Herpetic Corneal Infections

the royal victorian eye and ear hospital

Disclaimer

SEE ALSO: Microbial Keratitis, Herpes Zoster Ophthalmicus

DESCRIPTION

Herpes Simplex Virus (HSV) is typically a unilateral disease that can affect all layers of the eye. HSV may manifest as blepharitis, follicular conjunctivitis, keratitis, keratouveitis or more rarely, retinitis and optic neuritis. A history of cold sores elsewhere may or may not be present.

Please note that this CPG is a guideline only. Evidence is lacking for some treatment options for herpetic eye diseases, and clinical judgment remains important.

HOW TO ASSESS

Red Flags:

- HSV keratitis can appear similar to other eye conditions – Herpes zoster, Acanthamoeba, topical medication toxicity, healing abrasions
- Topical steroids can significantly worsen epithelial disease
- Stromal disease in the presence of an epithelial defect runs the risk of corneal perforation
- Think of HSV in a patient with uveitis and raised intraocular pressure (IOP)

On History:

- Symptoms: redness, pain, photophobia, blurred vision
- May be a history of topical steroid use
- Past history:
  - Previous HSV infections (skin, eye etc)
  - Treatments used in the past e.g. antivirals

On Examination:

Eyelid and conjunctival disease

- Vesicles on skin, lid margin, or bulbar conjunctiva
- Unilateral blepharoconjunctivitis or follicular conjunctivitis
- Palpable pre-auricular lymph node

Corneal epithelial disease (due to actively replicating viral particles)

- Test corneal sensation prior to instillation of local anaesthetic
- Dendritic lesions – dichotomous branching with terminal bulbs; unifocal or multifocal
- Geographic lesions – sharply demarcated corneal ulcers with scalloped margins

Stromal disease (usually due to immune response to non-replicating viral particles)

- Test corneal sensation prior to instillation of local anaesthetic
- Immune stromal keratitis
    - Focal, multifocal, or diffuse stromal opacities +/- mild anterior chamber reaction
    - No epithelial defect
    - Possible partial or complete immune ring
    - Called interstitial keratitis if accompanied by deep corneal vessels. May have lipid deposition.
- Necrotising stromal keratitis
    - Corneal opacity in presence of an epithelial defect and stromal thinning
    - Difficult to distinguish from other forms of microbial keratitis
    - May lead to corneal perforation
    - Frequently a significant anterior uveitis, and/or trabeculitis leading to raised IOP

Endothelial Disease

- Disciform keratitis
    - Localised endothelial dysfunction causing disc-shaped area of corneal oedema
    - Minimal inflammation of stroma
    - Usually has focal keratic precipitates (KPs) underlying the oedema
- Iridocyclitis
    - Granulomatous uveitis or non granulomatous uveitis may accompany necrotising stromal keratitis (herpetic keratouveitis) or occur independently of corneal disease
    - Often associated with high IOP caused by trabeculitis
    - May have segmental iris atrophy or synechiae from previous episodes

On Investigation:

- Viral swab for HSV in all patients unless previous swab was positive. Gently wipe the cotton tip across the surface of an epithelial defect or, in the absence of epithelial disease sample the tear film from the inferior fornix.

ACUTE MANAGEMENT:

- HSV epithelial keratitis (live virus) should be treated with antiviral medication but not with steroids.
- HSV stromal, endothelial, or uveitic disease (little if any live virus) requires steroids and consideration of antiviral prophylaxis.

Epithelial Disease

- Gently debride epithelium with a cotton tip and prescribe topical antiviral (aciclovir eye ointment 5 times per day for 10 days).
- Oral antivirals (e.g. aciclovir* 400mg orally 5 times per day for 2 weeks) may be considered, although generally not necessary and not covered by pharmaceutical benefits scheme (PBS) for this indication.
- Avoid topical steroids.

HSV Stromal Disease and HSV Endothelial Disease

- Topical prednisolone acetate 1%/phenylephrine eye drops (Prednefrin Forte®) 2 hourly by day.
- Antiviral cover to reduce risk of reactivation of epithelial disease: aciclovir* 400mg orally BD OR topical aciclovir eye ointment 5 times per day.
- Topical prednisolone acetate 1%/phenylephrine eye drops (Prednefrin Forte®) to taper every 1-2 weeks according to clinical improvement. Some clinicians elect to taper topical aciclovir concurrently.
- Prophylactic antiviral should continue until steroid dose is less than the equivalent of prednisolone acetate 1% one drop per day.

Necrotic Stromal Disease

- Perform a corneal scrape to exclude microbial keratitis.
- Initiate treatment with oral aciclovir 400mg 5 x per day OR topical aciclovir 3% 5 x per day, and topical fluoroquinolone, e.g. ofloxacin 0.3% eye drops hourly, day and night for microbial keratitis. Review daily and modify treatment according to laboratory results and clinical response.
- Topical prednisolone acetate 1%/phenylephrine eye drops (Prednefrin Forte®) QID or similar may be commenced on confirmation of negative bacterial and fungal scrape.
- Corneal perforation should be referred immediately to the Corneal Fellow.

Iridocyclitis

- In the absence of necrotising disease, treatment is as per uveitis, with addition of IOP lowering medications as indicated.
- Prophylactic topical aciclovir 5 x per day should be considered.
- There is only weak evidence (HEDS, Herpetic Eye Disease Study) for benefit of oral aciclovir (400mg 5 times per day).
- In the presence of concurrent epithelial disease, this should be treated first, prior to considering the addition of topical steroids (usually at least 72 hours later).

  *Note: Valaciclovir can be used as an alternative treatment. Dosage is Valaciclovir 500mg BD as treatment dose or 500mg daily for prophylaxis.

FOLLOW UP:

Epithelial disease, stromal disease, or endothelial disease:

- Review day 7 - 10

Necrotising Stromal Disease

- Consider admission or daily outpatient review.
- Steroid eye drops should be tapered very slowly over 8-12 weeks and may need to continue indefinitely, depending on the degree of clinical improvement.
- Continue treatment dose of aciclovir* (400mg oral 5 x per day) for 7 days and then reduce to prophylactic dose (400mg oral BD) until steroid drops are once daily or less. If using topical aciclovir, some clinicians elect to taper this after 7 days.

Long term management

- Prophylactic (oral aciclovir* 400mg BD) is useful in patients who have multiple recurrences, those who have scarring close to the visual axis, those who are using topical corticosteroids for stromal disease or those who are immunocompromised.

DISCHARGE INSTRUCTIONS:

- Education regarding the risk of recurrence, the need to present early and to report history of viral disease.
- Education regarding dangers of self-medicating with topical steroid drops in the absence of specialist examination.

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Evidence Table

Author/s	Title	Source	Level of Evidence (I – VII)	Comments
Barron BA, Gee L, Hauck WW, et al.	Herpetic Eye Disease Study. A controlled trial of oral aciclovir for herpes simplex stromal keratitis.	Ophthalmology. 1994;101:1871-1882.	II	
Wilhelmus KR, Gee L, Hauck WW, et al.	Herpetic Eye Disease Study. A controlled trial of topical corticosteroids for herpes simplex stromal keratitis.	Ophthalmology. 1994;101:1883–1895; discussion 1895–1896.	II	
	External Disease and Cornea. Basic and Clinical Science Course, Section 8.	American Academy of Ophthalmology 2011-2012.	VII	

The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynk and Fineout-Overholt (2011).

I Evidence obtained from a systematic review of all relevant randomised control trials.

II Evidence obtained from at least one well designed randomised control trial.

III Evidence obtained from well-designed controlled trials without randomisation.

IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.

V Evidence obtained from systematic reviews of descriptive and qualitative studies.

VI Evidence obtained from single descriptive and qualitative studies.

VII Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology.

CPG Suite General Disclaimer

These CPGs were written for use in the RVEEH speciality Emergency Department. They should be used under the guidance of an ENT or Ophthalmology registrar, and certain medications / procedures should only be undertaken by speciality registrars.

If you require clinical advice, please contact our admitting officer for assistance:
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