FUNGAL INFECTIONS IN NEONATES

Introduction
- Newborn infants are susceptible to invasive fungal infections (IFI) secondary to relative immunodeficiency.
- Colonisation is common (27% in VLBW) and mucocutaneous infection is common in those colonised with Candida (nearly 1/3rd).
- Incidence of IFI in the UK: 2.1% babies < 1000 g, 1% in babies < 1500 g, 0.6% > 2500 g, have high mortality (untreated 80%, treated 20-50%).
- Candida albicans and candida parapsilosis are the predominant candida species responsible for candidial infection in neonates. Candida albicans infection has more mortality than candida parapsilosis.

General Considerations

Congenital Infection:
- Intrauterine devices and cervical suture increase the risk.
- Mucocutaneous involvement often with pneumonia.
- Blood cultures are usually negative but gastric aspirates /skin swabs positive.
- Treat with Amphotericin and Flucytosine as below.

Acquired Systemic Infection:
- Preceding mucocutaneous candidiasis common (50%).
- Increased risk (cumulative), if VLBW (<1500 g), prolonged antibiotic therapy (especially 3rd generation cephalosporins), lack of enteral feeds (by day 3 of life), indwelling central catheters, endotracheal tubes, ventriculoperitoneal shunts.
- Systemic Candidiasis is usually late onset infection, highest risk from the end of first week into third month of life.
- Presentation similar to any sepsis, clinical features non-specific, can mimic NEC. Can have pneumonia, septicaemia, endocarditis, septic arthritis, osteomyelitis, endophthalmitis, intraperitoneal infections, liver abscess, meningitis, UTI.

Diagnosis:
- Thrombocytopenia is almost invariable feature but not diagnostic.
- Hyperthermia is a significant presenting feature of invasive fungal infection.
- Candida may grow slowly in culture contributing to the delay in the diagnosis.
- Once the diagnosis of invasive candida infection is suspected or confirmed, investigations for signs of dissemination must be undertaken (direct ophthalmologic examination, abdominal ultrasound, ECHO and neuroimaging).

Prevention:

Non-pharmacological:
- Early extubation, early enteral feeding and removal of central lines.
- Limit exposure to broad spectrum antimicrobial therapy.

Pharmacological:
- Prophylaxis reduces colonisation and infection.
- Prophylaxis with Fluconazole 3 mg/kg reduces in infants < 1500 g risk of invasive fungal infection by 90%, mortality by 24% and mortality attributable to candida species by 95%. No change in resistance patterns observed.
- Prophylaxis to be continued until no risk factors.
- Contraindications: ALT and AST > 150 IU/L, direct Hyperbilirubinemia.
Treatment:

**Mucocutaneous candidiasis:**
- Topical Clotrimazole 1% and enteral Nystatin suspension (neonatal formulary).

**Systemic candidiasis:**
- Test liposomal Amphotericin for anaphylaxis.
- For suspected infection use liposomal Amphotericin alone.
- For proven infection use liposomal Amphotericin and Flucytosine together.
- Percutaneous long line may be required for prolonged Amphotericin therapy.
- Duration of treatment for proven infection 3 - 4 weeks.
- Monitor for bone marrow suppression and liver damage weekly.
- Consider Fluconazole for renal Candidiasis.
Flowchart for Targeted Fungal Prophylaxis

- < 27 weeks CGA
- Birth weight < 750 g
- Neutropaenia (< 1000/microliter)

**Risk Factors:**
- Antibiotics > 5 days
- UAC/UVC/LL > 7 days
- Not on full enteral feeds by 2 weeks of age

- < 33 weeks CGA

- Antibiotics after first 48 h of life

- NEC or peritonitis
- Planned antibiotic treatment for ≥ 7 days

- Fluconazole (i.v./p.o.)
- Clotrimazole 1 % (topical)

- Nystatin (p.o.)
- Clotrimazole 1 % (topical)

- No prophylaxis