Title

Tools of the cornea specialist

Authors

Novack, Gary D

Mannis, Mark J

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BYLINE: GARY D. NOVACK, PHD[1,2] and MARK J. MANNIS, M.D.[1]

FOOTNOTES

From [1]Department of Ophthalmology & Visual Sciences, University of California, Davis and [2]PharmaLogic Development Inc., San Rafael CA.

Disclosure:

Gary D. Novack PhD consults with numerous pharmaceutical and medical device firms.

After tear duct surgery by an ophthalmic plastics specialist, a friend of mine had a cornea problem. She asked me to accompany her to a visit to a cornea specialist as a patient advocate. The specialist spent at least 30 minutes with my friend. Using a pen light and a slit lamp, the specialist diagnosed the problem and proposed therapy. I recall that a standard culture and sensitivity were also performed to define a possible infection.

Fortunately, the acute condition resolved with this therapy, although my friend now has chronic ocular surface disease. The specialist, who completed his fellowship at a premier academic department decades earlier, used a slit lamp and a pen light to make the clinical diagnosis. Standard microbiologic cultures would, presumably, pinpoint the pathogen, a maneuver that would help to modify the appropriate therapy.

My friend was pleased with this excellent care as well as the subsequent outcome. I was impressed with the time and obvious skill and experience of the specialist. Further, I realized that the instruments he used dated their origin to a previous century. That is, other than the extensive clinical experience of the specialist, everything used during that office visit was available to the specialist in his fellowship and well before that, in fact.

I contrasted this with examination of other ocular structures for other diseases. Examination of the retina today involves a host of imaging technologies in the diagnosis, treatment and the follow-up of patients. Examination for glaucoma uses not only automated perimeters, but also sophisticated imaging technologies. With the exception of confocal microscopy (to identify fungal or amoebic keratitis) and Polymerase Chain Reaction (PCR, for Herpes simplex), corneal specialists rely heavily on the clinical slit-lamp evaluation as well as standard culture and sensitivity data from specimen collection.

A similar theme was discussed by Russell van Gelder MD, PhD in his 2021 Jackson lecture as well as his American Ophthalmology Society thesis. He wrote: “If Edward Jackson, (who wrote a text in 1899)…were to watch an ophthalmologist in 2021 manage a corneal ulcer, he would feel immediately familiar with the process.”. Dr. van Gelder states that the Gram stain and blood agar plates, still used today, were well known in the late 1800’s. He then describes the Nobel

award-winning discovery of PCR and its use in contemporary medicine, and in particular, today's diagnosis of eye infections – in particular, epidemic keratoconjunctivitis and bacterial endophthalmitis.[1, 2]

The state of ocular examination by cornea specialists does not mean that therapeutics have stood still. In the current generation, several devices have been cleared by regulators for the diagnosis of tear film deficiencies. Moreover, numerous pharmaceutical and medical devices have been approved or cleared for the treatment of ocular surface disease (including meibomian gland disease). Still other therapies are used off-label or are derived from patients' serum.[3] Several useful symptom questionnaires have been developed and validated.[4, 5] And yet, ocular surface disease continues to be a prevalent disorder,[6] and every clinician has patients who are less than well served by today's therapies.

To date, the ocular signs used for approval of novel pharmaceutical agents are based upon "technologies" from the past – clinician judgement of corneal or conjunctival staining, Schirmer tests, etc. Many new systems are being developed, although they are of variable use in clinical medicine or in the development of novel therapies.[7] Indeed, the rapid proliferation of "point of care testing" will progressively objectify the clinical findings of the specialist in cornea and external disease.

However, we are still challenged in designing and conducting trials of novel therapies. Simply stated, quantification is challenging – a clinician's judgement at a slit-lamp is not like an automated sphygmomanometer. This leads to variability, requiring larger sample sizes to detect a given signal. Combined with the "vehicle" and "placebo" responses seen in clinical trials of novel agents in ocular surface disease,[8] this "signal-to-noise" issue means that clinical trials must have concurrent control groups, and samples sizes of at least 30 per group for adequate statistical detection power.[9] For the small firm trying to see if a novel therapy has enough efficacy to warrant development, this is a challenge.

Cornea and ocular surface disease clinics have been slower to adopt additional diagnostic measures and technologies compared to retina and glaucoma for instance where imaging is now

a standard part of most patient visits. Thus, we look to our colleagues in continuing methods for diagnosing the signs and symptoms of ocular surface disorders– both for better patient care as well as for the development of better tools to evaluate of novel therapies.

News from product related to the ocular surface

- Bausch +Lomb and Novaliq announced that the U.S. FDA accepted for review their New Drug Application (NDA) filing for investigational treatment NOV03 (perfluorohexyloctane) for the treatment of dry eye disease (September 2022).
- The U.S. FDA updated the guidance on generic cyclosporine ophthalmic emulsion (August 2022).

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