Standardized Clinical Management: Evidence of Reduction of Dengue Haemorrhagic Fever Case-Fatality Rate in Thailand

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Abstract

The first outbreak of dengue haemorrhagic fever (DHF) in Thailand occurred in 1958. There were 2,158 cases reported and 300 deaths, with a case-fatality rate (CFR) of 13.9%. Guidelines for the diagnosis and management of DHF were developed at the Children's Hospital, Bangkok, by Dr Suchitra Nimmannitya a few years after the outbreak. These guidelines were used widely in Thailand and have resulted in a marked reduction in the CFR from 14% to less than 1%. WHO adopted these criteria for the diagnosis and management of DHF in 1975 and has distributed it for worldwide use. The prognosis of DHF patients depends on early diagnosis and early detection of shock with proper management. This paper emphasizes on tourniquet test which is an important screening test for the diagnosis of dengue infection. CBC is an important laboratory test to be followed frequently in these patients. Leukopenia < 5,000 cells/cu mm and lymphocytosis indicate that the critical period is approaching within 24 hours and that warning signs and symptoms of shock should be told to the care-takers and they should be persuaded to bring the patient back to the hospital as soon as possible. Proper IV fluid management when the patients are in a critical period of 24-48 hours (when platelets are <100,000 cells/cu mm and 10-20% rising hematocrit) are explained in detail. Most DHF patients (60-70%) require only crystalloid solution (isotonic salt solution). Only 15-20% have massive plasma leakage and need colloidal solution for which dextran-40 with its hyperoncogenicity (about 3 times that of plasma) is recommended. Ten to 15% of DHF patients need blood transfusion. Platelet transfusion is recommended only for those with severe bleeding. With good medical and nursing care and appropriate management, all patients should recover rapidly and completely.

Key words: Dengue haemorrhagic fever, Tourniquet test, Leukopenia, Fluid Management, Colloidal solution

Introduction

The first case of dengue haemorrhagic fever (DHF) in Thailand in 1950 was diagnosed as "influenza with bleeding", and the first DHF epidemic occurred in 1958 when it was limited only to Bangkok. There were 2,158 cases reported with 300 deaths, and with a morbidity rate (MR) of 8.87/100,000 population and case-fatality rate (CFR) of 13.9%[1].

Guidelines for the diagnosis and management of DHF were developed at the Children's Hospital by Dr Suchitra Nimmannitya.[2,3,4] The use of these guidelines brought down the CFR from 13.9% to 5% in the first 8 years. After this period, the CFR was reduced gradually from 5% to 1% in about 10 years due to the spread of DHF to most big cities in the country. Since 1971, the number of reported cases has been continuously on the increase. However, CFR has stayed <1% since 1979 and was below 0.5% in 1989[1].

Critical areas in efficient case management

The clinical and laboratory criteria for the diagnosis of DHF developed at the Children's Hospital, Bangkok, during 1975[5] and which has been adopted by WHO, are based are based on the presence of major manifestations, in order of their appearance:

(1) High continuous fever for 2-7 days.

(2) Haemorrhagic manifestations, including at least a positive tourniquet test.

(3) Enlargement of liver.

(4) Circulatory disturbances (as shock in severe cases).

(5) Thrombocytopenia $\leq$ 100,000 cells/cu.mm.

(6) Haemoconcentration: hematocrit (Hct) increased by 20% or other evidence of plasma leakage i.e. pleural effusion and/or ascites.

These criteria meets 95% confidence level for making the diagnosis of DHF, but the diagnosis can be made only when a patient has completed his clinical course of illness.

DHF is classified into four grades according to the clinical hallmarks of bleeding and shock. Most patients of DHF grade I and II (non-shock) can recover spontaneously or shortly after a brief period of fluid therapy. In contrast, DHF grade III, and especially grade IV, patients need special attention and care from physicians and nurses with appropriate fluid resuscitation and judicious volume replacement. Correction of any metabolic and/or electrolytes abnormalities are critical in these patients. Concealed internal bleeding is likely in patients with prolonged shock.

Early detection of shock and proper management are the most important factors that determine the prognosis of DHF patients

The clinical course of DHF is divided into three phases:

(1) Febrile phase (2-7 days)

(2) Critical or leakage phase (24-48 hours)

(3) Convalescence phase (2-7 days)

The management of DHF cases[4,5,6] is divided according to these three phases.

1. Febrile phase

(a) Screen all suspected dengue patients.

- **Tourniquet test*** is an important tool for early screening of dengue patients from other viral/bacterial illnesses. It should be done in all children with high fever, flushed face, and without any focal signs and symptoms of infection. A positive tourniquet test is $\geq$ 10 dots/square inch. The tourniquet test is positive in 50% of the patients on the first day, in 60-70% on the second day and >90% on the third day onwards.

(b) Supportive and symptomatic treatment.

- Give paracetamol 10 mg/kg/dose prn T $\geq$ 39^{0}C q 4-6 hr., *aspirin and ibuprofen are contraindicated.*
- Apply tepid sponges if a patient still has high fever after a dose of paracetamol.
- For nutritional support, advise soft diet, fruit juice, milk or ORS.

(c) If a suspected patient has signs of dehydration and had severe vomiting, give 5% D/N/2 to correct dehydration and discontinue IV fluid as soon as possible, preferably within 24 hours. If IV fluid cannot be discontinued, give only a minimal amount - about half of the maintenance amount.

(d) Follow all suspected dengue patients closely everyday from day 3 of their illness.

During the febrile phase, it is difficult to differentiate between DF and DHF patients because they have almost the same clinical symptoms, except that maculopapular rash and myalgia/arthralgia are less frequent in DHF. So one has to follow carefully all suspected dengue infected patients until they are afebrile for 24 hours without the use of antipyretic. At the end of the febrile phase, DF patients will recover spontaneously while in DHF patients, the critical stage is reached. In mild DHF cases, the change in vital signs is minimal and transient. Patients will recover spontaneously or shortly after intravenous fluid administration. In more severe cases, the disease progresses rapidly into the stage of shock.

To follow these patients closely:

- Ask the history of bleeding (admit and give blood transfusion if there is a significant amount of blood loss, ~10% of total blood volume).
- Do physical examination:
  - Vital signs - signs of shock: rapid and weak pulse, narrowing of pulse pressure, hypotension - if present, give IV fluid immediately and admit.
  - Palpate the liver - liver enlargement and tenderness indicate nearness to or entering the critical phase; observe closely or admit.

* Tourniquet test is performed by inflating a blood pressure cuff on the upper arm to a point midway between the systolic and diastolic pressure for five minutes. Wait for one minute after the release of pressure before reading the test.

- Repeat tourniquet test if it was negative.

- Do CBC and follow CBC everyday:

  - Leukopenia $\leq$ 5,000 cells/ cu.mm. and lymphocytosis, increase in atypical lymphocyte indicates that *within the next 24 hours, the patient will have no fever* [7] and will enter critical phase if they are DHF cases.

  - Thrombocytopenia $\leq$ 100,000 cells/cu.mm. indicates that *the patient is entering a critical phase and needs close observation in the hospital.*

  - Rising Hct 10-20% indicates that *the patient is in the critical period and needs IV fluid therapy if he cannot have good oral intake. Admit this patient and give isotonic salt solution.*

(e) Advise caretakers about warning signs of shock so that parents should bring their children to the hospital as soon as possible.

- Clinical deterioration when defervescence occurs.
- Bleeding.
- Acute, severe abdominal pain/ vomiting.
- Very drowsy, patient looks weak and sleeps all the time.
- Refuses to eat or drink (some may complain of being very thirsty).
- Restless, irritable.
- Change in behaviour.
- Cold, clammy or mottling skin.
- Not passed urine for 4-6 hours.

(f) Indications for admission

- Very weak and cannot have adequate oral intake.
- Bleeding.
- Platelet $\leq$ 100,000 cells/cu.mm. and/or rising Hct 10-20%.
- Clinical deterioration when defervescence occurs.
- Acute, severe abdominal pain/ vomiting.
- Shock/impending shock.
- Rapid pulse and no fever.
- Capillary refill >2 seconds.
- Cold, clammy skin, mottling, restless.
- Pulse pressure $\leq$ 20 mm.Hg., e.g. 100/80, 90/70,
- Hypotension.
- No urine for 4-6 hours.
- Change of consciousness, stuporous or aggressive behaviour which may indicate more severe disease, encephalopathy.
- Parental anxiety, live far away from the hospital.

2. Critical/Leakage phase

Most of the admitted cases are more severe patients who cannot have adequate oral

intake, whether anorexia and/or vomiting during the critical/leakage phase.

(a) General management of patients

- Put all dengue patients together in the dengue ward or dengue corner for close observation. This ward should have mosquito net to prevent nosocomial dengue transmission.
- Vital signs should be measured q 1-2 hours; if unstable vital signs are present, it should be done more frequently, i.e. q 10-15 minutes.
- Hct should be done q 4-6 hours; if unstable vital signs and suspected internal bleeding, more frequently, i.e. q ?-1 hour. This is very critical, especially in cases with concealed bleeding.
- Record intake/output.
- Should have flow chart at bedside for recording clinical signs and symptoms, vital signs, Hct, intake/output, which is very important for adjusting the rate and type of fluid therapy.
- Give oxygen via face mask/nasal canular in cases with shock.
- Stop bleeding by proper methods, e.g. nasal packing in cases with epistaxis.
- Avoid unnecessary invasive procedures, e.g. do not insert naso-gastric tube in cases with upper GI bleeding.
- Closely observe the patients by both physicians and nurses.(

(b) High risk patients

The following types of patients are at risk, so nurses should notify attending staff as soon as possible. These patients need special laboratory investigations for they may have complications, e.g. internal bleeding, hypoglycemia, electrolyte imbalance (hyponatremia, hypocalcemia), metabolic acidosis, liver failure and renal failure. (The lab. investigations include, Hct, blood sugar, electrolyte + Ca, capillary or venous blood gas, coagulogram, liver function test, BUN and creatinine). These patients are:

- Young infants <1-year old.
- DHF grade IV or prolonged shock.
- Overweight patients.
- Patients with massive bleeding.
- Patients with changes of consciousness (encephalopathy).
- Patients with underlying diseases, e.g. thalassemia, G-6-PD deficiency, congenital heart disease, etc.
- Referred patients.

(c) Fluid management

Indication for IV fluid

- Thrombocytoperia <100,000 cells/ cu.mm., rising Hct 10-20%, platelet $\leq$ 100,000 cell/cu.mm. and patient cannot have adequate oral intake.
- Shock or impending shock.

Type of IV fluid

- Isotonic salt solution, e.g. Acetate Ringer (AR), Lactate Ringer (LR) or normal saline solution (NSS) with or without 5% dextrose (preferably with 5% dextrose).
- In young infants, during shock use isotonic solution; if not in shock, use 5% D/N/2.

Amount of IV fluid:

- During the critical period of plasma leakage (24-48 hours), DHF patients should receive the total amount of IV fluid for maintenance + 5% deficit (M + 5% D). Based on the observation that the average amount of IV fluid given through the period of leakage in DHF grade III patients is equal to that.
- In patients whose body weight is more than 40 kg, the total amount of IV fluid should be equal to 2 times the maintenance (2M) (because 2M is less than M + 5% D).
- In overweight patients, calculate IV fluid according to the ideal body weight (BW) [(BW X 2) + 8].
- In adults, calculate IV fluid based on average BW of 50 kg.

Rate of IV fluid

- In non-shock cases, start with:
  - 5 ml/kg/hr. (BW between 15-40 kg).
  - 3-4 ml/kg/hr. (BW > 40kg.).
  - 6-7 ml/kg/hr. (BW < 15 kg).
- In DHF grade III, start with 10 ml/kg/hr.
- In DHF grade IV, start with 10 ml/kg IV push or drip free flow for 10-15 minutes until blood pressure (BP) and pulse (P) can be measured, then reduce to 10 ml/kg/hr.

Adjusting the rate of IV fluid

It is very important to adjust the rate of IV fluid frequently to avoid fluid overload. In DHF patients, *IV fluid should be given at the minimal amount to keep intravascular circulation* because if more IV fluid is given, it will leak out into both the pleural and abdominal cavities and cause respiratory distress later. The rate of IV fluid should be adjusted according to:

- Clinical conditions: general appearance, capillary refill, appetite.
- Vital signs: BP, P, temperature (T) and respiratory rate (RR).
- Hct.
- Urine output.

The first 6-12 hours after shock, BP and P are the two important parameters to determine the rate of IV fluid, but later, consider all parameters together before adjusting the rate.

(d) Monitoring of shock

- After initial fluid resuscitation, evaluate the patient at 1-2 hours. If the rate of IV fluid cannot be reduced to <10 ml/kg/hr. because of unstable

vital signs (still narrowing of pulse pressure and rapid and weak pulse), *Repeat the Hct:*

- If there is an *increase*, change IV fluid to *colloidal solution* (Dextran-40 is preferred) at a rate of 10 ml/kg/hr.
- If there is a *decrease,* change IV fluid to *colloidal solution* (Dextran-40 is preferred) at a rate of10 ml/kg/hr. and c*ross match for fresh whole blood (FWB)* and re-evaluate the patient again after one hour whether he needs blood transfusion or not.
- In grade IV patients,
- If the initial Hct is very low, i.e. 40%-45%, think of possible internal haemorrhage and follow Hct more frequently and give blood transfusion as soon as indicated.
- Correct the possible metabolic and electrolyte disturbance, e.g. hypoglycemia, hyponatremia, hypocalcemia, acidosis.
- After 6 hours, if Hct is decreasing and in spite of a large amount of volume replacement, still cannot reduce the rate of IV fluid to < 10/ml/kg/hr., consider blood transfusion as soon as possible.

The recommended colloidal solution

- Dextran-40 (10% dextran-40 in NSS which is a plasma expander) is recommended because of its hyperoncogenicity (osmolarity ~3 times that of plasma), so it can hold the volume better. Other colloidal solutions, including plasma itself, are the plasma substitute and have osmolarity ~ 1-1.4 times that of plasma.
- The rate of dextran-40 should be 10 ml/kg/hr so that it can maintain maximum osmolarity when administered to the patients.
- The maximum dosage of dextran-40 is 30 ml/kg/day. Do not exceed this amount for it may cause acute renal failure.

Duration of IV fluid

- The duration of IV fluid administration should not exceed 24-48 hours.
- Indication for blood transfusion
- Significant amount of blood loss, i.e. > 10% of total blood volume (TBV). TBV = 80 ml/kg. Give FWB replacement equal to the amount observed.
- Patients with haemolysis due to their underlying diseases, e.g. G-6-PD deficiency, thalassemia.
- Patients with concealed bleeding. Hct dropped and unstable vital signs in spite of large amount of volume replacement, give FWB 10 ml/kg/dose or pack red cell (PRC) 5 ml/kg/dose at a time.

Indication for platelet transfusion

Platelet concentrate is indicated only in cases with massive bleeding. Give 0.2 unit/kg/dose.

3. Convalescence phase

In general, most DHF patients will recover rapidly without complication within 24 -48 hours after shock. Indicators for recovery include:

- Improved general condition.
- Gain appetite.
- Stable vital signs: wide pulse pressure, slow and strong pulse.
- Hct stable and decrease to baseline value, 35%-40%.
- Diuresis.
- Some (~ 30%) developed confluent petechial rash with characteristic, scattered small, whitish round areas on their lower extremities, may be itchy.
- Sinus bradycardia.

IV fluid should be discontinued immediately if they enter convalescence phase. If the patient does not gain appetite and has distended abdomen with decreased or no bowel sound, check for hypokalemia which is commonly found in this phase (due to diuresis). Fruit or fruit juice or KCl solution orally are recommended to correct this electrolyte abnormality.

4. Indications for discharge

- At least 24 hours after defervescence without using antipyretic.
- Good appetite.
- Visible good general conditions.
- Diuresis.
- Stable Hct at baseline value 35%-40%.
- At least 2 days after shock.
- No dyspnea or tachypnea.
- Platelet $\geq$ 50,000 cell/cu.mm.
- No complications.

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