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缅甸联邦第一特区卫生部

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

Neonatal Sepsis

Standard Operating Procedure (SOP)

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Neonatal Sepsis

It is a clinical syndrome of bacteraemia with systemic signs and symptoms of infection in the first four weeks of life.

Classification of Neonatal Sepsis

Early onset sepsis (EOS)

- *Presents within the first 72 hours of life*
- *EOS syndrome is associated with the following microorganisms from them other*
  - *Group B Streptococcous /GBS)*
  - *Escherichia coli*
  - *Coagulase negative staphylococcus*
  - *Haemophilus influenzae*
  - *Listeria monocytogenes*

Risk factors for EOS

- *Preterm or low birth weight Premature rupture of membranes*
- *Prolonged rupture of membranes (>18 hours)*
- *Spontaneous preterm onset of labour <37 weeks' gestation*
- *Maternal intrapartum fever: >37.5°C within 2 weeks prior to the delivery*
- *Signs of chorioamnionitis (e.g. smelly liquor) or malodorous baby*
- *Prolonged and difficult delivery with instrumentation*
- *Vaginal GBS colonization, previous baby with GBs sepsis*
- *Maternal history of urinary tract infection (UTI)*
- *Apgar scoring <4 at 1 minute of age*
- *More than 3 vaginal examinations during labour*

Late onset sepsis (LOs)

- *Usually presents after 72 hours of age*
- *4-90 days of life and is acquired from the care giving environment – nosocomial or community acquired*
  - *4-28 days- Late Onset Sepsis (LOs)*
  - *29-90 days- Late Late Onset Sepsis (LLOs)*
- *LOS syndrome is associated with the following microorganisms*
  - *Coagulase negative Staphylococci6Staphylococcus aureus0*

  - *Escherichia coli*
  - *Klebsiella*
  - *Pseudomonas*
  - *Enterobacter*
  - *Candida*
  - *Group B Streptococcous (GBS)*
  - *Serratia*
  - *Actinobacter*
  - *Anaerobes etc.*
- *The infant's skin, respiratory tract, conjunctiva, GI tract and umbilicus may become colonized from the environment, leading to the possibility of LOS from invasive organisms*
- *Gram negative nosocomial sepsis often presents with a more rapid deterioration and is commonly associated with shock and coagulation problems*

Risk factors for LOS

- *Prematurity/low birth weight*
- *NICU Admission*
- *Invasive Procedures/Endotracheal Intubation*
- *Prolonged IV line*
- *Prolonged hospital stays*
- *Frequent use of broad-spectrum antibiotics*
- *Contact from caregivers with bacterial colonization*
- *Poor cord care/Poor hygiene/Formula feeding*

Approach to Diagnosis of Neonatal Sepsis

History

- *Risk factors (See above)*
- *Risk factor for nosocomial infection from staff, relatives or other sick infants*

Physical examination

- *Asymptomatic (Risk Factors +)*
- *Symptomatic*
- *Close monitoring for progress of the disease*

(GBS, Esch. coli. etc., typically present with rapid and life threatening deterioration)

Investigations

- *Routine septic screen*
  - *Full blood count*
  - *Blood culture (should be taken before starting any antibiotic)*

- *Chest X-ray (if signs of respiratory distress present)*
- *C-reactive protein (if available)*
- *Coagulation profile (if DIC is suspected)*
- *Swab from any site of inflammation*
- *Throat and ear swab (in case of suspected early-onset infection)*
- *Urine microscopy and culture (if indicated)*

- *Additional routine tests, indicated by the clinical situation/availability*
  - *Lumbar puncture (CSF RE & Culture)-must be done in suspected LOS*
  - *Culture and Gram stain of gastric aspirate*
  - *Culture and Gram stain of maternal high vaginal swab*

Treatment

Antibiotic therapy in suspected sepsis

- *Selection of an empirical antibiotics should be based on*
  - *Postnatal age at the onset of the disease i.e. EOS vs. LOS*
  - *Patient specific factors (e.g. nature of the illness, previous antibiotic therapy)*
  - *Current Unit Protocol (must be based on routine bacterial surveillance)*
  - *Updated information on local predominant aetiological pathogens & their antibiotic susceptibility or resistance pattern in one's own hospital (or) one's own baby unit*
  - *Pharmacokinetic properties of the antibiotics*

Initial Empirical Therapy (EOS)

1. *Initial antibiotic treatment of unknown origin in EOS*
   Option (1) - V Ampicillin + IV Gentamicin (Situations where resistant strains are unlikely)
   Option (2) - IV Ampicillin + Iv Cefotaxime (especially in places where aminoglycoside resistance is high)
   (Note increased risk of antibiotic resistance and invasive fungal infections with third generation cephalosporins)
   **Add metronidazole if suspicion of anaerobic infection (e.g. NEC)*
2. *Antibiotic treatment of severely ill term/ preterm newborn, or preterm infants with a prenatal history indicating bacterial infection (e.g. maternal fever, foul smelling liquor, PROM > 18 hours etc.)*
   Option (l) - IV Ampicillin + IV Cefotaxime + IV Aminoglycoside (Gentamicin/Amikacin)
   Option (2) - IV Third generation Cephalosporin (Cefotaxime/Ceftazidime) + IV Aminoglycoside
   **Note-check maternal HVS result if available*
3. *Antibiotic treatment in cases of initial treatment failure and pathogens are stillun known (Blood C&S awaiting)*
   1st Line - IV Ceftozidime +IV Gentamicin/Amikccin

2nd Line - IV Sulperazone monotherapy (Cefoperazone + beta lactamase inhibitor Sulbactam)

3rd Line - IV Sulperazone combination therapy with other antibiotics if such combinations are indicated

e.g.IV Sulperazone + IV Gentamicin/Amikacin (suspected Gram. negative sepsis)
IV Sulperazone + IV Cloxacillin/Flucloxacillin (Suspected Staphylococcal sepsis)
IV Sulperazone + IV Vancomycin (suspected MRSA)

Initial Empirical Therapy (LOS)

Option (1) - IV Ampicillin or Cloxacillin + IV Gentamicin (Situations where resistant strains are unlikely)

Option (2) - IV Flucloxacillin plus Amoxicillin (i.e. Flumox®) + IV Gentamicin

Option (3) - Ampicillin + IV Cefotaxime (Especially in places where aminoglycoside. resistance is high and Staph infection is very unlikely)

Option (4) - IV Cefotaxime + Gentamicin/Amikacin

(Gram-negative infection is very likely)

Antibiotic treatment in cases of initial treatment failure and pathogens are still unknown i.e. Los not improving

1st Line - IV Ceftazidime + IV Gentamicin/Amikacin

2rd Line - IV Sulperazone monotherapy (Cefoperazone + beta lactamase inhibitor Sulbactam)

3rd Line - IV Sulperazone combination therapy with other antibiotics if such combinations are indicated

e.g. IV Sulperazone + IV Gentamicin/Amikacin (suspected Gram-negative sepsis) IV Sulperazone + IV Cloxacillin/Flucloxacillin (suspected Staphylococcal sepsis) IV Sulperazone + IV Vancomycin (suspected MRSA)

Last line - IV Extended specirum Penicillin (e.g. Piperacilin/Tazobactam) orCarbapenem le.g. Meropenam) + IV Aminoglycoside (Getamicin/Amikacin)

Continuing Antibiotic Therapy

- *The antibiotics started can either be continued as such or modified based on*
- *The culture report and/or the clinical condition of the baby*
- *If culture negative, consider stopping therapy*
- *Continue therapy if sepsis is very likely even though culture comes back as negative*

Table 1.7 Duration of antibiotic treatment

The clinical course and the laboratory findings do not verify the suspected infection.	*48 hours (Maximum)*
Infection is confirmed (evidence of pathogen plus laboratory studies and or clinical presentation)	*7 days*
Blood culture is positive and/ or severe illness.	*10 days*
Meningitis (some suggest treatment for an additional 1week after the last unremarkable CSF)	*14-21 days*
Osteomyelitis	*At least 3 weeks*

Supportive

- *Monitoring: Temperature, fluid balance, hydration state, weight, BGL*
- *Nurse the infant in a thermo-neutral environment taking care to avoid hypohyperthermia*
- *Maintain oxygen saturation in the normal range, assisted ventilation if necessary*
- *Administer IV fluids if the infant is haemodynamically unstable; regularly monitor for hypo/hyperglycaemia*
- *Avoid enteral feeding till the infant is haemodynamically stable*
- *Use crystalloids/colloids and inotropes to maintain normal tissue perfusion and blood pressure*
- *To manage anaemia/bleeding diathesis*
- *If DIC occurs*
  - *Check APTT, PT, Platelet count*
  - *Treat with FFP/cryoprecipitate/platelet or blood transfusion as indicated*

Important Points to Remember

- *Do your best to prevent infection by reinforcing infection control, particularly and washing, re-look at disinfection protocols, procedure asepsis, minimum invasion, equipment sharing, nurse-patent ratio, isolation policy and training*
- *Use antibiotics only if indicated and discontinue antibiotics as early as possible*
- *There is no role for prophylaxis antibiotics*
- *Avoid using broad-spectrum antibiotics as a baseline antibiotic.*
- *Use the narrowest spectrum of antibiotics possible, almost always any penicillin (e.g. Ampicillin/Amoxicillin-clavulanic acid) and an aminoglycoside (e.8. Gentamicin)*
- *Have a step-up protocol for antibiotic use*
- *As a rule, do not start first line-treatment, with a third-generation cephalosporin (e.g. Ceftazidime or Sulperazone)*

- *Reserve higher/newer antibiotics for use only after the sensitivity pattern indicate the use of such antibiotics*
- *Follow standard recommendations of dosage and duration of antibiotics in proven sepsis*
- *Develop an antibiotic policy using bacteriology surveillance data*
- *Maintain a record of culture sensitivity patterns; this will help in choosing the antibiotics*
- *Send a blood culture (and CSF and/or urine) before starting antibiotics*
- *In the absence of culture facilities, at least a sepsis screen should be done*
- *If blood cultures are negative at 2-3 days, it is almost always safe and appropriate to stop antibiotics*

Management of Neonatal Meningitis

- *Consider performing a lumbar puncture if any signs of sepsis in a neonate*
- *LP can safely be omitted in asymptomatic babies with only perinatal risk factors who are being evaluated for early sepsis*
- *Initial Blind Empirical therapy for meningitis*
  - *IV Ampicillin + IV Gentamicin + IV Cefotaxime*
- *Reassess therapy based on culture and antibiotic susceptibility result*
  - *If Group B Streptococcus, use high dose penicillin*
  - *Discontinue aminoglycoside when clinically stable and CSF is sterile*
  - *If Gram negative enteric, use Cefotaxime and an aminoglycoside. Discontinue aminoglycoside after two weeks and complete course with cefotaxime*
- *Continue IV antibiotic therapy for at least two weeks (GBS and Listeria) or three weeks (Gram negative bacteria) till CSF cultures sterile*
- *Role of repeat Lumbar puncture in neonatal bacterial meningitis during or after treatment*
  - *Do not perform a repeat LP in neonates who are receiving antibiotic treatment that the causative organisim is susceptible to and are making good clinical recovery*
  - *Do not perform a repeat LP before stopping antibiotic treatment in*
  - *neonates who are clinically well*
  - *Perform a repeat LP in neonates who have persistent or re-emergent pyrexia, clinical deterioration, new clinical findings (especially neurological findings), or persistently abnormal inflammatory markers*