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Small drop delivers big advancement

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Tsontcho Sean Ianchulev, MD, MPH

Article

The piezo-print microdosing delivers drugs in less than 80 milliseconds, beating the eye's 100-millisecond reflex.


The piezo-print microdosing delivers drugs in less than 80 milliseconds, beating the eye's 100-millisecond reflex. (Photo courtesy of Eyenovia)

Piezo-print technology directs a precise stream of micro-droplets to the ocular surface-in less than a blink of an eye.

From my perspective, first as an ophthalmologist and as someone who has brought many innovative technologies into our field, I have come to realize how antiquated and inadequate is the existing paradigm of topical drug delivery.

There is virtually no other situation in medicine where physicians prescribe a therapeutic to patients knowing that, most of the time, they do not receive the correct dose. In the case of pills and injectable drugs, we know that if have prescribed 250 mg of Augmentin or 10 units of insulin, for example, and that is what the patient gets.

When clinicians prescribe one drop of timolol twice a day, however, studies have demonstrated that patients get a drop into their eye only about half the time. When they do manage to get drops in the eye, patients often administer between 2 and 7 drops, or a 100% to 600% overdose.[1–7] Much of this excess goes directly into the blood stream through nasolacrimal drainage, explaining not only the high incidence of ocular side effects, but in the case of cardiotropic drop therapies like beta-blockers, systemic ones as well (eg, slowing heart and respiratory rates).

Another concern patients have about their drops is the frequency with which they run out of their medication because of the overdosing. This concern has been voiced by consumer advocacy groups who say patients are paying too much for wasted medication. They make the case that companies have a responsibility to provide drugs in accurate dosing containers which can deliver smaller drops, precisely as prescribed. This was escalated recently all the way to the Supreme Court which refused to consider industry's appeal.[8]

Overdosing the eye

Even when a single drop is administered correctly, about half the time, the eye is overdosed by 300%. The eye contains about 6 to 7Î¼L of tear film and yet the legacy eye dropper-the mainstay of topical eye delivery for more than 100 years-dispenses about 30 Î¼L to 50 microliters depending the dropper. Hence, the patient receives more drug, and more preservative, leading to more adverse events. About half of glaucoma patients experience adverse events from their drops,[9] and only half are adherent to their therapy.[1–7]

Not only are the issues associated with drops a barrier to patients' compliance, they are a stumbling block new drugs must overcome in clinical trials. For example, recent trials have shown adverse events associated with otherwise promising news agents, which can obscure the medication's potential.

Precisely targeted

Novel high-precision microtherapeutic delivery technology is being developed to change the way drops are administered to the ocular surface. Previous attempts with sprays have been tried and failed, because aerosols are imprecise and liquid jet sprays are hard on the eye. Instead, this technology uses breakthrough piezoprint technology which creates a micronized droplet stream. Piezo-print technology is how inkjet printers revolutionized the print industry, by using its ability to delivery pixel-sharp fluid stream of droplets to create elaborate images. High-precision piezo-print microdosing technology is leading the way with what we believe can replace the century-year-old legacy eyedropper and dramatically improve the precision of topical drug delivery.

New technology is poised to help usher in next-generation micro-therapeutics that will result in more than an 80% reduction in the eye's in exposure to the preservative and drug. Piezoprint microdosing delivers drugs in less than 80 milliseconds, beating the eye's 100-millisecond blink reflex. The technology also integrates smart electronics, allowing for dose monitoring thus enhancing compliance and disease management in a whole new area of smart microtherapeutics.

Glaucoma, myopia, and in-office dilation

When considering the best place to go with this technology, glaucoma was the obvious choice: it is a blinding disease, compliance is a major problem, and patients take the drugs for life. It is further realized that there is no FDA approved therapy for chronic angle-closure glaucoma, which accounts for 10% and 50% of all glaucoma diagnoses in the United States and China, respectively.[10] This indication is being pursued for an underserved population, and then following with expanded indications in the larger glaucoma market.

There is also interest in progressive myopia, it is recognized as a growing epidemic: about one-third of all American and European adults are myopic.[11,12] Multiple randomized controlled Studies from academic collaborative groups have shown that atropine slows the development of myopia by 60% to 70%, and its use is supported by a position paper from the American Academy of Ophthalmology citing level 1 evidence.13 Yet, there is no FDA approved drug because atropine needs to be administered in very low doses to allow for tolerability due to its side effects. This is a perfect candidate for microdosing technology, and we are preparing to initiate a phase III program for FDA registration during the next 12 months. Microdosing and the use of smart technology is a great fit for this savvy patient population who are not receptive to legacy eye drop delivery.

Also being explored is MicroStat for pharmacologic mydriasis; it would be a potential first in-class fixed-combination microformulation of phenylephrine 2.5% and tropicamide 1%.

More than 80 million people a year receive dilated office exams[14] and they overwhelmingly complain, finding it very unfriendly, awkward, and uncomfortable. Current preparations essentially "overdose" the eye; MicroStat can deliver the same efficacy as the drop that overdoses by 300%.

Improving compliance, outcomes

Using smart technology to precisely deliver drug to the corneal surface and thereby minimizing adverse events will define a whole new generation of smart microtherapeutics. Microdosing can be applied to many existing ocular drugs that are associated with significant toxicity side effects (e.g., hyperemia, prostaglandin-associated periorbitopathy).

When drugs are delivered precisely, clinicians can improve compliance, which means more treatment effect and better patient outcomes will follow.

Smart technology can make this happen. Drug makers will benefit from better compliance with more prescribers and revenue. Everyone will be happier, including insurers. Drugs are approved for efficacy, but patients and insurers buy effectiveness, after discounting for poor compliance.

There is a huge gap between what is shown in a clinical trial and what happens in the real world. When people run out of their drops, that is not a part of the study.

The aim is to price microdose agents in line with what patients and insurers pay for today's branded medications-and to have technology adopted as widely as possible and improve as many lives as possible.

Disclosures:

Sean Ianchulev, MD, MPH
E: tianchul@yahoo.com
Dr. Ianchulev is professor of ophthalmology and director of innovation and technology at New York Eye and Ear Infirmary of Mount Sinai. Dr. Ianchulev reports he is founder of Eyenovia and Iantech Technologies; chairman of the board for Iantech Technologies and on the board of Eyenovia; and the CEO of Eyenovia.

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Contact Info

2 Clarke Drive
Cranbury, NJ 08512

609-716-7777

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