Waikato District Health Board

Guideline

Candida infections and antifungal treatment in the newborn unit

Guideline Responsibilities and Authorisation

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Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
1	Catherine Dommett	March 2022	New guideline

Candida infections and antifungal treatment in the newborn unit

Contents

Candida infections and antifungal treatment in the newborn unit

1 Overview

1.1 Purpose

- To identify patients in the newborn unit at risk of fungal infection prompting further investigation.
- To inform treatment of invasive fungal infections in the neonate.
- To inform when to give prophylactic antifungal treatment.

1.2 Scope

Waikato District Health Board (DHB) staff working in Neonatal Intensive Care Unit (NICU): Consultants, Registrars, Neonatal Nurse Practitioners (NNP) & Neonatal Nurse Specialists (NNS), Registered Nurses (RN).

1.3 Patient / client group

Neonates at risk of fungal infection and those with suspected or proven fungal infections.

1.4 Definitions and acronyms

Invasive candidiasis	Systemic infection with candida species
NEC	Necrotising Enterocolitis
VLBW	Very low birth weight <1500g

2 Clinical management

Proven fungal infection

2.1 Oral candidiasis (thrush)

- Treatment is with topical (not nasogastric) nystatin to the oral mucosa at a dose of 1ml Q6H for 7 days or 48 hours after lesions disappear whichever is the longer. (See Nystatin oral liquid for neonates drug guideline).
- Observe closely for evidence of systemic candidiasis and investigate and treat as appropriate

2.2 Candida Dermatitis

- Generally in the nappy area
- Swab the area, then topical miconazole if well and not at high risk of invasive candidiasis
- See Prevention and Treatment of Nappy Rash in the Neonatal Intensive Care Unit (NICU) drug guideline

2.3 Invasive candida dermatitis

- A condition unique to VLBW infants. There is a variable appearance of lesions typically in intertriginous areas but these may be more widespread.
- Presents in the first 14 days after birth.
- Commonly becomes invasive so blood cultures must be performed.
- Treat with IV fluconazole.
- If blood cultures positive, investigate and treat as invasive candidiasis, refer to 3.5 for relevant investigations

2.4 Congenital candidiasis

Presents at or shortly after birth with a generalised eruption of 2-4mm papules with an erythematous base. The rash may be atypical in preterm infants. There may be associated oral thrush.

Increased risk in prolonged rupture of membranes or known maternal vaginal candidiasis.

Take skin swabs of the lesions, blood cultures, urine and cerebrospinal fluid (CSF) cultures if suspected.

May be treated with oral fluconazole in the well, term infant who is tolerating feeds, otherwise use IV fluconazole.

2.5 Invasive candidiasis

Generally late onset sepsis

Increased risk in extremely low birth weight infants (<1000g), broad spectrum antibiotic use, central venous access device (CVAD) access, parenteral nutrition, candida colonisation, NEC or previous abdominal surgery, intubated babies or postnatal steroid treatment.

Potential sites of infection: skin, central nervous system (CNS), liver, spleen, urinary tract, bone, eyes

Consider if signs of infection and instability not improving despite appropriate antibiotics, thrombocytopenia, hyperglycaemia and metabolic acidosis.

2.5.1 Investigations

Send blood culture, CSF and urine for culture, review sensitivities to determine treatment

Poor sensitivity on blood culture therefore may need to take further cultures if clinical suspicion remains and initial culture is negative

U+Es, LFTs, CBC at the start of suspected infection and monitor throughout infection

Swabs of any oral or skin lesions – (full examination of skin and mucocutaneous sites)

2.5.2 Treatment

- Remove any potential source of infection e.g. central lines, urinary catheters, endotracheal tubes if able.
- Fluconazole is often used instead of amphotericin B conventional for treatment of invasive neonatal candida infections because of its effectiveness and low incidence of side effects.
- Treat with maximal dose IV fluconazole, providing:
  - no prior exposure to fluconazole and
  - isolate is not one with predictable/likely fluconazole resistance (C.krusei/C.glabrata)
- Alternatively, commence IV amphotericin if confirmed candida infection or if high suspicion in a high risk patient as above (See Amphotericin B Liposomal (AmBisome) for neonates and Amphotericin B Deoxycholate (Conventional) for neonates drug guidelines).
- Amphotericin liposomal has theoretical risk of poorer renal tract penetration than amphotericin conventional.
- In renal infection and CNS infection amphotericin B Conventional is preferable to amphotericin B liposomal (See Amphotericin B Liposomal (AmBisome) for neonates drug guideline). In renal impairment or adverse drug effects amphotericin B (liposomal) is preferred.
- Review sensitivities once available, and use caspofungin for salvage therapy.

2.5.3 Length of treatment

- 14 days post negative culture in systemic infection
- 3 weeks in CNS infection
- 4-6 weeks of treatment may be recommended for focal infection of the eyes, heart, liver, kidney, spleen or bones. - Discuss with the Paediatric Infectious diseases team at Starship as a combination therapy with 5-flucytosine and amphotericin Liposomal may be beneficial.

2.5.4 Follow up

- Repeat cultures (blood, urine, CSF) after 2-3 days to assess for clearance
- If still infected, consider:
  - Eye examination
  - USS kidney, head, liver, spleen
  - Scan for osteomyelitis/ septic arthritis
  - Echocardiogram
- Please note advice for adverse effects monitoring during treatment within this guideline.

2.6 Candida Urinary Tract Infection

- Fluconazole is particularly useful for urinary tract infections, obtaining high concentrations in the urine. A loading dose should be given to obtain therapeutic serum concentrations in a timely manner.

2.7 Other non-candida fungal infection

- These are less common but do occur with species such as aspergillosis, cutaneous and intestinal zygomycosis, Malasseziasepsis, trichosporonosis, Pichia sepsis, cryptococcosis, coccidioidomycosis, blastomycosis, and dermatophytosis.
- These cases should be discussed with paediatric infectious disease team. Treatment should be based on results of cultures and sensitivities. If sensitivities are uncertain, treatment should be commenced with amphotericin conventional (See Amphotericin B Deoxycholate (Conventional) for neonates drug guideline).

3 Summary of Treatment Options

• Condition	• Recommended first treatment choice
• Oral candidiasis	• nystatin
• Candida dermatitis	• Topical miconazole
• Invasive candida dermatitis	• fluconazole
• Congential candida dermatitis	• fluconazole
• Invasive candidiasis	• fluconazole • - if no prior exposure • - if not C. krusei / C. glabrata • amphotericin conventional / amphotericin liposomal
• Invasive candidiasis with focal infection	• 5-flucytosine plus amphotericin liposomal
• Renal infection, CNS and side effects/intolerance	• amphotericin conventional better than amphotericin liposomal
• Candida UTI	• fluconazole
• Non-candida / mould	• amphotericin conventional – discuss with Paediatric Infectious Diseases team

4 Prophylaxis of fungal infection in babies at risk of systemic candidiasis:

- All premature infants <30/40 commenced on broad spectrum antibiotics should also be commenced on prophylactic nystatin cover.
- Also consider this in infants with a gestational age >30/40 who require >36 hours of antibiotics.
- All patients on long term parenteral nutrition who are eligible for the National Intestinal Failure Service (NIFS) registry (>30days IVN if GA<34/40; >20days IVN if GA≥34/40)

This is at a dose of 0.25 ml PO (not NG) Q6H and should continue for the duration of antibiotic treatment or while on parenteral nutrition (See Nystatin oral liquid for neonates drug guideline).

5 Evidence base

5.1 Bibliography

- UpToDate: Epidemiology and risk factors for Candida Infection in Neonates, 2019. Available from https://www.uptodate.com/contents/epidemiology-and-risk-factors-for-candida-infection-in-neonates
- UpToDate: Clinical Manifestations and diagnosis of Candida Infection in Neonates, 2021. Available from https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-candida-infection-in-neonates
- UpToDate: Treatment of Candida infection in Neonates, 2018. Available from https://www.uptodate.com/contents/treatment-of-candida-infection-in-neonates
- UpToDate: Unusual Fungal Infections in the Neonate, 2021. Available from https://www.uptodate.com/contents/unusual-fungal-infections-in-the-neonate
- Kaufman, DA. 2020. Fungal Infections in Preterm Infants. Medscape. Accessed from https://emedicine.medscape.com/article/980487-overview

5.2 Associated Waikato DHB Documents

- Nystatin Oral Liquid for neonates drug guideline (Ref. 6443)
- Prevention and Treatment of Nappy Rash in the Neonatal Intensive Care Unit (NICU) drug guideline (Ref. 2836)
- Amphotericin B Deoxycholate (Conventional) for neonates drug guideline (Ref. 0570)
- Amphotericin B Liposomal (AmBisome) for neonates drug guideline (Ref. 2901)