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Antimicrobial Management of Febrile Neutropenic Sepsis

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Date: August 2018

Approved by: Drugs & Therapeutics Committee
Date: October 2018

Implementation Date: November 2018

For Review: November 2020

Antimicrobial Management of Febrile Neutropenic Sepsis

[Read in conjunction with PAT/EC 5 Febrile Neutropenic Patients Management Guidelines]

Diagnosis of neutropenic sepsis (as per NICE guidelines Sept 2012) is patients having anticancer treatment whose neutrophil count is 0.5 x 10^9 /L or lower and who have either a temperature higher than 38^0C OR other signs or symptoms consistent with clinically significant sepsis.

This trust guideline includes patient with the above diagnosis and also includes patients who have a low neutrophil count of between 0.5 and 1.0 x 10^9/L, recent chemotherapy, a temperature of higher than 38^0C and clinically septic

***Table I*:** Details the first line, second line antibiotic therapy and antifungal therapy. Also see flowchart.

First line antibiotic should be commenced within one hour in patients with sepsis – see sepsis IPOC

***Table II*:** Prophylactic antiviral, antifungal and antibacterial therapy

The initial management should involve a thorough investigation looking for a source for sepsis and include the following:

- Detail history and examination
- Clinical examination to include skin, mouth, web-spaces , peri-anal area, Hickman line site, chest and abdomen
- Blood cultures – taken from the long line (through each lumen) and Peripheral cultures

- MSU
- Swab from Hickman site/skin lesions/mouth
- Faeces
- CXR – if clinically indicated

} If clinically indicated

- FBC, U/E, CRP, liver function and Lactate
- During the Flu season – all patients admitted with a temperature should have a throat swab sent for respiratory virus
- If a bronchoscopy is performed then send BAL sample for : routine culture and sensitivity, AFB, PCP, respiratory viruses and fungal culture

Table I :	Category		
	Neutrophil count ≤0.5 x 10^9/L **AND** Having anticancer treatment **AND** Temperature higher than 38 ^{0}**C OR** other signs and symptoms consistent with clinical sepsis	Neutrophil count of between 0.5 and 1.0 x 10^9/L **AND** Chemotherapy in the preceding 6 weeks **AND** Temperature greater than 38^{0}C Clinical sepsis, no obvious focus of infection	Neutrophil count of between 0.5 and 1.0 x 10^9/L **AND** Chemotherapy in the preceding 6 weeks, **AND** Temperature greater than 38^{0}C Clinically well
FIRST LINE ANTIBIOTIC THERAPY	IV Piperacillin/Tazobactam 4.5g 6hourly **Renal Impairment**: if CrCl≤40mls/min refer to pharmacy for dosing advice **Oral switch**: Co-amoxiclav 625mg 8hourly		Oral Co-amoxiclav 625mg 8hourly for 5 days
Non life -threatening penicillin allergy	IV Meropenem 1g 8 hourly **Renal Impairment**: if CrCl ≤50mls/min, refer to pharmacy for dosing advice		Oral Cefaclor 500mg tds + Metronidazole 400mg tds for 5 days
Life-threatening allergy to penicillin	IV Ciprofloxacin 400mg bd **AND** IV Teicoplanin 400mg 12-hourly for the first 3 doses, then 400mg once daily **Renal Impairment:** CrCl ≤80mls/min refer to pharmacy for dosing advice		Oral Levofloxacin 500mg bd for 5 days
MRSA positive swab **OR** **High suspicion of catheter related infection**	**ADD** IV Teicoplanin 400mg 12-hourly for the first 3 doses, then 400mg once daily (**unless already on Teicoplanin**) **Renal Impairment:** CrCl ≤80mls/min refer to pharmacy for dosing advice		
SECOND LINE	If the temperature persists at 48hrs but the patient remains clinically stable with no clinical deterioration then continue with the same antibiotic for another 24 hours. If temperature settles with 48-72hours – then stop antibiotics at 5 days If clinical deterioration at 48 hours or patient remain pyrexial at 72 hrs of 1st line therapy then switch to second line therapy		
Antibiotic therapy	IV Meropenem 1g 8 hourly (if had Piperacillin/Tazobactam first line). **Following all other first line regimes, discuss with Microbiologist.** **Renal Impairment**: if CrCl ≤50mls/min, refer to pharmacy for dosing advice		

THIRD LINE	If temperature persists and patient continues to deteriorate after a total of 5 days of antibiotic therapy, repeat examination and investigate **OR** Where antifungal therapy is necessary because of possible invasive fungal infection THEN consider antifungal therapy Patients not responding to first line anti-fungal agents should be investigated for invasive aspergillosis • Bronchoalveolar lavage • galactomannan enzyme assay • HRCT – halo sign and air-crescent sign • Transthoracic percutaneous biopsy	
Antifungal therapy	Caspofungin 70mg loading dose , then 50mg once daily if <79kg or 70mg once daily if >80kg Administered by slow intravenous infusion over approximately one hour. No dosage adjustment is necessary in renal impairment	
Invasive aspergillosis suspected	Voriconazole IV 6mg/kg every 12 hours for 2 doses, then 4mg/kg every 12 hours (Renal Impairment: if CrCl ≤50mls/min, refer to pharmacy for dosing advice) **OR** Voriconazole orally 400mg every 12 hours for 2 doses, then 200mg every 12 hours	
Antiviral therapy	**Agent**	**Comments**
Suspected herpes simplex virus lesions	IV Aciclovir 5mg/kg 8-hourly **Renal Impairment**: if CrCl ≤50mls/min, refer to pharmacy for dosing advice	Send swab in viral transport medium Use IBW for dosing if overweight (i.e. if >20% above IBW)
Suspected varicella-zoster virus (chickenpox/shingles) infection	Aciclovir 10mg/kg 8-hourly by IV infusion **Renal Impairment**: if CrCl ≤50mls/min, refer to pharmacy for dosing advice	Use IBW for dosing if overweight (i.e. if >20% above IBW) Exposure to chickenpox/shingles – see Policy for management of chickenpox/shingles PAT/IC 15 v2

Comments

Suspected CMV infection- discuss investigation with Microbiologist

If RSV positive consider treatment with aerosolised Ribavirin

Table II : PROPHYLAXIS			
		AGENT	**CAUTION**
AML patients and Myelodysplastic Syndrome receiving intensive chemotherapy	**First line**	Posaconazole 100mg tablets **Dose:** 300mg TWICE daily on first day then 300mg daily thereafter	Duration of therapy is based on recovery from neutropenia or immunosuppression. For patients with acute myelogenous leukemia or myelodysplastic syndromes, prophylaxis with posaconazole should start several days before the anticipated onset of neutropenia and continue for 7 days after the neutrophil count rises above 500 cells per mm3.
	Second line (if patient not tolerating the tablets)	Posaconazole suspension 200mg/5ml **Dose:** 200mg THREE times daily The syrup should ideally be taken with food to increase absorption	
Haematological malignancy where patients are receiving severely immunosuppressive chemotherapy		Oral Aciclovir 400mg 12 hourly OR 200mg 6 hourly	
AML patients receiving intensive chemotherapy with neutrophil count of 0.5 x 10^9/L or less and continue until resolution of neutropenia		Oral Ciprofloxacin 500mg 12hourly	High risk of *Clostridium difficle* infection - if diarrhoea develops consider stopping

Fig 1. Flow chart for first and second line antimicrobial management of febrile neutropenic sepsis