FLUID AND HEMODYNAMIC MANAGEMENT IN SEVERE DENGUE

Adisorn Wongsa

Phramnongkutklao Hospital, Bangkok, Thailand

Abstract. In the critical phase of dengue fever, the leakage of intravascular fluid into interstitial space and 3rd space can cause hemoconcentration and severe complications such as dengue shock syndrome (DSS), and it can lead to multiple organ failure, followed by death. Close monitoring, early detection and prompt management are the keys in successful treatment. In a hemodynamically unstable patient, crystalloid is the fluid of choice in initial management. However, if they are not responsive despite adequate resuscitation, a careful search for others causes is mandatory and fluids should be switched from crystalloid to colloid. If the leakage leads to restriction of the use of fluids (pulmonary edema), the addition of a vasopressor such as norepinephrine needs to be considered. After stabilizing the hemodynamics and clinical improvement, the physician has to know when to reduce and discontinue the fluid to avoid congestion and others complications.

Keywords: fluid management, hemodynamic, severe dengue

INTRODUCTION

In the critical phase of dengue fever, a severe complication is dengue shock syndrome (DSS), which may be caused by the leakage of intravascular fluid into interstitial space and 3rd space as well as from bleeding. This complication can lead to multiple organ failure and death.

In the World Health Organization guidelines on dengue (WHO, 2012), it is suggested that when frontline physicians encounter a severe dengue patient with signs of shock (cold, clammy extremities, prolonged capillary refill time and a weak pulse), or signs of severe bleeding or impaired consciousness, they should give intravenous fluid immediately. This should start with isotonic crystalloid solutions at 5-10 ml/kg/hour over one hour. Then the physician must urgently arrange to refer the patient to hospital.

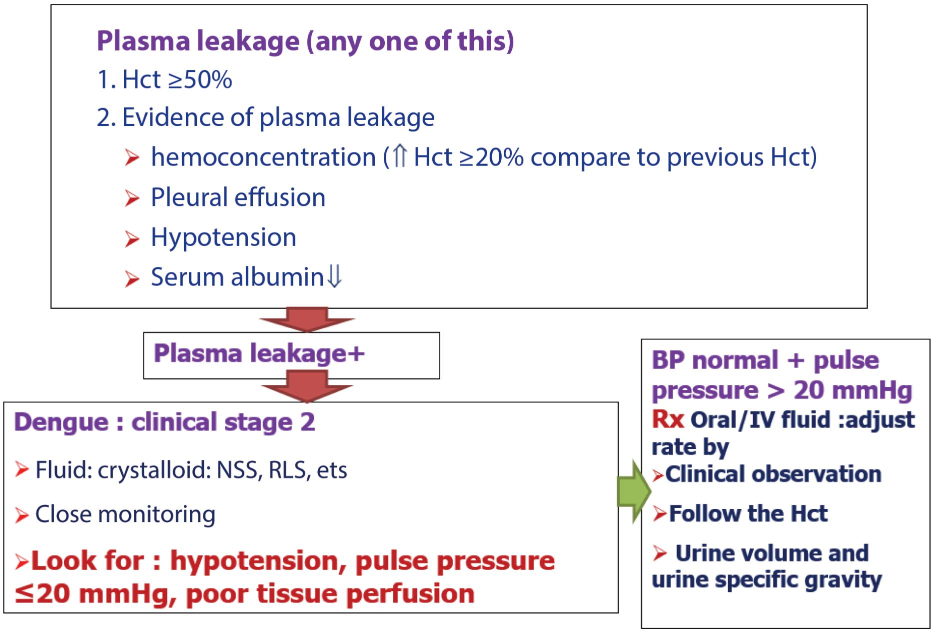
During the critical phase, the main pathophysiology is increased capillary permeability, leading to intravascular volume loss. The clinical management in this phase needs close observation of plasma leakage (Fig 1) (hemodynamically stable), and if patients have hypotension, they should receive the treatment (Fig 2).

FLUID MANAGEMENT IN PATIENT WITH PLASMA LEAKAGE

We can classify patients into 4 groups (Table 1) (modified from WHO, 2012).

1. Normal blood pressure and pulse pressure >20 mmHg.

Correspondence: Adisorn Wongsa, MD, Phramongkutklao Hospital, Ratchawithi Road, Bangkok 10400, Thailand.
E-mail: adisornwong@yahoo.com



Plasma leakage (any one of this)

1. Hct ≥50%
2. Evidence of plasma leakage
   - hemoconcentration (⇑ Hct ≥20% compare to previous Hct)
   - Pleural effusion
   - Hypotension
   - Serum albumin⇓

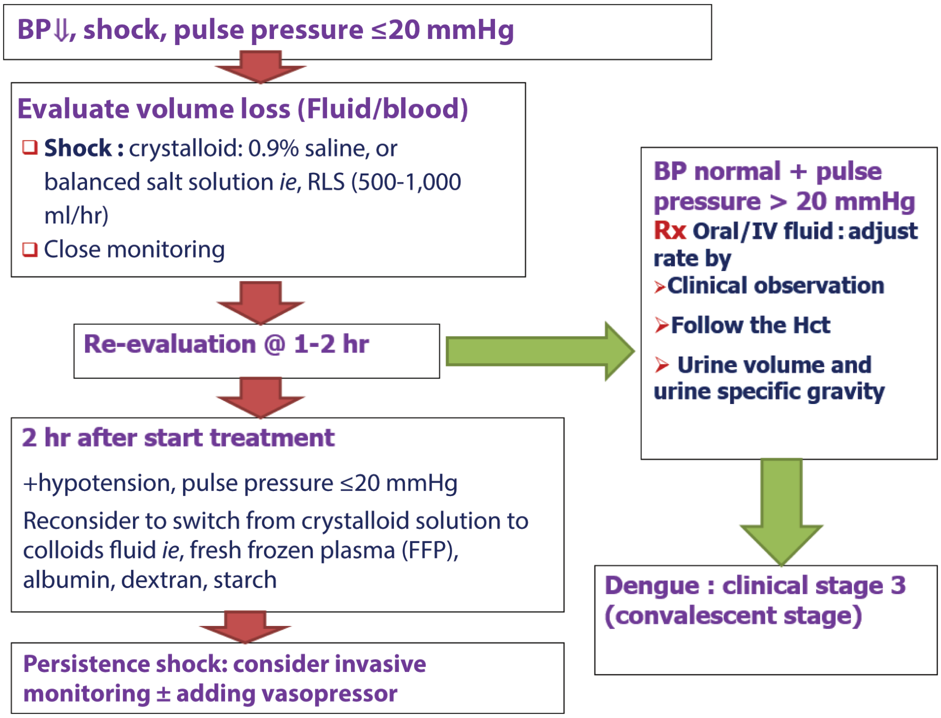
Plasma leakage+

Dengue : clinical stage 2

- Fluid: crystalloid: NSS, RLS, ets
- Close monitoring
- **Look for : hypotension, pulse pressure ≤20 mmHg, poor tissue perfusion**

BP normal + pulse pressure > 20 mmHg
Rx Oral/IV fluid :adjust rate by
- **Clinical observation**
- **Follow the Hct**
- **Urine volume and urine specific gravity**

Fig 1–Hemodynamically stable patient.



BP⇓, shock, pulse pressure ≤20 mmHg

Evaluate volume loss (Fluid/blood)
- ☐ **Shock :** crystalloid: 0.9% saline, or balanced salt solution *ie*, RLS (500-1,000 ml/hr)
- ☐ Close monitoring

Re-evaluation @ 1-2 hr

2 hr after start treatment

+hypotension, pulse pressure ≤20 mmHg

Reconsider to switch from crystalloid solution to colloids fluid *ie*, fresh frozen plasma (FFP), albumin, dextran, starch

Persistence shock: consider invasive monitoring ± adding vasopressor

BP normal + pulse pressure > 20 mmHg
Rx Oral/IV fluid : adjust rate by
- **Clinical observation**
- **Follow the Hct**
- **Urine volume and urine specific gravity**

Dengue : clinical stage 3 (convalescent stage)

Fig 2–Hypotensive patient.

Table 1
Hemodynamics management.

Normal blood pressure and pulse pressure >20 mmHg	Hypotension and/or pulse pressure ≤20 mmHg	Shock	Persistent shock despite adequate crystalloid replacement
Target end point Normal blood pressure and pulse pressure >20 mmHg Urine sp.gr. 1010-1020 and urine output 0.5-1.0 ml/kg/hr Hct ~40%-45%			
Limitation Fluid resuscitation can increase amount of plasma leakage into the 3rd space that increases the possibility of pleural effusion, ascites, and pulmonary edema.			
Treatment	Treatment	Treatment	Treatment
Oral fluid intake in most of case. IV fluid (5%D/saline, 0.9% saline) in patients who are unable to have adequate oral intake. Amount of fluid: 40-80 ml/hr and adjust according to vital signs, urine parameter, and Hct.	IV isotonic crystalloid *eg*, 0.9% saline or RLS 5-7 ml/kg/hr for 1-2 hr. If the clinical status & parameters are improved, decrease the rate to 3-5 ml/kg/hr for 2-4 hr, and then 2-3 ml/kg/hr until stable vital signs. If clinical status and parameters are worsened or not improved, increase the rate to 7-10 ml/kg/hr for 1-2 hr and re-evaluate. If not improved, the patient should be managed as “shock”.	IV isotonic crystalloid; *eg*, 0.9% saline or RLS 10-20 ml/kg/hr (500-1,000 ml) for 1-2 hr. If clinical status & parameters are improved, decrease the rate to 7-5 ml/kg/hr for 1-2 hr and then gradually decrease the rate. If clinical status and parameters are worsened or not improved, change to colloid solution: 5% albumin, Dextran, FFP 10 ml/kg/hr for 1 hr. If not improved, the patient should be managed as “persistent shock despite adequate crystalloid replacement”.	Evaluate for other co-morbidities, *eg*, condition: severe bleeding, severe sepsis, metabolic acidosis, or pneumothorax. Start vasopressor, *eg*, norepinephrine 0.1-0.2 µg/kg/min. Adjusted dosage every 10-15 min (max dose 1-2 µg/kg/min). Decrease the dose when clinical status & parameters are improved. Note: Patients with shock should have their vital signs and parameters closely monitored until resolution of shock.

2. Hypotension and/or pulse pressure ≤20 mmHg.

3. Shock.

4. Shock despite of fluid resuscitation with crystalloid solution.

The end point of treatment is to bring their hemodynamics back to normal (that is, normalized blood pressure, pulse pressure >20 mmHg, urine specific gravity 1010-1020, urine output 0.5-1 ml/kg/hr, and Hct 40-45 vol%).

For groups 1-3, the main treatment is

crystalloid solution, which has some limitation because of increasing the volume of leakage into the 3rd space, which can lead to pleural effusion, ascites, or pulmonary edema.

MONITORING THE PATIENTS DURING MANAGEMENT

1. Vital signs, peripheral perfusion and clinical status should be assessed every 15-30 minutes until the shock is resolved, and then assessed every 1-4 hr.

2. Hematocrit should be monitored 1-4 times per day according to clinical status.

3. Urine output and specific gravity should be monitored every 1 hr during unstable hemodynamics, and then monitored every 4-6 hr when the clinical status is stable.

4. Monitoring of other parameters such as oxygen saturation, acid-base balance, liver function, and renal function depends on each clinical situation.

TYPE OF FLUID

A study in Vietnamese children (Wills *et al*, 2005) found that moderately severe shock should be treated with fluid therapy using Ringer's lactate solution, and severe shock should be treated with starch over dextran. However, there is no clinical study in adult dengue infection to compare fluid management between crystalloid and colloid in volume resuscitation. Evidences comparing crystalloid and colloid for volume resuscitation in critically ill patient from other causes exist. A report for the WHO secretariat by Pablo Perel found that there is lack of effectiveness of colloid compared to crystalloid (Perel *et al*, 2013).

Also, a study of Dextran 70 in adults with septic shock showed a higher rate of severe bleeding in patients who received Dextran 70 compared with crystalloids (Hvidt and Perner, 2012). Other studies have found no significant differences in the effectiveness of crystalloid or colloid. A study in critical patients compared hydroxyl starch to saline for fluid resuscitation, and found no significant differences in mortality outcome between these 2 types of fluid (Myburgh *et al*, 2012). A recent study comparing albumin to saline in severe sepsis and septic shock also had the same result (Caironi *et al*, 2014). These recent evidences suggest that fluid resuscitation in adult dengue patients should be crystalloid. If the patient has limitation in crystalloid therapy such as developing pulmonary edema then physician should consider using colloid. Because hydroxyl starch has an increased risk of renal complications (Myburgh *et al*, 2012), and Dextran is associated with major bleeding (Hvidt and Perner, 2012), albumin or fresh frozen plasma might be considered as the colloids of choice.

VASOPRESSOR

Administration of vasopressor should be evaluated individually because they may raise blood pressure despite inadequate intravascular volume, and this leads to inadequate tissue perfusion, which can increase morbidities. However, in situation of prolonged shock in a patient who has adequate volume resuscitation or a patient who develops signs and symptoms of fluid overload such as pulmonary edema, vasopressor has a role in maintaining their perfusion pressure.

Currently, there are not any direct studies of the efficacy of vasopressors in DSS. According to the international guidelines for management of septic shock: 2012 (Surviving Sepsis Campaign), vasopressors could be applied in this situation (Dellinger *et al*, 2013). Norepinephrine should be considered as the first line agent, and vasopressin or epinephrine should be added if the patient does not respond to norepinephrine. Dopamine should be avoided because it increases risk of arrhythmia (De Backer *et al*, 2010).

WHEN TO STOP THE FLUID

During fluid therapy in the critical phase, the concern of treatment is plasma leakage, which can cause death. Then the fluid therapy should be reduced or discontinued when:

1. Patient has signs of cessation of plasma leakage.
2. Hemodynamics are stable (BP, pulse, and peripheral perfusion).
3. Hct decreases in the presence of a good pulse volume.
4. Apyrexia (without the use of antipyretics) for more than 24-48 hours.
5. Resolving bowel/abdominal symptoms.
6. Improving urine output.

Continuing intravenous fluid therapy beyond the 48 hours of the critical phase will put the patient at risk of pulmonary edema and other complications such as thrombophlebitis.

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