INSTRUMENTS

Maintained concentration

Bill Harvey tries out the i-Pen osmolarity system a useful addition to clinical practice

A few years back, measurement of tear osmolarity was a concept discussed only in research laboratories. Recently, the idea of tear osmolarity as an indicator of the state of the tears, and therefore of dry More eye severity, has entered the mainstream. This is in no little part thanks to the inclusion of tear osmolarity into the latest definition of dry eye disease (DED) in the TFOS DEWS2 report which came out last year.[1] This defines dry eye disease as follows:

'Dry eye is a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.'

POINTS TO CONSIDER

The TFOS DEWS2 report includes an important review of the literature on the significance of tear osmolarity and its measurement. Here are a few key points worth citing:

- Spatial and temporal variations in tear osmolarity might affect tear film stability.
- There is greater inter-eye variability of osmolarity in DED than in normals and the inter-eye differences increase with disease severity. Moreover, this inter-eye variability has been shown to substantially reduce over time with successful treatment of DED.
- While repeated (osmolarity) measurements over a period of time have been shown to be low and stable in normal subjects, DED subjects showed relatively elevated and unstable readings.
- A link has been reported between hyperosmolarity and tear instability with increases in osmolarity measured at the centre of areas of rupture of the tear film .
- Tear osmolarity has been demonstrated (in some studies) to have the highest correlation to disease severity of clinical DED tests, and has been frequently reported as the single best metric to diagnose and classify DED.
- However, other studies have indicated current measurement techniques to be highly variable. Osmolarity generally increases with disease, classified as normal (302.2 ± 8.3 mOsm/L), mild-to-moderate (315.0 ± 11.4 mOsm/L) and severe (336.4 ± 22.3 mOsm/L).
- These data support the 316 mOsm/L cut-off as a specific threshold to better differentiate moderate to severe DED, or when used in parallel with other specific tests, while the 308 mOsm/L cut-off has become a widely accepted, more sensitive, threshold for use in routine practice to help diagnose mild to moderate subjects.

5

7

So accurate measurement of tear osmolarity would appear to be an important tool in both the diagnosis and classification of DED, and also in monitoring the effectiveness of any intervention.

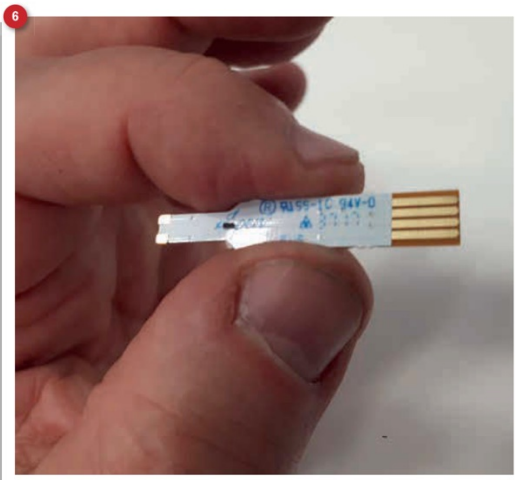
THE I-PEN

The i-Pen osmolarity system (**1**,**2**) is a small hand-held device allowing a measurement of the osmolarity of the ocular surface to be taken in a few seconds. Use is simplicity itself. After removal of the sensor cap, depression of the on/off switch reminds you to insert the single use sensor or SUS (**3** and **4**). The single use sensor must be carefully handled as if either of the metallic ends are touched then accurate measurement is impossible. Once in position, and after a 'beep' is heard, the display indicates you are ready to measure (**5**,**6**). Initially, placing the sensor in the unit and then approaching the patient to take the reading took longer than the 30 seconds it takes for the unit to go into 'sleep' mode. As the sensor is for one use only, this meant a few sensors were wasted during the practice phase.

Measurement relies upon the sensor being held upon the palpebral conjunctiva being able to detect and record the electrical impedance of the saline concentration of the fluid on the surface between two small electrical terminals on the sensor (**7**). This is achieved by having the patient look up, having first squeezed their lids tightly shut for 30 to 60 seconds, and approaching their exposed inferior palpebral conjunctiva from an angle 30 to 45 degrees above the horizontal. As long as the two gold terminals are in contact with the conjunctiva for several seconds, a 'beep' should sound and a reading display on the pen (**8**). Reuse of a sensor is not possible, and the display shows this if you attempt to do so (**9**).

8

6



CONCLUSION

The i-Pen offers an easy way to take a rapid and minimally invasive measurement of the tear osmolarity. With the limited time I had available, I can confirm that the system detected asymmetry in a dry eye sufferer, showed increased osmolarity in a contact lens wearer as the day proceeded, and confirmed normal values cited in a young and healthy individual (my daughter).

As yet, the i-Pen has not been available long enough for any significant body of evidence regarding its accuracy and repeatability to have been published. One peer reviewed study,[2] however, certainly indicates the instrument to be both reliable and accurate. This study found that 'findings suggest that ocular surface osmolarity cut-offs may be lower than previously reported when using the i-Pen osmometer'. Also, 'the observed cut-off between normal and mild DED noted in this study's cohort of 290 mOsm/L may be lower due to the lack of variables with the i-Pen *in vivo* method of measurement and therefore being more representative of true ocular surface osmolarity. With sensitivity of 91.8% and specificity of 71.4%, it would seem this lower threshold is in fact reasonable and can be explained by current understanding of the interaction between ocular surface osmolarity and corneal nociceptor stimuli.

The i-Pen is certainly worth your attention and I await further publications regarding its use with great interest.

- For further information contact www.graftonoptical.com.

REFERENCES

1 TFOS DEWS 2 can be downloaded from http://dx.doi.org/10.1016/j.jtos.2017.05.001
2 Maharaj J. https://imedpharma.com/wp-content/uploads/2018/04/CRO-28-1-Maharaj.pdf

9