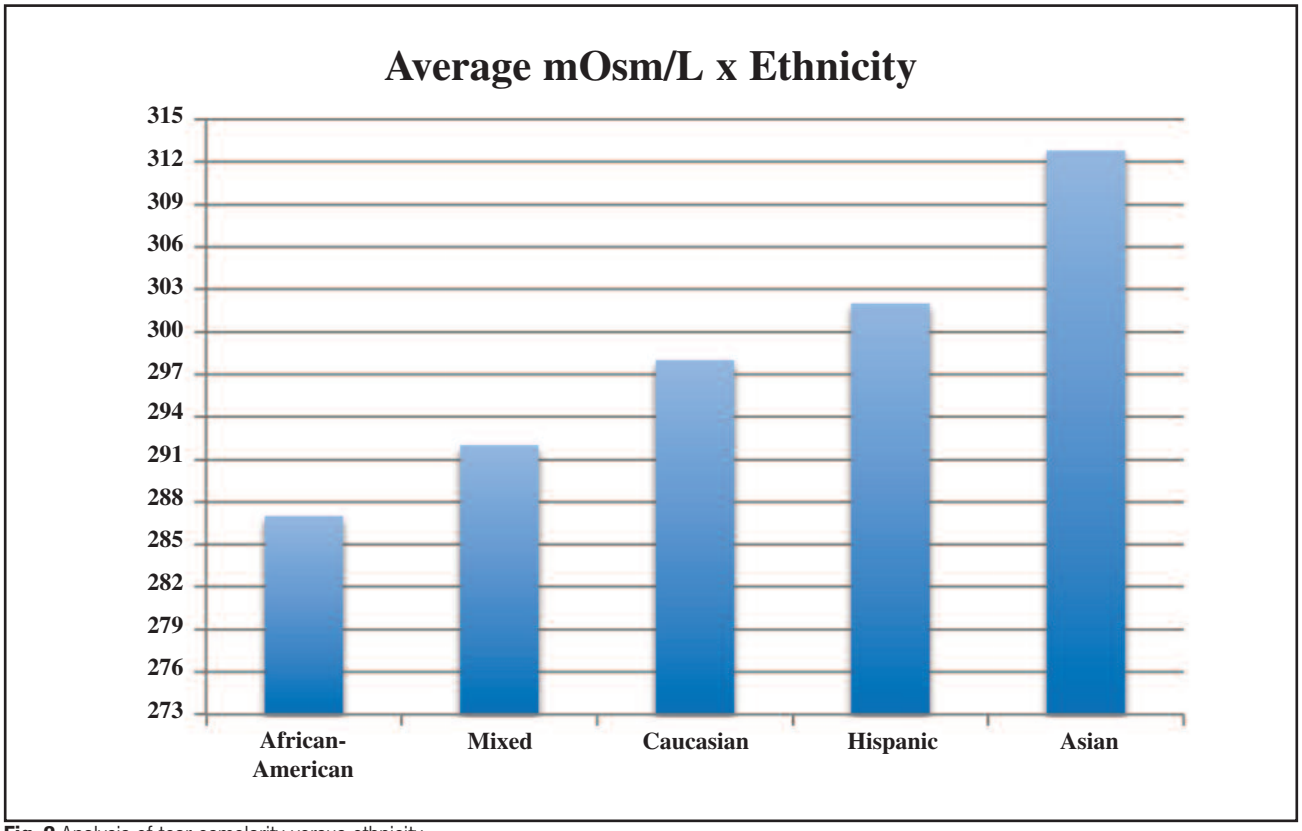

Fig. 2 Analysis of tear osmolarity versus ethnicity

Results

According to the i-Pen user manual, the mean osmolarity value in normal patients was 300 mOsm/L and a range from 275 to 316 mOsm/L was documented.

The mean tear osmolarity encountered in this study was 295 mOsm/L, with an average of 300.85 mOsm/L. Exam values ranged from 276 to 336 mOsm/L (Fig. 1), with a statistically higher upper reference limit (URL)

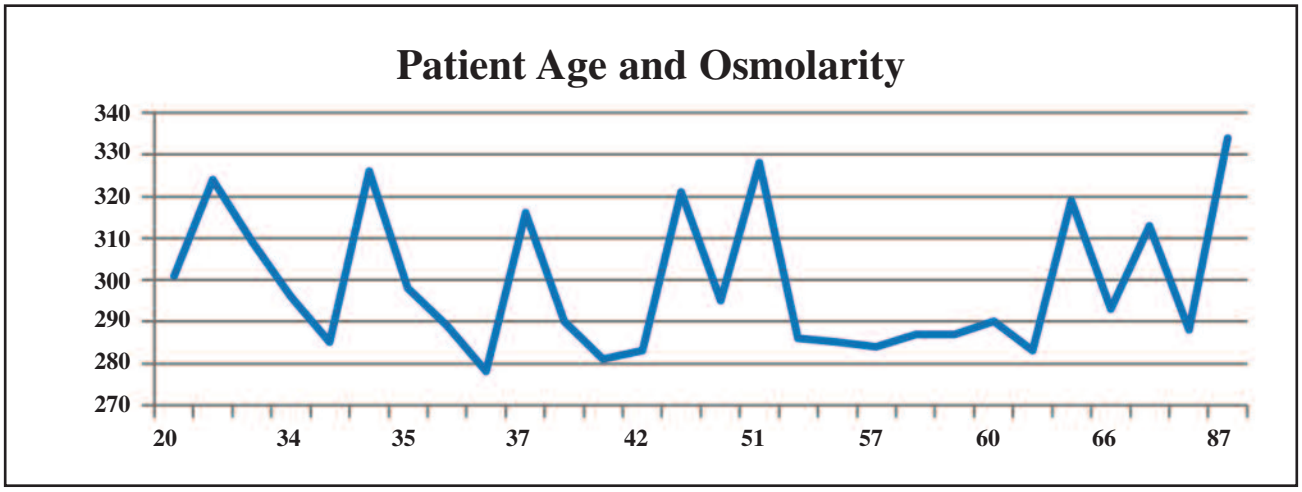

Fig. 3 Analysis of tear osmolarity versus patient age yielded no statistical significance.

when compared to the URL published by the manufacturer. In view of that discrepancy, one might claim that most symptoms of OSD have no defined, sudden onset, leading to a proportionally small group of those patients being classified as normal. OSD symptoms might be initially masked or subclinical, leading to artificially low questionnaire scores in patients that would otherwise be classified as positive for ocular surface disease.

The analysis of tear osmolarity in different ethnical groups unveiled a statistically significant variance (Fig. 2), with patients of African-American descent presenting with the lowest average value (287 mOsm/L), followed by Mixed (292 mOsm/L), Caucasians (298.36 mOsm/L), Hispanic (302.22 mOsm/L) and lastly Asians (312.8 mOsm/L).

No statistical significance was observed when analyzing the distribution of tear osmolarity by age or time of testing (Fig. 3).

The i-Pen True Negative Rate (TNR), also known as Specificity (SPC), was calculated as 91.7%. This is considered clinically significant, as most tests that present SPC values over 90% are considered reliable; despite the fact that a quintessential gold standard test would display both sensitivity and specificity of 100%. Furthermore, a direct TNR comparison between the two commercially available osmometers, TearLab® (TearLab Corp, San Diego, CA) and i-Pen® (I-MED Pharma, Montreal, QC) indicates that both options have similar test specificity, with 88% for the former and 91.7% for the latter.

Conclusion

The inclusion of tear osmolarity in ocular surface disease diagnostic algorithms is strongly encouraged by the authors. The test has proved to have high specificity, allowing eye care practitioners to exclude OSD in most cases where osmolarity testing is negative. It is also important to consider the statistically significant correlation between ethnicity and ocular surface osmolarity, and be conscientious when analyzing dry eye questionnaires, as some patients might neglect to report symptoms in early stages of the condition. ❑

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