OPTOMETRISTS AND DISPENSING OPTICIANS BOARD
Te Poari o ngā Kaimātai Whatu me ngā Kaiwahakarato Mōhiti

CONDITION: HERPES ZOSTER OPHTHALMICUS (HZO)

Description

Herpes zoster represents a reactivation of the varicella zoster virus (VZV) which leads to characteristic skin lesions and, in many cases, ocular complications. Age (usually over 60 years) is the most common risk factor for reactivation (Liesegang, 2008; Weinberg, 2007), but herpes zoster may be seen in younger patients especially those with HIV/AIDS or other forms of immunosuppression (Waife, 2003). The incidence of herpes zoster has been found to be increasing (Li, 2018).

Significance

The lifetime risk of herpes zoster is approximately 25%, which increases to 50% in patients more than 85 years of age (Johnson & McElhaney, 2009). Recurrent attacks of shingles occur in 4 to 7% of patients. It is important to remember that this inflammatory reaction can happen in almost all ocular tissues (from the skin of the eyelids to the cornea, conjunctiva, sclera, uvea, retina and optic nerve) (Liesegang, 2008) so the eye must be carefully inspected from lids to retina, with a special emphasis on IOP.

Incidence

Over 90% of 12-year-olds have been found to be seropositive for VZV (chicken pox virus) and this number increases to approximately 99% of 40 year olds. Herpes zoster affects 20-30% of the population at some point in their lifetime. Herpes zoster ophthalmicus (HZO) is defined as the involvement of the ophthalmic division of the fifth (trigeminal) cranial nerve, accounting for around 10-20% of herpes zoster cases Approximately half of these patients will develop ocular signs (Liesegang, 2008). Despite the name ‘ophthalmicus’ it is important to note that HZO can occur with or without ophthalmic involvement (Li, 2018).

Management Category

Optometric management to resolution is appropriate if there is isolated corneal involvement, episcleritis or anterior uveitis. The optometrist should undertake first aid measures and urgent referral to an ophthalmologist for patients with scleritis, raised intraocular pressure (IOP) or posterior segment involvement. All immunocompromised patients should be referred for ophthalmological consultation.

Signs and symptoms

Patients may report general malaise, tiredness and fever in the days preceding the appearance of the rash. Symptoms on the affected side of the face include pain or altered sensation.

1. **Skin lesions:**
   These are painful and appear as a unilateral red vesicular rash involving eyelids and forehead, which progresses to crusting over 2 to 3 weeks. Resolution of this rash often involves scarring. The presence of skin lesion(s) on the tip of the nose (Hutchinson's sign) is associated with twice the usual incidence of ocular complications, however, ocular manifestations are also seen in about 30% of patients who do not present with Hutchinson's sign.

2. **Ocular signs (Salmon, 2020):**
   a. Mucopurulent conjunctivitis – this can be follicular and/or papillary.
   b. Episcleritis.
   c. Scleritis (uncommon).
   d. Keratitis: All layers of the cornea can be affected. Punctate epitheliopathy is the most common sign (50% of cases), however HZO keratitis may also present as a pseudo-dendritic lesion (tapered ends without terminal bulbs), nummular keratits (granular subepithelial deposits with a halo of surrounding stromal haze), disciform lesions (less common than in herpes simplex), or endothelial changes with associated keratitic precipitates, up to one month following onset of skin lesions (Womack & Liesegang, 1983).
   e. Neurotrophic keratitis: because of decreased corneal sensitivity a neurotrophic ulcer can develop. All suspected cases of neurotrophic keratitis should be referred to a corneal specialist for further evaluation.
   f. Anterior uveitis is common.
   g. Posterior segment complications: optic neuritis, optic atrophy, retinitis, retinal necrosis, secondary glaucoma (due to trabeculitis). A dilated fundus examination is mandatory in all cases of suspected HZO.
   h. Nerve palsies: 3rd, 4th and 6th cranial nerve palsies are not uncommon.

   Post-herpetic neuralgia is the most common complication and occurs in approximately 30% of patients, and is chronic and severe in approximately 7% of patients. It is characterised by constant or intermittent, and usually severe, pain, burning or piercing pain that occurs almost daily (Womack & Liesegang, 1983).

Differential diagnosis

Ocular lesions should be differentiated from Herpes Simplex Keratitis / bacterial keratitis / acanthamoeba keratitis. Cutaneous skin lesions should be differentiated from cellulitis and contact dermatitis.

Management

The role of therapy is to reduce viral replication, control inflammation and prevent scarring. Specific goals are: to shorten the course of active disease; to provide analgesia; to prevent ocular and

systemic complications; and to decrease the incidence of post-herpetic neuralgia. The only way to achieve this is through early intervention with antiviral treatment.

1. **Oral Treatment**

Randomised controlled trials have shown that oral anti-viral drugs reduce virus shedding and accelerate resolution of symptoms (Cobo *et.al.,*n.d.; and Wood *et.al.,* 1996). Many studies have found oral acyclovir (as well as famciclovir (Tyring *et.al.,* 1995) and valacyclovir (valaciclovir) (Colin *et.al.,* 2000) started within 48-72 hours of rash onset to be safe and effective in treating active disease and preventing post-herpetic neuralgia (Harding & Porter, 1991). Early treatment with acyclovir reduces the prevalence of ocular complications from about 50% of patients with herpes zoster to 20-30%. Importantly, the earlier the treatment is started the better, (Cobo, 1988) and this is where optometric prescribing of oral acyclovir has its main potential advantage, i.e. reducing delay to treatment.

Currently, the Zoster Eye Disease Study (ZEDS), a double-masked, placebo-controlled, multicentre, randomised clinical trial, is investigating whether prolonged suppressive oral antiviral treatment (specifically with valacyclovir 1000 mg per day) reduces complications and improves clinical outcomes in HZO (in epithelial, stromal and endothelial keratitis, and iritis) in individuals without immune compromise. The secondary aim of the study is to determine whether antiviral treatment for 12 months (same dose as above) reduces duration or severity of post-herpetic neuralgia. The estimated study completion date is mid-2024 (clinicaltrials.gov).

The standard dosage of acyclovir for herpes zoster infections in adults is 800mg five times a day (at approximately 4 hourly intervals) (Huff *et.al.,* 1988). Treatment should continue for 7-14 days. It is largely well tolerated with few side effects, but caution is advised when administering acyclovir to patients with renal impairment and dosage may need to be reduced – these patients are best seen by an ophthalmologist or co-managed with an appropriate medical professional.

The standard treatment regimen for valacyclovir is 1000 mg, three times per day for 7-14 days, and for famciclovir, it is 500 mg per day for 7 days (Tyring *et.al.,* 2001). As with acyclovir, the dosage of valacyclovir will need to be adjusted in patients with renal impairment. Famciclovir is not subsidised in New Zealand (NZ Formulary accessed October 2021), and is indicated as a single treatment for genital herpetic disease.

2. **Topical Treatment**

- Ocular lubricants/artificial tears, topical NSAIDs.
- Topical corticosteroids (e.g. prednisolone acetate (Pred Forte®) 1% 4-6 times daily) along with cycloplegic agents (e.g. cyclopentolate 1%, 2 to 3 times daily) in cases of anterior uveitis or stromal keratitis (once HSV, bacterial and acanthamoeba keratitis have been ruled out). Refer if this is required as once started, corticosteroids usually need to be continued for many months, sometimes indefinitely, due to rebound inflammation on cessation.

3. **Review**

Patients should be reviewed every 1 to 5 days within an appropriate time frame to monitor IOP and inflammation risk factors, and for topical therapy to be adjusted where appropriate.

Referral criteria

1. All patients with renal impairment should be referred to or co-managed by an appropriate medical professional.
2. All immune-compromised patients should be referred for management by an ophthalmologist.
3. Patients with posterior segment involvement will require management with systemic (IV or oral) antivirals and steroids, and require urgent referral to a retinal specialist.
4. Oral steroids (prednisolone) have been shown to significantly shorten healing time and reduce symptoms in patients with moderate to severe pain (Huff *et.al.,* 1988). These patients should be referred to an appropriate medical practitioner for co-management of their condition.
5. Patients with elevated IOP/iridocyclitis require immediate referral for ophthalmological assessment.
6. Patients with moderate to severe post-herpetic neuralgia require referral to a pain management specialist (Huff *et.al.,* 1988).

Warnings and precautions

Acyclovir is eliminated by renal clearance and its dose should be modified for patients with renal impairment. All elderly patients are likely to have some degree of renal impairment and the need for dose reduction must be considered for this group of patients. Consultation with the patients General Practitioner is therefore recommended for elderly patients and those with potentially compromised renal function.

Acyclovir has been associated with reversible encephalopathic changes and should be used with caution in patients with neurological abnormalities.

Systemic dosing in rabbits, mice and rats did not produce embryotoxic to teratrogenic effects. There have been no human birth defects associated with acyclovir use, however, its use should only be considered when potential benefits outweigh the risks. Caution is advised in breast-feeding mothers as acyclovir has been detected in breast milk following oral administration.

Precautions for valacyclovir are similar to those listed for acyclovir above.

Side effects:

The most common side effects reported for both acyclovir and valacyclovir are: headache, dizziness, nausea, vomiting, diarrhoea and abdominal pain. Patients may also report pain, fever, pruritus, rashes and photo-sensitivity.

For a full list of side effects see:

http://www.medsafe.govt.nz/profs/datasheet/z/zoviraxtab.pdf

Informed consent

As with all healthcare interventions, the therapeutic optometrist is responsible for ensuring that the patient has been advised of the possible benefits and risks associated with the prescription medication, in order that the patient can make an informed decision and provide consent to the treatment plan.

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Please note: These guideline documents are not exhaustive and should be considered 'living' documents that will be added to over time. Conditions outside those described in these guidelines may be deemed out of scope for independent optometric management and require referral to a medical practitioner. If in doubt, please check with the Board for advice.

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