Systematic Review Snapshot

TAKE-HOME MESSAGE

Treatment of herpes simplex virus keratitis can be accomplished with either topical trifluridine or ganciclovir, which have similar efficacy. Oral acyclovir is an acceptable treatment option in cases for which compliance with a topical ophthalmic regimen may be of concern.

METHODS

DATA SOURCES

The authors searched more than 14 databases, as well as hand searched the older ophthalmologic literature. A search of gray literature was also conducted through multiple Web sites and reports made during meetings.

STUDY SELECTION

Studies were selected according to interventions for patients who had received a diagnosis of herpes simplex virus epithelial keratitis. Follow-up at 7 or 14 days after enrollment for evaluation of corneal healing was required.

DATA EXTRACTION AND SYNTHESIS

Data were extracted according to an intention-to-treat analysis whenever possible. Certain treatment groups were combined within studies to simplify the statistics, such as similar doses and procedures. The primary outcome was corneal healing. Heterogeneity was assessed through an inconsistency index. Results were summarized with relative risk (RR). Quality was assessed according to method of randomization, blinding, and the potential for forms of bias,

What Is the Most Effective Treatment of Herpes Simplex Keratitis?

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Results

Systematic review summary results for corneal healing.

Comparisons	RR (95% CI)	Number of Trials (Number of Patients)
Idoxuridine vs placebo	1.7 (1.0–2.9)	2 (63)
Vidarabine vs placebo	1.8 (1.1–3.0)	1 (43)
Interferon vs placebo	1.3 (1.1–1.6)	2 (110)

Two hundred eighty studies were found to be relevant, and ultimately, 116 were included in the analysis and review. Topical trifluridine, acyclovir, and ganciclovir were all shown to be equally effective compared with one another and more effective than idoxuridine. There was no difference in the effect size estimate for oral acyclovir versus topical treatments (RR 0.9; 95% confidence interval [CI] 0.8 to 1.1).[1] Similarly, there was no difference in the primary outcome between interferon treatment and antivirals (RR 1.2; 95% CI 0.9 to 1.6).

Commentary

It is estimated that herpes simplex virus keratitis has an incidence of approximately 12 to 31 people per 100,000 annually.[2,3] Although it is a relatively uncommon diagnosis in the emergency department setting, initiation of appropriate treatment is critical, given the potential to lead to serious visual impairment. There have been a number of treatments proposed for this ophthalmologic condition, and this comprehensive Cochrane review assessed both medical and surgical therapy. Avoiding topical steroids has been a principle of treatment during active herpes

including performance, attrition, and detection bias. Although plans for meta-analysis were in the protocol, the meta-analysis was limited to a small number of select studies because of substantial heterogeneity and exclusions because of high risk of bias for the primary outcome.

simplex virus infection of the ocular surface because of the risk of serious complications.[4]

Idoxuridine and vidarabine are earlier topical antiviral treatments for herpes simplex virus keratitis that have been demonstrated to be less effective than the newer topical antiviral agents (eg, trifluridine, ganciclovir). Oral acyclovir may be considered as a treatment option for patients for whom there is concern for compliance with the somewhat onerous eye drop protocol required. Although surgical debridement of the area plus a topical antiviral was demonstrated to be no more effective than a topical antiviral alone (RR 1.1; 95% CI 0.9 to 1.2), for patients for whom follow-up may be a problem, referral to an ophthalmologist for surgical debridement remains a valid treatment option.

Editor's Note: This is a clinical synopsis, a regular feature of the *Annals*' Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is:
Wilhelmus KR. Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev.* 2015;(1):CD002898. http://dx.doi.org/10.1002/14651858.CD002898.

1. Collum LM, McGettrick P, Akhtar J, et al. Oral acyclovir (Zovirax) in herpes simplex dendritic corneal ulceration. *Br J Ophthalmol*. 1986;70:435-438.
2. Labetoulle M, Auquier P, Conrad H, et al. Incidence of herpes simplex virus keratitis in France. *Ophthalmology*. 2005;112:888-895.
3. Young RC, Hodge DO, Liesegang TJ, et al. Incidence, recurrence, and outcomes of herpes simplex virus eye disease in Olmsted County, Minnesota, 1976-2007: the effect of oral antiviral prophylaxis. *Arch Ophthalmol*. 2010;128:1178-1183.
4. Williams HP, Falcon MG, Jones BR. Corticosteroids in the management of herpetic eye disease. *Trans Ophthalmol Soc U K*. 1977;97:341-344.

Michael Brown, MD, MSc, Alan Jones, MD, and David Newman, MD, serve as editors of the SRS series.