Management of dengue haemorrhagic fever/dengue shock syndrome.

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INTRODUCTION

The major pathophysiology in dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) is an acute increase in vascular permeability that leads to leakage of plasma through the endothelium.[1,2] The onset of plasma leakage is acute and the haematocrit rises sharply. If uncorrected, intravascular hypovolaemia leads to tissue hypoperfusion, tissue anoxia, metabolic acidosis and organ failure.

Other haemostatic changes in DHF are thrombocytopaenia and coagulation disorders. 80% of patients with DSS have an abnormal coagulation profile, suggesting a consumptive coagulopathy with thrombocytopaenia, prolonged partial thromboplastin time (PTT) and decreased fibrinogen levels. In dengue infection with liver dysfunction, the prothrombin time will be prolonged. In cases of uncontrolled shock, coagulation disorders may cause severe bleeding and may play an important role in the development of lethal shock.

Assessment of the circulation should include the following considerations:

1. Fluid intake for the previous 24-36 hours and vomiting losses.
2. Urine output for the past 24 hours and time of last micturition.
3. Frank haemorrhage and amount.
4. Presence of abdominal pain may indicate gastrointestinal haemorrhage, acute liver enlargement or hypovolaemia with intestinal ischaemia.
5. Degree of dehydration: sunken eyes, dry tongue, skin turgor.
6. Peripheral circulation: cool peripheries, peripheral cyanosis, delayed capillary return, weak volume pulses.
7. Tachypnoea, presence of pleural effusion and ascites indicate loss into 'third space'.
8. Mental status: often overlooked. Headache, irritability, combativeness, drowsiness, coma, seizures may indicate reduced cerebral perfusion, cerebral oedema, encephalopathy, intracranial haemorrhage.

DO NOT WAIT FOR THE BLOOD PRESSURE TO DROP - IT WILL BE TOO LATE

It is important to realise that "shock" is not synonymous with "hypotension" and that compensatory adjustments to progressive hypovolaemia may maintain blood pressure up to a point despite hypoperfusion of certain organs. Vasoconstriction of the vascular beds of the kidneys, lungs, intestines, skin and muscle is an attempt to maintain perfusion of the brain and heart. Overt hypotension is a late event in the evolution of the hypoperfusion state. Even with early intervention, acute renal failure as a consequence of ischaemic renal tubular injury is a common accompaniment to shock.

Early and effective fluid replacement with isotonic fluid and electrolyte solution results in a favourable outcome in most cases. With early and adequate fluid administration, DSS should be rapidly reversible. Rapid intravenous replacement will usually prevent clinical disseminated intravascular coagulation (DIC). Good prognosis depends on early recognition of plasma leakage and hypovolaemia based on careful monitoring of the clinical condition: conscious level, peripheral circulation, heart rate, blood and pulse pressure, urine output, urine specific gravity, repeated platelet and haematocrit determination~.

Investigations

1. The following are essential to the management and must be obtained upon insertion of an intravenous cannula:
   a) Full blood count, particularly platelet count and haematocrit.
   b) Blood urea and electrolytes (and serum creatinine if oliguric).
   c) Group and cross match.

2. The following should be obtained as soon as resuscitation has been started or upon admission to the ward:
   a) Liver function tests and liver enzymes for grades 3 and 4 DHF/DSS;
   b) Prothrombin time and partial thromboplastin time.

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3. The following are necessary for confirmation of DF/DHF/DSS:
   a) Blood for dengue serology[3] and virus isolation.[4]

4. Patients with raised liver enzymes must have the following measurements:
   a) Serum ammonia.
   b) Fibrinogen degradation product, fibrinogen levels.
   c) Thrombin time.

5. Patients with grades 2-4 DHF. A request must be made for fresh frozen plasma (FFP), platelet concentrates and whole blood.

Grades 1 and 2 dengue haemorrhagic fever

At our hospital we consider that children with DSS who develop complications decompensate in a short period of time. Paediatric patients who are relatively stable with DF or mild DHF (WHO grades 1 or 2) are admitted to the general paediatric ward for observation. An indwelling intravenous cannula is inserted in all patients. Stable patients are encouraged oral fluids. The blood pressure, pulse pressure, pulse rate and respiratory rate are observed regularly. The fluid intake, urine output and urine specific gravity are monitored with the haematocrit, haemoglobin and platelet count 2 to 3 times daily. The critical period occurs during the transition from the febrile to the afebrile phase which is usually after the third day. Serial determinations of haematocrit and platelet count are essential guidelines to therapy because they reflect the degree of plasma leakage and the need for intravenous fluids. Haemoconcentration usually precedes changes in pulse pressure and rate. Patients who are unable to take orally and patients with evidence of plasma leakage are given intravenous fluids: 4.3% Dextrose-0.45% NaCl at 1 to 2 times the maintenance rate to produce an adequate urine flow. These observations are continued until the temperature returns to normal for 1 or 2 days.

Dengue shock syndrome

Ill patients, i.e. those in shock, preshock, those who are restless and agitated, are admitted to the paediatric intensive care unit (PICU) for close monitoring. The most urgent consideration is to establish intravenous access even though this can be difficult in a patient with poor peripheral circulation. Placement of a central venous line in a hypovolaemic patient with abnormal coagulation may be hazardous. Alternative routes of intravenous access include the femoral vein or

intraosseous route, the latter using a 16 or 18 gauge bone marrow aspiration needle to puncture the antero-medial aspect of the tibia 2 to 3 cm below the tibial tuberosity. The intraosseous route of infusion can be discontinued when peripheral venous access is established following restoration of the intravascular volume.

Haemaccel or 0.9% NaCl of about 10-20 ml/kg is infused as rapidly as possible. This dose may be repeated until the peripheral circulation, pulse volume and blood pressure return to normal. When the tips of fingers and toes are warm, and capillary refilling occurs within 3 seconds, the peripheral circulation is fully restored. If peripheral circulatory status remains compromised following infusion of up to 40 ml/kg of crystalloid, plasma or human albumin solution (15 to 20 ml/kg) should be administered. On the average a patient in grades 3 or 4 DSS will require 30 to 40 ml/kg of fluid in the initial resuscitation period.

Metabolic acidosis is secondary to tissue hypoperfusion and is usually corrected by fluid resuscitation. However, if metabolic acidosis is severe, 1 mmol/kg sodium bicarbonate should be given as an infusion. A second or third intravenous line may be necessary to infuse platelets and fresh frozen plasma at the same time. Hypoglycaemia must be vigorously treated especially if liver failure is present.

Continued replacement of plasma losses is based on peripheral perfusion, blood pressure, urine output, urine specific gravity, frequent haematocrit and platelet count determinations and serial measurements of blood urea and creatinine. In general, the patient will require further intravenous fluids (0.45% NaCl or 0.9% NaCl) at 1.5 to 2 times the maintenance rate for 24 to 48 hours after admission.

Correction of electrolyte and metabolic disturbances

Hyponatraemia is common and metabolic acidosis occurs occasionally. Electrolyte levels and blood gases should be checked periodically in the critically ill patient. Hypoglycaemia may occur in liver failure and should be corrected with an appropriate concentration of glucose infusion.

Oxygen

Oxygen therapy should be given to all patients in shock. Sometimes the presence of the oxygen mask can increase the child's apprehension. The apprehensive, hypoxic child should never be

sedated as this may precipitate respiratory arrest.

Intra-arterial line

The critically ill child experiencing rapid shifts between fluid compartments must have an intra-arterial line (IAL) for continuous arterial pressure monitoring. IAL also facilitates sampling for blood gas, haematology and biochemical studies. It is particularly necessary in an oedematous child and it saves the peripheral veins for infusion therapy.

Renal aspects of management

The majority of patients will respond to fluid resuscitation with improvement in the peripheral circulation and the passage of concentrated urine of high specific gravity. With rehydration the urine output improves and its specific gravity decreases.

A small but significant number of patients are hypovolaemic and anuric for more than 10 hours before admission. These patients are at risk of renal tubular damage and acute renal failure (ARF). Following adequate fluid resuscitation they remain oliguric (<0.5 ml/kg/hr urine) with poor quality urine and a high blood urea and creatinine.

Once the diagnosis of ARF is made, it is essential to take great care in managing all aspects of the patient with ARF in order for spontaneous recovery to take place after about 1 to 3 weeks. Survival and return of renal function is likely to occur if the patient does not die of DHF and does not develop infectious or metabolic complications of ARF.

The first step in managing an oliguric patient is to ensure the adequacy of intravascular volume. Physical examination may indicate the presence of hypovolaemia or hypervolaemia. A chest X-ray should be done for signs of pulmonary oedema and cardiomegaly. A central venous pressure (CVP) line is invaluable in assessing the state of intravascular volume and the response to therapeutic measures.

In the absence of evidence of hypervolaemia a fluid challenge of 10 ml/kg 0.9% NaCl should be given. This volume load should always precede diuretic administration lest diuretics decrease renal perfusion by exacerbating pre-existing hypovolaemia. If there is no response to fluid challenge, frusemide should be given to distinguish prerenal oliguria from established renal failure, or to convert oliguric to non-oliguric renal failure, whereupon fluid management will become much easier. Frusemide 1 mg/kg i.v.

should be given to euvolaemic patients. If there is no response in 30 minutes, incrementally higher doses up to 10 mg/kg may be used, although at such a dose level one may be concerned about ototoxicity and interstitial nephritis. Low dose dopamine at 2-5 microg/kg/min should be added. If these therapeutic manoeuvres do not improve urine output or if, despite increased urine output, blood urea and creatinine levels continue to rise, then established renal failure has occurred. Meticulous supportive care is essential to avoid complications during the period prior to recovery of renal function, whch usually begins in 5 to 10 days. The principles of conservative mananagement are to:

a) normalise intravascular volume, systemic blood pressure and renal blood flow,

b) maintain normal sodium, potassium and acid base balance,

c) minimise accumulation of nitrogenous waste by restricting protein intake while providing adequate caloric intake to prevent a catabolic state and to promote renal repair,

d) take special care to avoid infectious complications.

Patients with ARF and "third space" losses may become hypovolaemic. It is imperative that hypovolaemia be detected and appropriately corrected as failure to do so can cause recurrent renal vasoconstriction, with resultant exacerbation and prolongation of ARF. The circulatory status should be carefully monitored and fluid balance meticulously recorded. The volume of fluid administered should be determined by CVP measurement.

In the critically ill oliguric patient receiving FFP, platelet concentrates and other blood products it may be difficult to limit intravenous fluids to maintain homeostasis. If fluid overload develops it may be better to remove excess water and solute with haemofiltration or peritoneal dialysis.

Control of haemorrhage

It is important to prevent gastrointestinal haemorrhage because it is difficult to control once it has occurred. There are many causes of haemorrhage including coagulopathy, renal failure, hepatic failure and stress gastritis. Severe gastrointestinal haemorrhage is associated with high mortality. It is our practice to administer a H, receptor antagonist and vitamin K parenterally. A gastric tube should be passed through the

oral route to empty the stomach and to enable gastric lavage to be performed.

Coagulopathy must be corrected with the infusion of fresh frozen plasma, cryoprecipitate and platelet concentrates. Blood transfusion is indicated in cases with significant haemorrhage. Plasma leakage and haemorrhage tend to shift haemoglobin levels in opposite directions. It may be difficult to recognise internal haemorrhage in the presence of haemoconcentration. A drop in the haematocrit without clinical improvement despite adequate fluid replacement suggests significant internal haemorrhage.

Pleural effusion and ascites

These are seen in about 75% of grades **3** and 4 DHF/DSS. Careful attention to the cardio-respiratory status is necessary. Massive ascites can compromise cardiac output by decreasing venous return and decrease pulmonary gas exchange by reducing functional residual capacity. Pleural effusion *per se* usually does not require drainage unless it is massive, bilateral and associated with ascites where it can cause respiratory distress. Haemorrhagic pleural effusion may contribute to the fall of haemoglobin. Overinfusion of fluids can cause massive pleural effusion and ascites.

Hepatic failure

Hepatic failure is manifested by hypoglycaemia, raised hepatic enzymes, bilirubin and prolonged prothrombin time. In the absence of gastrointestinal haemorrhage, serum ammonia levels are usually within normal limits. A euvolaemic state and normal electrolytes should be maintained. Blood glucose levels must be monitored and normoglycaemia maintained. Hepatic regeneration occurs over 1 to 6 weeks even in cases of severe hepatic necrosis."

Encephalopathy

Encephalopathy is a serious manifestation of DHF/DSS and requires urgent management. Restlessness and drowsiness are signs of cerebral oedema. In severe cases, therapy should include elective ventilation, sedation and paralysis with muscle relaxants.

It is useful to monitor intracranial pressure via an intraventricular catheter. The main hazards associated with intracranial pressure monitoring are infection and uncontrolled haemorrhage.

Reabsorption phase

The period of plasma leakage usually lasts 24 to 48 hours. A good urine output indicates sufficient circulatory volume. Reabsorption of extravasated plasma takes place and the urine volume improves even without additional intravenous fluids. A strong pulse and blood pressure are additional reassuring signs and are indications that further intravenous fluids should be reduced or stopped.

The majority of patients have an uneventful recovery. **A** small minority may encounter some problems. These patients have a markedly positive fluid balance during plasma leakage. They have gross peripheral oedema, pleural effusion and ascites with or without renal failure. During reabsorption, hypertension is seen, accompanied by bradycardia. This is not cerebral oedema but is due to fluid overload and is an indication to reduce intravascular volume with diuretics.

During the reabsorption period, expansion of the intravascular volume leads to increased venous return and increased right and left ventricular end diastolic volume. In a normal myocardium, stroke volume increases with preload, up to a point. In a child without increased metabolic demands, as stroke volume increases, heart rate decreases in order to maintain a normal cardiac output. Therefore, hypertension and bradycardia in the reabsorption phase of DSS is a sign of circulatory overload and a myocardium that is still able to cope with the increased fluid load. Nonetheless, intravenous fluids must be reduced at this stage because further increases in preload will lead to congestive heart failure.

Hypertension associated with tachycardia and tachypnoea is a worrying sign because it heralds acute pulmonary oedema and left ventricular failure. Patients with DSS and ARF are at particular risk of this complication. This is because reabsorption of extravasated fluids takes place before recovery of renal function. Patients in ARF are also predisposed to infections which increase the metabolic needs and place more demands on the fluid-loaded heart. These patients are seriously ill and will require intravenous diuretics, inotropic and respiratory support. Intravenous fluids should be reduced.

CONCLUSION

The management of DHF/DSS requires early recognition of the disease, close monitoring for the pathophysiological changes of DHF/DSS, prompt replacement of hypovolaemia with appropriate intravenous fluids and reduction of fluids during the reabsorption period.

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