

SUPPORT DOCUMENT IV: Combining Antiviral Agents

There is insufficient evidence to conclude that the combination of two antiviral agents treats HSV epithelial keratitis more effectively than a single antiviral agent.¹⁻³

Topical acyclovir plus topical vidarabine performed as well as topical acyclovir alone for the treatment of dendritic HSV epithelial keratitis in one randomized double blind placebo controlled trial.² Oral acyclovir plus idoxuridine ointment healed ulcers more quickly than idoxuridine ointment alone in one clinical trial without randomization, masking, or placebo control.¹ In the HEDS Epithelial Keratitis trial, The HEDS Group aimed to evaluate the efficacy of oral acyclovir in preventing stromal keratitis or iritis in patients with HSV epithelial keratitis.³ In this study, patients with HSV epithelial keratitis were treated with topical trifluridine alone or in combination with a three week course of oral acyclovir 400 mg five times daily. A secondary outcome to this study (without statistical analysis) compared the ability of these two treatment modalities to resolve HSV epithelial keratitis. It appears that patients treated with topical trifluridine alone experience corneal ulcer healing just as quickly as patients treated with a combination of trifluridine solution and oral acyclovir. This was a secondary outcome to the study and lacked any statistical analysis making it difficult to assess the value of the observation. Additionally, the two aforementioned studies compared antiviral agents that are no longer used, idoxuridine¹ and vidarabine,² making it difficult to extrapolate to the antiviral agents used today; thus reducing the value of these results.

1. Srinivas C. Combination therapy of acyclovir and idurine in herpetic keratitis. *Afro-Asian Journal of Ophthalmology* 1993;12:336-7.
2. Colin J, Chastel C, Kaufman HE, Kissling GE. Combination therapy for dendritic keratitis with acyclovir and vidarabine. *J Ocul Pharmacol* 1987;3:39-42.
3. HEDS. A controlled trial of oral acyclovir for the prevention of stromal keratitis or iritis in patients with herpes simplex virus epithelial keratitis. The Epithelial Keratitis Trial. The Herpetic Eye Disease Study Group. *Arch Ophthalmol* 1997;115:703-12.