Research issues: Early detection & clinical management of Nipah virus infected patients

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Early detection

• Proactively detect new cases
• Prompt management
• Prevention of transmission including human to human transmission
Kerala outbreak

- One index case and 18 confirmed cases (12 M and 7 F)
- Clinical presentations – Encephalitis, ARDS or Myocarditis
- One patient had only fever, headache, tiredness, cervical adenopathy
- Two survivors – different spectrum
- Myocarditis, Encephalitis. ARDS and dysautonomia
- Flu like illness
Clinical features

- Fever
- Profound tiredness
- Headache
- Vomiting
- Disorientation
- Breathlessness
- Cough
- Diarrhoea
- Convulsions / myoclonic jerks
Information to be collected

• Demographics
• Presenting symptoms of illness
• Exposure to ill patients
• Exposure to animals in the surrounding area, and other possible risk factors like hospital visits
• The degree of contact with the patient, and type of barrier precaution used during patient care.
Early detection - implications

- Early initiation of management
- Training of health care workers
- Prevention of transmission
- Excluding treatable causes
- Effective implementation of triage system
Case definitions

Adapted from NCDC interim guidelines, WHO Bulletins, updated 23/05/2018, DHS

Suspect Nipah case
Person from an area / locality affected by a Nipah virus disease outbreak who has:

• Acute Fever with new onset of altered mental status or seizure and/or
• Acute Fever with severe headache and/or
• Acute Fever with Cough or shortness of breath
Probable Nipah Case

Suspect case-patient/s who resided in the same village where suspect/confirmed case of NIPAH were living during the outbreak period and who died before complete diagnostic specimens could be collected. OR

Suspect case-patients who came in direct contact with confirmed case patients in a hospital setting during the outbreak period and who died before complete diagnostic specimens could be collected.
Confirmed Nipah Case

• Suspected case who has laboratory confirmation of Nipah virus infection either by:
  – Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid.
  – Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid.
Definition of a contact

Close contact - as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways.

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah virus disease
- Has had direct close contact with the suspect/confirmed case of Nipah virus disease during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah virus disease at a funeral or during burial preparation rituals
- Has touched the blood or body fluids (saliva, urine, vomitus etc.) of a suspect/confirmed case of Nipah virus disease during their illness
- Has touched the clothes or linens of a suspect/confirmed case of Nipah virus disease
Concerns

- Case definition – Probable – having contacts with confirmed case
- Lab facilities for investigations – before diagnosis, confirmed cases
- Contact tracing and listing - Definition
- Confirmed cases – blood, throat swab, urine & CSF
Investigations

• Baseline, specialised, ABG, Trop I
• Which sample – eg: CSF, other body fluids and tissues
• Imaging including POCUS, MRI, ECHO
• EEG
• Exclude other causes – definite treatment
• Blood, Urine, throat swab and CSF – Nipah RNA RT PCR
Management

• General measures – ABCDE approach

• First step - Ensure personal safety. Wear apron and gloves as appropriate.

• Proper Triaging
Standard of care of encephalitis

Patients with increased ICP
- Management of fever, pain, control of cough and other strains.
- Prevention of seizures
- Control systemic hypertension
- Elevate head
- Furosemide 20mg IV and/or mannitol 1-2 mg/kg IV over 30-60 minutes - provided circulatory volume is protected
  Hyperventilation - PaCO2-30mmhg

Seizures
- Lorazepam 4 mg IV
- Phenytoin 100mg IV q6-8h
- Fosphenytoin 150PE q8h IV
- Levetiracetam 500mg q8-12h IV
Standard of care of myocarditis

Supportive therapy for symptoms of acute heart failure with use of diuretics, nitroprusside, ACE inhibitors.

**Inotropes**-

- **Dobutamine**: 2–5 micrograms/kg/min, titrated up to 20 micrograms/kg/min - Inotrope and potential vasodilator; lowers blood pressure; give as individual agent as long as systolic blood pressure (SBP) ≥90. Can use with dopamine.
  - **Dopamine**: 3–5 micrograms/kg/min, titrated up to 20–50 micrograms/kg/min as needed - Inotrope and vasoconstrictor; increases left ventricular end-diastolic pressure and causes tachycardia. Can use with dobutamine.
  - **Norepinephrine**: 2 micrograms/min, titrate to response - Vasoconstrictor and inotrope; preferred as a single agent over dobutamine if SBP <70. Can use combined with dobutamine.
Standard of care of ARDS

• Severe ARDS is often associated with refractory hypoxemia, and early identification and treatment of hypoxemia is mandatory.
• For mechanical ventilation specific settings are recommended: limitation of tidal volume (6 ml/kg predicted body weight), adequate high PEEP (>12 cmH2O), a recruitment manoeuvre in special situations, and a ‘balanced’ respiratory rate (20-30/min).
Standard of care of ARDS

• Because intubation and mechanical ventilation may be associated with an increased incidence of complications, such as barotrauma and nosocomial pneumonia, alternatives to mechanical ventilation such as a high-flow nasal cannula or noninvasive positive-pressure ventilation (NIPPV) may be beneficial in patients with ARDS.

• So For mild and moderate ARDS, NIV stands as the first-line approach.
Standard of care of ARDS

• Patients who have a diminished level of consciousness, vomiting, upper GI bleeding, or other conditions that increase aspiration risk are not candidates for NIPPV.

• Other relative contraindications include hemodynamic instability, agitation, and inability to obtain good mask fit.
Specific treatment

• No therapeutics approved for human use
Ribavirin

- Dose 2 g stat, 1 g 6 hourly 4 days followed by 500mg 6 hourly for 5 days (based on WHO guideline for other haemorrhagic fevers)
- Started on confirmation of NiV
- Ribavirin has broad activity against RNA and some DNA viruses
- Experience – HCV, hemolytic anemia, teratogenicity, dose 400mg twice daily
- Used in Malaysian outbreak in an open label trial – 36% reduction in mortality, animal models further proved ineffective
Flavipravir

- Purine analogue
- Effective in Syrian hamster model – twice daily oral or once daily SC for 14 days
- Has efficacy against broad spectrum of RNA viruses
- Approved for use in Japan in emerging influenza strains

https://www.nature.com/articles/s41598-018-25780-3
Favipiravir

• Recommended dosage and schedule of influenza antiviral medications for treatment in Japan (as of 2016)
  • 1600 mg twice daily as initial dose
  • 600 mg twice daily for following 2–5 days
  • Oral
• Not recommended in chemoprophylaxis

Monoclonal antibody m102.4

- Recognizes the G envelope protein of NiV
- Appears to block the receptor binding site on the protein
- Preventing adhesion to the Ephrin B2 protein
- Thereby inhibiting viral entry into the host cell
Challenges

• Early identification of suspect/probable
• Early diagnosis – Lab facilities
• Implementing infection control practices
• Providing uniform usual standard of care for everyone
Challenges

• Infection control in health care settings is vital to reduce risks for other patients, for caregivers and health workers.
• Safe burial in a dignified manner
• Long term follow up of survivors