News
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***Acyclovir shows promise in treating ocular herpes

DALLAS--It is the leading cause of infectious corneal blindness in the United States. And in the world, it is second only to traucoma -- an inflammatory disorder affecting the mucous membrane lining the eyelids.

Epithelial herpes simplex keratitis, better known as ocular herpes, affects thousands of Americans. A progressive disease, it first attacks the epithelial or surface layer of the eye, later penetrating the inner tissues and attacking the deeper cornea. It becomes a blinding disease when corneal scarring occurs and is one of the primary reasons for corneal transplantation surgery in the United States.

Most cases of ocular herpes can be managed effectively with current drug therapy, says Dr. James P. McCulley, chairman of Ophthalmology at The University of Texas Health Science Center at Dallas. However, the treatments do produce undesirable side effects with prolonged use and success is limited when treating the more advanced stages of the disease.

Now, McCulley says, a new antiviral drug, Acyclovir, shows promise of overcoming many of these problems. This antiviral drug requires activation by herpes-infected cells and doesn't destroy normal cells like the other antivirals. It is also capable of penetrating to the inner tissues of the eye unlike the other drugs.

Acyclovir is also showing promise in treating other forms of herpes. At UTHSCD, another research study in the Infectious Disease Unit is studying the new drug's effectiveness against genital herpes. That study is headed by Dr. James Luby, director of the unit in Internal Medicine and is still in progress.

Working with five other medical centers, McCulley's recently completed study compares the new antiviral drug to idoxuridine (IDU), one of the drugs currently used to treat ocular herpes. He recently presented a paper on his work at the annual meeting of the American Academy of Ophthalmology in Atlanta.

In a double-masked study, two groups of patients (30 in the first group, 34 in the second) were treated with either Acyclovir ointment or IDU ointment for 14 days. In some cases, patients treated with Acyclovir healed faster. In all cases there were fewer side effects noted. There was no significant difference between the two groups in the frequency of development of deeper disease.

"Our study showed that, in terms of efficacy, Acyclovir is as effective as the currently available antivirals. It is also much less toxic." The study did not prove, McCulley said, that Acyclovir prevents or is an effective treatment for deeper disease. However, because it is known that the drug will penetrate to the deeper tissues of the eye and because it has been shown to suppress herpes virus, he believes this could someday be a possibility.

"With the other drugs we have no hope of reaching the deeper involvement of the disease."

McCulley also added that there are still many unanswered questions about the disease itself that complicate treatment.

"We know that ocular herpes can be either of the type one or type two strain. Type one is generally not sexually transmitted and can be spread from herpes fever blisters on the lips or from one individual to another just by the spray of the virus.

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"Type two, the genital strain, can be sexually transmitted by physical contact and tends to cause a more severe ocular disease." Symptoms of ocular herpes vary from patient to patient, McCulley said, but the classic signs are an inflamed, watering, red eye. With recurring attacks, the disease travels to the deeper tissues of the trigeminal ganglione or corneal nerve ending. The herpes virus destroys the normal sensation of the eye and discomfort lessens.

McCulley estimates that about a third to a half of the patients will develop deeper involvement.

"The surface disease is not a major problem in contrast to deeper involvement. We don't know for sure what the mechanisms in the deeper disease are. We think that, as the virus goes deeper into the eye, it replicates for a short period of time leaving behind a pool of viral antigen. The viral antigens are substances that induce certain inflammatory defense mechanisms in the body.

"We think it is this response that leads to tissue damage, scarring and decreased vision," McCulley said.

Currently the deeper inflammation is treated with topical steroids. But these drugs have a big drawback -- they potentiate the live viral disease on the eye surface should this be present or recur during treatment.

"We have to cover these patients with topical antivirals as long as they are on the steroids. The antivirals we now use will help prevent recurrence of the surface disease but not without associated toxic damage to the surface of the eye."

McCulley says the topical steroids could result in a minimally scarred cornea. Cataracts or steroid-induced glaucoma could also occur as side effects. Most of the side effects will disappear when the drugs are stopped so they are safe for short-term use. It is with long-term use that they become more damaging.

"The steroids will also decrease local defense mechanisms," McCulley added. "This leads to a greater risk for other ocular infections.

"Steriod therapy is not a very satisfactory treatment at all."

If Acyclovir does not prove directly beneficial in treating the deeper involvement of ocular herpes, McCulley feels it will at least be beneficial because it is less toxic when used in combination with steroids.

Other variables like the virulence of the virus and the patient's response to the drugs are also factors in successful treatment.

McCulley believes that further studies will show that the timing of ocular herpes treatment is also critical.

"A week of live viral replication gives the virus enough time to penetrate, replicate in the deeper tissues and set up an inflammatory response.

"If we can treat patients early -- within the first week of live viral replication -- and treat them with a penetrating antiviral like Acyclovir, we might be able to prevent deeper involvement altogether."

McCulley admits that how successful acyclovir will be at filling these needs is still a question. But he and other researchers are excited about the new drug's potential. "The way I look at it, Acyclovir may be somewhat analogous to events in the antibacteria era: We had sulfa drugs and then penicillin came along. Penicillin wasn't just another sulfa drug, it was a major advance.

"I think our currently used antivirals represent first generation antivirals and Acyclovir now represents a major leap forward -- because it is nontoxic and because it will penetrate.

"It offers great hope if we can discover how to use it effectively."

McCulley's research is supported by the Burroughs Wellcome Company. Other researchers and institutions contributing to the research are: Perry S. Binder, M.D., University of California at San Diego; Herbert E. Kaufman, M.D., Louisiana State University Medical School; Denis M. O'Day, M.D., Vanderbilt University School of Medicine and Robert H. Poirier, M.D., University of Texas Health Science Center at San Antonio.

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