A Comparison of *In Vivo* and *In Vitro* Osmometers for the Assessment of Dry Eye Disease

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Abstract

***Purpose*: To evaluate the efficacy of two commercially available osmometers in the assessment of dry eye patients. *Methods*: We included 100 eyes of 50 patients diagnosed with dry eye disease (DED). The study assessed 20 patients with mild DED and 30 with moderate DED at Focus Eyecare Centre, a full-scope optometric practice located in Burnaby, BC, Canada. All subjects completed the Ocular Surface Disease Index (OSDI) questionnaire and underwent comprehensive examinations including tear osmolarity [TearLab® (TearLab Corp) and i-Pen® (I-MED Pharma Inc.)], Keratograph® 5M (Oculus Inc.) dry eye assessment, slit lamp examination and SM Tube. Subjects were divided into 2 groups: Group 1 had the osmolarity assessed with i-Pen, followed by a TearLab osmolarity measurement 30 minutes later. Group 2 was initially assessed with TearLab and a second osmolarity measurement with i-Pen was acquired 30 minutes after the initial one. *Results*: Tear osmolarity values (mOsm/L) for Group 1 were 321.10 +/- 34.50 for i-Pen and 321.40 +/- 35.00 for TearLab. Group 2 yielded osmolarity values of 323.78 +/- 30.05 for i-Pen and 332.82 +/- 29.10 for TearLab. Patients diagnosed with mild DED presented with average tear osmolarity readings of 307.67 with i-Pen and 316.52 with TearLab. Those with moderate DED averaged 332.28 with the i-Pen and 334.16 with the TearLab. *Conclusions*: Both devices showed similar performance in a clinical setting for the diagnosis of dry eye disease. Tear osmolarity values were comparable in mild dry eye patients, but i-Pen acquired lower measurements in moderate dry eyes when compared to TearLab. The order in which these tests were performed also influenced the results in Group 2, due to reflex tearing induced by TearLab. Tear osmolarity should be considered as the key biomarker in the diagnosis of DED.**

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Introduction

Dry eye disease (DED) is a complex, multifactorial condition that affects the anatomy and physiology of the eyelids and ocular surface. Intrinsically an inflammatory condition, it disrupts the lacrimal functional unit and leads to tear film instability and ocular surface damage. Patients commonly experience symptoms that range from reduced visual acuity to discomfort, pain and epiphora. Approximately 5% to 30% of adults over 50 years of age present with DED according to the 2007 International Dry Eye Workshop.[1]

This chronic aggression to the cornea leads to an inflammatory cascade that results in goblet cell apoptosis and increased tear film osmolarity.

A variety of studies have been published which demonstrate that including tear osmolarity assessment in every comprehensive dry eye protocol is of paramount importance (Fig. 1).[2-16] Furthermore, some authors postulate that, in patients with dry eye symptoms who present with normal tear osmolarity values (290 mOsm/L or lower with an inter-eye difference inferior to 5 mOsm/L), a cause other than dry eyes should be present 90% of the time.[4]

The Canadian Association of Optometrists has stated in its National Dry Eye Disease Guidelines for Canadian Optometrists that osmolarity is the most accurate and objective test for dry eye disease. The aforementioned rationale leads to a logical debate; while tear osmolarity is an integral component in current DED protocols, studies comparing commercially available tear film osmometers in a clinical setting are scarce. This study seeks to elucidate

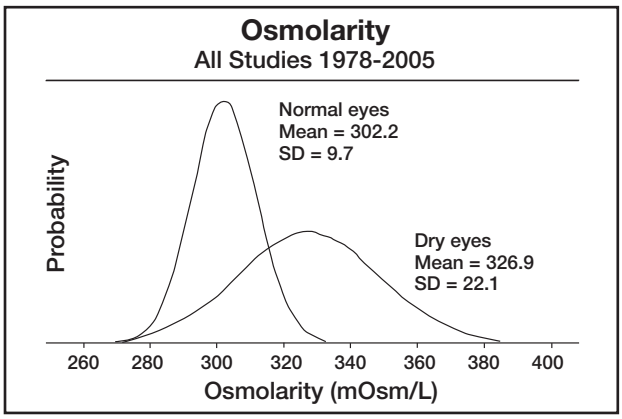

Fig. 1 Distribution of osmolarity (mOsm/L) in studies from 1978 to 2005.[8]

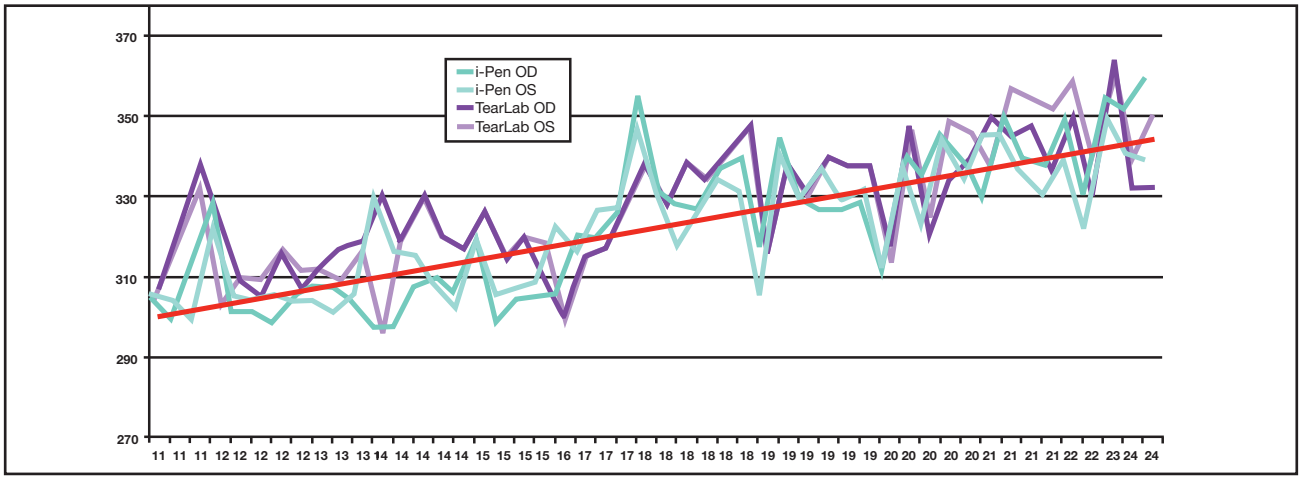

Fig. 2 Osmolarity values (mOsm/L) versus OSDI scores

if TearLab® (TearLab Corp, San Diego, CA) and i-Pen® (I-MED Pharma Inc., Montreal, QC) yield comparable results in a clinical setting, in patients diagnosed with mild to moderate dry eye disease.

Methods

The authors have included 50 patients referred to the Focus Eyecare Dry Eye Centre (n=100). Subjects ranged from age 30 to 65. 21 were male (42%) and 29 female (58%).

The selection criteria included both objective and subjective examinations traditionally used for the diagnosis of DED[17]:

1. Ocular Surface Disease Index (OSDI)
2. Keratograph 5M Non-Invasive Break Up Time (K5M NIBUT))
3. Slit lamp assessment (SLE) of corneal and conjunctival staining (Oxford).
4. SM Tube.

OSDI from 9 to 16 and from 17 to 24 were included in the study. Patients with normal OSDI or values of 25 and higher were excluded according to the Modified Thompson Tau method. K5M NIBUT was considered positive when values ranged from 1 to 9. Patients with unmeasurable BUT or ranging 10 and higher were excluded from the study. SLE Oxford Protocol was utilized to include patients ranging from Grade I to IV. SM Tube was also utilized to confirm K5M NIBUT findings and patients ranging from Grade 1 to 5 were considered for the study. It is important to point out that tear osmolarity was not included in the selection criteria to prevent selection bias.

The exclusion criteria eliminated from the study subjects with positive history for ocular surgery, active ocular infection, use of contact lens and/or artificial tears (preserved or not) in the previous 24 hours.

Subjects had the severity of their condition assessed and were subsequently classified as having mild, moderate and severe DED. Severe DED patients were not included in the study mainly due to the criteria that excluded patients who had used artificial tears within the last 24 hours.

The study included 20 patients with mild DED and 30 with moderate DED (n=100). Subjects were divided into 2 groups. Group 1 underwent tear osmolarity assessments with i-Pen and TearLab, 30 minutes apart. Group 2 was tested in reverse order, also respecting a 30-minute interval between measurements.

A trained optometric technician with CCOA designation ensured proper technique, and the devices were utilized according to their manufacturer manuals.

Results

Tear osmolarity values (mOsm/L) for Group 1 were 321.10 +/- 34.50 for i-Pen and 321.40 +/- 35.00 for TearLab. Group 2 yielded osmolarity values of 323.78 +/- 30.05 for i-Pen and 332.82 +/- 29.10 for TearLab.

Patients diagnosed with mild DED presented with average tear osmolarity readings of 307.67 with i-Pen and 316.52 with TearLab. Those with moderate DED averaged 332.28 with the i-Pen and 334.16 with the TearLab (Fig. 2). Inter-eye difference averaged 6.66 with i-Pen and 6.74 with TearLab. This value was lower among mild dry eye patients, with i-Pen yielding 6.3 and TearLab 5.25. Moderate DED patients showed a higher inter-eye osmolarity difference of 6.9 measured with i-Pen and 7.73 with TearLab (Fig. 3) No statistically significant differences between the devices were found for the group mean and group standard deviation (paired t-test, p=0.04). The osmometers provided results that were statistically aligned with OSDI scores and SLE assessment, but did not show correlation with K5M NIBUT and SM Tube measurements.

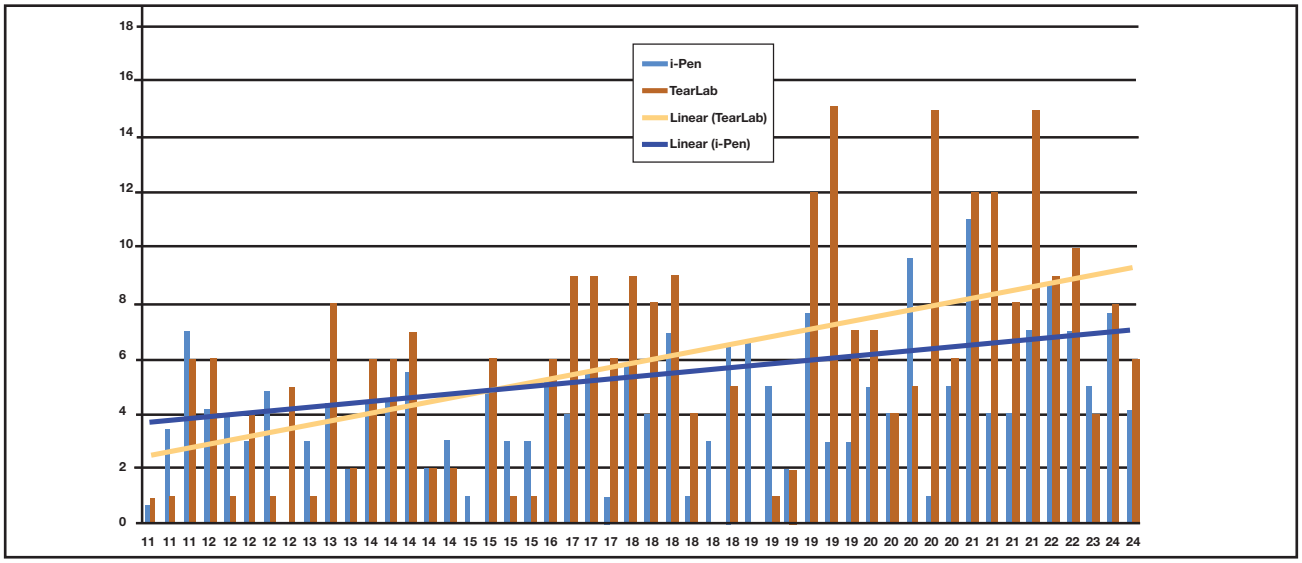

Fig. 3 Absolute inter-eye difference in osmolarity (mOsm/L) versus OSDI

The coefficient of variation CV%=(SD/Xbar)100 was 3.2% and 4.1% for i-Pen and TearLab, respectively, indicating good method performance.

It is important to note that Group 1 did not present a significant change in value when having the second test performed, whereas Group 2 showed a statistically significant lower mOsm/L even after a 30-minute interval. The authors attribute this finding to potential reflex tearing induced by TearLab. Subjects assessed with i-Pen, in contrast, presented with minimal reflex tearing. Inter-eye mOsm/L difference corresponded to OSDI scores, with similar significance between the two devices. Mean values differed 0.52, however TearLab showed greater inter-eye variance when compared to i-Pen, with 2.14 and 0.908, respectively.

Conclusion

TearLab and i-Pen, two commercially available osmometers, showed consistent correlation with OSDI and slit lamp examination, proving to be reliable and objective devices in DED management. No statistically significant difference in performance between the osmometers could be demonstrated in a clinical setting under a strict study protocol. Adequate technique and rigorous patient selection should be observed in order to achieve reliable results. The authors advise optometrists and ophthalmologists to include tear osmolarity in the assessment of every dry eye patient. ❑

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