Sandwell and West Birmingham Hospitals NHS
NHS Trust

GUIDELINES FOR THE MANAGEMENT OF FUNGAL KERATITIS

Reference	SWBH/BMEC/Ophth/039
Category	Birmingham and Midland Eye Centre / Ophthalmology
Date Approved	23-05-2011
Date of Next Review	23-05-2014

POLICY PROFILE

Overview

Key overall purpose of policy	
Principal target audience	Ophthalmology clinical staff
Application	Trust wide
Accountable Executive Director	Clinical Director Ophthalmology Surgery B
Author(s)	Lead Ophthalmic Pharmacist
Impact Assessment	
Resource implications	
Training implications	
Communications implications	
Date of initial equality impact assessment	
Date of full equality impact assessment (if appropriate)	
NHSLA risk management standards/ CQC core standards	
Consultation and referencing	
Key stakeholders consulted/involved in the development of the policy	
Complementary Trust documents for cross reference	
Approvals and monitoring	
Approving body	Divisional Governance Group – Surgery B Drugs and Therapeutic Committee
Date of implementation	23-05-2011
Monitoring and audit	

DOCUMENT CONTROL AND HISTORY				
Version No	**Date Approved**	**Date of Implementation**	**Next Review Date**	**Reason for Change** **e.g. full rewrite, amendment to reflect new legislation, updated flowchart, etc.**
1	23-05-2011	23-05-2011	23-05-2014	

1.0 Background

Fungal infection of the cornea is rare and is usually seen in the context of trauma (frequently organic in nature), tissue devitalization, or immunosuppression, including topical corticosteroid use. Other predisposing factors include a hot humid climate, agricultural work, dry eye or a neurotrophic cornea. Fungal infective agents can be divided into moulds (filamentary fungi) and yeasts. Of the former, *Fusarium* and *Aspergillus* commonly infect the cornea, and of the latter, *Candida* is a common infective organism.

2.0 Clinical Signs

In the case of yeast infections, the corneal involvement is often localized, with a 'button' appearance, an expanding stromal infiltrate and relatively small epithelial ulceration. Filamentary fungal infections initially produce a feathery, branching pattern. A severe anterior uveitis and hypopyon may develop. As the condition progresses, the characteristic patterns may disappear, and the appearance closely resembles an advanced bacterial keratitis.

3.0 Management

All patients suspected of microbial keratitis should have a proper corneal scrape for full microbiological analysis, including urgent Gram stain. This should include bacterial, fungal and viral isolation (*Herpes simplex*) and special media for *Acanthamoeba* if clinically indicated. See protocol for corneal scrapes.

A careful history should be taken to exclude systemic disease, e.g. autoimmune disease, immunosuppression (spontaneous or iatrogenic) or evidence of other opportunistic infection. Consider systemic work-up: FBC, U+Es, LFTs, vasculitic screen, blood cultures if pyrexial, CXR and ECG.

Most patients with severe microbial keratitis need admission to hospital for intensive antimicrobial treatment. Some mild cases can be managed as an outpatient. The decision on whether to admit or not must be left to clinical judgement of the managing doctor.

As soon as relevant specimens have been taken, intensive topical therapy should be prescribed on the in-patient prescription chart:

3.1 Topical therapy

- Patients should be treated initially empirically with econazole 1% eye drops preservative-free, given hourly day and night for the first 24–48 hours. If

there is no response to econazole then non-formulary drugs may have to be used. Authorisation for the use of a non-formulary drug is obtained by contacting an officer of the Drug & Therapeutics committee.

- If the patient has existing ocular surface disease, amphotericin 0.15% eye drops preservative-free (non-formulary) may be used.

  NB. Amphotericin 0.15% eye drops preservative-free are available from Moorfields Pharmaceuticals who prepare them one weekly on a Wednesday and delivered on a Thursday. Orders must be received by Thursday of the previous week for a Thursday delivery.

  (Voriconazole eye drops 1% (non-formulary) have been used in the treatment of fungal keratitis, often with good effect. It is however not routinely available. Therefore, with Consultant permission, enquiries regarding availability should be made to pharmacy)

- Cycloplegic drops should be given: atropine 1% eye drops twice daily or cyclopentolate 1% eye drops twice daily.

- Topical steroids should be added at the discretion of a senior Ophthalmologist – usually starting 48 hours after topical antifungal therapy: dexamethasone sodium phosphate 0.1% eye drops preservative-free, one drop daily.

3.2 Intraocular therapy

Intracameral amphotericin (10 micrograms in 0.1 ml) may be given in cases where treatment response is poor, particularly in the presence of a hypopyon. This should be performed after an anterior chamber washout, with the washings being sent for microbial culture.

Where a secondary endophthalmitis develops, intravitreal amphotericin (5–10 micrograms in 0.1 ml) may be given, preceded by a vitreous biopsy where possible.

In cases of resistance to amphotericin, voriconazole may be used at a dose of 10 to 50 micrograms in 0.1ml (non-formulary) for both intracameral and intravitreal injection. Contact Microbiology for advice.

Intrastromal voriconazole 50 micrograms in 0.1ml (non-formulary). has been used in resistant cases.

3.3 Systemic treatment

This is not obligatory, but should be strongly considered for cases of secondary endophthalmitis and penetrating keratomycosis, and given in addition to topical therapy. Adjunctive systemic therapy should be considered in all immunosuppressed hosts. It should be given in liaison with

microbiologists and physicians. Liver & renal function must be monitored before and during treatment.

3.3.1 Yeast infection

Oral fluconazole should be given for 7–14 days where candidal infection is suspected or proven. A dosage of 50–100mg daily is required for those with a keratitis who are immunosuppressed. Where a secondary endophthalmitis is present, 200–400mg should be given. Liver function must be monitored before and during treatment, on a weekly basis.

Intravenous flucytosine (non-formulary) may be considered for invasive yeast infections, at a dosage of 200 mg/kg daily in 4 divided doses, for no more than 7 days. Contact Microbiology re plasma concentration monitoring.

3.3.2 Mould infection

Voriconazole is first-line systemic treatment for mould infections, Contact microbiology before using it. Voriconazole is also indicated for fluconazole-resistant *Candida* spp. For patients > 40 kg body weight this may be given orally (400 mg twice daily for 2 doses, then 200 mg twice daily, increasing if required to 300 mg twice daily), or intravenously (6 mg/kg twice daily for 2 doses, then 4 mg/kg twice daily). Children 2–12 years, oral (suspension recommended – the suspension is non-formulary) 200 mg every 12 hours; intravenous - 7 mg/kg every 12 hours (reduced to 4 mg/kg every 12 hours if not tolerated).

3.4 Antifungal therapy in pregnancy and lactation

Topical administration of econazole, amphotericin and voriconazole is not considered to be harmful in pregnant and lactating women. There are however contraindications to the use of systemic antifungal therapy in pregnancy and lactation. It is therefore imperative to contact the Microbiologists before starting systemic therapy for this patient group.

Flowchart for the Management of Fungal Keratitis

Suspect Fungal Keratitis if risk factors

Ocular trauma (organic)
Immunosuppression
Ocular surface disease
Dry Eyes

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Take a detailed history

Check for systemic disease
Immunosuppression (topical steroid use)
Other opportunistic infections

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Undertake slit-lamp examination for clinical signs suggestive of fungal keratitis

Corneal epithelial defect + stromal infiltrates with feathery branching pattern
Satellite lesions
Hypopyon

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Perform early and adequate corneal scrapes

Urgent Gram stain
Culture for bacteria, fungus and virus (HSV)
Culture for *Acanthamoeba* if clinical suspicion

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Admit patient and fill in-patient chart for intensive topical treatment

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Consider systemic work-up

Check for diabetes
FBC, U&E, LFT

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Topical *antifungal* therapy
Initial treatment

Econazole 1% pres free eye drops hourly day and night for 48 hrs + atropine 1% eye drops or cyclopentolate 1% eye drops twice daily

If co-existing ocular surface disease

Replace econazole with amphotericin 0.15% pres free eye drops hourly (non-formulary – obtain authorisation from DTC)

Treatment required for many weeks and tapered based on clinical response

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If response to treatment is poor

Consider voriconazole 1% eye drops (non-formulary)

Consider anterior chamber washout + **intracameral** amphotericin injection (10 micrograms in 0.1 ml). Send the washout for culture

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If resistance to Amphotericin

Consider **intracameral** voriconazole injection (10 to 50 micrograms in 0.1 ml) (non-formulary)

Consider **intrastromal** voriconazole injection (50 micrograms in 0.1 ml) (non-formulary)

If secondary endophthalmitis

Consider vitreous biopsy + **intravitreal** amphotericin injection (5 to 10 micrograms in 0.1 ml)

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Adjunctive systemic antifungal treatment

In cases of secondary endophthalmitis, penetrating keratomycosis and immunosuppressed patients.
Liaise with Microbiologist and Physician
Monitor liver and renal function

1. For yeast infection

Oral fluconazole for 7-14 days:
Immunosuppressed patients (50 to 100 mg daily)
Secondary endophthalmitis (400mg daily)

Intravenous flucytosine (non-formulary) for up to 7 days:
Penetrating keratomycosis (200 mg/kg daily in 4 divided doses)
Monitor plasma concentrations

2. For filamentous infections (Moulds)

Patients >40 kg
Oral voriconazole**: (**400 mg twice daily for 2 doses, then 200 mg twice daily, increasing to 300 mg twice daily) OR
Intravenous voriconazole: (6 mg/kg bd for 2 doses, then 4 mg/kg twice daily)

Children 2 to 12 years:
Oral voriconazole (suspension): (200 mg twice daily)
Intravenous voriconazole: (7 mg/kg every 12 hours, reduced to 4 mg/kg every 12 hours if not tolerated)

Guidelines for the management of fungal keratitis