Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

Solution-induced corneal staining: Insights from the laboratory

August 14, 2013

Maud Gorbet is an assistant professor in the Department of Systems Design Engineering at the University of Waterloo, Canada. She is also cross-appointed with the UW School of Optometry and Vision Science, and collaborates with the Centre for Contact Lens Research.

The introduction of silicone hydrogel lenses and their daily wear use with multi-purpose solutions (MPS) has been paralleled by the realization that preserved MPS interact differently with different lens materials.[1] Uptake and release of various MPS components by contact lenses has been reported to affect the microbial efficacy of the MPS[2,3] and is also believed to affect corneal biocompatibility.[4,5]

Certain lens-solution combinations induce corneal staining

One common method to determine biocompatibility is to assess the degree of corneal staining that is observed with a particular lens-solution combination. Certain lens-solution combinations have been identified as inducing increased amounts of corneal staining (often referred to as "solution-induced corneal staining" or SICS).[6,7]

SICS continues to be a controversial topic, as the cellular mechanisms involved in fluorescein staining of corneal epithelial cells following exposure to MPS-lens combinations are poorly understood.[8-11] The phenomenon of hyperfluorescence and hyper-reflectivity observed with certain MPS-lens combinations through slit lamp bio-microscopy[6,7,12,13] respectively, falls short of providing mechanistic clues as to why these cells are highlighted.

The concept that fluorescein stains live corneal epithelial cells is not new. In 1992, Feenstra and Tseng reported that sodium fluorescein was uptaken by cells in vitro.[14] In 1995, using rabbit corneas that had been exposed to different stress conditions, Wilson et al. demonstrated fluorescein-stained cells in vivo.[15]

Ex vivo and laboratory studies: Insights and limitations

To begin to understand SICS, it is necessary to characterize the response at the cellular level, and thus both ex vivo and laboratory studies are paramount in identifying the mechanisms involved in fluorescein staining of cells. One approach is to simplify the cell to its basic level and to represent the cell by its membrane alone. The use of model membranes (or liposomes) has provided relevant information related to NaFl quenching and its potential interaction with phospholipids, the main components of the cell membrane.[16]

However, the physiological implications of this model are limited by the fact that liposome-based models do not take into account the active transport mechanisms that are present in live cells. The cell membrane is also recognized to change structure under different stress conditions[17,18] and this process is not easily reproduced by a model membrane.

Fluorescein staining: an intracellular phenomenon in live cells

The role of active transport in the ability of fluorescein to stain cells has been recently identified both directly

and indirectly by three separate investigators using different cells. Using fibroblasts, fluorescein staining at a temperature of 4°C (the temperature at which active transport is significantly suppressed) resulted in a significant reduction in fluorescein staining of cells[19]. In presentations by Bandamwar[20,21] and Cira[22,23] fluorescein-stained corneal epithelial cells were clearly identified as live cells, and dead cells were shown to display minimal (background) to no staining at all.

The association of fluorescein with live cells strongly infers the requirement of some form of active transport, which is absent in a dead cell. Furthermore, confocal microscopy of fluorescein-stained shed cells (collected non-invasively from the cornea after fluorescein instillation, such as that described by Luensmann et al.[24]) indicated that fluorescein was indeed present within the cells.[25] Some of these fluorescein-stained cells have also been found to be apoptotic (apoptosis is a mechanism of programmed cell death).[21,25] These laboratory studies were performed with cells under both stress and normal conditions, using both in vitro and ex vivo models, but all point to a mechanism whereby fluorescein enters live cells.

The bottom line: We don't yet understand the significance of SICS

In Cameron Postnikoff's review of Mokhtarzedeh's and colleagues' paper, it is clear that studying corneal staining of cells in dry eye patients may provide further insight into SICS. Why NaFl actually enters certain corneal epithelial cells and what SICS is really highlighting remains to be determined. What does it mean physiologically for the cornea, for ocular health, and for lens-solution biocompatibility? We have yet to answer these questions unequivocally.

To identify the cellular mechanisms involved in fluorescein staining and their relation to SICS and lens-solution biocompatibility will require more laboratory-based studies using in vitro and ex vivo models. Understanding SICS is not a question about a specific product, it is a scientific quest about understanding the underlying cellular mechanism such that, one day, clinicians will truly understand what these punctate spots on the cornea truly mean.

REFERENCES

1. Jones L and Powell CH. Uptake and release phenomena in contact lens care by silicone hydrogel lenses. Eye Contact Lens 2013;39(1): 29-36.
2. Shoff ME, Lucas AD, Brown JN, et al.. The effects of contact lens materials on a multipurpose contact lens solution disinfection activity against Staphylococcus aureus. Eye Contact Lens 2012;38(6): 368-73.
3. Clavet CR, Chaput MP, Silverman MD, et al.. Impact of contact lens materials on multipurpose contact lens solution disinfection activity against Fusarium solani. Eye Contact Lens 2012;38(6): 379-84.
4. Gorbet M and Postnikoff C. The impact of silicone hydrogel-solution combinations on corneal epithelial cells. Eye Contact Lens 2013;39(1): 42-7.
5. Robertson DM. The effects of silicone hydrogel lens wear on the corneal epithelium and risk for microbial keratitis. Eye Contact Lens 2013;39(1): 67-72.
6. Andrasko G and Ryen K, Corneal staining and comfort observed with traditional and silicone hydrogel lenses and multipurpose solution combinations. Optometry 2008;79(8): 444-54.
7. Carnt N, Willcox M, Evans V, et al.. Corneal staining: The IER matrix study. Contact Lens Spectrum 2007;22(9): 38 – 43.
8. Morgan PB and Maldonado-Codina C. Corneal staining: do we really understand what we are seeing? Cont Lens Anterior Eye 2009;32(2): 48-54.
9. Ward KW. Superficial punctate fluorescein staining of the ocular surface. Optom Vis Sci 2008;85(1): 8-16.
10. Fonn D, Peterson R, Woods C. Corneal staining as a response to contact lens wear. Eye Contact Lens 2010;36(5): 318-21.
11. Efron N. Putting vital stains in context. Clin Exp Optom 2013;99(4): 400-421.
12. Schneider S, Simpson T, et al.. Hyper-reflective cells observed by confocal microscopy as an indicator of lens and lens care

interactions. Optom Vis Sci 2008; e-abstract 80028

13. Bandamwar KL, Garrett Q, and Papas E. Significance of hyper-reflective corneal epithelial cells during confocal microscopy. Contact Lens Ant Eye 2011;34 (supplement 1): S19.
14. Feenstra RP, Tseng SC. Comparison of fluorescein and rose bengal staining. Ophthalmology 1992;99(4): 605-17.
15. Wilson G, Ren H, Laurent J. Corneal epithelial fluorescein staining. J Am Optom Assoc 1995;66(7): 435-41.
16. Bright FV, Merchea MM, Kraut ND, et al.. A preservative-and-fluorescein interaction model for benign multipurpose solution-associated transient corneal hyperfluorescence. Cornea 2012;31(12): 1480-8.
17. Choy CK, Cho P, Boost MV, et al.. Do multipurpose solutions damage porcine corneal epithelial cells? Optom Vis Sci 2009;86(5): E447-53.
18. Dutot M, Pouzaud F, Larosche I, et al.. Fluoroquinolone eye drop-induced cytotoxicity: role of preservative in P2X7 cell death receptor activation and apoptosis. Invest Ophthalmol Vis Sci 2006;47(7): 2812-9.
19. Bakkar M, Maldonado-Codina C, Morgan P, et al.. Underlying mechanisms of fluorescein staining using an in vitro model of solution-induced corneal staining (SICS). Contact Lens & Anterior Eye 2012;35S: e21.
20. Bandamwar KL, Garrett Q, Papas E. Sodium fluorescein of corneal epithelial cells in response to wounding: An in vitro evaluation. The 6th International Conference on the Tear Film & Ocular Surface Society 2010: 46.
21. Bandamwar KL, Garrett Q, and Papas E. Superficial micropunctate corneal staining with fluorescein: what does it mean at a cellular level? Invest Ophthalmol Vis Sci 2011;52: e-abstract 6496.
22. Cira D, Peterson R, Postnikoff C, et al.. Ex vivo and in vitro investigation of diagnostic dyes fluorescein and lissamine green on human corneal epithelial cells. Contact Lens & Anterior Eye 2010;33(6): 280.
23. Gorbet M, Cira D, Luensmann D, et al.. The acute effect of benzalkonium chloride and sodium fluorescein on epithelial cells collected from the human ocular surface. Contact Lens & Ant Eye 2012;35S: e22.
24. Luensmann D, Moezzi A, et al.. Corneal staining and cell shedding during the development of solution-induced corneal staining. Optom Vis Sci 2012;89(6): 868-74.
25. Situ P, McCanna DJ, et al.. Confocal images of human corneal epithelial cells during and after contact lens wear. Invest Ophthalmol Vis Sci 2012;52: e-abstract 4698.