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Pretreatment With Topical Capsaicin (0.25%) Does Not Prevent UV Light-induced Reactivation of Herpes Labialis(HL). J. Dumois, S. Straus, B. Savarese, C. Wohlenberg, A.L. Notkins, and J. Rooney*. NIDR and NIAID, NIH, Bethesda, MD, USA and Burroughs Wellcome Co., Research Triangle Park, NC, USA.

Capsaicin is a substance P inhibitor that induces topical analgesia and can prevent reactivation of latent herpes simplex virus(HIV) infection (HSV) in guinea pigs. We are studying the ability of topical capsaicin to prevent UV light-induced reactivation of HL. In a Phase I dose range-finding study, 15 patients with a history of HL applied either 0.025%, 0.1%, or 0.25% capsaicin cream to the lips 3 times daily for 3 days and rated levels of discomfort. The maximum tolerated dose was 0.25%. In a phase II uncontrolled pilot trial, 10 patients with a history of HL applied 0.25% capsaicin to the lips 3 times daily for 3 days and were then exposed to UV light of an intensity shown in our prior controlled study to reactivate HSV in 71% of subjects. One patient withdrew because of intolerance to medication. 5/9 patients(56%)developed a recurrence of HSV within 7 days. Although capsaicin did not appear effective in this study, preliminary evidence suggests that a greater analgesic effect can be achieved with a longer period of use; if tolerated, this may inhibit HSV recurrences.

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Evaluation of Retinal Toxicity and Efficacy of a Phosphorothioate Antisense Against Herpes Retinitis in a Rabbit Model.

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Phosphorothioate oligonucleotides have been shown to specifically inhibit gene expression in a variety of in vitro systems. Systemic delivery of oligonucleotides is currently impratical because of the cost of synthesis and capacity limitations of current synthesis protocols. In patients with retinitis, intravitreal delivery may be a practical route of administration. We therefore evaluated the retinal toxicity of ISIS 4015, a phosphorothioate oligonucleotide complementary to HSV RNA in fifteen New Zealand white rabbits. We injected four different doses intravitreally ranging from 3 μM to 320 μM (initial intravitreal concentration). Toxicity was assessed through electroretinography, clinical examination with slit lamp and indirect ophthalmoscopy and histologically with light and electron microscopy. Inflammation and outer retinal disorganization were seen. The highest dose found not to be toxic to the retina was 10 μM. We evaluated the drug's ability to treat HSV-1 retinitis in a rabbit model that we have previously described. Fifteen Dutch pigmented rabbits were used. All animals were pretreated one day before HSV-1 virus inoculation with 4015 at three different concentrations (3,10 and 32 μM) or ganciclovir 100 μg per eye. Both the 32 and 10 μM doses were effective in preventing HSV-1 retinitis, but inflammatory response in the vitreous was seen at the former higher concentration. The 3 μM dose and ganciclovir treatment did not prevent HSV retinitis. This represents the first successful treatment of retinal infection with a phosphorothioate oligonucleotide.

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