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The Union of Myanmar, SR(1) Department of Health

Infective Endocarditis

Standard Operating Procedure (SOP)

Contents

Infective Endocarditis

It is not a very common condition but very important to clinicians as it has a significant morbidity and mortality if diagnosed late or untreated.

Common Symptoms

Unexplained remitting fever >1 week, loss of weight and appetite and myalgia

Diagnosis

The diagnosis of infective endocarditis requires a multifaceted approach involving clinical suspicion and examination, laboratory investigation by means of inflammatory markers and microbiological analysis and imaging with echocardiography.

The need for robust diagnostic criteria uniting these means of investigation was shown by the Duke criteria in the 1990s.

Modified Duke Criteria

Pathological criteria
• *Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments. or intracardiac abscess content)*

Major criteria
• *Two positive blood cultures showing typical organisms consistent with infective endocarditis, such as Streptococcus viridans and the HACEK* group (OR)* • *Persistent bacteraemia from two blood cultures taken >12 hours apart or three or more positive blood cultures where the pathogen is less specific, such as Staphylococcus aureus and Staphylococcal epidermidis (OR)* • *Positive serology for Coxiella burnetti, Bartonella species, or Chlamydia psittaci (OR)* • *Positive molecular assays for specific gene targets* • *Positive echocardiogram showing oscillating structures, abscess formation, new valvular regurgitation, or dehiscence of prosthetic valves*

Minor criteria
• *Predisposing heart disease* • *Fever >38°C* • *Immunological phenomena such as glomerulonephritis, Osler's nodes, Roth spots, or positive rheumatoid factor* • *Microbiological evidence not fitting major criteria*

- *Elevated C reactive protein or erythrocyte sedimentation rate*
- *Vascular phenomena such as major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae, or purpura*

Definite infective endocarditis
• *Pathological criteria positive (OR)* • *Two major criteria (OR)* • *One major and two minor criteria (OR)* • *Five minor criteria*

**HACEK group: Haemophiles species, Actinobacilius actinomycetemcomitans, Cardio. bacterium hominis, Eikenella corrodens, and Kingella kingae*

Underlying Risk Factors

Prior congenital or rheumatic heart disease and repaired congenital heart disease

Preceding dental, urinary tract or intestinal procedure in patients with underlying heart diseases; congenital or acquired

Prosthetic heart valve

Intravenous drug use

Immunocompromised patients with central venous catheter

Investigations

- *Blood cultures*
  Three to five separate blood collections should be obtained after careful preparation of the phlebotomy site. The timing of collection is not important because bacteraemia can be expected to be relatively constant, Antimicrobial pretreatment of the patient reduces the yield of blood cultures to 50-60%.
- *ESR - Elevated; may be low with heart or renal failure*
- *CRP - Elevated*
- *FBC - Anaemia, Leucocytosis*
- *Urine RE to look for hematuria*
- *U&E - Azotemia, high creatinine (Glomerulonephritis)*
- *Echocardiography; the absence of vegetations does not exclude endocarditis. Vegetations are often not visualized in the early phases.*

Treatment

- *Antibiotic therapy should be instituted immediately once a diagnosis is suspected after taking appropriate blood cultures whenever possible*
- *High serum bactericidal levels must be maintained long enough to eradicate organisms*
- *Total of 4-6 weeks of treatment is recommended*
  (If symptoms ≤3 months, treat for4 week and if>3 months, treat for 6 weeks)

- *Depending on the clinical and laboratory responses, antibiotic therapy may require modification and in some instances more prolonged treatment is required*
- *No relationship exists between the infecting organism and the type of congenital defect, the duration of illness, or the age of the child. However,*
  - *Viridans groups streptococcal infection is more common after dental procedures*
  - *Group D enterococci-in lower bowel or genitourinary manipulation*
  - *Staphylococcal endocarditis - in patients with no underlying heart disease*
  - *Pseudomonas aeruginosa or Serratia marcesens-in intravenous drug users*
  - *Coagulase-negative staphylococci - in indwelling central venous catheter*

Table 3.11 Recommended Antibiotic Treatments for Pediatric Infective Endocarditis

Organism/condition	*Recommended Antibiotic*	*Alternative Antibiotic*
Initial empirical therapy	*IV Ampicillin-sulbactam + IV Gentamicin +/- IV Vancomycin*	*IV Vancomycin + IV Gentamicin*
Streptococci • *Streptococci viridans* • *Group D Streptococci* • *(5. bovis. S. eqwinus)* • *Non-enterocci Group ABCG*	*IV Penicillin G or IV Ampicillin + IV Gentamicin (IV Gentamicin Enterococci - whole course Non-enterococci-2 wk)*	*For Enterococci IV Vancomycin + IV Gentamicin For Aminoglycoside resistant or intolerant patient IV Ampicillin + IV Ceftriaxone for Non enterococci IV Ceftriaxone + IV Gentamicin*
Staphylococci (S, aureus or coagulase negative staphylococci)	*IV Penicillinase-resistant penicillin (e.g. cloxacillin, Amoxicillin-Clavulanic acid, Ampicillin-Sulbactum, Cefoparazone - Sulbactum) ± IV Gentamicin (3-5 days)*	*IV Vancomycin*
Methicillin resistant S. aureus (MRSA)	*IV Vancomycin*	
Gram-negative enteric bacilli	*IV Ceftazidime or Ceftepime or Cefotaxime or Ceftriaxone + IV Gentamicin or Amikacin*	*IV Piperacillin/tazobactam + IV Gentamicin or Amikacin*

HACEK group Vancomycin resistant or intolerant	*Iv Cefotaxime or Ceftriaxone or IV Ampicillin-sulbactam*	*IV Ampicillin + IV Gentamicin or Amikacin*
Fungi Candida spp Aspergillus spp	*Surgical resection + IV Amphotericin 8 +/- Flucytosine*	*Amphotericin B followed by Imidazole (eg, Fluconazole, Itraconazole, Voriconazole) suppression if surgery cannot be performed.*
Culture Negative Endo-carditis	*IV Ampicillin-sulbactam + IV Gentamicin or IV Vancomycin + IV Gentamicin + IV/ Oral Ciprofloxacin*	*Vancomycin is recommended only for patients who are una. ble to tolerate penicillins*

Table 3.12 Dosage Regimens

Name	*Dosage*	*Route*	*Interval*
Amikacin	*15 mg/kg/day*	*IV*	*every 8-12 hr*
Amoxicillin Clavulanic acid	*100 mg /kg/day*	*IV*	*every 8 hr*
Amphotericin B	*1 mg/kg/day*	*IV, over 3-4 hr*	*OD*
Amphotericin liposomal/lipid- associated (3 formulations)	*3-5 mg/kg/day*	*IV*	*OD*
Ampicillin	*200-300 mg/kg/day Max. 12 g*	*IV*	*every 4-6 hr*
Ampicillin-sulbactam	*200-300 mg/kg/day Max. 12 g*	*IV*	*every 4-6 hr*
Ceftriaxone	*100 mg/kg/day Max.4 g*	*IV*	*every 12 hr*
Cefepime	*100 mg/kg/day*	*IV*	*every 12 hr*
Cefoperazone/sulbactum	*100-150 mg/kg/day*	*IV*	*every 8-12 hr*
Cefotaxime	*200 mg/kg/day Max. 12 g daily*	*IV*	*every 6 hr*
Ceftazidime	*100-150 mg/kg/day Max. 2-4 g*	*IV*	*every 8 h daily*
Ciprofloxacin	*20-30 mg/kg/day*	*IV/PO*	*every 12 hr*
Cloxacillin	*200 mg/kg/day*	*IV*	*every 6 hr*
Flucytosine	*150 mg/kg/day*	*PO*	*every 6 hr*
Gentamicin	*3-6 mg/kg/day*	*IV*	*every 8 hr*

Penicillin G	*200 000-300 000 U/ kg/day* *Max. 12-24 million U*	*IV*	*every 4 hr daily*
Piperacillin/tazobactam	*240 mg/kg/day* *Max.18 g*	*IV*	*every 8 hr daily*
Vancomycin:	*Initial empirical therapy: 60 mg/kg/ day, ax. 2 g*	*IV*	*every 6h*
	Others: 40 mg/kg/day *Max.2 8*	*IV*	*every 8-12 hr daily*

Prevention

The existing evidence does not support the extensive use of antibiotic prophylaxis recommended in previous guidelines. Prophylaxis should be limited to the highest risk patients (patients with the highest incidence of infective endocarditis and/or highest risk of adverse outcome from infective endocarditis). Frequent unnecessary use of antibiotics could cause allergic reactions and encourage emergence of antibiotic resistant strains of organisms causing infective endocarditis thereby increasing morbidity and mortality.

NB: Good oral hygiene and regular dental review are of particular importance for prevention of infective endocarditis.

Cardiac conditions for which infective endocarditis prophylaxis is recommended when a high risk procedure is performed

1. *Patients with any prosthetic valve or prosthetic material which was used for cardiac repair.*
2. *Patients with a previous episode of infective endocarditis.*
3. *Patients with congenital heart disease:*
   - *Any type of cyanotic congenital heart disease.*
   - *Any type of Congenital heart disease repaired with a prosthetic material whether placed surgically or by percutaneous techniques up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.*

   Antibiotic prophylaxis is not recommended in other forms of valvular or congenital heart diseases.

Procedures for which antibiotic prophylaxis in highest risk patients need to administered:

1. *Manipulation of gingival tissue or periapical region of teeth or perforation of oral mucosa*
2. *Established infection of gastrointestinal (GI) or genitourinary tract (GU) or for those who receive antibiotic to prevent wound infection or sepsis associated with GI or GU procedure*
3. *Patients with enterococcal urinary infection or colonization*
4. *An invasive procedure of the respiratory tract that involves biopsy or incision of the respiratory mucosa*

5. *Any procedure involving infected skin, skin suture or musculoskeletal tissue*
6. *Placement of prosthetic valves or intravascular or intracardiac material*

Table 3.13 Antibiotic regimen for a dental procedure at risk

Situation	*Agent*	*Dose*
Oral	*Amoxillin*	*50 mg/kg*
Unable to take oral medication	*Ampicillin (or)* *Cefazolin (or)* *ceftriazone*	*50 mg/kg (IM or V)*
Allergic to penicillins or ampicillin (oral)	*Cefalexin (or)* *Clindamycin (or)* *Azithromycin or* *Clarithromycin*	*50 mg/kg* *20 mg/kg* *15 mg/kg*
Allergic to penicillins or ampicillin and unable to take oral medication	*Cefazolin or* *ceftriazone (or)* *Clindamycin*	*50 mg/kg (IM or IV)* *20 mg/kg*

(Regimen single dose 30 to 60 minutes before the procedure)

Source: Habib G6 et al. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J2015:36:3075-3128

- *In patients with established infection of GI or GU tract or for those who receive antibiotics to prevent wound infection or sepsis associated with Glor GU procedures*
  - *Prophylaxis should include antibiotics active against enterococci such as Penicillin, Ampicillin, Piperacillin or Vancomycin.*
  - *Antibiotic prophylaxis is not recommended for patients who undergo routine GI or GU procedures, including diagnostic esophagogastroduo denostomy or colonoscopy*
- *In patients with enterococcal urinary infection or colonization,*
  - *It is important to eradicate enterococci from the urine prior to an elective cystocopy or manipulation of the urinary tract.*
  - *If the procedure is not elective, antimicrobial regimen should contain drugs active against enterococci such as amoxicillin or ampicillin. If the patient cannot take orally, vancomycin should be used*
- *In patients who undergo an invasive respiratory tract procedure,*
  - *The choice of antibiotic would depend on the organism known or suspected to cause the infection.*
  - *If Streptococcus viridans is suspected the regimen is similar to that for dental procedure. If Staphylococcus aureus is suspected the regimen should contain*

antistaphyloccocal penicillin, cephalosporin or vancomycin. If the patient cannot tolerate penicillins or if MRSA is suspected vancomycin should be administered.

- *In procedures involving infected skin or musculoskeletal tissue*
  - *Prophylaxis should be covered with antibiotics active against staphylococci and β hemolytic Streptococci such as penicillin or cephalosporin. Vancomycin or clindamycin should be administered if patient is not able to tolerate β lactams*
- *For patients undergoing the placement of prosthetic valves or any other material in the heart or in the vascular system,*
  - *Intravenous preintervention prophylaxis with a first or second generation cephalosporin is recommended, This should be given within 30 minutes before procedure. If the procedure is longer than 4 hours, a second dose can be given intraintervention, Prophylaxis should not be continued longer than 24 hours.*
  - *For the penicillin-allergic patient or in hospitals in which there is a high prevalence of MRSA or methicillin-resistant or S. epidermidis, vancomycin should be considered.*

Indications to Surgical intervention

- *Failure to sterilize the blood despite adequate antibiotic levels, myocardial abscess, recurrent emboli and increasing size of vegetations while receiving therapy*
- *(Active infection is not a contraindication)*
- *Severe aortic or mitral valve involvement with intractable heart failure*
- *Mycotic aneurysm, rupture of aortic sinus or dehiscence of an intracardiac patch*