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Dr.N.C.Gowrishankar Editor-in-Chief	**Dr.S.Thangavelu** Executive Editor

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TOPIC OF INTEREST - "FLUID AND ELECTROLYTE DISTURBANCE"

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FLUID AND ELECTROLYTE DISTURBANCE

COMPOSITION OF BODY FLUIDS AND MAINTENANCE FLUID THERAPY

***Nammalwar BR**
****Sudha E**

Abstract: *Holliday and Segar recommended the use of the maintenance intravenous fluids in children. This fluid contained sodium 30 mEq/L and was markedly hypotonic compared to plasma with sodium of 140 mEq/L. The resultant intravascular hyponatremia and the osmotic gradient can push fluid from the intravascular space into the intracellular space. In vital organ like brain, it can cause cellular swelling and neurological damage. Sick children both acute and non acute, have been found to have increased levels of anti-diuretic hormone secretion which reduces their ability to excrete water and can worsen the hyponatremia. The recent randomized controlled trials and guidelines recommend the use of maintenance intravenous fluids with a 0.9% sodium chloride to decrease the risk of hyponatremia and its adverse effects. Holliday and Segar recommended per day maintenance fluid rate based on daily caloric requirements of healthy children. In reality, caloric demands of sick children are much less than normal children and hence their daily fluid requirement will be much less. For sick children without dehydration hypotonic maintenance intravenous fluid at one half to two third of the standard maintenance rate per day is recommended.*

Keywords: *Children, Hyponatremia, Neurological damage, Maintenance intravenous fluid, Fluid rate.*

Holliday and Segar recommended the use of the maintenance intravenous fluids in children as early as 1950. The aim was to maintain adequate effective circulating volume and normal electrolytes without causing fluid overload. However, serious complications can arise not only from the wrong volume, inappropriate composition of IV fluid but also IV cannula related complications including extravasation, infection or thrombosis. Care should be taken in the prescription, administration and monitoring of IV maintenance fluid in children.

Darrow, et al contributed significantly to our understanding of body fluid physiology, foremost being the concept of "deficit therapy" as a method of replacing previous losses from the extracellular and intracellular fluid spaces and later the concept of "maintenance therapy" as the provision of fluid and electrolytes to replace anticipated loss from breathing, sweating and urine output.[1,2]

Physiology of body fluids

Brief knowledge of normal size and make up of body fluid compartments is essential for appropriate fluid and electrolyte management. Total body water (TBW) content changes drastically from fetal period until one year of age. At 24 weeks gestational age, a TBW content in fetus is close to 80% of total body weight. This can be 70% or higher in a newborn which slowly decreases until the child is around one year of age, when TBW content is about 60% of total body weight. The TBW in most adults is between 50% and 60% of total body weight.[3] Approximately two-thirds of TBW is in the intracellular space and one-third in the extracellular space. The extracellular space comprises of two compartments: interstitial space (75%) and plasma or vascular space (25%) (Fig.1).[4]

The electrolyte content within each compartment is distinctly different from that of the other. The extracellular fluid (ECF) contains sodium as its primary cation, with

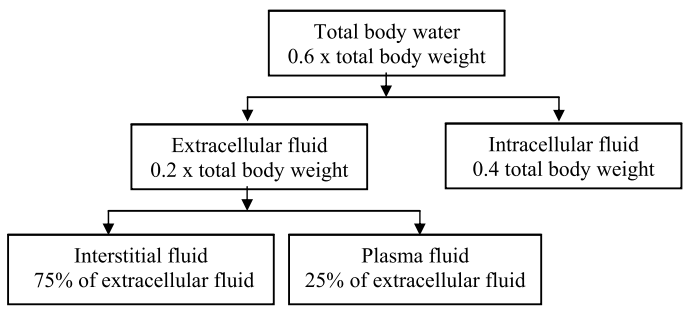

Fig.1. Body fluid compartments

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chloride and bicarbonate as its primary anions. The intracellular fluid (ICF) contains potassium as a primary cation with phosphate as the primary anion. Water moves freely across cell membranes to ensure equal osmolalities in ECF and ICF.

Sodium determines tonicity of ECF. It has the main role in the distribution of water between intracellular and extracellular compartments and therefore is the main determinant of extracelluar fluid volume. Sodium regulates water movement across cell membranes. This explains the development of intracellular edema that occurs in the presence of hyponatremia which can be detrimental as in brain where small increases in intracellular fluid may lead to disproportionately large increases in intracranial pressure. Children are at greater risk of neurological sequelae secondary to hyponatremia because their brain has a larger intracellular fluid volume per total skull volume.

In clinical practice, fluid and electrolyte restoration in the body is of prime importance followed by fluids for maintenance and ongoing losses. The most commonly used technique to calculate IV maintenance fluids for children is the Holliday-Segar method. This method estimates the fluid requirements based on the amount of kilocalories expended and is therefore indirectly related to the patient's weight (Table I). Accordingly for every 100 kilocalories expended for metabolism, 100 mL of fluid is needed in normal children. But a point to note is that energy expenditure in critically ill children may be as low as 50-60 kcal/kg/day. Requirement for sodium is 3 mEq/kg/day, while the requirement for potassium is 2 mEq/kg/day. Chloride requirement which is 5 mEq/kg/day is met by administering sodium and potassium as sodium chloride and potassium chloride salts.[5]

Tonicity of maintenance fluid - Controversy

Based on the content found in both human and cow's milk, 3 mEq/kg/day of sodium was proposed as maintenance by Holliday and Segar in healthy patients. When combining 3 mEq/ kg/day of sodium with the 100 ml/kg/day of maintenance fluid volume, the prescribed fluid contained approximately 30 mEq/L of sodium. This fluid is markedly hypotonic. Sick children are likely to release anti-diuretic hormone (ADH) as a response to illness which along with hypotonic fluids leads to water retention and subsequent hyponatremic encephalopathy and increased mortality.

One of the earliest studies reported more cases of neurologic morbidity and also mortality resulting from hospital-acquired hyponatremia in children who were receiving hypotonic IV fluids. Administration of isotonic saline in IV maintenance fluids was recommended as the prophylactic measure to prevent the development of hyponatremia.[6]

In a meta-analysis of ten RCTs that compared isotonic to hypotonic maintenance IV fluid therapy in hospitalized children, there was a significantly greater fall in plasma sodium in those children who received hypotonic maintenance IV fluids but there was no significant difference for the risk of hypernatremia between the two interventions.[7]

In a meta-analysis in 2014, ten studies were identified as independent randomized controlled trials, five in the intensive care setting, four in regular wards and one in a mixed setting. Hyponatremia was seen more often in those receiving hypotonic fluids than in those receiving isotonic fluids, with an overall relative risk of 2.37. A subgroup analysis of hypotonic fluids with half-normal saline also found a relative risk of hyponatremia of 2.42. The meta-analysis concluded that in intensive care and postoperative settings, the administration of hypotonic maintenance fluid increases the risk of hyponatremia when compared with administration of isotonic fluids; data was insufficient for children in the general wards.[8]

A Cochrane review of 10 studies with 1106 children concluded that those who received isotonic fluid had a substantially lower risk of hyponatremia though it was unclear whether there is an increased risk of hypernatremia when isotonic fluids are used. The majority of the children were intensive care patients and/or surgical patients.[9]

All these studies had certain short comings which preclude a blanket recommendation for use of isotonic fluid in general wards or in non-acutely ill children. Majority of

Table I. Holliday-Segar formula for maintenance fluid requirements by weight

Weight (kg)	mL/day	Water (mL/hr)
0–10 kg	100/kg	4/kg
11–20 kg	1000 + 50/kg for each kg >10	40 + 2/kg for each kg > 10
> 20 kg	1500 + 20/kg for each kg > 20	60 + 1/kg for each kg > 20

these studies were done in postoperative patients or ICU patients (except the study by Foster, et al) with use of various types of hypotonic fluids and statistically were not adequately powered.[10]

In a more recent study of 690 children in a broad pediatric population, 319 received IV isotonic fluid containing 140 mEq/L of sodium and 322 received IV fluid containing 77 mEq/L of sodium. Fewer patients given fluid containing 140 mEq/L of sodium than those IV fluid containing 77 mEq/L of sodium developed hyponatremia (4% vs. 11%). No clinically apparent cerebral edema occurred in either group. The authors recommend that isotonic fluid should be used for maintenance therapy in children.[11]

It is interesting to note that hyponatremia has been observed even with isotonic or near-isotonic fluids in the perioperative period. This was due to generation of electrolyte free water due to excretion of hypertonic urine. This was termed, as "desalination" phenomenon. The pathophysiology is said to be related to the increased volumes of infused saline, increased ADH, natriuretic peptide, glomerular filtration and suppression of aldosterone. The risk of hyponatremia is further aggravated if a hypotonic solution is administered. The other mechanism to explain hyponatremia with isotonic fluids is the intracellular shift and redistribution of sodium due to increased membrane permeability, a 'disorder of microcirculation' known as translocational hyponatremia or sick cell hyponatremia.

Physiological aberrations in the use of normal saline

Owing to the 'strong ion' Cl^- and the lack of buffering capacity, normal saline (NS) infusion can be complicated by metabolic acidosis. Advocates of the alternative Stewart approach, introduced in 1983, argue that the change is direct due to infusion of the 'strong ion' Cl^-. Excessive chloride loading leads to disproportionate urinary bicarbonate loss. Secondly, chloride ions suppress renin release and leads to reduced aldosterone availability and also decreases bicarbonate retention. Thirdly metabolic acidosis is due to renal vasoconstriction and decreased glomerular filtration rate.[12]

Rate of maintenance fluid - Controversy

Those in favor of isotonic solutions argued that fluids containing higher sodium and therefore tonicity, would reduce the risk of iatrogenic hyponatremia and its sequelae in the setting of an inability to excrete free water. Those in favor of hypotonic solutions argued that iatrogenic hyponatremia is related to excess fluid volume administration (hence restrict fluid intake) and not due to the aberrant production of ADH and retention of free water which decreases serum sodium concentrations. Further the fluids containing higher sodium increases the risk of hypernatremia and fluid overload.

Analyzing the complications of isotonic IV fluids, this study reports that developing hypernatremia was not significantly increased. The development of hyperchloremic metabolic acidosis and other manifestations of volume overload (e.g., congestive heart failure, pulmonary edema) were not reported in any of the 11 studies included in a systematic review in 2015.[13] As a fall out of these speculations, studies have examined the impact of the rate of maintenance IV fluid administration on hyponatremia.

Three different IV fluid regimes to compare the incidence of hyponatremia in hospitalized children from 3 months to 12 years of age were analysed. The children were randomized to three IV fluid groups: Group A, 0.9% saline in 5% dextrose at the standard maintenance rate; Group B, 0.18% saline in 5% dextrose at the standard maintenance rate and Group C, 0.18% saline in 5% dextrose at two-thirds of the standard maintenance rate. 14.3% of the children in Group B who were administered 0.18% saline in 5% dextrose at the standard maintenance rate developed hyponatremia compared with 1.72% of the children in Group A and 3.8% of those in Group C. The administration of 0.9% saline in 5% dextrose as IV maintenance fluid helps in reducing the incidence of hospital-acquired hyponatremia among children.[14]

In another study of 50 children, 0.9% saline, 0.18% dextrose saline at either the traditional maintenance fluid rate or 2/3 of that rate was compared for their effect on sodium level. At the end 24 hours 0.18% dextrose saline full maintenance rate produced a greater fall in plasma sodium than restricted rate, but the difference was small and non-significant.[15]

In a prospective, randomized, non blinded study, 124 children admitted for surgery received 0.9% NS or 0.45% saline solution at 100% or 50% maintenance rates. Plasma sodium concentrations fell in both 0.45% saline groups at 8 hours but not at 24 hours. The study concluded that the risk of hyponatremia was decreased by isotonic saline solution but not by fluid restriction.[16]

Points to ponder

Sick children are prone for non-osmotic stimuli for ADH release that will lead to preferential retention of free water, which will thereby decrease serum sodium concentrations and hence the need for isotonic IV fluids.

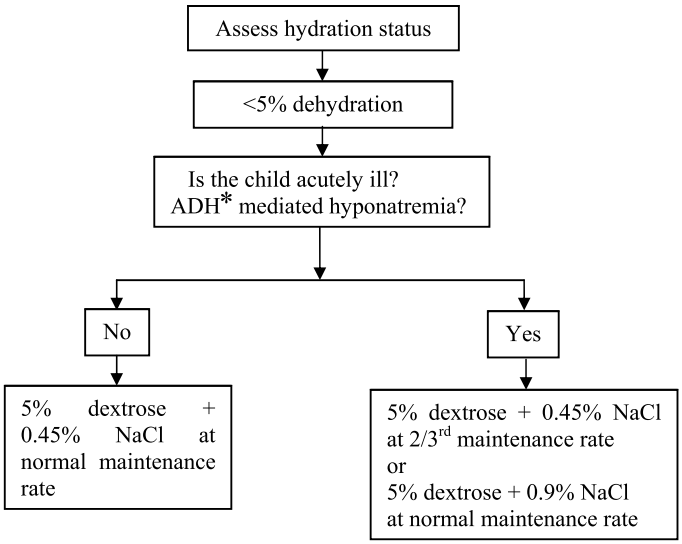

Fig.2.Algorithm for initial maintenance fluid with <5% dehydration

*(*Risk of excess ADH secretion due to non-osmotic stimuli – Bronchopneumonia, CNS infection, post operative state, critically ill child)*

The Holliday-Segar method estimates the IV fluid requirements with the amount of kilocalories expended and therefore indirectly related it to the weight of children. Accordingly for every 100 kilocalories expended for metabolism, 100 mL of fluid is needed in well, active children with a normal metabolism and normal renal function. But it should be noted that energy expenditure in critically ill children may be as low as 50-60 kcal/kg/day. Hence, the actual fluid requirements in unwell children would actually amount to half of that suggested by Holliday and Segar method.[17] In 2013, WHO recommended that "children who require IV fluids for maintenance should be managed with Ringer's lactate with 5% dextrose, or 0.9% sodium chloride (NS) with 5% dextrose or 0.45% sodium chloride (½ NS) with 5% dextrose.[18]

In 2015, the National Institute for Care Excellence (NICE) recommended that if children and young people need IV fluids for routine maintenance, initially use isotonic crystalloids that contain sodium in the range 131-154 mmol/L should used. During acute illness, if there is a risk of water retention associated with non-osmotic ADH secretion, either restricting fluids to 50-80% of routine maintenance needs or reducing fluids, calculated on the basis of insensible losses within the range 300-400 ml/m^2/ 24 hrs plus urinary output should be considered.[19] Based on the above concepts an algorithm for initial maintenance fluid for <5% dehydration and >5% dehydration is given in Fig.2 and Fig.3 respectively.[19]

Replacement

Clinical situations where replacement fluids are needed include patients with chest tubes in place, uncontrolled vomiting, profuse diarrhea, or externalized cerebrospinal fluid shunts. In these situations IV fluids that contain sodium in the range of 131(RL) to 154(NS) mEq/L should be considered.[20]

Unaddressed issues

Dextrose: The appropriate dextrose concentration in intravenous fluids for children at different ages is not clear and probably cannot be generalized, as it is pathology specific. There is a lack of evidence that it is beneficial to add glucose to intravenous fluids in children. The standard prescription is 5% dextrose solution. 10% dextrose solution may result in hyperglycemia.

Potassium: Whether potassium should be added to standard intravenous fluids and if so how much to be added is not addressed in the studies. Holliday-Segar formula recommends 20 mEq/L.

Fluid and electrolyte therapy requires clinical judgment to modify the therapy as circumstances dictate.[5] This discussion will not extend to the neonates who have their own unique fluid and electrolyte requirements. Maintenance fluid as discussed above is the usual water and electrolyte requirements for a 24 hours period in a child with no associated confounding factor. The need for fluid requirements increases in patients with high solute loads, such as glucosuria and diabetic ketoacidosis, or severe catabolism with high protein losses, such as burns or crush injuries, uncontrolled diabetes insipidus, increased insensible losses from fever or an increased respiratory rate. Decreased free water requirements is seen in SIADH as in postoperative stress, persistent nausea, coma, head injury and positive pressure ventilation. Reduced maintenance requirements are seen in oliguric conditions and ventilator use with fully humidified air.[21] There is a growing body of evidence that balanced crystalloids (Plasma-Lyte A or Ringer's lactate) are preferred over normal saline in clinical practice.[12,22]

Guideline for IV fluid therapy[22]

1. Monitor the total fluid intake (TFI)**.** Monitor the fluid which the child actually received rather than the volume ordered or prescribed. Experience shows that the TFI is often in excess of the volumes that are prescribed. At each assessment consider whether oral fluids could be commenced.

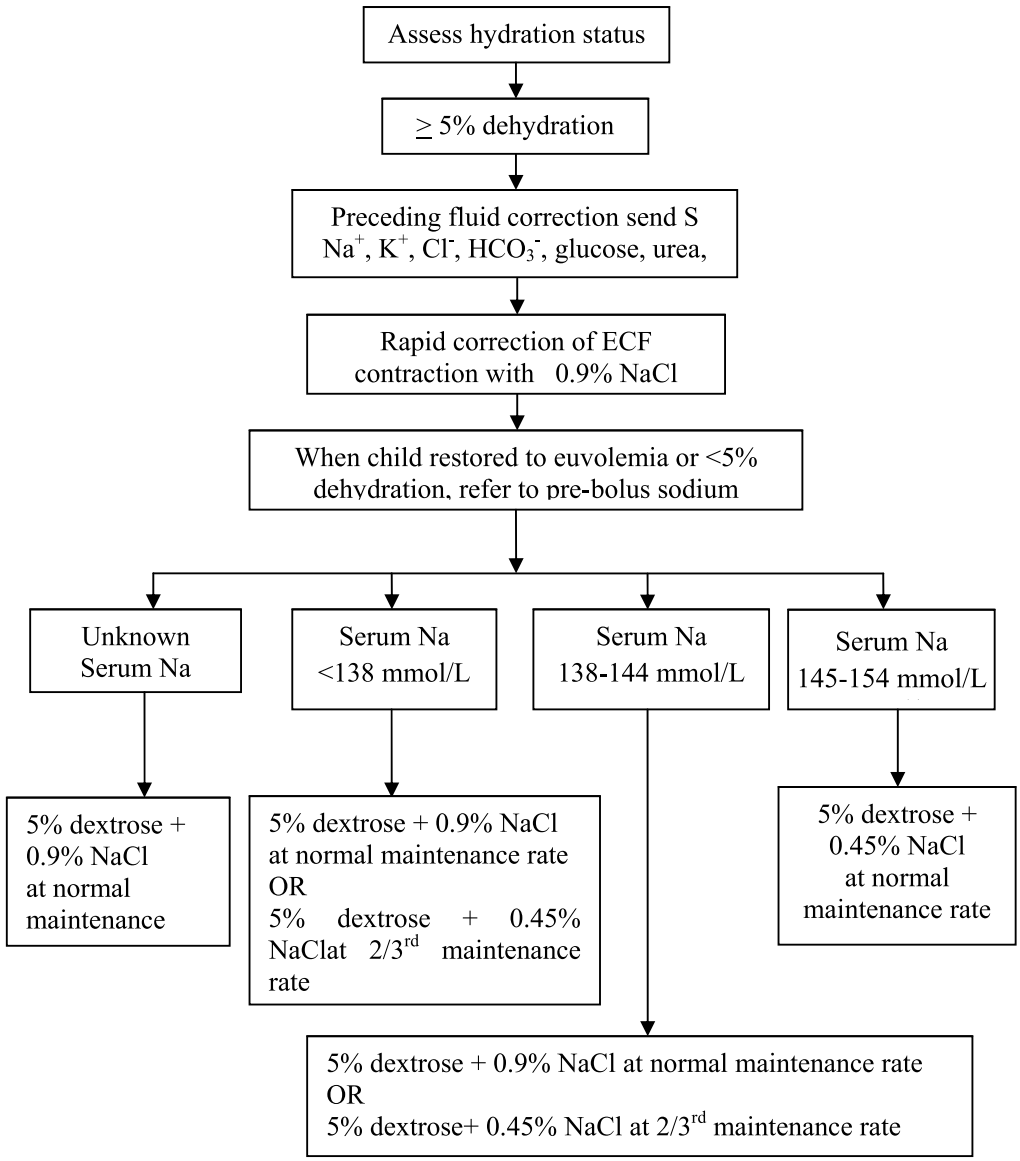

Fig.3. Algorithm for initial maintenance fluid with >5% dehydration

2. Children receiving intravenous fluids should be weighed daily**.** An increase in weight of 5% or more over 24 hours indicates fluid overload. If so IV fluids should be stopped and the serum sodium measured. A decrease in weight of 5% or more indicates dehydration. It is advisable to weigh on the same scales in similar light-weight clothing for more accurate monitoring.
3. Check for edema every day**.** If either puffy eyes and lower limb swelling is present, intravenous fluids should be reduced or stopped and reassessed. It is necessary to check for signs of dehydration, especially if the child has ongoing abnormal losses (e.g. diarrhea or vomiting).
4. Every child receiving 50% or more of maintenance volumes of intravenous fluids should have the serum electrolytes checked daily. If the serum sodium is below 130 mmol/L or has fallen by more than 5 mmol/L since admission, the type and volume of intravenous fluid given is reassessed. If the serum sodium is 150 or above, or has risen by 5 mmol/L from the time of admission the possible causes should be reviewed (dehydration, sodium excess).
5. In infants less than 6 months on IV fluid, blood glucose should be measured every 6-12 hours. If the blood glucose is less than 50 mg/dL, correct the hypoglycemia and intravenous fluid should be changed from that containing 5% to 10% glucose. Child is fed if possible.

Points to Remember

- ***Be aware of the risks of inappropriate hypotonic maintenance intravenous fluid.***

- ***Isotonic maintenance intravenous fluids similar to sodium concentration of plasma or its tonicity are recommended.***
- ***In non-dehydrated children, consider 0.9% sodium chloride in 5% dextrose or 0.45% sodium chloride in 5% dextrose at a reduced rate for maintenance intravenous fluids.***

(Acknowledgment: We thank Dr Vinodh Choudhury, Junior Consultant, Department of Pediatric Nephrology, Dr Mehta Multispecialty Pvt Ltd., for the assistance in collecting the references).

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FLUID AND ELECTROLYTE DISTURBANCES IN CHILDHOOD DIARRHEAL DISEASES

*Sadagopan Srinivasan
**Rangan Srinivasaraghavan

Abstract: *Acute gastroenteritis (AGE) is the most common illness leading to dehydration in children, especially in developing nations. It is often associated with fluid and electrolyte disturbances, which is responsible for the morbidity and mortality associated with diarrheal diseases. The disease severity depends on the degree of dehydration. Correct assessment of severity of dehydration and identification of underlying electrolyte imbalance is an essential step in management plan. Most of these children can be successfully treated by timely use of oral rehydration solution. This review focuses on the pathophysiology and management of the fluid and the common electrolyte disturbances associated with childhood diarrheal diseases.*

Keywords: *Diarrhea, Fluid and electrolyte balance, Child, Fluid therapy.*

Acute gastroenteritis (AGE) is the most common illness leading to dehydration, especially in children in developing nations with poor sanitation, environmental hygiene and inadequate access to safe drinking water.[1] According to the World Health Organization (WHO), diarrheal disease is the second leading cause of underfive mortality, accounting for 760,000 deaths per year in this age group.[2] Most of these diarrheal deaths are due to acute infectious diarrhea, commonly referred to as acute gastroenteritis and its ensuing complication, dehydration which is largely preventable with home available fluids and easily treatable with oral rehydration solution (ORS).[3,4] The disease severity often depends on the degree of dehydration.[5] Assessment of the "dehydration status" of these children by both history and physical examination forms the essential step in formulation of the management plan. Most of these children are not dehydrated and can be successfully treated at home with replacement of ongoing fluid losses. Timely use of ORS has saved millions of children in developing nations. The routine use of antibiotics and anti-diarrheal agents is not recommended for treatment of acute diarrhea and strongly discouraged as their use may be often harmful.

Acute diarrhea is defined as abrupt onset of increased fluid content of the stool above the normal value of approximately 10 mL/kg/day. Usually, this implies an increased frequency of bowel movements, which are more than 3 times per day.[3] Though this definition mentions the amount and frequency in definitive terms, diarrhea in an individual child refers to more than his/her "usual" passage of stools - i) increase in amount, ii) increase in frequency and iii) increase in the fluid state (water content).[4] The increased water content of the stools is the result of an imbalance in the function of the small and large intestinal processes involved in the absorption and secretion of electrolytes, organic substrates and thus water.

Diarrhea - Classification

Classifying diarrhea based on duration and content is clinically more useful. This type of categorization helps to guide evaluation and management decisions.[6]

Four clinical types exist for diarrheal conditions:

(i) Acute watery diarrhea lasting upto 14 days which generally is viral or toxin mediated. Reassurance and replacement of ongoing fluid losses usually are all that is required. No specific testing is required.

(ii) Acute dysentery (diarrhea with blood in stool) - This presentation requires quick action. Blood in a diarrheal stool is a sign of infection, allergies such as cow milk protein allergy or immune-mediated inflammation as in inflammatory bowel disease.

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Table I. Infectious diarrhea in children – Causes

	Causative organisms
Virus	Rotavirus, Noroviruses, Sapovirus, Adenovirus, Astrovirus
Bacteria	Escherichia coli (ETEC, EIEC, EHEC, EAEC), Shigella species, Vibrio cholerae, Non-typhoidal salmonella, Campylobacter jejuni, Clostridium difficile
Parasites	Giardia lamblia, Entamoeba histolytica, Cryptosporidium parvum
Fungal	Candida

(iii) Persistent diarrhea lasting 14 days or longer - if the beginning of the episode is well marked, often with weight loss. In chronic diarrhea, a definite starting point cannot be often obtained as it is insidious in onset.

(iv) Diarrhea with severe malnutrition, which places the child at high risk for complications and mortality.

Infectious diarrhea: AGE, common intestinal communicable infection in children in their earlier years, causes fever, vomiting and diarrhea. Mostly it is viral, but in some cases may be bacterial and in a few, parasitic (Table I).[4] Seasonal and sporadic community outbreaks are also reported periodically.

Non-infectious inflammatory diarrhea: This indicates the presence of an inflammatory process in the absence of viral, bacterial, or parasitic infection - Cow's milk allergy and other food allergies (infancy and early years of life), inflammatory bowel diseases and rarely due to bowel ischemia, radiation or chemical injury. Inflammatory bowel diseases may be episodic and often associated with mucoid and bloody stool, tenesmus, fever and severe crampy abdominal pain.

Non-inflammatory diarrhea: This is usually watery, large-volume, frequent stool (>10 to 20 per day). Volume depletion is possible due to high volume and increased frequency of bowel movements. This is characterized by absence of tenesmus, blood in the stool, fever, or fecal leukocytes. Non-inflammatory diarrhea can be classified into: Secretory diarrhea and osmotic diarrhea.

(i) Secretory diarrhea: There is an altered transport of ions across the mucosa, which results in increased secretion and decreased absorption of fluids and electrolytes from the GI tract, especially in the small intestine. Secretory diarrhea tends not to decrease by fasting. Examples of causes are:

- Enterotoxins: These can be from infection such as Vibrio cholerae, Staphylococcus aureus, enterotoxigenic E coli, and possibly HIV and rotavirus.
- Hormonal agents: Vasoactive intestinal peptide (VIP), small-cell cancer of the lung, and neuroblastoma.
- Other causes: Laxative use, chronic diarrhea with celiac sprue, collagenous colitis, hyperthyroidism, and carcinoid tumours.

(ii) Osmotic diarrhea: Stool volume is relatively small (compared with secretory diarrhea) and diarrhea improves or stops on withholding those probable offending dietary items known to be osmotically active. It results from the presence of unabsorbed or poorly absorbed solute (magnesium, sorbitol and mannitol) in the intestinal tract that causes an increased secretion of liquids into the gut lumen. Measuring stool electrolytes shows increased osmotic gap (>50), but the test has very limited practical value. Stool (normal or diarrhea) is always isosmotic (260 to 290 mOsml/L). Osmotic diarrhea can be due to:

- Maldigestion - Refers to impaired digestion of nutrients within the intestinal lumen or at the brush border membrane of mucosal epithelial cells. It can be seen in pancreatic exocrine insufficiency and lactase deficiency.
- Malabsorption - Refers to impaired absorption of nutrients. It can be seen in small bowel bacterial overgrowth, mesenteric ischemia, post bowel resection (short bowel syndrome) and in mucosal disease (celiac disease).

Complications of acute diarrhea

1. Severe dehydration and shock leading to mortality - Children manifest with cold clammy peripheries with rapid thready pulses and severely reduced urine output. The BP is low. CNS hypoperfusion causes lethargy. There is associated acute kidney injury of pre-renal type (acute tubular necrosis). The urine output improves dramatically with fluid therapy.
2. Dyselectrolytemia- Hyponatremia, hypernatremia, hypokalemia.

a. Hypokalemia - Can cause paralytic ileus (distended abdomen with absent bowel sounds) and arrhythmias.

b. Hyponatremia - Can cause seizures and altered sensorium

c. Hypernatremia - Child presents with shrill, high pitched and irritable cry (due to intracellular dehydration) with doughy skin feel on pinching the abdomen skin. It can also cause altered sensorium.

3. Acute tubular necrosis leading to acute kidney injury

4. Hypercoagulable state - Hemoconcentration due to fluid loss can cause venous thrombosis in infants. Cortical vein thrombosis and renal vein thrombosis are rare complications of dehydration.

5. Metabolic acidosis - Normal anion gap acidosis is often associated with severe diarrhea. The anion gap remains normal because the bicarbonate that is lost in the body fluids through the GI tract is compensated by chloride retention.

6. Sepsis - Bacterial causes of diarrhea are more likely to produce sepsis, mostly in neonates and infants

7. Lactose intolerance - This may follow an episode of acute gastroenteritis where it is called secondary lactose intolerance. It results in osmotic diarrhea. If plenty of lactose is given in diet, undigested lactose can offer an osmotic effect to absorb more fluid to lumen resulting in more liquid stools. Undigested lactose can reach colon and get fermented by the colonic bacteria. This produces greenish, acidic stools which is very frothy. The frequent passage of acidic watery stools causes perianal excoriation.

8. Hemolytic uremic syndrome (HUS) after dysentery - Common in infants. Suspect HUS in a child with recent history of dysentery or diarrhea presenting with pallor and reduced urine output. The pallor is caused by microangiopathic hemolytic anemia. HUS leads to acute kidney injury of intrinsic renal injury type. Fluid therapy will not result in improvement of urine output.

9. Persistent diarrhea and malnutrition - Acute weight loss may result in pushing a child to malnutrition.

Dehydration refers to the state of hypovolemia resulting from occurrence of a negative balance of water and electrolytes from the fluid compartments of the body (intravascular, extravascular or both), due to various causes leading to increased loss of fluids.

The loss may be from i) GI tract (AGE, congenital adrenal hyperplasia leading to increased urinary salt and water losses due to mineralocortical deficiency), ii) kidneys [polyuria as in renal tubular acidosis (RTA), use of diuretics], iii) skin (cystic fibrosis, scorpion sting envenomation, high grade fever, sweating, burns), iv) lungs (hyperventilation).

Decreased intake (anorexia, altered mental status, local oro-buccal-palatal conditions, e.g., cleft lip / palate, pharyngitis, stomatitis, etc) and movement of water out of the intravascular space (burns, ascites, paralytic ileus, anaphylaxis, infections like dengue, sepsis, peritonitis, etc.) also can cause dehydration.

Pathophysiology of dehydration in acute gastroenteritis

Dehydration occurs due to loss of water and electrolytes. Initially these losses occur from the extracellular space, leading to compensatory shifts of fluid from the intracellular to the extracellular space. There can be loss of sodium, potassium and chloride (more in vomiting) and bicarbonates (more from intestinal losses). Depending on the relative loss of the major electrically charged cation e.g. Sodium (Na+) and water from the extra cellular compartment following watery diarrhea and vomiting, the dehydration state has been classified as isonatremic, hyponatremic or hypernatremic dehydration.

Isonatremic (Isotonic) dehydration: There is a proportional loss of water and sodium due to AGE. Plasma sodium level (135-145 mmol/L) and hence the plasma osmolality (275-295 mOsm/kg) are maintained within the normal range. The state of dehydration is termed isotonic dehydration. Nearly 80% or more of diarrheal dehydration is isonatremic.

Hyponatremic dehydration: 5%-10% of diarrheal dehydration. The serum Na^+ is less than 130 mEq/L and the osmolality of the plasma is low. It occurs, when there is a proportionately more loss of sodium when compared to fluids during AGE, or when a child is administered plain water or inappropriately dilute fluids for treatment.

Hypernatremic dehydration - 10%-15% of diarrheal dehydration - The serum Na^+ is more than 150 mEq/L and the osmolality of the plasma is high. It is commonly seen in neonates and infants or it may be due to administration of concentrated high sodium fluids to the child.

Clinical history in acute diarrheal disorders in children

The objectives of history taking (Table II) are to i) assess the hydration and nutritional status of the child, ii) understand the site of GIT involved, iii) get an insight into the cause of the diarrheal disorder and pathogenesis,

Table II. History to be obtained with regard to assessment of dehydration

Symptom	Characteristics
Stools	Frequency, consistency, amount, presence of blood, mucus, duration
Vomiting	Frequency, amount, presence of bile
Fever	Absent, grade (low /moderate/high)
Thirst	Same as in usual state, thirsty asking for water or excessively (craving for) thirsty (highly suggestive of hypernatremic dehydration)
Passing of urine	Frequency, amount (after onset of diarrhea) in the previous 8-12 hours (same or decreased than before)
General appearance	Well as before / unwell (sick/ very sick) after onset
Activity (motor)	Normal / reduced / lying down all the time (weak)
Attitude, behaviour irritable	Normal, drowsy - sleepy/lethargic (indicative of hyponatremia), "excessively" and peevish (Highly suggestive of hypernatremic dehydration)
Skin : Anything unusual noticed	Mottling or pale appearance
Feel of the extremities (feet and hands)	Colder than body
Type of fluids given at home or by health providers	Water, dilute or concentrated commercial drinks like fruit juices, colas, sodas, etc
Types of dietary food items given and method of feeding	Before illness - Breastmilk, bottle feeds, cereals, fruits, etc., and during illness
Any treatment given	

iv) institute the plan and place of management – triaging to treat dehydration and v) find out the indication for use of antibiotics and choice of antibiotics.

Historical clues towards etiology and etiopathogenesis of diarrheal disorders

Although nausea and vomiting are nonspecific symptoms, they indicate infection in the upper intestine. Fever suggests an infective process but also occurs as a result of dehydration or co-infection (e.g. urinary tract infection, otitis media). Fever is common in patients with infective diarrhea. Features such as nausea and vomiting and absent or low-grade fever with mild to moderate periumbilical pain and watery diarrhea indicate small intestine involvement and also reduce the likelihood of a serious bacterial infection. Severe abdominal pain and tenesmus indicate involvement of the large intestine and rectum. Distended abdomen may be seen with hypokalemic paralytic ileus.

Ingestion of contaminated food followed by rapid onset of nausea and vomiting within 6 hours can be by preformed toxins of Staphylococcus aureus, with possible fever, abdominal cramps, and diarrhea within 8-72 hours while watery diarrhea and abdominal cramps after an 8-16 hours incubation period are associated with enterotoxin-producing Cl perfringens and B. cereus.

Traveller's diarrhea with history of recent travel to endemic area followed by abdominal cramps and watery diarrhea after a 1-2 days incubation period and can be due to enterotoxigenic E.coli. Cryptosporidium and cyclospora can cause recurrent diarrhea or persistent diarrhea in a setting of immunodeficiency.

Several organisms, including Salmonella, Shigella, C. jejuni, Yersinia enterocolitica, enteroinvasive or hemorrhagic (Shigatoxin-producing) E. coli and V. parahemolyticus can cause fever, tenesmus and diarrhea that can contain blood as well as fecal leukocytes.

Box 1. Children who are at "Higher" Risk

- Neonates and infants <1 year
- Low birth weight neonates (Preterms & IUGR)
- Severe acute malnutrition
- Obese children
- Infants, unable to breastfeed during illness
- Those with > 5 watery, loose motions (as in cholera) in < 24 hours
- Those with repeated vomiting, not accepting or retaining ORS/feeds
- Those with altered sensorium or excessively tired and lethargic

Bloody diarrhea and abdominal cramps after a 72-120 hours incubation period are associated with infections from Shigella and also Shiga toxin-producing E. coli, such as E. coli O157:H7. Organisms associated with dysentery or hemorrhagic diarrhea can also cause watery diarrhea alone without fever initially. In antibiotic associated diarrhea there is onset of diarrhea a few days after starting antibiotic. Children who are at higher risk in diarrheal diseases is given in Box 1.

Evaluation: The objectives of evaluation of a child with acute diarrhea include to i) assess presence or absence of dehydration, its severity, presence of signs of acidosis, signs of hypokalemia, ii) assess the nutritional status of the child with diarrhea, iii) decide the triaging and further management plan A, B or C (Home/ ORT centre/ Inpatient treatment - with ORS/ initial I.V parenteral fluids) and iv) get an insight into the cause of diarrheal disease to decide about the need for antibiotic therapy.

Rapid assessment of hydration status and the degree of dehydration

a) Observe: General appearance, behaviour, sensorium and mental status, alertness, general motor activity, depressed fontanelle, sunken eyes, tears, moistness /dryness of conjunctiva, cornea, oral mucous membrane and tongue, abdominal distension, perianal excoriation, nutritional status (normal, obese, malnourished), presence of fast, deep and sighing breathing (acidotic). If the child is admitted in ORS area / centre the child's stools - colour, fluidity, amount, presence of mucus or blood - and urine (amount, frequency and colour) should be noted.

b) Touch and feel: Distal extremities (warm or cool and pale), temperature (rectal in malnourished infants), pulse-rate, rhythm and volume, capillary refill, skin turgor by skin

Table III. Dehydration - Classification

Symptoms / Signs	Dehydration		
	No	Some (Mild and Moderate)	Severe
Sensorium/ Mental Status	Well, alert	Irritable, fatigued, restless	Apathetic/lethargic Unconscious
Thirst	Normal	Thirsty, eager to drink	Poor / Inability to drink
Eyes	Normal	Slightly sunken	Deeply sunken
Tears	Present	Decreased	Absent
Mouth and tongue	Moist	Dry	Parched
Skin turgor (Skin fold recoil)	Instant	Slow in <2 sec	Very slow in >2 sec
Capillary refill (CFT)	Normal	Prolonged	Markedly prolonged
Extremities	Warm	Cold	Cold, mottled, cyanotic
Pulse volume	Normal	Normal	Weak, thready, impalpable
Breathing	Normal	Normal	Deep, acidotic
Heart rate	Normal	Normal/ Increased	Tachycardia
Urine output	Normal	Reduced	Minimal
Fluid deficit (Body weight loss in%)	< 3%	>3% but <10%	>10%

Table IV. Low-osmolarity WHO - UNICEF ORS (from 2002)

Constituents		mmol /litre	
Sodium Chloride	2.6g	Sodium	75
Potassium chloride	1.5g	Potassium	20
Trisodium citrate	2.9g	Chloride	65
		Citrate	10
Glucose	13.5g	Glucose	75
Osmolarity			245
The entire contents have to be diluted in 1 litre of water			

Box 2. Low osmolarity ORS – Advantages

i) Lower stool volumes;

ii) Less vomiting resulting in better acceptance by mothers and caregivers

iii) Fewer instances of unscheduled switch over to parenteral fluid administration

iv) Shorter duration of diarrhea by 24-48 hours

v) No instance of hypernatremia

vi) Overall increased efficacy over the previous high osmolarity (311mOsm/L) ORS

vii) Reduces stool bulk by favouring water movement from gut lumen into body

pinch over the abdomen, vital signs including BP recording in presence of moderate to severe dehydration. Classification of dehydration based on clinical symptoms and signs is given in Table III.

Management

Diagnostic tests/investigations: Almost all guidelines and evidence based recommendations "do not recommend" routine ordering of laboratory tests. In severe diarrhea, renal function tests- serum creatinine, blood urea, serum electrolytes (sodium, potassium) and if child is in shock obtain venous blood gas and blood cultures are done.

Microscopic examination of stool for ova / cyst for parasites, mucus, blood and leukocytes is done in select situations. Stool cultures may be obtained in dysentery with suspected hemolytic-uremic syndrome and in immune suppressed children with diarrhea.

Treatment: The two pillars of management in AGE are immediate attempts at oral rehydration and rapid reintroduction of regular feeding following initial fluid rehydration.[7,8,9]

Oral rehydration therapy: Described as "potentially the most important medical advance of the 20th century" by the Lancet, oral rehydration solution has resulted in a significant reduction in number of deaths associated with diarrhea.[10] Despite being one of the most important scientific discoveries that has helped millions, the recognition given to the researchers like Richard A Cash, Nathaniel Pierce, Dilip Mahalanabis, David R Nalin and others, who worked to prove the benefits of ORS has been disappointing.

Mechanism of action: ORS works because of the "Sodium Glucose Co-Transport System - (SGLT-1)" in the jejunum which contain SGLT-1 transporter proteins. Sodium transport and glucose transport are coupled in the small intestine so that glucose accelerates absorption of solute and water. If sodium and glucose are consumed in 2:1 ratio, the SGLT-1 channel actively transports both from the gut across epithelial wall into the cells. An osmotic imbalance is created wherein the osmolarity of the cells increases due to the influx of sodium and glucose molecules and hence to maintain osmolarity water is absorbed from the gut and into the body. Thus both fluid and electrolytes are instantly replenished. Previously used higher osmolarity ORS (1975 – 2002) has been replaced by low-osmolarity ORS (WHO-Unicef) (Table IV).[11] The advantages of low osmolarity ORS (WHO-UNICEF) over the earlier WHO high osmolarity ORS is given Box 2.

Rehydration steps with ORS in children with some dehydration

Proper demonstration and education on ORS administration is mandatory by health staff. Start initially with 1-2 ml/kg every 5 minutes of "low osmolar" ORS-administer with a spoon, syringe, paladai or dropper. When child accepts and drinks, increase the amount from 5 ml to 10 ml every 10 minutes. Over the next 2-4 hours, administer as much as 50-100 ml/kg of ORS. Never feed or push fast and but after 10 minutes if the child vomits out. Subsequent ongoing episode of diarrhea and vomiting will be replaced by about 60-120 ml of ORS in a child less than 10kg and 120-240ml. ORS. Encourage mothers to continue breastfeeding during rehydration with ORS. Educate mothers to avoid carbonated drinks, commercial beverages and fruit juice concentrates, coffee, bottle feeding. The guidelines for correcting mild and moderate dehydration with ORS is given in Table V.

Table V. Dehydration correction with with ORS - Guideline

Weight (kg)	Mild dehydration (3%–5%) Total volume over 4 hours	Moderate dehydration (6%–9%) Total volume over 4 hours
5	150–250 mL	300–450 mL
10	300–500 mL	600–900 mL
15	450–750 mL	900–1,350 mL
20	600–1,000 mL	1,200–1,800 mL
25	750–1,250 mL	1,500–2,250 mL
30	900–1,500 mL	1,800–2,700 mL

Evidence for efficacy of ORS: Most children with gastroenteritis and mild-moderate dehydration can be successfully rehydrated with oral rehydration solutions either by mouth or nasogastric tube. Adequate evidence has shown beyond doubt the efficacy of "ORS" in the correction of diarrheal dehydration. For every 25 children getting the earlier WHO-UNICEF promoted high osmolarity ORS orally or by nasogastric rehydration, only one failed and required IV therapy. But when using the lower osmolarity WHO-UNICEF ORS (245mMol/L) solution, only one in 100 children failed oral rehydration therapy (ORT). Similar percentages of children with improved dehydration scores after 2 hours and successful rehydration by 4 hours when comparing those receiving IV fluids and ORT have been reported. Side effects of ORT are minimal.

Other ORS variants

ReSoMal (Rehydration Solution for Malnutrition) is a specially designed ORS preparation recommended by WHO to help rehydrate malnourished children with diarrhea (Table VI). These children have severe depletion of total body potassium, magnesium and essential trace elements like zinc and copper needed for immunocompetence and important mitochondrial enzymatic functions. The low sodium content of ReSoMal is very important as these children are more prone to develop cardiac failure with ORS containing higher sodium load. The mental apathy noted in these children is reported to recover earlier with the use of ReSoMal.

Cereal (Rice) based ORS: Starch polymers containing a complex carbohydrate such as rice when slowly broken down into glucose have shown to improve transport of sodium and water across the intestinal epithelium and were found to be effective without increasing stool output.[10]

Table VI. Rehydration solution for malnutrition (ReSoMal)

Constituents	mmol / L
Glucose	125
Sodium	45
Potassium	40
Chloride	70
Citrate	7
Magnesium	3
Zinc	0.3
Copper	0.045
Total osmolarity	300

Box 3. ORS therapy – When ineffective ?

1. High purge rate
2. Uncontrolled vomiting
3. Severe dehydration
4. Hypovolemic or septic shock
5. Altered sensorium
6. Severe electrolyte disturbances

Such cereal derived carbohydrate polymer replaced glucose in low osmolar ORS formula.

Super ORS - Amino acids (L-alanine or glycine or glutamine) fortified or oligopeptides enriched starch from rice powder ORS (instead of glucose) have been found to reduce stool volume, shorten duration of diarrhea and allow early introduction of feeding, mostly in cholera. But its main disadvantages are requirement of prior cooking, shorter half life after preparation (ferments within 8-12 hours rendering it useless) and not effective in children with non-cholera diarrhea.

ORS therapy may be ineffective under certain circumstances (Box 3). Under such states, the child needs to be admitted and IV fluids administered.

Indication of parenteral fluid therapy in diarrheal dehydration

Standard of therapy in some (mild and moderate) dehydration is ORT. But in severe dehydration IV fluid replacement is essential.

Table VII. Correction of severe dehydration in a peripheral centre*

Age	Initial 30 mL/kg	Then 70 mL/kg
Infants above 2 months	0 – 1 hour	1 – 5 hours
Older child > one year	0 – 30 min	30 min – 3 hours

** Fluid used is NS or RL; Check blood glucose, if low correct it.*

Correction of severe dehydration (Shock) in peripheral centre: Assessment is done as per PALS principles. This is followed by administration of oxygen and securing IV or IO access without any delay. There are many ways of administering IV fluid therapy for a child with severe dehydration which depends on the level of health care facility. It is different in a peripheral centre or a small hospital from tertiary care centre with emergency room or Pediatric Intensive Care Unit (PICU). Table VII gives the correction of severe dehydration (shock) in a peripheral centre or a smaller hospital (fluid plan as per WHO). After shock correction continue the rehydration process (Box 4).

Box 4. Fluid management of severe dehydration after shock correction

Fluid management of severe dehydration after shock correction

e.g. One year old infant weighing 10 kg presented with severe dehydration (shock).

Shock corrected after two 20 ml/kg fluid boluses. i.e 400 mL

a) Deficit correction: Body weight in kg X % of fluid loss (10% or 100 mL/Kg) = 10 X 100 = 1000 mL

b) Maintenance fluid: 10 X 100 = 1000 mL

Total fluid = 2000 mL for 24 hours

Deduct 400 ml given as fluid bolus (2000 – 400 mL = 1600 mL

Administer as 5% dextrose normal saline / 5% dextrose one half normal saline with kCl 20 mEq/L over 24 hours. Ensure normal renal function before adding potassium.

- Give 50% of 1600 mL ie 800 ml over 0 - 8 hours
- Second 50% ie 800 mL over 9 - 24 hours

Table VIII. Electrolyte loss in various dehydration

Types of dehydration *	Water loss (ml/kg)	Na^+mmol/L	K^+mmol/L	Cl^-mmol/L
Isonatremic (S.Na: 130-150)	100-120ml/kg	8 – 10	8 – 10	8 – 10
Hyponatremic (S.Na: <130)	100-120ml/kg	10 – 12	8 – 10	10 – 12
Hypernatremic (S.Na: >150)	100-120ml/kg	2 – 4	0 - 4	2 – 6

Table IX. Composition of available IV fluids

IV Fluids	Na	K	Cl	Others	Tonicity	Osmolality
Normal saline	154	-	-	-	Isotonic	308
D5 Normal saline	150	-	150	-	Isotonic hyper-osmolar	586
Ringer lactate	131	4	109	Calcium-3	Isotonic, iso-osmolar	278
D5 one half Normal saline	77	-	77	-	Hypotonic, hyper-osmolar	432
Plasmalyte A	140	5	98	Magnesium-1.5	Isotonic, iso-osmolar	295
Plasmalyte 148	140	5	98	Dextrose-5% Magnesium-3	Isotonic, Hyperosmolar	547
Isolyte M	39	28	37	Acetate-21	Hypotonic, hyper-osmolar	415
Isolyte G	63	7	150	Ammonia-70	Hypotonic, iso-osmolar	274
Isolyte P	23	20	20	Acetate-20	Hypotonic, hyper-osmolar	369

Box 5. IV Fluid management in a child with moderate dehydration

e.g One year old infant weighing 10 kg presented with moderate dehydration.

a) Deficit correction: Body weight in kg X % age of fluid loss (7% or 70 mL/Kg) = 10 X 70 = 700 mL

b) Maintenance fluid: 10 X 100 = 1000 mL
Total fluid = 1700 mL for 24 hours

- Initially plan for rapid volume repletion: 20 mL/kg normal saline or Ringer lactate (maximum = 1 L) over 2 hr. In this child 200 mL is given for rapid volume repletion. (To prevent the child slipping into severe dehydration from moderate dehydration)
- Rest of the fluid 1700 – 200 = 1500 mL
- Administer as 5% Dextrose Normal saline/ 5% Dextrose half Normal saline with KCL 20 mEq/L over 24 hours.
- Give 50% of this maintenance fluid ie 750 ml over 0 -8 hours
- Second 50% ie 750 mL over 9 – 24 hours

Ongoing losses : *For diarrhea: Provide 5 -10 mL per kg of ORS for every episode of diarrhea*
For vomiting: Replace the volume mL/mL with IVF (NS + Potassium 10 mEq/L)

Box 6. Basic principles of dehydration, fluid loss and deficit correction

Mild dehydration	: < 5% in infants and < 3% in older children
Moderate dehydration	: 5 - 10% in infants and 3 - 6% in older children
Severe dehydration	: > 10% in infants and > 6% in older children

Correction of severe dehydration (shock) in an emergency room of a tertiary care centre: Infuse 20 mL/kg of NS/RL over 20 min. Reassess and repeat the IV fluid bolus till 60 mL is given over 60 minutes. Once shock is corrected, continue rehydration (Box 4).

Deficit correction in some (mild and moderate) dehydration: ORT is the standard way of dehydration correction in this situation. But IV fluid therapy may be considered as the next choice when oral administration fails or not possible, as in the presence of uncontrolled vomiting, inability to drink because of extreme fatigue or abdominal distension with ileus. Calculate the fluid requirement for a) deficit correction and b) maintenance fluid. A general approach is given based on the physiological principles, even though there are many approaches in fluid calculation (Box 5). The principles behind different approaches in dehydration is given in Box 6. The amount of electrolyte lost in various dehydration and the composition of various IV fluids with their osmolality is given in Table VIII and IX respectively.

Other supportive measures

The other important aspects of management of acute gastroenteritis in children include enteral feeding and diet selection, zinc supplementation and additional therapies such as probiotics.

Zinc: Zinc supplementation in children with diarrhea has been proven to reduce duration and severity of diarrhea and could potentially prevent a large proportion of cases from recurrence. All children older than 6 months of age with acute diarrhea in at-risk areas should receive oral zinc (20 mg/ day) for 10-14 days. The role of zinc in well nourished, zinc replete populations in developed countries is less certain.

Prebiotics and probiotics: Their role in acute diarrhea is not clear though they have a definite role in antibiotic associated diarrhea.

Antibiotics and anti-parasitic drugs: Antibiotics are not indicated in a majority of acute diarrheal disorders in infants and young children. They are given in preterm and neonates in institutional deliveries, children with SAM, acute bacillary dysentery and parasite associated diseases. In acute bacillary dysentery and parasite associated diseases, appropriately selected based on local resistance and sensitivity pattern can reduce the duration and severity of illness and prevent complications (Table X).

Antiemetics: Ondansetron therapy in the dose of 0.2 mg/ kg has been shown to decrease the risk for persistent vomiting, the need for IV fluids and the risk of immediate hospital admission in children with vomiting related to AGE.

Table X. Antimicrobials in diarrhea – Indication and drugs

Organism	Treatment
Shigella, Salmonella	Oral Cefixime / Inj.Ceftriaxone
ETEC traveller's diarrhea	Oral azithromycin
Campylobacter jejuni	Oral azithromycin
Entamoeba histolytica	Metronidazole
Crytosporidium	Nitazoxanide

But pediatricians should be aware that increased diarrheal frequency is one of the most common adverse effects of ondansetron. Also, it is recommended to use ondansetron with caution and under electrocardiographic monitoring in patients with electrolyte abnormalities because they may be at risk for developing prolongation of the QT interval that can lead to an abnormal and potentially fatal ventricular tachy-dysrhythmia.

Antimotility agents: Never use antimotility agents, such as loperamide and diphenoxylate should never be used as their use is contraindicated in children with acute diarrheal disorders and dysentery. The risk of toxic megacolon or ileus with deterioration and even deaths have been reported especially those younger than age 3 years. Enkephalinase inhibitor racecodotril also has no role in children with acute watery diarrhea.

Dietary management: Enteral feeds to be continued. Foods with complex carbohydrates (rice, wheat, potatoes, bread, and cereals), lean meats, yogurt, fruits, and vegetables are also tolerated. Fatty foods or foods high in simple sugars (juices, carbonated sodas) should be avoided. Breastfeeding must be continued in infants. Withdrawal of milk and replacement with specialized (and expensive) lactose-free formulations are unnecessary.

Green banana diet: Green banana-supplemented diet has been found to hasten recovery from acute and prolonged diarrhea. The underlying mechanism of action of green banana is postulated to be mediated by its high content of amylase rich starch (ARS), which is not digested in the small intestine of humans. On reaching the colon, it is fermented by resident bacteria into the short-chain fatty acids (SCFA) - butyrate, propionate, and acetate. In the colon, SCFA stimulate salt and water absorption, as well as provide energy and induce a trophic effect on the colonic as well as small-bowel mucosa.[12] Unripe, green banana has been used in the folk treatment of various intestinal disorders including diarrhea.

Green banana diet may be prepared by peeling three green bananas, cooking and mashing with a cup of cooked rice and pinch of salt. The mix may be made up to a litre of water to meet the fluid requirements. If dehydration is not a problem, a thicker consistency may be acceptable in older children. In severe cases or non-response to this, the diet may be prepared without rice. This diet may not necessarily meet the entire caloric needs of the child but will definitely decrease the stool output early enough to be able to start a more calorie and protein sufficient lactose free diet in a few days.

Points to Remember

- ***Classifying diarrhea based on timing and content is clinically more useful for deciding on the management.***
- ***Four clinical types are commonly seen- acute watery diarrhea lasting several hours to days, acute bloody diarrhea, prolonged diarrhea lasting more than a week and diarrhea in the setting of undernutrition.***
- ***Severe dehydration and sodium imbalance are common complications associated with diarrhea.***
- ***Osmolality disturbances need to be considered while giving treatment for the associated sodium imbalance conditions.***
- ***Children who are at higher risk of complications due to diarrhea are- infants <1 year, children with underlying severe acute malnutrition, repeated vomiting/ refusal to accept oral feeds, and children with poor sensorium.***
- ***The two pillars of management in AGE are immediate attempts at oral rehydration and rapid reintroduction of regular feeding following initial fluid rehydration.***
- ***Green banana diet has been found to hasten recovery from acute and prolonged diarrhea and may be a useful adjunct therapy in resource limited settings.***

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CLIPPINGS

Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture Pediatrics.

Among the 7766 infants <60 days of age, without clinical suspicion of meningitis lumbar puncture was done to identify the CSF cell count, proteins and glucose. CSF WBC counts and proteins were higher in infants <28 days of age (upper limit: 15 cells/mm^3) than in infants 29 to 60 days of age (upper limit: 9 cells/mm^3; P < .001), in infants < 28 days of age (upper limit: 127 mg/dL) than in infants 29 to 60 days of age (upper limit: 99 mg/dL; P< .001). CSF glucose concentrations were lower in infants <28 days of age (lower limit: 25 mg/dL) than in infants 29 to 60 days of age (lower limit: 27 mg/dL; P< .001). Above values may be useful in interpreting lumbar puncture results in infants <60 days of age.

Thomson J, Sucharew H, Cruz AT, Nigrovic LE, Freedman SB, Garro AC, et al., Pediatric Emergency Medicine Collaborative Research Committee (PEM CRC) HSV Study Group. Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture. Pediatrics 2018; 141(3): e20173405; DOI: 10.1542/peds.2017-3405.

Infant Hospitalizations and Mortality After Maternal Vaccination.

Influenza, reduced diptheria, acellular pertusis and tetanus are recommended immunisations for the antenatal women and is in practice. There is scarcity of data on the safety of infants born to mothers who received immunisation during pregnancy. Recent study has confirmed the safety of such recommendations. Influenza, reduced diphtheria, tetanus toxoid and acellular pertusis vaccines are not associated with increased risk or hospitalisation or death in infants. Two doses of influenza during any time of pregnancy and one dose of reduced diphtheria, acellular pertusis and tetanus during 27-36 weeks of gestation reduced the occurrence of the disease in infants. Maternal immunization with influenza and Tdap vaccines allows for passive antibody transfer and protection to infants for the respective diseases when they are most vulnerable

Lakshmi S, McCarthy NL, Kharbanda EO, Vazquez-Benitez G, Lipkind HS, Jackson L, Infant Hospitalizations and Mortality After Maternal Vaccination. Pediatr 2018; 141(3): in press.

FLUID AND ELECTROLYTE DISTURBANCE

FLUID RESUSCITATION IN SHOCK

Anand Shandilya

Abstract: *Shock is a common emergency in children and hypovolemic shock is one of the commonest type of shock to present as an emergency in our country. The first medication to be administered to a child with shock after oxygen is fluids. It is essential to understand the physiology, use and limitations of fluid therapy to successfully manage this emergency. It must be understood that fluid therapy is only one component of a complex hemodynamic resuscitation strategy with the aim of restoring intravascular volume. When shock is fluid refractory, adjunctive therapies to augment cardiac contraction and venous return will be needed in the form of inotropes. Besides intravascular volume end organ function also needs to be monitored.*

Keywords: *Shock, Fluid resuscitation, Management.*

Shock is a common emergency seen in pediatrics which can be recognized clinically. Once shock is diagnosed, rapid institution of fluid therapy can be lifesaving. It must be understood that fluid therapy is only one component of a complex hemodynamic resuscitation strategy with the aim of restoring intravascular volume. When fluid therapy alone does not lead to improvement of shock, adjunctive therapies to augment cardiac contraction and venous return will be needed in the form of inotropes. Besides intravascular volume, end organ function also needs to be monitored.[1]

Shock

Shock is a clinical state characterized by a circulation which is unable to meet the metabolic demands of tissues. This implies that the circulatory compromise is such that the tissues don't receive enough oxygen and nutrients to allow the cells to function. This ultimately leads to cellular death, progressing to organ failure and finally, if untreated, death.[2]

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Recognition of shock

Assessment of circulatory function consists of direct assessment of the circulation and indirect assessment of the organs perfused. In direct assessment, heart rate, the quality of peripheral and central pulses and the blood pressure are evaluated. Three organs - skin (temperature and capillary refill time), brain (sensorium, muscle tone and pupils) and the kidneys (urine output) are evaluated in indirect assessment.[2] Hepatomegaly, basal crepitations and a raised JVP suggests cardiac etiology. Presence of hypotension (systolic blood pressure less than 5th centile for age) categorizes the severity as hypotensive shock which helps in deciding the urgency of management. The blood pressure values for deciding if the shock is hypotensive is determined by the values are shown in Table I.[2]

Table I. Criteria for hypotension by age

Age	Systolic blood pressure in mm Hg (Fifth percentile)
0 to 1 month	< 60
> 1 month up to 1 year	< 70
1-10 years	< 70+(2 X age in years)
>10 years	< 90

Severity and type of shock

While assessing a child with shock the aims are to evaluate the severity and type. The first is to decide the severity of shock which will decide the tempo of resuscitation. The blood pressure classifies the shock as compensated or hypotensive. If the shock is categorized as hypotensive, the resuscitation has to be rapid. The second aim is to decide the type of shock and treatment strategy. Shock is categorized as hypovolemic, distributive (septic, anaphylactic and neurogenic), cardiogenic and obstructive. It is usually possible to determine the type of shock based on the assessment mentioned above as well as history.[2]

Increased susceptibility of children to fluid loss - Reasons

Children normally require a much higher fluid intake per kilogram of body weight than adults. This is because they have a higher surface area-to-volume ratio and a higher basal metabolic rate. Children may therefore suffer fluid deficits if they are unable to take oral fluids, additional fluid losses due to fever, diarrhea, increased insensible losses (e.g. due to increased sweating or tachypnea) or loss of the normal fluid-retaining mechanisms, e.g. burns, the permeable skin of premature infants, increased urinary losses or capillary leak.[3]

Importance of fluid resuscitation

The three determinants of cardiac output are preload, myocardial contractility and afterload. Derangement in these factors leads to shock. Of these, the preload is affected in all types of shock. There is hypovolemia which may be absolute as in hypovolemic shock or relative as in distributive or cardiogenic shock. Fluid resuscitation corrects the deficits in the preload. Only when the preload is optimized and the shock is unresponsive, other modalities of treatment are considered. Hence fluid resuscitation is the first vital component of therapy after oxygen. Fluids are used for volume replacement, delivery of medications and correction of metabolic abnormalities like acidosis.[3] Table II shows the change in preload, contractility and afterload in various categories of shock. This will help in deciding the aliquot of the bolus therapy.

Type and amount of fluid

The amount of fluid to be administered is determined by the type of shock. The initial bolus of fluid is 20 ml per kg, the exception being cardiogenic shock where the initial bolus is 5-10 ml per kg. The recommendation for rate of administration has changed. The recommendation was to give the bolus very fast over 5 to 10 minutes. It was observed that with such fast rates of administration, the need for mechanical ventilation was higher.[4] This was specially seen in critically ill children in resource limited settings. Hence, the rate of administration now recommended is slower over 20 minutes to an hour with monitoring and more so in resource limited settings.[5,6]

Table II. Preload, contractility and afterload in shock

Category	Preload	Contractility	Afterload
Hypovolemic	↓	N or ↑	↑
Distributive	N or ↓	N or ↓	Variable
Cardiogenic and Obstructive	Variable	↓	↑

The ideal resuscitation fluid should be one that produces a predictable and sustained increase in intravascular volume, has a chemical composition as close as possible to that of extracellular fluid, is metabolized and completely excreted without accumulation in tissues, does not produce adverse metabolic or systemic effects, and is cost-effective in terms of improving patient outcomes. Currently, there is no such fluid available for clinical use.[1] But there are two options available at present namely - crystalloids and colloids.

Crystalloid solutions, which are isotonic, are the most preferred fluids used in resuscitation of shock. The advantage of crystalloids are that they are cheap and easily available and are effective in most situations. The disadvantage is that only 30 % of the fluid is retained in circulation after the infusion and hence multiple boluses may be needed. Fluids of choice are normal saline and lactated Ringer's solution.[1] There is no role of hypotonic fluids in fluid resuscitation.

Normal saline: This fluid is the most appropriate for fluid boluses, compatible with blood products and most drugs. 0.9% NaCl has an osmolarity of 308 mOsm/L, slightly higher than that of plasma.

Lactated Ringer's (LR): This fluid is also good for fluid boluses but is hypo-osmolar when compared to plasma, resulting in approximately 114 ml of free water per liter of LR. Hence normal saline is the preferred solution in situations associated with abnormalities of sodium (hyponatremia and hypernatremia).

Dextrose containing solutions should not be used for boluses as they are likely to cause hyperglycemia. Hyperglycemia is associated with poor neurological outcomes. The dose of glucose for treating hypoglycemia is 0.5 to 1 g per kg. An intravenous fluid which contains 5% dextrose has 5g glucose / 100 ml. If a bolus of a 5% dextrose containing fluid is given at 20 ml/kg, this solution will deliver 1g glucose/kg. This is the maximum dose of glucose used to treat hypoglycemia. Subsequent boluses with the same solution will result in hyperglycemia.[7]

The other category of fluids which are available are colloids. Colloid refers to a liquid that exerts osmotic pressure due to large molecular weight (greater than 30,000) particles in solution. A variety of colloid solutions are available for use in hospital. Examples of colloids used are, protein (5% albumin and plasma) and starch derivatives.

Theoretically these solutions have the potential to stay longer in the intravascular compartment and hence are more effective in restoring circulatory volume compared to crystalloids. In reality, in shock, there is increased vascular permeability, leading to leakage into the extravascular space. Hence this fluid also does not stay in the intravascular compartment. These fluids also inhibit platelet function and reduce the activity of factor VIII and may precipitate a coagulopathy. Fluids in this category are hydroxyethyl starch, pentastarch and dextran solutions (dextran 40 and dextran 70). Dextrans have an osmotic pressure similar to plasma. Dextrans interfere with normal coagulation partly by hemodilution of clotting factors and partly by "coating" platelets and the vascular endothelium. They may also promote renal failure.[1]

Studies have found no benefit of colloids over crystalloids. In fact, there is an increased risk of mortality when colloids are used. There is a higher risk of adverse events and allergic reactions with colloids. Colloids are also expensive and not readily available.[1] Hence crystalloids are the fluid of choice in resuscitation of shock.

Volume of bolus in different types of shock

Hypovolemic shock has an absolute deficit in preload. Hence, in these children multiple boluses of 20 ml per kg are needed. It is necessary to assess the response to the bolus after administering it before deciding on the next aliquot.

Cardiogenic shock does not have an absolute deficit in preload and usually the problem is with myocardial contractility. If the usual bolus of 20 ml per kg is infused, the child may be pushed in to further decompensation. However, there may be a relative deficit in preload as the myocardial pumping is inadequate. A slow and cautious infusion over a longer duration may help with monitoring of the heart rate, liver span and appearance of basal crepitations. The usual dose used in cardiogenic shock is 5 to 10 ml per kg.[7]

Distributive shock is characterised by relative hypovolemia as the vital central vascular beds are deficient and hence these patients may require larger boluses of fluids to restore the deficit in preload, especially in warm distributive shock. Cold distributive shock behaves like cardiogenic shock and hence will require lesser fluids.[7]

In obstructive shock**, c**ardiac filling pressures are usually increased owing to outflow obstruction, impaired ventricular filling or decreased ventricular compliance. Therefore the clinical mani-festations of cardiogenic and obstructive shock may be similar. Hence, obstructive shock will require a more cautious administration of fluids.[7]

Blood during resuscitation in shock

The commonest indication for using blood in shock is in hemorrhagic shock. The initial fluid to be used would still be a crystalloid since it is cheap, easily available and easy to administer. If shock is persistent after two to three boluses of crystalloids in hemorrhagic shock, one can use blood (20ml / kg) or packed red blood cells (10 - 15 ml /kg).

Therapeutic endpoints while managing shock

The shock is said to be reversed when the patient has a normal mental status, normal heart rate and BP for age, normal pulses, warm extremities, a CRT <2 sec, an adequate urine output (UO > 0.5 to 1ml/kg/hr), decreased serum lactate, reduced base deficit, central venous oxygen saturation (ScvO2) > 70 % and MAP >65 with CVP 8-12. These goals are to be achieved as fast as possible. If not achieved with initial fluid resuscitation, then stepping up therapy would be the next action. Appearance of crepitations, worsening respiratory distress, puffiness around the eyes and an increase in liver span suggest myocardial dysfunction and/ or fluid overload.

Best route of administration of fluids

The most important dictum is that no child should die due to a lack of vascular access. In the critical pediatric patient, the time to establish access should be kept to a minimum. The old teaching was to limit to "3 pricks in 90 seconds". Keeping the dictum in mind one should establish vascular access as fast as possible. Usually peripheral veins are preferred, but if there is likely to be a delay in getting vascular access, there should be no hesitation to establish an intraosseous access. When there is expertise available in the right setting, central veins may be cannulated.[2]

In conclusion, fluid resuscitation is one of the most important interventions in the management of shock after oxygen therapy. This is true for all grades of severity and types of shock. The preferred fluid is a crystalloid and among the crystalloids normal saline is the optimal fluid. The dose of the bolus is 20 ml per kg with the exception of cardiogenic and obstructive shock where the dose is 5 to 10 ml per kg. In hemorrhagic shock if crystalloids are unable to restore circulation, blood has to be administered. An important point to note is that patients don't suddenly deteriorate but health care professionals suddenly notice! Hence, clinical monitoring is vital. Assiduous clinical monitoring is usually adequate to determine the response to therapy.

Points to Remember

- ***Shock is one of the commonest emergencies seen in pediatric practice.***
- ***Hypovolemic shock is the commonest type of shock.***
- ***All children with shock should be administered oxygen as the first therapy.***
- ***Crystalloids are the fluid of choice in the acute resuscitation of a child with shock and normal saline is the fluid of choice.***
- ***The clinical state of the patient will determine the volume and rate of fluid administration.***
- ***Fluids should be administered with the same caution and care as with any intravenous drug.***
- ***Assiduous clinical monitoring during and after therapy is mandatory.***

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CLIPPINGS

Clinico-laboratorical spectrum of malaria in children: Emerging new trends.

Recently, a significant change in clinical presentation of malaria and various laboratory parameters has been reported worldwide.In changing clinical spectrum of malaria, Plasmodium vivax is predominantly associated with severe malaria. Most common complication was prostration. Followed by abnormal bleeding, severe anemia, impaired renal impairments, shock, altered sensorium, convulsion and pulmonary edema. Among laboratory parameters, thrombocytopenia and deranged hepatic functions were observed. Presence of thrombocytopenia, severe anemia, bleeding tendencies in a patient of acute febrile illness should alert the clinician the possibility of malaria. *Plasmodium vivax* was most common etiology of severe malaria in children. It should no longer be considered as benign malaria

Meena HM, Sharm BS, Gupta ML, Sharma A, Choudhary R and Prity Sharma. Clinico-laboratorical spectrum of malaria in children: Emerging new trends. Current Pediatric Research 2017; 21(3): 384-388.

NEWS AND NOTES

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FLUID AND ELECTROLYTE DISTURBANCE

HYPONATREMIA AND HYPERNATREMIA

Amish Udani

Abstract: *Dysnatremias occur due to imbalance either in total body water (TBW) or in sodium balance or both. Volume of extracellular fluid compartment helps us to assess the total body sodium status while serum sodium levels suggest TBW status. The kidney regulates serum sodium concentration between 135-145mEq/L primarily by its ability to regulate free water excretion especially in hyponatremia. The primary prevention from developing hypernatremia is thirst. It is important to find out the etiology of dysnatremias to guide treatment for appropriate corrections in serum sodium levels per hour to prevent morbidity and mortality.*

Keywords: *Dysnatremias, Total body water, Total body sodium.*

HYPONATREMIA

Total body water (TBW) is 70% in term infants, 65% in young children and 60% in older children and adolescents,[1] of which 2/3 is intracellular fluid (ICF) and 1/3 is extracellular fluid (ECF) (Fig.1). Sodium is an effective osmole in extracellular compartment to maintain extracellular fluid volume (ECFV) besides glucose. If the total body sodium in ECF increases, it will result in ECFV expansion and will be seen clinically as edema or ascites, pleural effusion or pulmonary edema. Conversely if the total amount of sodium in the ECF decreases it will result in ECFV depletion and will be seen clinically as poor skin turgor, feeble pulses, tachycardia, hypotension and prolonged capillary refill time.[2]

Extracellular sodium concentration is the main determinant of plasma tonicity which can result in movement of water from one compartment to another. Tonicity determines the cell size and hydration, particularly of the brain. When there is decrease in the tonicity of ECFV, water will move into the intracellular compartment resulting in cerebral edema and conversely increase in the tonicity of ECFV will lead to intracellular dehydration because of water leaving the brain cells. Hence, the serum sodium level does not tell us about total amount of sodium in ECF compartment or ECFV. It only tells about the amount of water relative to amount of sodium.[3] When ECFV increases, mechanisms to increase sodium excretion are activated and when ECFV decreases, pathways for sodium retention in the kidneys are activated by various hormones acting on renal tubules.[3]

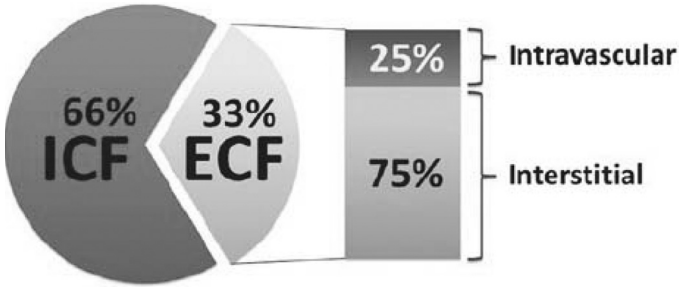

Fig.1. Body fluid compartments

Approach to hyponatremia (Serum sodium <135mEq/L)[4]

A low serum sodium level (TBW imbalance) can be associated with decreased, normal or increased total body sodium depending upon history and clinical examination for presence of dehydration or edema.[5] Hyperproteinemia or hyperlipidemia can result in pseudohyponatremia as serum sodium concentration is measured per decilitre of total plasma volume.

Plasma osmolality, which is determined by total solute concentration in fluid compartment, is measured per litre of plasma water and hence will be normal in these conditions.[6] Plasma osmolality can also be calculated as [2 x plasma sodium (mEq/L) + Glucose (mg/dL)/18 + BUN (mg/dL)/2.8]. The difference between the measured and calculated osmolality is called osmolal gap. If the difference is more than 10mOsm/L then it suggests presence of exogenous ingestion of osmotically active substance(s) other than sodium, glucose and urea. As compared to sodium and glucose, urea is not an effective osmole because it crosses cell membrane easily and does not contribute to water movement. Tonicity is different from osmolality as it refers to ability of a solute for e.g. sodium in extracellular

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compartment to cause water movement from one compartment to another.[3]

The diagnosis of true hyponatremia is made[5] after pseudohyponatremia and hyponatremia with hyperosmolality either because of hyperglycemia or presence of substances like methanol, mannitol or maltose etc., are ruled out. The causes of true hyponatremia are listed in Table I.

True hyponatremia results from impaired renal water excretion in the presence of continued water intake. Impaired renal water excretion may be due to renal failure, ECFV depletion because of extra-renal or renal fluid losses, edematous states, SIADH, use of diuretics, hypothyroidism or adrenal insufficiency.

In renal failure due to decreased glomerular filtration rate (GFR), ingested water load cannot be excreted. In the early stages of renal failure, large amount of water is needed to result in hyponatremia without developing edema, while in the late stages with GFR <15ml/min/1.73m^2 there is a progressive solute and water retention with presence of edema.

In patients with ECFV depletion due to extra renal losses, hyponatremia will develop only if they drink or are administered hypotonic fluids, leading to relative water repletion compared to solute. Severe depletion of ECFV results in release of ADH which also contributes to development of hyponatremia. As sodium and water are retained by proximal tubule, urine sodium is typically <20mEq/L and often, there is oliguria with obvious signs of dehydration in such situations.

The opposite findings are seen in renal tubulopathies and hypoaldosteronism. Additionally serum potassium and acid base imbalance are seen along with hyponatremia in renal tubular disorders. Cerebral salt wasting is characterized by polyuria, ECFV depletion and elevated urinary osmolality. ECFV depletion differentiates it from SIADH who are clinically euvolemic. Brain natriuretic peptide mediated antagonism of ADH and other hormones is believed to cause polyuria, natriuresis and lack of thirst in this condition.[7]

In edematous conditions of high total body sodium there is decreased cardiac output, peripheral vasodilatation and decreased oncotic pressure which is perceived falsely as decrease in intravascular space of extracellular compartment by compensatory mechanisms. This perpetuates more water retention with progressive expansion of interstitial space of extracellular compartment causing hyponatremia (Fig.1). The urine sodium concentration is often low <20mEq/L in edematous state because of abnormal renal sodium retention in these conditions.

In SIADH, circulating ADH is not suppressed despite normal plasma osmolality. Central nervous system diseases, lower respiratory tract illnesses, malignancy, pain, stress, hypoxia and certain medications are some of non-osmotic stimulus associated with inappropriate ADH release. SIADH is characterized by absence of kidney, adrenal and thyroid disease along with normal acid-base and potassium balance, euvolemic, elevated urine sodium concentration >20mEq/L, urine osmolality >100 mOsm/kg and hypouricemia from volume expansion resulting in decreased proximal tubular sodium and uric acid reabsorption.[5]

Diuretics induced salt and water loss cause ECFV depletion resulting in ADH release and increased thirst. In the presence of ADH when thirsty individual drink hypotonic fluid there will be retention of more water as compared to sodium by renal collecting tubules. Thiazide diuretics are contraindicated in all patients with

Table I. True hyponatremia (Hyponatremia with hypo-osmolality)

Low total body sodium (Hypovolemic)	High total body sodium (Hypervolemic)	Normal total body sodium (Euvolemic)
GI fluid losses like emesis, diarrhea, stoma output Bleeding Skin fluid losses like burns, cystic fibrosis Renal fluid losses like diuretics, renal tubular diseases, hypoaldosteronism, cerebral salt wasting	Congestive heart failure Cirrhosis Nephrotic syndrome Multiorgan dysfunction syndrome Late stages of renal failure	Early stage of renal failure SIADH* Adrenal insufficiency Hypothyroidism

**SIADH, syndrome of inappropriate antidiuretic hormone secretion*

hyponatremia including those with edematous state. Loop diuretics affect osmolality of medullary interstitium at the loop of Henle and therefore interfere with water reabsorption as well at the collecting tubule whereas thiazides donot affect the medullary interstitium. Hence ingested water can be maximally reabsorbed at the collecting tubules exposing the patient to the risk of severe hyponatremia.

In adrenal insufficiency, mineralocorticoid deficiency inhibits sodium reabsorption in renal collecting tubule leading to increased urinary salt and water losses. ECFV depletion results in ADH release and cortisol deficiency also adds to unregulated ADH release as cortisol normally inhibits ADH release from hypothalamus. Decreased cardiac output and decreased GFR with increased ADH release might be the reason for hyponatremia in hypothyroidism though this mechanism is still unclear.[8]

The symptoms depend upon how rapid and how severe the reduction of serum sodium levels occurs. It can manifest as nausea, vomiting, headache, lethargy, confusion, obtundation, seizures, coma and even death. The symptoms correlate directly with the degree of intracellular overhydration in brain. With movement of water intracellularly, cells extrude sodium, potassium, chloride via membrane channels initially and later synthesize new solutes such as glutamate, taurine, myoinositol etc., to prevent further movement of water in intracellular compartment.[9] These new solutes induce water loss minimizing brain swelling and hence fewer symptoms are seen in chronic hyponatremia.

The treatment of hyponatremia depends on the underlying cause, duration of hyponatremia and presence or absence of symptoms. Hypertonic 3% saline which has 513 mEq of sodium per litre should be judiciously used in symptomatic patients to rapidly decrease cerebral edema until patients becomes asymptomatic. This can be accomplished by increasing serum sodium by 5 mEq/L over 2 to 8 hours, hence approximately 1ml/kg of 3% saline infusion will increase serum sodium by 1 mEq/L over 2 to 8 hours. It is important to monitor serum sodium every 2 to 4 hours during this correction.[9] The commonest cause of hyponatremia is because of either extra renal or renal losses. Isotonic saline (0.9% Normal Saline) is indicated for volume repletion. Once dehydration is corrected, the sodium correction of not more than 0.5mEq/L/hour should be done with appropriate sodium containing intravenous (IV) fluid. Along with maintenance fluid, deficit correction according to percentage of dehydration and ongoing losses should be accounted for calculating daily fluid requirement. In renal tubular diseases, correction of potassium and acid base imbalance should also be addressed. Discontinuation or adjustment of dose of diuretics is all that is needed to normalize serum sodium in patients with hyponatremia on diuretics.

In SIADH, along with treatment of underlying etiology, fluid restriction to 2/3rd of daily maintenance fluid is the most important aspect for correcting hyponatremia. Severe fluid restriction to 500ml/m^2/day might also be needed in certain cases. If hyponatremia persists, furosemide, vaptans (vasopressin receptor antagonists) or demeclocycline may be given to promote water excretion by kidneys.[10]

In hyponatremia with excess total body sodium, fluid restriction, with or without diuretics should be the initial treatment. In renal failure due to decreased GFR, salt restriction, in addition to above treatment may be needed. If hyponatremia still persists then dialysis should be started to correct fluid overload, hypertension, pulmonary edema and refractory hyponatremia. In nephrotic syndrome, control of proteinuria will correct TBW excess. It is important to reemphasize, that in the absence of hyponatremia there is no indication to restrict water. If there is edema (ECFV excess) alone, restrict only sodium with or without diuretic. If there is hyponatremia and edema, restrict both water and sodium.[3] An approach to management of hyponatremia is given in Fig.2.

HYPERNATREMIA

Hypernatremia is relatively less common as compared to hyponatremia. Patients will develop hypernatremia only if there is loss of water, failure to adequately replace the water loss (relative decrease in TBW) or increase in total body sodium.[11] When there is water loss there is increase in plasma osmolality which will make the kidneys to generate highly concentrated urine through ADH which helps to conserve water. However, there is an obligatory water loss in urine for the solutes to be excreted and water loss from skin as well. Hence, maximum urine osmolality which can be generated is 1200 mOsm/kg in humans as compared to camels which can concentrate urine twice more than us.[3] Patients who have intact thirst mechanism and free access to water do not develop hypernatremia. In patients with excess total body sodium due to iatrogenic administration of hypertonic sodium, mechanisms to increase sodium excretion are activated in the kidneys.

Approach to hypernatremia (Serum sodium >145mEq/L)[2]

Hypernatremia also can occur in presence of decreased, increased or normal total body sodium.[5] The causes of hypernatremia are listed in Table II.

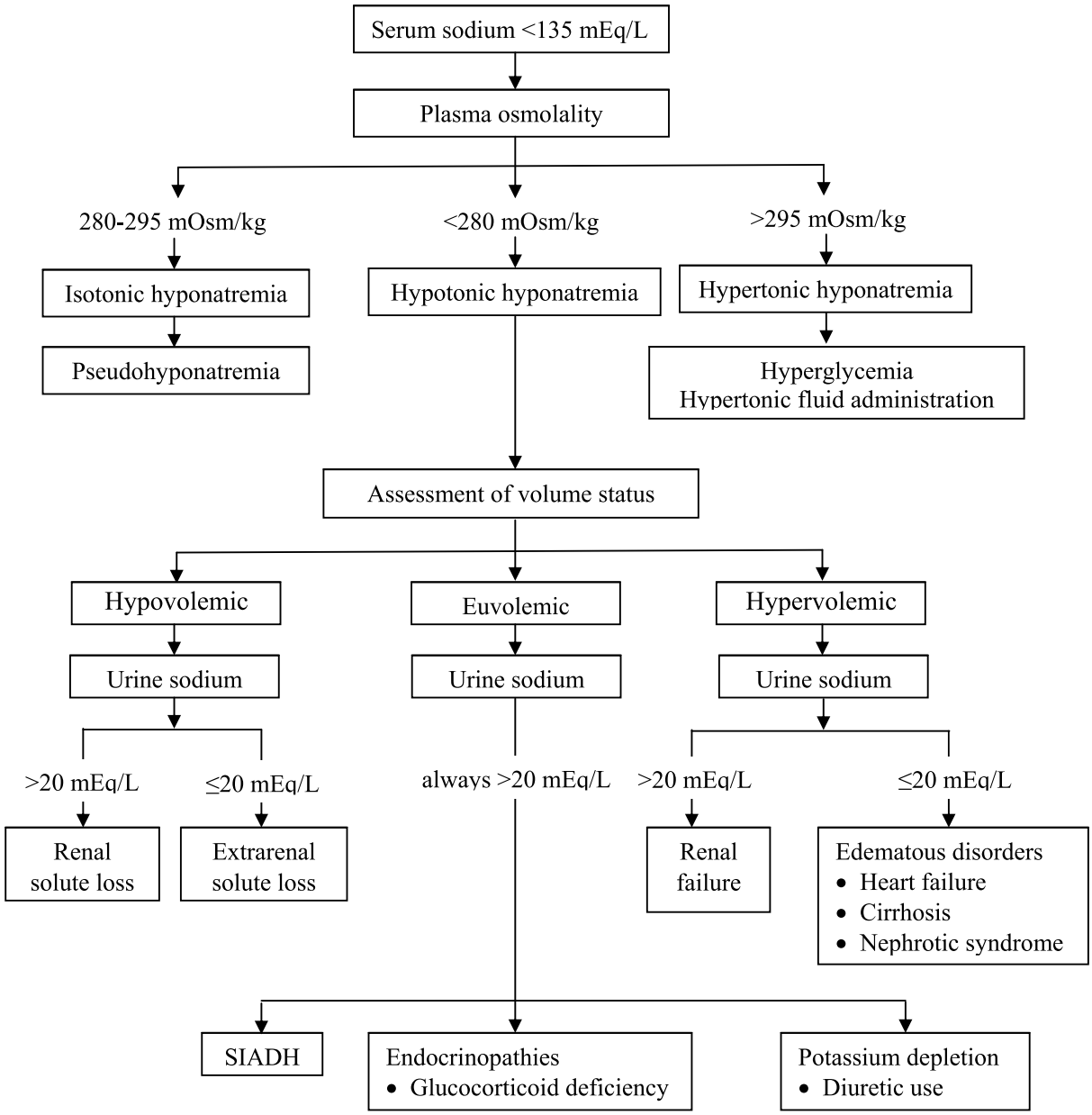

Fig.2. Approach to hyponatremia

In extra-renal or skin losses, hypernatremia develops if water losses exceed sodium loss. Infants with diabetes insipidus (DI), who do not have free access to water present with failure to thrive, dehydration and polyuria either because of defect in secretion of ADH (Central DI) or presence of end organ resistance to ADH (Nephrogenic DI).[9] Both types of DI can have congenital or acquired causes.[12] Important causes are listed in Table III.

To differentiate between the two, administer vasopressin after making diagnosis of DI on water deprivation test. In central DI, urine output will decrease and urine osmolality will increase >50% from baseline after administration of vasopressin where as in nephrogenic DI, there will be no rise or <50% rise in urine osmolality. Also, serum ADH levels can be done to differentiate between the two at the end of water deprivation test. If low then it confirms lack of secretion of ADH in central DI while ADH levels will be high in nephrogenic DI is due to end organ resistance to circulating ADH in renal tubules. Older children with intact thirst mechanisms who have free access to water present with polyuria and hypernatremia without dehydration (normal total body sodium). Hypernatremia with increased total body sodium is seen in salt water drowning, iatrogenic administration of hypertonic sodium solutions or inadvertent ingestion of ORS.

Table II. Causes of hypernatremia

Low total body sodium (Hypovolemic)	High total body sodium (Hypervolemic)	Normal total body sodium (Euvolemic)
GI fluid losses like emesis, diarrhea, stoma output	Inadvertent ingestion of infant formula or oral rehydration solution or salt water drowning	Early stages of insensible losses through skin in fever, prematurity, phototherapy or radiant warmers
Late stages of skin fluid losses due to sweat or cystic fibrosis	Iatrogenic administration of sodium bicarbonate during cardiopulmonary resuscitation or metabolic acidosis	Insensible losses through lungs in hyperventilation, use of unhumidified air during mechanical ventilation
Renal losses like central or nephrogenic diabetes insipidus in infants or osmotic diuresis with glucose or mannitol		In older children with central or nephrogenic diabetes insipidus who have free access to water
Immature renal concentrating ability in infancy		

Apart from symptoms mentioned for hyponatremia, children with hypernatremia may present with intracranial bleed or venous sinus thrombosis. In acute stages, due to movement of water from intracellular to extracellular space there is shrinkage in the cell size of the brain. Brain which is attached to bony skull by membranes that contain blood vessels rupture during brain cell shrinkage.

In chronic hypernatremia, there is intracellular generation of osmoles which prevent movement of water extracellularly from intracellular compartment. It would take few days to metabolize these osmoles by the brain cells. Hence, during treatment of chronic hypernatremia rapid fall in extracellular osmolality with free water would allow intracellular osmoles to shift extracellular water intracellularly leading to cell swelling and cerebral edema.[9]

In hypernatremic dehydration, isotonic saline bolus is used to correct hemodynamic instability. After initial fluid bolus, correction of hypernatremia with hypotonic fluid should be done to provide free water with aim of fall of serum sodium not more than 0.5mEq/L/hour. To calculate free water deficit (FWD) with the above aim, one of the formulas can be used:

FWD (litres) = 0.6 x weight (kg) x {[serum sodium/Desired sodium] – 1} or

FWD (ml) = 4ml x weight (kg) x Desired change in serum sodium in 24 hours (approximately 10mEq/L per day)

For e.g. if the weight of the child is 10 kg, to decrease serum sodium from 170 to 160mEq/L per day, one can give 375 ml of FWD by first formula or 400 ml by second formula. So approximately 750-800 ml of 0.45 normal saline per day should be the fluid prescription.

Change in serum sodium per litre of IV fluid used can be calculated as follows:

(Infusate sodium – serum sodium) / (0.6 x weight +1) or

({Infusate sodium + infusate potassium} – serum sodium)/ (0.6 x weight +1)

Table III. Central and nephrogenic diabetes insipidus (DI) - Causes

Central DI	Nephrogenic DI
Congenital Autosomal dominant - AVP-NP11 gene defect Central nervous system malformations	Congenital X linked recessive – AVPR2 gene defect Autosomal recessive – AQP2 gene defect
Acquired : CNS - tumors, injury, infections and aneurysm	Acquired - hypercalcemia, hypokalemia, inerstitial nephritis, obstructive uropathy Drugs - lithium, demeclocycline

So, as per this formula if 1 litre of 0.45% sodium chloride without potassium is used, the fall in serum sodium per day will be 13.5mEq/L. If 10mEq/L of potassium in 1 litre of 0.45% sodium chloride is added, the fall in serum sodium per day will be 12.1mEq/L in the above child. Serial serum sodium monitoring 4 hourly should guide further treatment. In central DI, intranasal vasopressin of 5-30 microgram per day in 1-2 divided doses can be used to correct hypernatremia along with treatment of underlying etiology in acquired conditions.[9] Ongoing water loss in the form of polyuria (>4ml/kg/hour) in nephrogenic DI should be replaced volume to volume with either distilled water or 5% dextrose. So if urine output is 8ml/kg/hour, then volume to be replaced per hour should be 4ml/kg. In case of salt poisoning, salt restriction with or without diuretics should correct hypernatremia. In hypernatremic dehydration with oliguric renal failure, peritoneal dialysis can be done to prevent volume overload with addition of 3% saline in peritoneal dialysis fluid to prevent rapid fall in serum sodium.

To conclude, patients with abnormal ECFV size (depletion or overload) are due to problem with sodium control mechanism. Patients with abnormal serum sodium concentration (hyponatremia or hypernatremia) are due to abnormal water control mechanisms. Patients with both, abnormal ECFV size and serum sodium level have abnormalities of both sodium and water control mechanisms respectively and hence diagnosis and treatment should be stressed on to correct both sodium and water control mechanisms.

Points to Remember

- ***Sodium homeostasis is essential for maintaining intravascular volume and is tightly linked to water balance.***
- ***The diagnosis of true hyponatremia is made after ruling out pseudohyponatremia and hyponatremia with hyperosmolality.***
- ***The symptoms of hyponatremia correlate directly with the degree of intracellular overhydration in brain.***
- ***The treatment of hyponatremia depends on the underlying cause, duration of hyponatremia and presence or absence of symptoms.***
- ***In the child with hypernatremic dehydration the first priority is restoration of intravascular volume with isotonic fluid. During treatment fall of serum sodium should not be more than 0.5mEq/L/hour and serial serum sodium monitoring 4 hourly should guide the treatment.***

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FLUID AND ELECTROLYTE DISTURBANCE

HYPOKALEMIA AND HYPERKALEMIA

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Abstract: *The ions and molecules which are dissolved in our body should be at the normal range at any point of time. Either a decrease or an increase in the level of these ions are always associated with some clinical disturbance and may increase the risk of morbidity and mortality. Normal range of serum potassium is crucial as it is essential for muscle, nerves and cardiac electrical activity. High intracellular potassium concentration is required for cellular processes including DNA and protein synthesis, cell growth, apoptosis, mitochondrial enzyme function, maintenance of cell volume and acid base balance.*

Keywords: *Potassium, Hypokalemia, Hyperkalemia.*

The most abundant intracellular cation of our body is potassium of which 98% is located within the cells, predominantly in muscle and the concentration ranges from 100 to 150 mEq/L. The remaining 2% is in the extracellular fluid (ECF) and the levels vary between 3.5 to 5 mEq/L.[1] The dietary intake of potassium widely varies between 35 to 110 mEq/day between the various age group.[2] Homeostatic mechanism of a healthy individual precisely maintains the extracellular fluid (ECF) potassium level between 3.5 to 5 mEq/L. Approximately 90% of potassium intake is excreted by the kidney and 10% by gastrointestinal system. Unlike adults, children need positive potassium balance for their somatic growth.

Regulation of potassium balance

The internal potassium balance and distribution of potassium across the cells is largely maintained by Na^+K^+ ATPase pump. It is modulated by insulin, sympathetic nervous system and acid base balance. Majority of the external potassium homeostasis is maintained by the kidneys through excretion of the same. Almost 90% of the filtered potassium is reabsorbed in proximal convoluted tubule and loop of Henle. Only 10% of the filtered potassium is delivered to the distal convoluted tubule and collecting duct. The most important regulator of potassium secretion within the cortical collecting duct is aldosterone which promotes tubular secretion and urinary excretion of potassium. This response is predominant during hyperkalemia.[3,4] Potassium imbalance is one of the important electrolyte abnormalities seen in children and its approach from a pediatrician's perspective is very important in its management. Proper management requires definitive diagnosis as well as the treatment of primary disease.

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HYPOKALEMIA

Hypokalemia is defined as serum potassium less than 3.5mEq/L. The causes for hypokalemia is varied (Table I). Mild and Chronic hypokalemia (3 to 3.5mEq/L) may not be symptomatic. Children may become symptomatic with the potassium concentration less than 2.5 or 3.0 mEq/L.[5] Hypokalemia can have effects on various systems of the body. Approach to the management of hypokalemia is given in Fig.1.[6]

Effects of hypokalemia on various systems

Cardiovascular system: Various cardiac arrhythmias like premature atrial and ventricular beats, sinus bradycardia, paroxysmal atrial or junctional tachycardia, atrioventricular block ventricular tachycardia or fibrillation can occur. Characteristic electrocardiographic changes include depression of the ST segment, decrease in the amplitude of the T wave and an increase in the amplitude of U waves, which occur at the end of the T wave. Systemic vascular resistance can increase.

Neuromuscular effects: Muscle cramps, skeletal muscle weakness (usually starts with lower extremities and progress to trunk and upper extremities; may involve respiratory muscles), rhabdomyolysis and smooth muscle dysfunction such as paralytic ileus and urinary retention can occur.

Renal effects: Polyuria (decreased urinary concentrating ability), reduced sodium excretion, increased renal

Table I. Causes of hypokalemia

Spurious hypokalemia	Can occur in patients with leukemia or elevated white cell counts as K^+ will be taken up by these metabolically active cells in the test tube
Transcellular shift of potassium from ECF to ICF (Normal total body potassium)	Stress, hypothermia, beta 2 adrenergic agonists, insulin, aldosterone, metabolic alkalosis, xanthines, hypokalemic periodic paralysis, thyrotoxicosis, barium ingestion, following treatment of megaloblastic anemia with vitamin B12 and folic acid and paraneoplastic hypokalemia
True potassium depletion (Reduced total body potassium) - Non renal causes	Hypokalemic metabolic acidosis – Diarrhea, malabsorption, intestinal fistulas, ureterosigmoidostomy Hypokalemic metabolic alkalosis -Vomiting, naso-gastric suction, congenital chloride diarrhea Hypokalemia with unpredictable acid base balance - Prolonged poor oral intake of potassium, undernutrition, laxatives, potassium binding resins and burns
True potassium depletion (Reduced total body potassium) - Renal causes	Hypokalemic metabolic acidosis- Renal tubular acidosis type I & II Hypokalemic metabolic alkalosis - Bartter syndrome, Gittelman syndrome, diuretics (loop and thiazide), magnesium depletion and following high dose antibiotics like penicillin Hypokalemia with unpredictable acid base balance - interstitial nephritis, post-obstructive release diuresis, recovering acute kidney injury
Hypokalemia with high blood pressure	Renal artery stenosis, malignant hypertension, primary hyperaldosteronism, Liddle syndrome, apparent mineralocorticoid excess and congenital adrenal hyperplasia (11-β-hydroxylase or 17-α-hydroxylase deficiency)

ammonium production (more generation of HCO3) may be observed. Long standing hypokalemia may cause hypokalemic nephropathy characterized by interstitial fibrosis, tubular atrophy, cyst formation in the renal medulla.

Endocrine and metabolic effects: Growth retardation due to negative nitrogen balance, glucose intolerance, decreased aldosterone release and increased renin secretion.

Management of hypokalemia

The goal of therapy is to prevent or treat life threatening complications like cardiac arrhythmias and paralysis. Asymptomatic patients with potassium level of 3 to 3.5 mEq/L can be corrected with diet rich in potassium like tender coconut water, fruit juices with high potassium content (Orange and tomato) and treating the underlying causes like acute gastroenteritis. Mild and chronic hypokalemia (2.5 to 3 mEq/L) is better tolerated and is less likely to require emergency intervention. They can be treated with oral potassium supplementation. Alkali therapy is the main stay of treatment for renal tubular acidosis (RTA) type 1 and 2 which can be given in the form of potassium citrate. Requirement of alkali will be higher in proximal RTA (15 to 20 mEq/kg/day) compared to distal RTA (2 to 4 mEq//kg/day). Readymade liquid form of potassium citrate is available (1ml gives 2 mEq of potassium and 3mEq of citrate). Potassium in the form of potassium chloride, 1 to 3 mEq/kg/day is used in Bartter syndrome along with potassium sparing diuretics and indomethacin. Oral form of potassium chloride can be used (15ml gives 20mEq of potassium). Always check the magnesium level as hypomagnesemia may cause refractory hypokalemia.[7] Children with symptomatic hypokalemia like muscle weakness and arrhythmias should receive parenteral potassium correction under continuous ECG monitoring. Intravenous potassium chloride (1ml KCL gives 2mEq potassium) is usually given over a period of 1 to 2 hours. Infusion should not exceed 0.5 to 1 mEq/kg/hour with the maximum of 40 mEq/L. The concentration should not exceed 40 mEq/L in peripheral and 60 mEq/L in central venous line. It is a high alert medication and always mixed with normal saline (potassium and normal saline at the ratio of 1:10 to 20). Ringer's lactate (potassium 4 mEq/L), PlasmaLyte A, PlasmaLyte 148 (both have potassium 5 mEq/L) are the isotonic potassium containing IV fluids. Serum potassium level needs to be monitoredas there is a risk of rebound hyperkalemia. It is mandatory to correct potassium levels prior to the correction of metabolic acidosis.

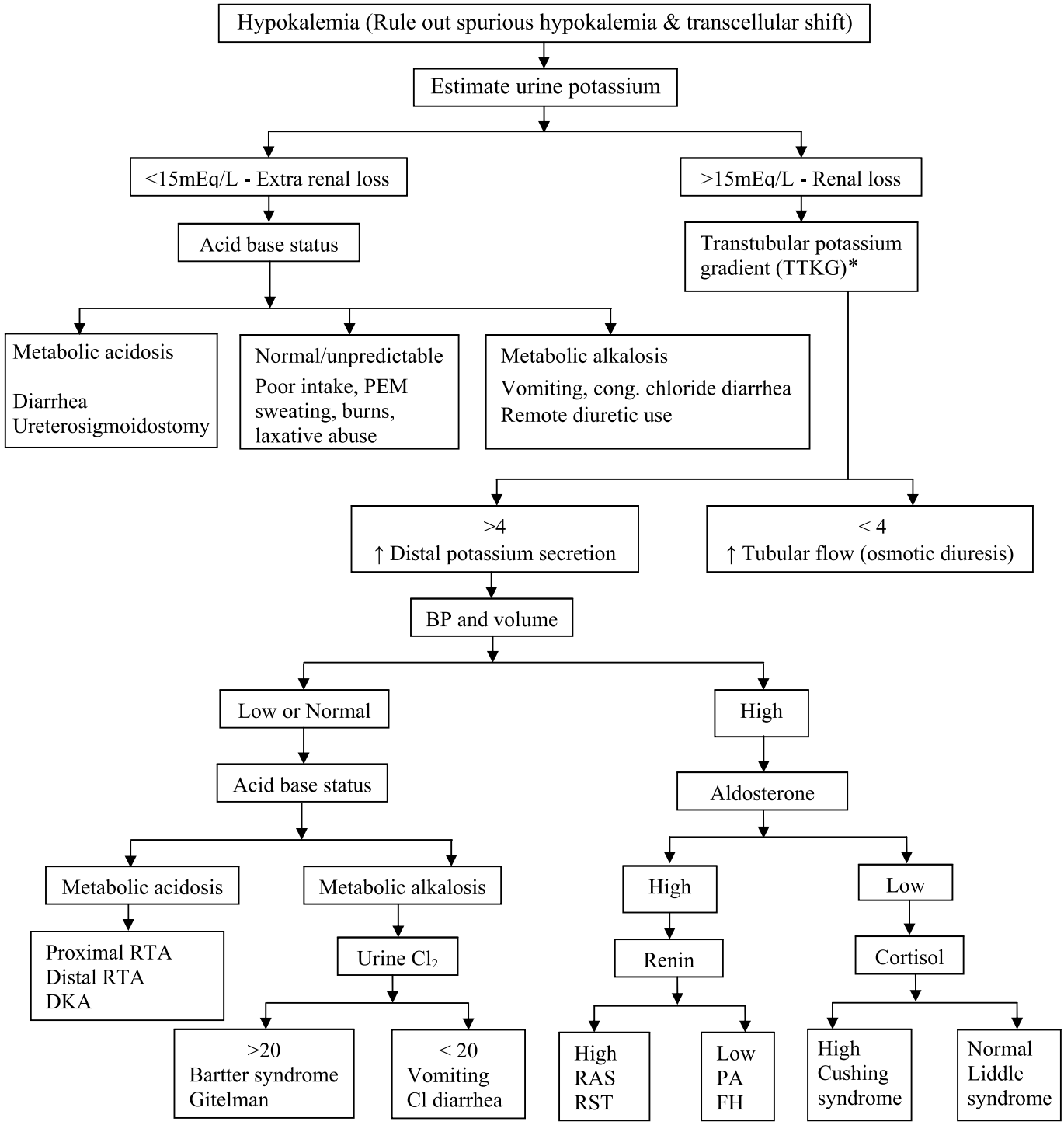

Fig.1. A step by step approach in the management of hypokalemia

(RAS – Renal artery stenosis, RST- Renin secreting tumors, PA- Primary aldosteronism, FH- Familial hyperaldosteronism)

$$*\text{Trans tubular potassium gradient (TTKG)} = \frac{\text{Urine potassium X Serum osmolality}}{\text{Serum potassium X Urine osmolality}}$$

(Pre requisites: Urine sodium should be >20 mmol/L and Urine osmolality > Serum osmolality)

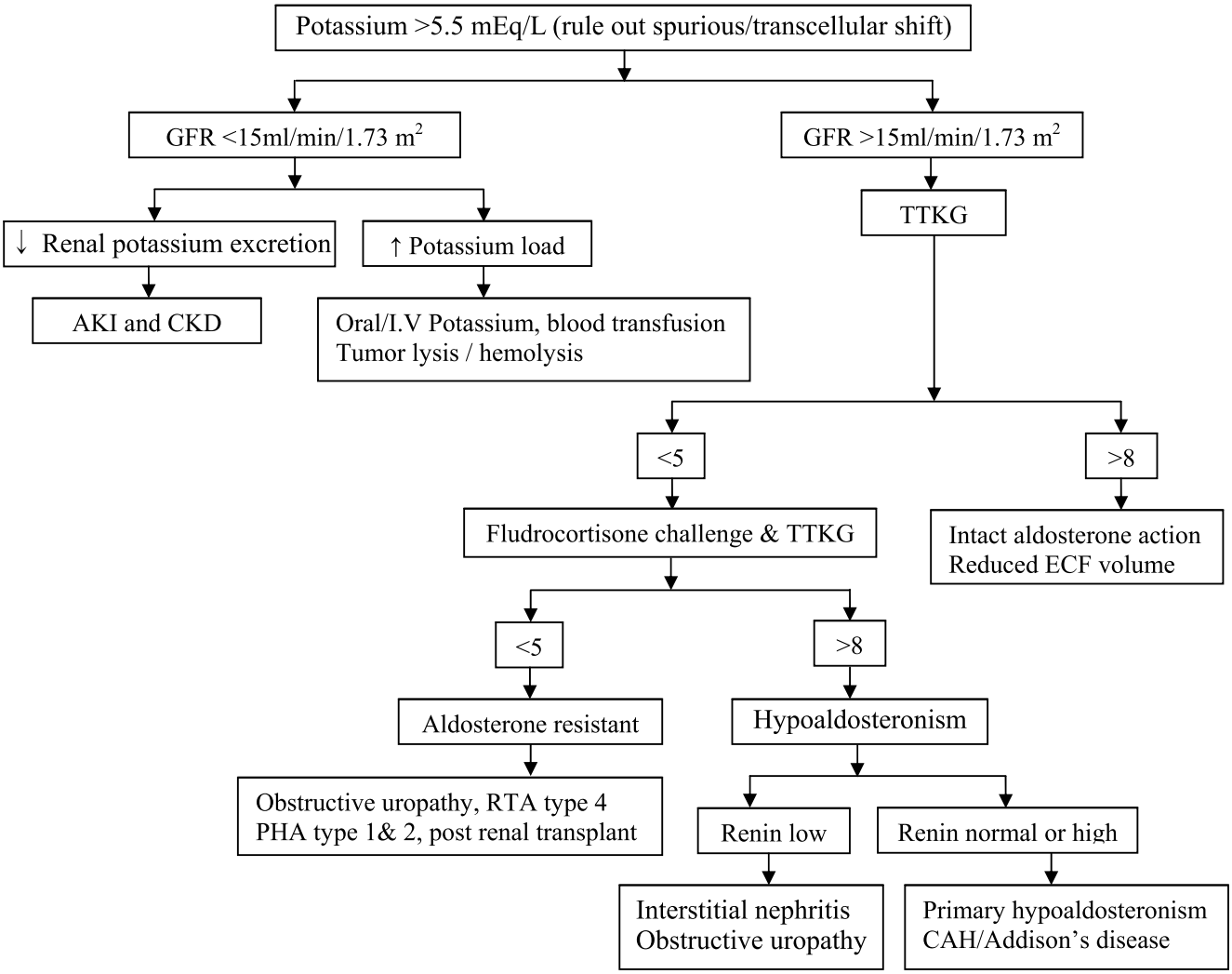

Fig.2. Management of hyperkalemia - Approach

HYPERKALEMIA

Serum potassium level more than 5.5mEq/Lis hyperkalemia. Symptoms and signs of hyperkalemia tend to occur only with rapid rise and high levels of potassium (>6 mEq/L).[8,9] Severity of hyperkalemia is defined as mild (5.5 to 6 mEq/L), moderate (6 to 7 mEq/L) and severe (>7 mEq/L). The causes for hyperkalemia is given in Table II and their symptoms and signs are in Table III.

Effects of hyperkalemia on various systems

Cardiovascular system: Cardiac arrhythmias - ventricular ûbrillation and standstill are the most severe consequences. The characteristic electrocardiographic changes include peaked tall T wave with shortened QT interval followed by progressive lengthening of the PR interval and QRS duration. There is decrease in systemic vascular resistance.

Neuromuscular effects: Skeletal muscle weakness and smooth muscle dysfunction.

Renal effects: Increased sodium excretion and decreased renal ammonium production (less generation of HCO_3).

Endocrine and metabolic effects: Increased aldosterone release and decreased rennin secretion.

Management of hyperkalemia

Look for reversible causes like hypovolemia, medications, parenteral fluids and metabolic acidosis. Life threatening hyperkalemia needs emergency attention. Dialysis is indicated in children who donot respond to conservative antihyperkalemic therapy (Table III). Approach to the management of hyperkalemia is given in Fig.2.[6]

Table II. Causes of hyperkalemia

Spurious hyperkalemia	Potassium movement out of cells during or after blood is withdrawn, tissue ischemia during venepuncture, hereditary spherocytosis
Increased potassium load	Intravenous or oral potassium, blood transfusion
Transcellular shift of potassium from ICF to ECF	Insulin deficiency, extracellular hypertonicity, increased tissue catabolism (severe hemolysis, rhabdomyolysis, tumor lysis syndrome, immediately after cardiac surgery), heavy exercise, familial hyperkalemic periodic paralysis, hyperkalemia of premature infant
Impaired renal potassium excretion	Acute kidney injury and Chronic kidney disease Drugs- Potassium sparing diuretics, calcineurin inhibitors, non steroidalanti inflammatory drugs, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and heparin Hyperreninemic hypoaldosteronism: Addison disease, salt-losing congenital adrenal hyperplasia (21-hydroxylase deficiency) Hyporeninemic hypoaldosteronism: idiopathic, complicating acute nephritic syndrome Pseudohypoaldosteronism Type 1 Primary due to reduced epithelial sodium channel activity or mutations in gene for mineralocorticoid receptor Secondary due to complicated obstructive uropathy, systemic lupus erythematosus, sickle cell disease, renal transplantation and renal amyloidosis Pseudo hypoaldosteronism Type 2 Familial hyperkalemic hypertension or Gordon syndrome

Table III. Anti-hyperkalemic measures

Medication	Dosage	Onset of action	Mechanism
10%Calcium gluconate	0.5 ml/kg with maximum of 20 ml with 20 ml 10% dextrose over 15 minutes	Immediate	Stabilization of cardiac membrane and prevents arrhythmias
Insulin and glucose	0.1unit/kg insulin with maximum of 10 units and 0.5 g/kg dextrose over 30 minutes (watch for hypoglycemia)	10 to 20 minutes	Increased transcellular shift of potassium inside the cell by enhancing Na^+K^+ATPase.
Inhaled beta adrenergic agonist-salbutamol	Neonate- 0.4 mg in 2 ml NS Children<25 kg-2.5 mg in 2 ml NS>25 kg to 50 kg-5 mg in 2 ml NS>50 kg- 10 mg in 4 ml NS	30 min- 1 hour	Transcellular shift of potassium inside the cell
Sodium bicarbonate (8.4%)	1mEq/kg (max. 50 mEq) IV over 20 minutes	20 minutes	Transcellular shift of potassium inside the cell
Diuretics (Frusemide)	1mg/kg (maximum of 40 mg) I.V	1 to 2 hours	Removes potassium from the body
Cation exchange resins (Calcium polystyrene sulfonate)	1g/kg (max.30grams) oral/enema 8^{th} hourly		Exchanges sodium for potassium across the large intestine and potassium is excreted

Conclusion

Growing children need a net positive potassium balance for their appropriate somatic growth. Both hypokalemia and hyperkalemia are associated with adverse consequences hence it is essential to maintain the potassium within normal range. Always try to find out the underlying etiology causing potassium imbalance so that the management becomes easy.

Points to Remember

- ***Understanding the basics of potassium distribution in our body is essential to treat both hypo and hyperkalemia.***
- ***Hypokalemia is more common in children than hyperkalemia. Always look for the reversible causes like volume depletion, medications, etc.***
- ***Intravenous potassium chloride is a high alert medication and hence should be used cautiously under cardiac monitoring.***
- ***Moderate to severe hyperkalemia is a life threatening medical emergency and needs urgent intervention***.

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CLIPPINGS

A study on toothbrush wear index and wear rate in some kindergarten children.

Toothbrush wear index and wear rate in some kindergarten children was evaluated in order to study proper toothbrush management method among children 6-12 years of age. A toothbrush used once a day for 50 kindergarten children was collected for 1 week and 4 weeks. The change in the toothbrush shape varied according to the usage period. In addition, the tips of the toothbrush used for 4 weeks were cracked and many microorganisms inhabited the cracked tips.It should be recommended that toothbrushes be kept in a dry place with low humidity so as to prevent microbial hatching, and children's toothbrushes characterized by fine bristles be replaced sooner than 3 months, the known average replacement interval.

Yu-Jin Choi, Su-Bin Lee, Chae-Eun Jeon and Jung-Ok Choi. A study on toothbrush wear index and wear rate in some kindergarten children. Current Pediatric Research 2017; 21(4):577-581.

FLUID AND ELECTROLYTE DISTURBANCE

FLUID AND ELECTROLYTE MANAGEMENT IN DIABETIC KETOACIDOSIS

** Vijai Williams*
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Abstract: *Diabetic ketoacidosis (DKA) is a preventable but serious complication of type 1 diabetes and carries a mortality rate of 0.3-0.5% in developed economies and much higher in developing economies (about 10%). New onset diabetes presenting for the first time as DKA is quite common in children. The diagnosis in these children is not always apparent and requires a high index of suspicion. Immediate treatment includes adequate intravenous fluids, parenteral insulin and careful clinical and biochemical monitoring. Pediatricians in resource limited settings encounter a higher incidence of complicated DKA due to delayed presentations, poor compliance to therapy and higher co morbidities like malnutrition and sepsis. These warrant modifications in established international guidelines to avoid over as well as under treatment with respect to fluids and insulin. In our settings children with DKA should preferably be managed by a specialist multidisciplinary team during and after an episode. Since parents play a key role in the day to day management, emphasis should be on sustained patient/ parent education to avoid recurrence.*

Keywords: *Diabetic ketoacidosis, Children, Fluids, Electrolytes, Insulin therapy*

Diabetic ketoacidosis (DKA) is a pathological state of severe metabolic acidosis caused by insulin deficiency leading to accumulation of ketoacids that exceeds the normal buffering capacity of the body. DKA occurs due to interplay between insulin (deficiency) and counter-regulatory hormones (excess). Insulin is the key regulator of glucose and fatty acid metabolism and helps maintain a balance between catabolism and anabolism. Insulin deficiency leads to hyperglycemia and ketosis. Hyperglycemia is a result of both decreased glucose storage and utilization in the peripheral tissues, while ketosis results from inhibition of lipolysis and increased oxidation of ketones in the peripheral tissues, thus resulting in both an overproduction as well as underutilization of ketones. The hyperglycemia is further aggravated by counter-regulatory hormones (epinephrine, cortisol and growth hormone) released in response to stress, which blocks the action of insulin and enhance the release of glucagon, resulting in increased glycogenolysis in the liver. The biochemical criteria that define diabetic ketoacidosis are in Box 1.[1] Rarely DKA can present with normal glucose values especially if the patient is partially treated or is severely malnourished. Risk factors depend on the patient being a known case or a newly diagnosed case of type 1 DM (Table I).

Box 1. DKA - Diagnostic criteria

- Hyperglycemia with random blood glucose (BG) > 200 mg/dL
- Venous pH<7.3 or bicarbonate <15 mmol/L
- Ketonemia (>3mmol/L) and ketonuria (>2+)

Table I. Risk factors for DKA in Type 1 DM

A. New onset Type 1DM	B. Known Type 1 DM
• Younger age (<2 years)	• Insulin omission
• Delayed diagnosis	• Insulin pump failure
• Lower socioeconomic status	• Previous episodes of DKA Poor metabolic control
• Infection	• Puberty and adolescence
	• Psychiatric (including eating) disorders
	• Infection

Clinical features of DKA

Most of the manifestations can be attributed to osmotic symptoms and volume loss. Ketoacidosis leads to

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Table II. DKA classification based on severity

Parameter	Mild	Moderate	Severe
Arterial pH	7.3- 7.2	7.2 - 7.1	< 7.1
Serum bicarbonate (mmol/L)	10-15	5-10	< 5
Urine ketones	> ++	> ++	> ++
Level of consciousness	Alert	Alert/drowsy	Stupor/coma

tachycardia, deep and rapid (Kussmaul's) respiration, a fruity odour of the breath, nausea and vomiting. Abdominal pain mimicking an acute abdomen is a very common manifestation of DKA. Confusion and drowsiness are common; progressive worsening of consciousness is seen with delayed presentation and is an ominous sign. Fever is uncommon and if present, is usually indicative of an underlying infection. In children with DKA, there is poor correlation between clinical features and severity of acidosis and degree of dehydration[3]. Hence, children suspected to have DKA should be considered critically ill until evaluation proves otherwise. The classification of DKA based on severity is given in Table II.

Differential diagnosis

The other major hyperglycemic crisis associated with diabetes/non-diabetes is the hyperglycemic hyperosmolar state (HHS). In contrast to DKA, there is usually enough insulin to suppress ketogenesis, but not to control blood glucose. Typically, these children present with disproportionately high blood glucose (BG) with mild or no ketosis (Box 2).[2] On the other hand in DKA since ketoacidosis manifests early much before BG can rise, the BG levels are lower than hyperglycemic hyperosmolar state (HHS).

Box 2. Diagnostic criteria for hyperglycemic hyperosmolar state

- Blood glucose >600 mg/dL
- Arterial pH >7.30; venous pH >7.25
- Serum bicarbonate >15 mmol/L
- Mild ketonuria, absent to small ketonemia
- Effective serum osmolality >320 mOsm/kg in presence of stupor, coma or seizures

Challenges of managing DKA in a resource limited set-up

Unlike the West, where timely treatment is sought, most children with DKA in India, reach late to any healthcare facility due to delayed health seeking behaviour and lack of awareness about symptoms. Poor socioeconomic status, poor adherence to therapy, associated malnutrition, co morbidities like sepsis and inadequate treatment at first contact healthcare facility puts these children at higher risk for severe and complicated DKA.[4] Therefore, international treatment recommendations cannot be completely extrapolated to our population. A protocol based management anticipating complications at every step is presented keeping in mind the difficulties faced in a resource limited set up like ours.

Management

Goals of therapy are (i) Assess and appropriately correct dehydration to restore renal perfusion and facilitate peripheral glucose utilisation, (ii) Arrest ketogenesis with insulin therapy, (iii) Anticipate and replace ongoing fluid and electrolyte losses, (iv) Assess and treat precipitating cause (e.g. infection) and (v) Anticipate and intervene rapidly if complications occur (e.g. cerebral edema).

Immediate steps of stabilisation in an emergency room (ER)

Immediate stabilisation of airway, breathing and circulation are same as for any other critical illness. Acute management should follow the general principles of Advanced Life Support (ALS) and some of the important steps are given below

- Airway measures (basic and advanced) may be needed in children with DKA who are deeply comatose with features suggestive of cerebral oedema.
- All children should be started on supplemental oxygen (whichever delivery device is available).
- Continuous nasogastric aspiration is essential to decompress a hugely dilated stomach.
- Two peripheral lines must be secured for fluids and insulin infusion.
- Hypotension is rare in DKA, if present, indicates either severe uncorrected hypovolemia or associated septic shock. Volume resuscitation will be required in children with shock.
- All children must be under continuous cardiac monitoring.

Table III. Diabetic ketoacidosis - Treatment guidelines

Protocols	Milwaukee1988	BSPED[#]2004 & 2007	ISPAD[##]2009 & 2014
Fluid to be started	NS (normal saline)	NS	NS
Minimal duration of NS	1 hour	12 hours at least	4 hours at least; preferably 12 hours
Bolus	10-20 ml/kg	10 ml/kg	20 ml/kg only if in shock
Insulin (IU/kg/hr)	0.05-0.1	0.1	0.1
Fluid and insulin	Start together	Start insulin 1 hour after fluids	Start insulin 1-2 hours after fluids
Duration of correction	23 hours	48 hours	48 hours

[#] *British Society for Paediatric Endocrinology and Diabetes*

[##] *International Society of Paediatric and Adolescent Diabetes*

- Bladder catherization may be required in children with low GCS.
- Consider antibiotics in a febrile child after obtaining appropriate cultures.
- Children with severe DKA are better managed in PICU.

Fluid therapy

Rationale: Children with DKA have volume depletion that activates the renin-angiotensin-aldosterone axis and also triggers the release of corticotrophin releasing hormone (CRH). These hormones act towards preserving the intravascular volume but at the same time increase insulin resistance. Fluid therapy by improving dehydration causes a decline in CRH, enhances renal glucose clearance (following improved renal perfusion) and augments insulin sensitivity.[5] This in turn causes significant improvement in blood glucose, hypertonicity and acidemia. Hydration alone has been shown to reduce glucose concentration by 17-80% during a period of 12-15 hours, which represents an average plasma glucose reduction rate of 25-50 mg/hour.

Goals: Fluid resuscitation goals include expansion of the intravascular, interstitial and intracellular volume and restoration of renal perfusion. Slow and even rehydration without major osmolar shifts is the key.

Assessment of dehydration: Clinical assessment of dehydration is difficult and unreliable in children with DKA due to several reasons. Conventional signs of dehydration like decreased skin turgor, dry oral mucosa, sunken eyes, and capillary refill time >2 seconds are absent in DKA as they tend to have preserved intravascular volume due to hyperosmolarity. Additionally, acidosis itself can cause dry oral mucosa and peripheral vasoconstriction. The assumption of an average overall 10% dehydration in patients with DKA was found to overestimate dehydration. Subsequently, the assumed deficits were reduced to a range of 6.5-8.5% following studies which showed that median absolute measure of dehydration as calculated by body water estimation was 8.7%.[3] This estimate was the best fit to avoid risks of over-hydration as well as under-hydration. DKA is one clinical condition where the 'one size fits all' policy seems more appropriate.

Fluid resuscitation

Though various protocols are available, treatment guidelines are still evolving with multiple ongoing trials on the type, rate and amount of fluid therapy (Table III). Despite these, normal saline (0.9 %) still remains the initial fluid of choice for resuscitation.

Children in shock may require volume expansion with 20 ml/kg bolus of isotonic saline over 30-60 min. In compensated shock, bolus can be given slowly over 1 hour followed by slow correction as described below.

In children who are hemodynamically stable, deficit for dehydration correction is taken as a rough estimate of 6.5 to 8.5% (A). This is added on to the 36/48-hour maintenance fluid (B). All initial resuscitation boluses received need to be subtracted from total calculated deficits (C). Fluid replacement is guided by clinical examination, hemodynamic, hydration status, serum electrolyte levels and urine output. Urinary losses need not routinely be replaced. If any child develops cerebral edema during therapy, fluid should be tailored to suit the needs of raised ICP management. Strict assessment of fluid balance is essential in all children.

Weight	Fluid (mL/kg)
< 10 kg	100
10- 20 kg	1000ml + 50
>20 kg	1500ml+ 20

Fluid calculation: Total fluid requirement = (A + B) – C

A. Maintenance fluid calculation: From the Holliday-Segar equation which roughly estimates fluid requirement based on weight.

B. Deficit calculation: % dehydration assumed x body weight.

C. All isotonic fluid boluses, if received during resuscitation, need to be subtracted from the total volume.

Fluid requirement is calculated for 36-48 hours and hourly infusion rate is obtained. Urine output monitoring may not be reliable, as the child may have polyuria due to glycosuria and urinary losses need not be replaced routinely.

Fluid type to be used

Isotonic saline used for initial resuscitation may be continued for the initial 4-6 hours before replacing it with N/2 saline (0.45%).This switch is determined by the serum sodium and osmolality levels and more importantly the availability of plain N/2 saline (without dextrose). In case of non-availability, normal saline can be continued. A recent RCT comparing slower versus rapid fluid administration using either 0.45% saline or 0.9% saline failed to show any significant differences in the frequency of either altered mental status or cerebral edema and long-term neurocognitive outcomes.[6] Continued use of large volumes of NS can however cause hyperchloremic metabolic acidosis due to their high chloride content. What was once thought to be a transient and innocuous side effect, has now been shown to be associated with acute kidney injury and delayed resolution of acidosis. Balanced fluids (containing lower chloride) have been found to be better in preventing kidney injury; however further studies are needed to establish them as standard of care. Currently, therefore isotonic saline remains the preferred choice till further recommendations emerge.

Rate of fluid correction

Rate of fluid correction is another area of debate. Many centres prefer a slow and even correction spaced over 36-48 hours, as this has been shown to reduce the risk of cerebral edema. The rate of correction is determined by the initial BG levels, serum osmolality, corrected sodium, severity of acidosis, presence of acute kidney injury and depth of altered sensorium. Slower correction is recommended for children with severe DKA and those having very high BG, osmolality and corrected sodium.

Insulin therapy

Rationale: Insulin replacement is the mainstay of therapy in type 1 DM. It facilitates glucose utilisation and halts ketosis. The goals are to decrease hyperglycemia and arrest ketosis.

When to start?: Current guidelines do not recommend bolus insulin administration, as it was found to be associated with increased incidence of cerebral edema. Also greater incidence of cerebral oedema was noted in children who received insulin within first hour of starting fluids.[7] Regular insulin is therefore recommended to be initiated following fluid resuscitation, as an infusion at a rate of 0.1 U/kg/hr. Lower dose (0.05 U/Kg/hr) as continuous infusion has been tried and found to be as effective as standard low dose regimen (0.1 U/kg/hr). The authors' unit follows the 0.05 U/Kg/hr regimen as it was found to have similar time to resolution of DKA as compared to standard therapy, with lesser incidence of hypoglycemia.[8,9]

Administration: Separate intravenous access for insulin is necessary. The entire line has to be adequately flushed with the insulin solution as insulin tends to adhere to the tubing and may not be delivered appropriately, unless flushed prior to the start of the infusion. Fresh insulin in appropriate dilution needs to be used.

Alternatives to IV route: Prospective randomized control trials have tried newer rapid acting subcutaneous insulin analogues in place of intravenous regular insulin, and have found them to be safe and effective.[10] They were more cost effective, especially in patients admitted to the ICU without major co-morbidities. Their use in moderate to severe DKA, however, still needs further evaluation.

Non-response to insulin: Before escalating dose or changing insulin, the patency of IV cannula, insulin preparation and expiry date, appropriateness of dilution have to be checked apart from adequate flushing of lines. Insulin dose can be hiked if all above parameters are checked and found correct.

Anticipated electrolyte abnormalities and reason

Potassium

Hypokalemia in DKA occurs secondary to osmotic polyuria, excretion of ketoanions and due to low potassium

stores in malnourished children. Furthermore during therapy, serum potassium decreases quickly as K + is driven into the intracellular compartment by insulin and acidosis correction. All children need to be monitored with ECG which can show hypokalemia related changes. Anticipate hypokalemia in a child with DKA if serum potassium level is normal or low in presence of severe acidosis and in presence of malnutrition.

Potassium replacement is started when the serum potassium concentration falls below normal levels with a goal to maintain serum potassium between 4.0 and 5.0 mEq/L. If the child is hypokalemic at admission, potassium correction has to be started immediately along with addition of maintenance potassium at 40 mmol/L, after ensuring adequate urine output. Administration of insulin has to be delayed in severe hypokalemia and may be started after fluid and potassium replacement. One-third of potassium replacement may be administered as potassium phosphate either as intravenous or as phosphate enema. This may offset the chloride load from IV fluids and prevent hypophosphatemia.

Phosphate

Whole-body phosphate depletion is a hallmark of poorly controlled diabetes but typically remains asymptomatic. The routine use of phosphate in the treatment of DKA is not recommended.[11,12] Replacement is indicated in those with anemia, cardiac dysfunction, respiratory depression, muscle weakness or in patients with serum phosphate lower than 1-1.5 mg/dL. When considered necessary, one third of potassium replacement can be given as potassium phosphate as described above.

Hyperchloremia

Hyperchloremia results from ongoing loss of bicarbonate from renal tubules, with retention of chloride, further compounded by excessive infusion of chloride containing fluids like normal saline. Recent reports suggest that hyperchloremia may be associated with acute kidney injury. The resultant normal anion gap metabolic acidosis though self-limiting, may be erroneously interpreted as non-resolution of ketoacidosis, if careful AG estimation is not done at bedside. Balanced fluids with lower chloride content may decrease this complication and are being increasingly studied.

Bicarbonate

Bicarbonate replacement is a controversial issue in DKA and is not routinely recommended, as metabolic derangements tend to correct with insulin and fluids. Therefore, the objective must be to address the root causes for acidosis such as hypovolemia, ketoacidosis, tissue hypoperfusion and acute kidney injury rather than chase the pH. Alkali therapy may benefit children with severe diabetic ketoacidosis with pH <6.9 associated with life threatening hyperkalemia or compromised cardiac function. Studies have failed to support bicarbonate use in DKA, rather they have shown impaired ketone and lactate clearance with bicarbonate therapy.[13]

Monitoring during therapy

Clinical and biochemical: All children during therapy need continuous cardiac monitoring. Complete neurological examination is mandatory with special emphasis on pupils, Glasgow coma scale (GCS) and deep tendon reflexes (DTR) anticipating cerebral edema during therapy. Hourly blood glucose monitoring is essential. Fluid balance needs to be calculated periodically.

Laboratory tests: Blood glucose, blood gases, serum electrolytes, urea, creatinine and hematocrit should be repeated 2–4 hours or more frequently, as clinically indicated, in severe cases. Blood beta hydroxybutyrate concentrations, if available, needs to be done every 2 hourly. Lipids and triglycerides can be grossly elevated causing the blood sample to show a visible rim of lipids.

Anion gap (AG) estimation [AG= Na - (Cl+HCO3); normal 8-12] helps in monitoring; closure of anion gap indicates correction of ketoacidosis. Persistent high anion gap acidosis in DKA suggests non-response to insulin, uncorrected hypovolemia or concomitant lactic acidosis. Significant hyperchloremia results in normal anion gap hyperchloremic acidosis. Calculation for corrected sodium and effective osmolality is given in Box 3.

Targets for gradual reduction of effective serum osmolality is analogous to "Slow and steady wins the race"

The desired rate of fall of BG is 50-100 mg/dL/hour after starting insulin. The pH is expected to increase by 0.03/hr. Serum sodium should increase by 0.5 mmol/L for

Box 3. Calculation for corrected sodium and osmolality

- Corrected sodium = Measured Na+2 [(plasma glucose-5.6)/5.6] mmol/L or measured Na+2 [(plasma glucose-100)/100] mg/dL.
- Effective osmolality (mOsm/kg)=2×(plasma Na) + plasma glucose (mmol/L).

each 1 mmol/L decrease in BG with least variability in corrected sodium. Rate of fall of serum osmolality should be 3-8 mOsm/kg/hour for HHS and more gradual for DKA, so as to reduce cerebral edema. Severity of extracellular fluid contraction can be assessed by serum urea and hematocrit. Urinary ketones should not be used to monitor clearance of ketonuria or ketonemia, as commercially available kits generally measure acetoacetate which continues to appear even after resolution of DKA.

Persistent acidosis: Persistent acidosis is defined as bicarbonate <10 mEq/mL despite 8-10 hours of therapy for DKA. The first step before proceeding further is to calculate the AG. High AG acidosis at this juncture suggests the following - Improper insulin dose, dilution and rate of infusion, incorrect administration (avoided by flushing the IV line completely before starting insulin) and rarely may be secondary to lactic acidosis/renal compromise. Normal AG acidosis at this juncture suggests hyperchloremia due to administration of chloride containing fluids like normal saline.

End points of therapy are normal sensorium with good oral tolerance, resolution of acidosis pH>7.3 or bicarbonate > 15 mmol/L and closed anion gap. There is considerable variability in the definition of end-points used in different studies.

Transition to subcutaneous insulin

Once the acidosis is passive, oral acceptance and tolerance is good. A subcutaneous insulin regimen can be initiated at 1 U/kg/day of regular insulin in 4 divided doses. This can be later changed to basal bolus or spilt mix regimen. There should be an overlap of 1- 2 hours between the first dose of sub-cutaneous insulin and stopping intravenous insulin infusion to prevent a precipitous drop in serum insulin levels and consequent hyperglycemia and ketoacidosis. In a known type 1 DM on home insulin regimen, their home dose of insulin may be restarted and titrated for desired blood glucose levels.

Complications

Cerebral edema: Children have higher incidence of symptomatic cerebral edema (CE) as compared to adults, particularly in those with new onset diabetes.[14] It remains a major complication of DKA with a mortality rate of 10-25%.[14,15] The cerebral edema model proposed for DKA is the two hit hypothesis: First hit is before DKA therapy is initiated wherein the dehydration and cerebral hypoperfusion cause ischemia related cerebral injury. Second hit occurs after fluid therapy is started and is due to reperfusion injury.[16,17] Akin to other hyperosmolar states, 'idiogenic osmoles' are generated in the brain cells to protect them against intracellular dehydration and shrinkage. Rapid decrease in extracellular osmolality draws fluid into the intracellular compartment favouring development of cerebral oedema. This may be secondary to rapid reduction of blood glucose, too vigorous fluid replacement with failure of corrected sodium to rise with therapy and bicarbonate use.[18] This underscores the importance of avoiding both under hydration as well as overhydration during management of DKA.

Cerebral edema usually occurs few hours after start of DKA therapy with varied symptomatology, ranging from headache to abrupt neurological deterioration and coma. A high index of suspicion for cerebral edema is therefore needed and should be considered in patients with impaired sensorium persisting despite improvement in pH>7.3 and blood glucose <300 mg/dL and in those with early subtle neurological signs. It may be too late to react at the time of profound neurological depression and respiratory arrest. When cerebral edema is suspected, close monitoring of blood glucose and electrolytes is essential to avoid osmotic disequilibrium. Osmotherapy with mannitol may be used to counter cerebral edema. Fluid volume administered should be curtailed and other anti-raised ICP measures should be initiated.

Hypoglycemia: Hypoglycemia as a therapy related complication in the West has decreased considerably with use of low dose insulin infusion. However, the incidence in resource limited settings despite low dose insulin is still high due to associated malnutrition.[19] Hourly monitoring of blood glucose and early addition of dextrose (when BG reaches 250 mg/dL) to fluid regimen especially in malnourished children is recommended. This allows for continuation of insulin till ketosis is reversed and prevents hypoglycemia. It is advisable to have a 2 bag system containing 10% dextrose (1st bag) and no dextrose (2nd bag) so that there is a smooth transition to varying dextrose concentration.[20,21]

Acute respiratory distress syndrome: Non-cardiogenic pulmonary edema is a result of reduced colloidal oncotic pressure in pulmonary capillaries due to exclusive crystalloid replacements in DKA. In hypoxemic patients with increased pulmonary alveolar-arterial gradient, one should suspect pulmonary edema. It can be avoided by judicious fluid replacement.

Acute kidney injury: Acute kidney injury is a common complication encountered during DKA management. Elevated chloride level is an independent predictor of AKI and there is a possible beneficial role of balanced solutions in preventing this morbidity.

"Sick day rules" - Prevention is better than cure

Since the principal reason for DKA recurrence is omission of insulin, most cases can be avoided by proper patient education. Clear guidelines must be issued to patients on sick day management; not stopping insulin, monitoring blood glucose and urine ketones regularly, ensuring usual carbohydrate intake with plenty of fluids and seeking early medical help.These measures will help prevent the occurrence of DKA.

Points to Remember

- ***The features of DKA are attributable to the osmotic effects of high blood glucose and loss of body fluid.***
- ***Correcting the dehydration by appropriate IV fluid, arresting the ketogenesis by insulin therapy and treating the precipitating cause(s) forms the basis of treatment in DKA.***
- ***Correct dose, rate, technique and duration of insulin infusion is a must.***
- ***Anticipating electrolyte abnormalities and treating them as and when it occurs is essential.***
- ***Managing a child with DKA needs to be in the intensive care unit with a good lab support.***

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CLIPPINGS

Risk factors for poor outcomes of children with acute acalculous cholecystitis.

147 children with acute acalculous cholecystitis (AAP) were evaluated for identifying the risk factors for poor outcomes. AAC was defined by presence of fever and an echo proven thickened gallbladder wall exceeding 4 mm. Anemia, thrombocytopenia, gall bladder sludge, hepatitis and sepsis plus hepatitis are the predictors likely to help clinicians identify patients who are at a high risk of poor prognosis and make appropriate clinical decision.

Yi-An Lu, Cheng-Hsun Chiu, Man-Shan Kong, Han-I Wang, Hsun-Chin Chao, Chien-Chang Chen. Risk factors for poor outcomes of children with acute acalculous cholecystitis. Pediatrics and neonatology 2017; 58(6): 497–503.

Point-of-Care Ultrasound for the Diagnosis of Skull Fractures in Children Younger Than Two Years of Age.

Study was undertaken to determine the accuracy of skull point of care ultrasound (POCUS) for identifying features in children younger than 2 years of age with signs of head trauma and the ability of POCUS to identify the type and depth of fracture depression. Of all the 115 enrolled, 88 (76.5%) had skull fractures. POCUS had a sensitivity of 90.9% (95% CI 82.9-96.0) and a specificity of 85.2% (95% CI 66.3-95.8) for identifying skull fractures. Agreement between POCUS and CT to indentify the type of fracture as linear, depressed or complex was 84.4%. Emergency physicians should consider POCUS as an adjunct to clinical evaluation and prediction rules for traumatic brain injuries in children younger than 2 years of age.

Point-of-Care Ultrasound for the Diagnosis of Skull Fractures in Children Younger Than Two Years of Age. Parri Niccolò, et al. The Journal of Pediatrics, DOI: https://doi.org/10.1016/j.jpeds.2017.12.057 in Press.

NEWS AND NOTES

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FLUID AND ELECTROLYTE DISTURBANCE

FLUID AND ELECTROLYTE MANAGEMENT IN SEVERE ACUTE MALNUTRITION

***Praveen Kumar**
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Abstract: *Fluid management in children with severe acute malnutrition (SAM) is controversial due to lack of strong evidence. As a result of the reductive adaptive state in SAM, there is high intracellular sodium and low potassium. Thus, there is high risk of fluid overload and sodium retention with overzealous management of shock and dehydration. WHO has recommended conservative approach for fluid resuscitation preferably oral or nasogastric rehydration unless child has shock or other contraindications. When WHO recommended ReSOMal is unavailable, modified ORS using low osmolarity ORS, potassium, glucose and mineral solution is the preferred ORS for children with SAM. All children with severe acute malnutrition on intravenous or oral rehydration should be closely monitored for signs of overhydration. Additionally, due to common deficiencies, potassium and magnesium supplementation is recommended.*

Keywords: *Fluid, Malnutrition, Shock, Rehydration.*

Malnutrition may be defined as the cellular imbalance between supply of nutrients and body's demand for them to ensure growth, maintenance and specific functions. Severe Acute Malnutrition (SAM) is defined as weight for height below -3 SD score of the median WHO child growth standards and/or mid upper arm circumference below 11.5 cm and/or presence of bilateral pedal edema in children aged 6 months to 5 years. Mid upper arm circumference (MUAC) criteria is not applicable for infants less than 6 months.[1]

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According to estimates, malnutrition affects 8.1 million under-five children with 0.6 million deaths and 24.6 million disability adjusted life years (DALYs).[2] In hospitalized Indian children, malnutrition has been shown to increase the risk of mortality up to six times in diarrhoea and in acute respiratory tract infections.[3] A recent survey of National Family Health Survey (NFHS-4) showed that 7.5% of children under 5 years of age are severely wasted.[4] Protocol based management decreases this mortality significantly. Fluid therapy in children with severe malnutrition is an area which is controversial due to lack of strong scientific evidences.[5] In this article we have attempted to put together current evidences on fluid and electrolyte administration.

Need for different fluid strategy in SAM

Due to energy deficiency, several physiological and metabolic changes occur in children with severe acute malnutrition which is also known as reductive adaptation.[6,7] Edematous malnourished children typically have high intracellular sodium and a tendency to retain fluids. By comparison, intracellular potassium is lost to the extracellular space and total body potassium is often very low. These changes at cellular level occur as part of the overall adaptive responses to repeated infections and damage to cell membranes by free radicals. Non-edematous SAM children also have depleted intracellular and total body potassium and similarly experience adaptive physiological changes such as reduced renal and cardiac output.

Malnutrition not only affects the muscles but also other internal organs. The heart become weak and may fail if it has to pump large volumes of fluid. Viartet al compared clinical and hemodynamic parameters of 43 Jamaican children who were marasmic kwashiorkor with 24 convalescent children. In the malnourished children, hemodynamic parameters were abnormal when compared with convalescent patients. Red cell volume and total blood volumes in malnourished childrenwere 51% and 66% of the convalescent children while cardiac and stroke indices averaged 58% and 62% of the convalescent children values respectively.[8] These changes predispose them to pulmonary edema when rapid and large volume of fluid is given. Similarly, an observational study from India by Singh, et al

reported that malnourished children had smaller cardiac mass. In particular, left ventricular mass was less and indicators of left ventricular function were reduced.[9] As a result, they are prone to fluid retention and susceptible to fluid changes and in particular, have reduced tolerance to rapid changes in circulating blood volume. For these reasons, fluid management is complex in all children with severe acute malnutrition.

Fluid therapy in SAM and shock

Shock results from an acute failure of circulatory function causing inadequate amounts of nutrients, especially oxygen, delivered to body tissues and inadequate removal of tissue waste products. Inadequate tissue perfusion resulting in impaired cellular respiration (i.e. shock) may result from defects of the pump (cardiogenic), loss of fluid (hypovolemic), abnormalities of vessels (distributive), flow restriction (obstructive) or inadequate oxygen-releasing capacity of blood (dissociative). Advanced Pediatric Life Support (APLS) Guidelines provide lists of clinical signs that, if present, indicate that a child is in "shock". However, these guidelines do not indicate how many signs must be present in order for shock to be diagnosed. The clinical definition of shock used by WHO, which can be used in resource-limited settings, is the presence of three clinical signs at one time, i.e. cold extremities with capillary refill time >3 seconds and a weak and fast pulse. The presence of one or two of these signs indicates nonspecific circulatory impairment that could be due to conditions other than circulatory shock. WHO refers only to "shock" with no other sub-classifications. If a child has only one or two of the three signs, the diagnosis is only circulatory impairment, whereas if all three signs are present the child is in "shock".[10]

Shock in children with severe malnutrition is often difficult to assess and manage. The management of shock in children with severe malnutrition remains very controversial due to lack of strong scientific evidence.[10] As previously described, children with severe malnutrition should be managed with different type and rate of fluid administration and need close monitoring. Sometimes children with severe malnutrition have circulatory signs suggesting shock, but have septic shock rather than hypovolemia. In children with SAM it is preferable to administer fluids orally or through nasogastric tube. Only if the child is lethargic or unconscious and cannot swallow or tolerate an NG tube (e.g. vomiting), use of IV fluids 0.45% normal saline (N/2) with 5% glucose or Ringer's lactate with 5% glucose at 15 ml/kg in 1 hour is recommended.[11] One randomized controlled trial conducted in Kenya which compared the efficacy of Ringer's lactate isotonic fluid (RL), half-strength Darrow's in 5% dextrose (HSD/5D) and4.5% human albumin solution (HAS) in SAM children with shock was prematurely terminated due to the high mortality and inadequate correction of shock in all study arms.[11]

All SAM children who are on IV fluids need close monitoring by checking the pulse and respiratory rate every 5-10 minutes. The intravenous infusion should be stopped if there are signs of overhydration (increase in pulse by 15/minute, respiratory rate by 5/minute). If the child shows signs of improvement and able to take orally then switch to oral or nasogastric rehydration. If the child fails to improve after the first 15 ml/Kg IV it has to be assumed that the child has septic shock unless there is profuse diarrhoea and/or vomiting to explain no improvement. Fluid therapy algorithm for shock in a SAM child is summarized in Fig.1.

Fluid therapy in diarrhea with dehydration

Misdiagnosis and inappropriate treatment for dehydration is the commonest cause of death in a malnourished child. Most of the clinical signs used for assessment of dehydration are unreliable in severely acute malnourished children. Assessment of hydration status is difficult because many of the normally used signs are unreliable. Skin turgor appears poor in children with marasmus owing to the absence of subcutaneous fat; their eyes may also appear sunken. Loss of skin turgor may be masked by edemain children with kwashiorkor. In both types of malnutrition, the child's irritability or apathy make assessment of the mental state difficult. Signs that remain useful for assessing hydration status include: eagerness to drink (a sign of some dehydration), lethargy, cold and clammy extremities, weak or absent radial pulse and reduced or absent urine flow (signs of severe dehydration). Thus, the management of diarrhoea and dehydration in SAM is much more uncertain and difficult than in normal children. Incorrect and over-diagnosis is very common and treatment is often given inappropriately. In children with severe malnutrition it is also often impossible to distinguish reliably between some and severe dehydration. The main diagnosis can be assumed from the history of fluid loss due to acute watery diarrhea rather than from the examination.[5,6]

Rehydration in malnourished children - Recommendations

WHO recommended management guideline for diarrhea in children with severe acute malnutrition is slow rehydration over 10-12 hours with close monitoring for signs of fluid overload by monitoring the vital parameters (pulse rate and respiratory rate), the liver size and auscultation

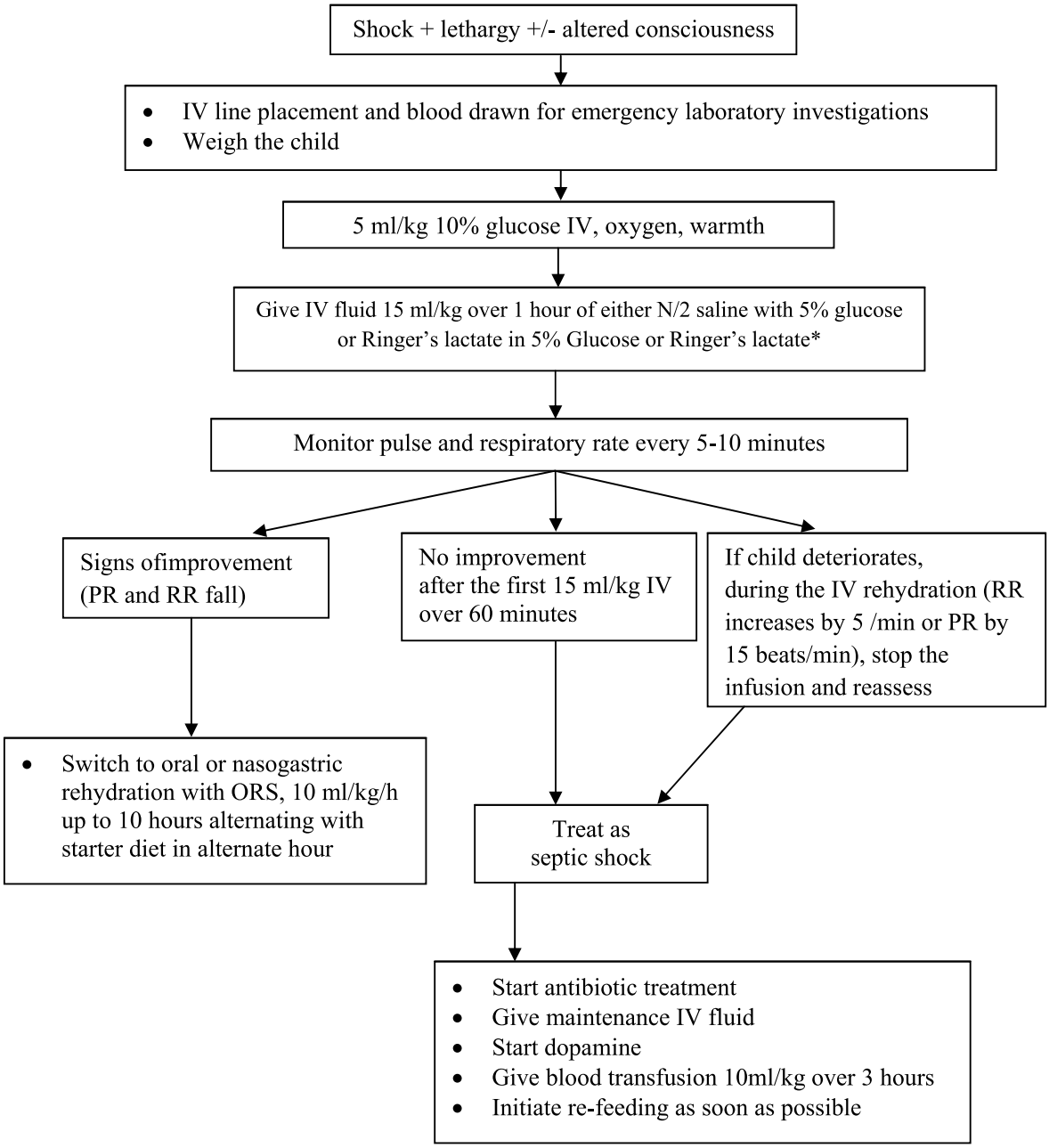

Fig.1.Fluid therapy in a child with severe acute malnutrition and shock

** If profuse diarrhea or suspected cholera, repeat 15 ml/kg of IV fluid*

for chest crepitation. It is recommended to rehydrate the child orally or by nasogastric tube unless the child is in shock or has any other contraindication like intestinal obstruction or paralytic ileus. Since, WHO recommended ORS for SAM children (ReSoMal) is not commercially available in India, low osmolarity ORS may be modified for SAM by dissolving one sachet (1litre) of low osmolarity oral rehydration salt in 2 litre (instead of 1Litre) and adding and dissolving 50g of glucose/sugar and 45 ml of potassium chloride syrup or 30 ml of potassium chloride injection containing 60 mEq of potassium (M-ORS). The amount of ORS to be given is based on the child's weight, that is 5 ml/kg body weight every 30 minutes for the first 2 hours followed by 5-10 ml/kg/hr alternating with F 75 diet for up to 10 hours.[6,7] Weight should be monitored closely in these children and the amount of ORS should be modified as shown in Fig.2. However, if the child has profuse watery diarrhoea or if cholera is suspected, it is recommended to use low osmolarity ORS without any modification for rehydration.[5]

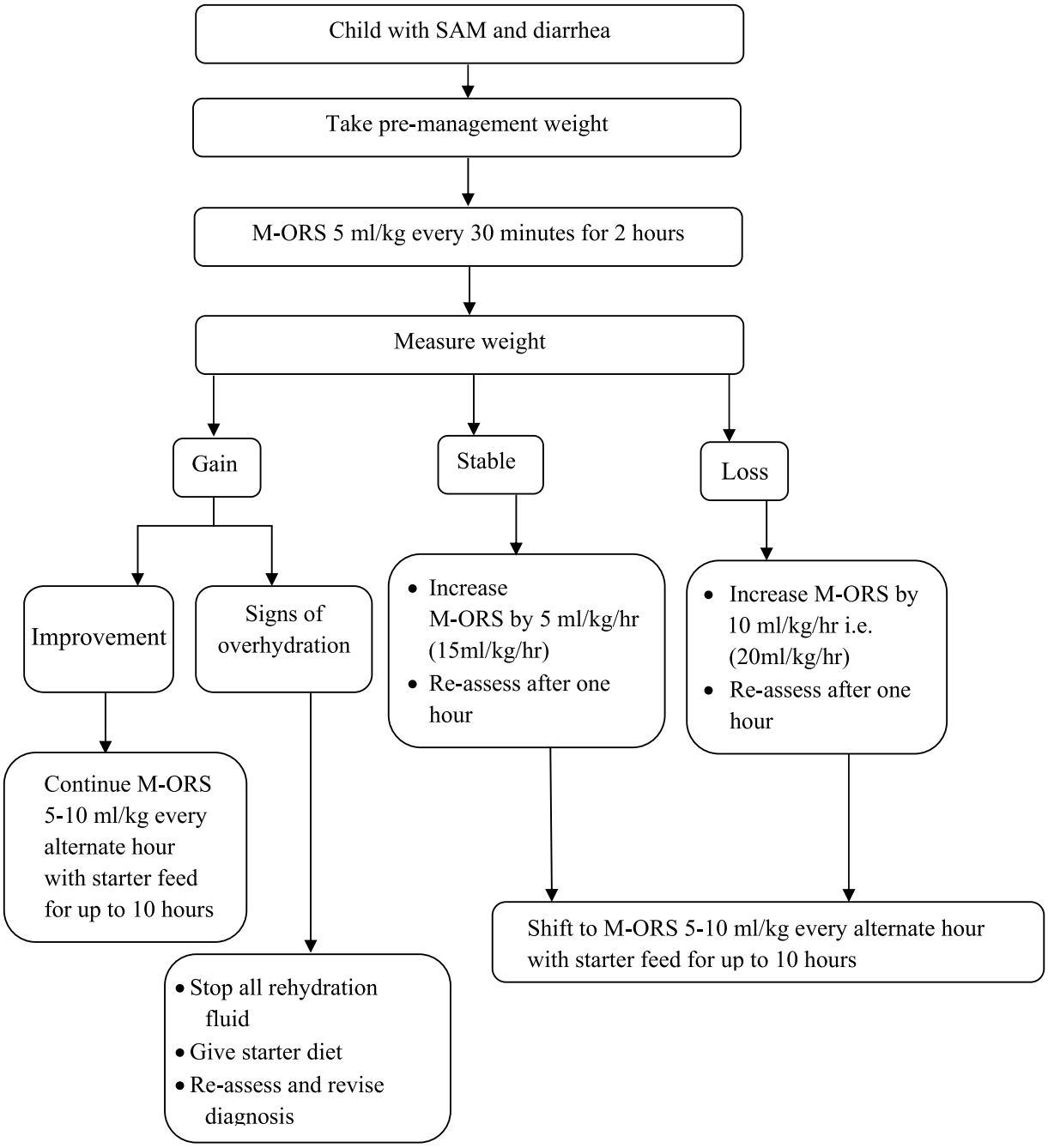

Fig.2. Rehydration algorithm for SAM with diarrhea

Rehydration - Type of fluid

WHO recommends a special oral rehydration solution known as ReSoMal which has lower sodium (45mEq/L) and high potassium (40 mEq/L) as compared to currently available low osmolarity 75mEq/L sodium and 20 mEq/L potassium ORS. However, these recommendations are not based on strong scientific evidence.[5] A systematic review which examined the effectiveness of different interventions like hypo-osmolar ORS (H-ORS), a modified WHO-ORS (ReSoMal), an ORS containing glucose, glucose plus amylase resistant starch (ARS) or rice powder and supplementation with zinc concluded that ReSoMal did not perform better over the standard WHO-ORS in rehydrating these children.[12] Rice-ORS appeared to be more favourable than glucose - ORS in treating children with cholera.[13] A recent study which compared the safety and efficacy of low-osmolarity ORS with modified ReSoMal for treatment of children with SAM and diarrhea reported comparable success rate of rehydration in both the groups. Though the children in modified ReSoMal group achieved early rehydration, a higher proportion (15.4%) developed

hyponatremia as compared to 1.9% on low osmolarity ORS.[14]

Electrolyte imbalances - Management

Normally the body requires energy to maintain appropriate balance of potassium inside the cells and sodium outside the cells. Due to less energy, balance is disturbed leading to excess sodium in their cells. This requires restricted sodium and extra potassium supplementation to make up for loss. Magnesium is also essential for potassium to enter the cells and to be retained. Hence, all children with SAM should also receive magnesium supplementation. WHO recommends potassium supplementation at 3-4 mEq/kg/day for at least 2 weeks. Magnesium sulphate 50%IM once (0.3 mL/kg up to a maximum of 2 ml on day 1) and thereafter 0.2-0.3 ml/kg of same preparation of magnesium orally to be given daily for 2 weeks.[6,7]

New evidence on intravenous fluid (IVF) in SAM

A recent review on use of IVF in malnourished child with diarrhea which included four studies and 883 children, all of which were conducted in low resource settings.[15] It concluded that there was no evidence of fluid overload or other fluid-related adverse events, including children managed on more liberal rehydration protocols and concluded that children with SAM with severe dehydration, managed on WHO protocol continued to be under hydrated. However, the review also included a large percentage (33%) of the patients who had cholera, which probably explains the higher need of fluid and cannot be extrapolated to non-cholera patients. More quality studies with well-defined outcome parameters are needed before practicing more liberal fluid therapy.

Conclusion

Children with severe acute malnutrition have profound disturbances of normal physiology, including electrolyte imbalances and altered fluid distribution. As a result of the reductive adaptive state, they are prone to fluid and sodium retention and in particular, have reduced tolerance to rapid changes in circulating blood volume. For these reasons, fluid management continues to remain complex in all children with severe acute malnutrition. WHO recommends a cautious approach to fluid management, especially if children have diarrhea, with ongoing assessment for signs of over hydration as it is a common cause for high mortality in such children. Strict monitoring of vitals during fluid therapy should always be done.

Points to Remember

- ***Children with severe acute malnutrition are in a state of reductive adaptation with high intracellular sodium and low potassium.***
- ***Misdiagnosis and overestimation of dehydration is common in children with severe acute malnutrition.***
- ***Fluid therapy in children with SAM is challenging due to risk of fluid overload and heart failure.***
- ***Rehydration by oral route or through nasogastric tube is the preferred method.***
- ***IV fluid should be given only to children with shock.***
- ***All children on IV fluid or ORS should be closely monitored for signs of deterioration and overhydration.***

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CLIPPINGS

Pilot Clinical Trial of High-Flow Oxygen Therapy in Children with Asthma in the Emergency Service.

The efficacy of high-flow nasal cannula (HFNC) oxygen therapy and safety in children with asthma and moderate respiratory failure in the emergency department (ED) was undertaken among 62 children as a pilot trial. Patients with a pulmonary score (PS) >6 or oxygen saturation <94% with a face mask despite initial treatment (salbutamol/ipratropium bromide and corticosteroids) were randomized to HFNC or to conventional oxygen therapy. PS had decreased by >2 points in 16 patients in the HFNC group (53%) compared with 9 controls (28%) (*P*=.01). HFNC appears to be superior to conventional oxygen therapy for reducing respiratory distress within the first 2 hours of treatment in children with moderate-to-severe asthma exacerbation refractory to first-line treatment.

Ballestero Y, De Pedro J, Portillo N, Martinez-Mugica O, Arana-Arri E, Benito J. Pilot Clinical Trial of High-Flow Oxygen Therapy in Children with Asthma in the Emergency Service. The Journal of Pediatrics 2018; 194: 204 - 210.e3.

NEWS AND NOTES

4th NATIONAL PEDIATRIC CRITICAL CARE CME & DR MEHTA ENDOWMENT ORATION

Organised by Dr.Mehta Hospital and IAP-CCB

Venue: Hotel Savera, Chennai.

27.04.2018 – PG Quiz on "Pediatric Acute Care"

28.04.2018 – Workshop on "Disease Specific Ventilation"

29.04.2018 – Critical Care CME on "Tropical Infections in Pediatric Acute Care"

Contact

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FLUID AND ELECTROLYTE DISTURBANCE

FLUID MANAGEMENT IN DENGUE

*Priyavarthini Venkatachalapathy
**Suchitra Ranjit

Abstract: *Dengue, an arboviral illness, has the potential to cause significant morbidity and mortality if not recognised and managed appropriately. Treatment is entirely supportive, with fluids being the mainstay of therapy. This seemingly simple intervention can be quite challenging and complex even for the most experienced physician. Most patients can be managed as outpatients with simple oral rehydration measures and by educating the parents regarding warning signs. Those with warning signs and severe dengue need carefully titrated isotonic crystalloids and in some instances, timely use of colloids. Severe bleeding and multi-organ failure is almost always preceded by a period of protracted shock which may have been unrecognised and under-resuscitated. On the other hand, excessive fluid administration may result in fluid overload, massive third space fluid collections and increased mortality. Repeated close clinical monitoring and serial measurement of hematocrit are the key to successful outcomes in children with dengue.*

Keywords: *Dengue, Fluid, Crystalloids, Colloids, Shock, Bleeding, Fluid overload, Monitoring, Hematocrit, Children.*

Dengue infection is a major public health problem causing a broad spectrum of clinical presentation ranging from an undifferentiated febrile illness to shock and multi-organ failure.[1] Though historically dengue is said to be an urban disease, incidence in rural areas is increasingly reported.[2]

As specific antiviral agent is not available, fluid management remains the cornerstone of therapy. No other infectious disease probably warrants as much close monitoring of fluid status as dengue, since both under resuscitation and overzealous resuscitation have potentially disastrous consequences. In this article, we focus on management of fluids in dengue including fluid overload status.

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Pathophysiology

The pathophysiology of severe dengue is attributed to complex and poorly understood immunological cascades, the most important of which is massive T-cell activation and apoptosis. The resultant cytokine storm is responsible for the increased vascular permeability, which is the pathophysiological hallmark of severe dengue infections.[3]

Clinical course and phases of illness

The clinical course of dengue is highly variable and can be divided into three distinct phases- febrile, critical and recovery phase. The febrile phase is non-specific with constitutional symptoms, resembling any other viral illness. The critical phase starts during defervescence, when a variable degree of capillary leak occurs. The degree of capillary leak is highly variable in that it may go completely unnoticed without any overt clinical evidence or can cause profound circulatory compromise.[1] Children who have no/minimal plasma leak improve rapidly once fever subsides, whereas in the severe forms of dengue, hypovolemic shock occurs from loss of plasma volume into the interstitial space. If the hypovolemic shock is prolonged and uncorrected,

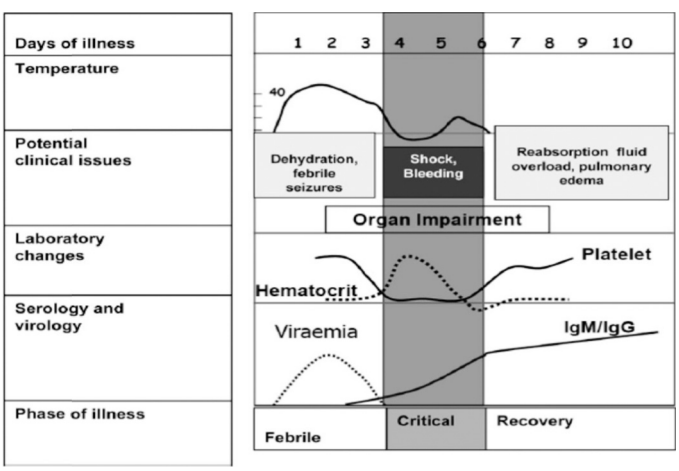


Fig.1. Dengue illness – Course

(Reproduced from Handbook for Clinical Management of Dengue, World Health Organization 2012)

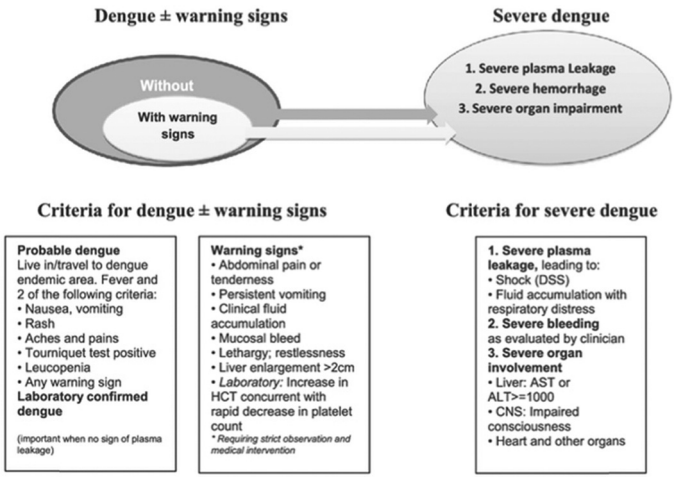


Fig.2. Classification of Dengue cases based on severity

(Reproduced from Handbook for Clinical Management of Dengue, World Health Organization 2012)

severe metabolic acidosis occurs which in turn can set off a vicious cycle of coagulopathy, bleeding, refractory shock and worsening acidosis.[1] Other manifestations during this phase include pleural effusion and ascites, the degree of which depends on the severity of capillary leak and the volume and type of flu ids (both oral and intravenous) given. The recovery phase is characterised by the resorption of fluid from the interstitial spaces. This phase can be complicated by features of fluid overload if not recognised and when fluid resuscitation is continued (Fig.1). Children with dengue cases can be classified into dengue without warning signs, dengue with warning signs and severe dengue (Fig.2).

Fluid management

It is remarkable that a disease of such complexity and potentially high mortality can be managed quite well and mortality decreased to <1% by appropriate fluid management alone, especially in the early phases of the disease.[1] This highlights the crucial role of primary care physician and other health care personnel at the field and front-lines areas, in recognising the disease early and tailoring fluid therapy appropriately.

Management of a child with dengue depends on the phase of the illness, presence or absence of warning signs and if he/she fits into the criteria for severe dengue. Children with no warning signs of dengue, who have normal sensorium and are able to eat and drink fluid can be managed on an outpatient basis with antipyretics and oral fluids. The caregivers must be instructed not only on the type of fluids to be given but also the importance of noting the frequency and quantity of urine output. It should be

Table I. Indications for hospitalisation and PICU care

For hospitalisation	For emergency treatment/ PICU admission
• Presence of warning signs	• Severe plasma leakage
• Inability to take orally	• Major bleeding
• Inability to quantify urine output properly	• Severe organ impairment
• Infants, even if there are no warning signs	
• Other co-morbid conditions like diabetes, renal disease and morbid obesity	
• Social circumstances like poor access to health care facilities,poor understanding or awareness of the disease and inability to monitor the child well at home	

ensured that the patient voids urine at least once in every six hours even at nights and the amount must be measured by using a measuring jar.[4]

It may be useful to teach parents to maintain a chart containing the nature and volume of fluids consumed along with the urine output. They need to be informed about the minimum expected fluid intake (based on normal maintenance fluid requirements), the minimum expected urine output (at least 1ml/kg/hour) in every 4-6 hour time period and when they should report to the care-giver in the event that the intake or output is inadequate. It is also important to teach the type of fluids to be consumed (e.g. tender coconut water, soups, oral rehydration solution) and to avoid drinks with very high sugar content (>5% sugar e.g. commercial drinks and fruit juices) as they can induce osmotic diuresis and spuriously normal/high urine output.[4] The chart can be reviewed by physicians every day during follow up which is mandatory until the child crosses the critical phase of the illness. The indications for hospitalisation and PICU admission is given in Table I.[4]

Management principles in hospitalised patients with dengue

It includes (1) replacement of plasma losses, (2) timely

identification and treatment of hemorrhage and (3) prevention and treatment of fluid overload.

(1) Replacement of fluid losses

In hospitalised children with dengue, obtain baseline hematocrit, blood grouping and cross matching along with other diagnostic investigations during the first point of contact. This can be followed up with serial measurements at given intervals depending on the clinical status to guide fluid therapy and to detect occult bleeding early. A rising hematocrit alone without any other sign of hypoperfusion is not an indication for beginning or increasing fluid therapy. However, these children need repeated clinical assessments looking for worsening in perfusion and clinical status.[1]

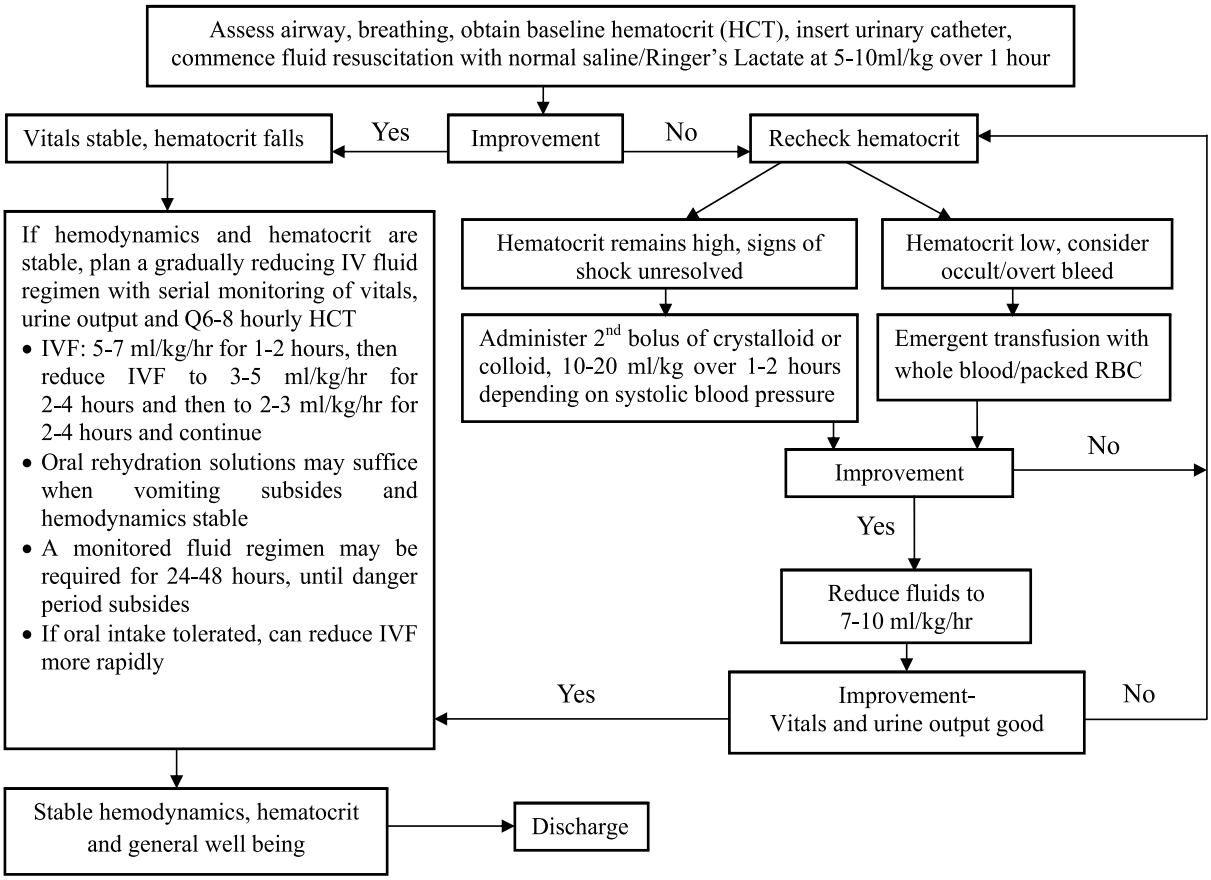
Rehydration with intravenous fluids is the single most important intervention that determines outcome. The goal is to maintain an adequate "effective" circulating volume that is "just enough" to maintain organ perfusion while minimizing fluid overload. The rate of fluid administration depends on the presence or absence of shock and hypotension. Patients with only warning signs do not need fluid boluses but they need titrated fluid therapy to match their ongoing plasma losses. Rapid fluid boluses are indicated if there is hypotension whereas slower boluses over an hour are advocated if blood pressure is maintained. The endpoints for fluid resuscitation are normal blood pressure, urine output of >0.5 to 1 ml/kg/hour, stable hemodynamics, pulse pressure >30 mmHg and steady, gradual decrease in hematocrit. If urine output exceeds 1.5 to 2 ml/kg/hr for even an hour, it's advisable to reduce the fluid rate to prevent fluid overload.[1] For this reason, it may be wiser to have a urinary catheter inserted (with utmost caution to prevent trauma and bleed) early during resuscitation to titrate the amount of fluids. It is important to note that all fluid calculations have to be based on ideal body weight in obese patients.[4] Separate maintenance fluids are not required for most patients unless they are prone for hypoglycemia.[1] All patients need close clinical monitoring for a period of 24 to 48 hours until they show consistent signs towards recovery. Documentation should include clinical status of the child, intake, output, fluid balance and serial hematocrit measurements. Box 1 gives the volume replacement flowchart for the management of dengue children with warning signs.[1] Suggested algorithms for the management of dengue children with compensated shock and hypotensive shock are given in Fig.2 and Fig.3 respectively.[1]

In case of refractory dengue shock, the caregiver must be alert for the presence of certain unrecognised issues that may be perpetuating the hemodynamic abnormalities. These include occult bleeds, coexistent bacterial sepsis, malaria, myocardial dysfunction- both systolic and diastolic, abdominal compartment syndrome (ACS) and uncorrected metabolic abnormalities.[1] These need to be addressed appropriately for reversal of shock. However, in a few patients, especially in late presenters, extensive hypoxic - ischemic injury can cause vasoplegic shock (low systemic vascular resistance and refractory hypotension) with no response to any form of treatment and these patients have a high mortality risk which again emphasizes the importance of early recognition.[1]

Box 1.Volume-replacement flowchart for patients with dengue with "warning signs"

- Assess airway and breathing and obtain baseline hematocrit level
- Commence fluid resuscitation with normal saline/ Ringer's lactate at 5-7 mL/kg over 1-2 hours
- If hemodynamics and hematocrit level are stable, plan a gradually reducing IVF regimen
- Titrate fluids on the basis of vital signs, clinical examination, urine output (aim for 0.5-1 mL/kg/hour), and serial hematocrit level
- IVF - 5-7 mL/kg/hour for 1-2 hours, then reduce to 3-5 mL/kg/hour for 2-4 hours and then to 2-3 mL/kg/ hour for 2-4 hours
- Continue serial close clinical monitoring and every 6-8 hourly hematocrit level
- Oral rehydration solutions may suffice when vomiting subsides and hemodynamics stabilize
- A monitored fluid regimen may be required for 24-48 hours until danger period subsides

Choice of fluids: The choice of resuscitation fluids has been controversial, but evidence is in favour of using non-dextrose containing isotonic crystalloids, such as 0.9% saline or lactated Ringer's solution during the initial phases of resuscitation in patients with warning signs and compensated shock.[1,4-6] Hypotonic solutions such as 0.45% saline and blood products, e.g. platelets and fresh frozen plasma,[7] must also not be used for fluid resuscitation. Large volumes of 0.9% saline can cause hyperchloremic acidosis and it is preferable to use lactated Ringer's solution if the pH, anion gap and chloride levels are suggestive of the above.[4] Hyperchloremic acidosis may confuse the clinical picture in a patient with shock. However, it should be remembered that lactated Ringer's solution may not be ideal in dengue patients with liver failure as lactate metabolism is impaired in these patients.[4]



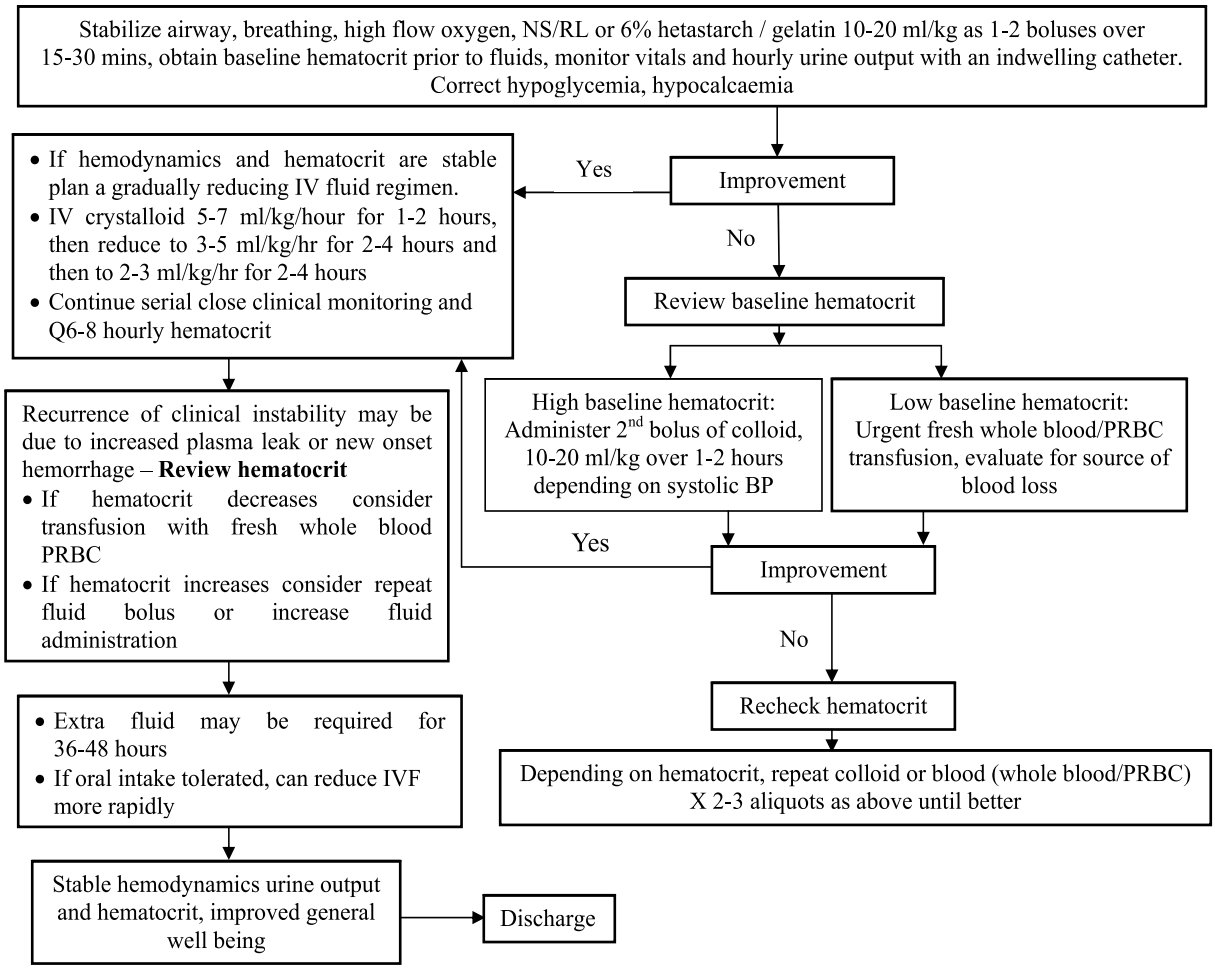
Note: Recurrence of clinical instability may be due to increased plasma leak or new onset hemorrhage: Review hematocrit

Fig.3. Volume-replacement flowchart for patients with severe dengue and compensated shock

Crystalloids are safe, inexpensive and reaction free, but their main drawback is the dilutional effects on coagulation. While colloids are attractive as their osmotic potential can result in lower volume of infused fluids, some have allergic risks and there are reported adverse effects on coagulation and renal function. Three large randomized controlled trials (RCT) concluded that there was no clear advantage of colloids over crystalloids in fluid resuscitation of dengue shock.[5,6,8] However, colloids might be preferable in severe dengue with hypotension, and in those with pulse pressure <10 mm Hg,[5,6,8] repeated shock, high rates of fluid requirement after >20 to 30 ml/kg of crystalloids, and if hematocrit remains persistently elevated with features of shock despite resuscitation with crystalloids.[4]

With regard to the choice among colloids, the RCTs in dengue fluid therapy show no clear-cut superiority of one colloid over the other.[5,6,8-10] These studies have been done using various preparations of gelatin, hydroxyethyl starch and dextran, apart from crystalloids. Amongst colloids, dextran has the largest impact on coagulation, whereas gelatin has the least. But, gelatin has the maximal allergic potential.[4] Considering all the above, the choice of colloid is left to the physician who has to make a reasonable choice based on personal experience, local availability, cost and the side effect profile.

Albumin (5%) can be used when colloids are indicated as a continuous infusion at a dose of 1 g/kg over 6 to 8 hours: in the event 5% solution is unavailable, 20% albumin is co-infused with 0.9% saline or Ringer's lactate via a 3-way tap. The mixing of 20% albumin and the crystalloid occurs beyond the 3- way connection to make it 5% albumin as mixing externally is not advocated due to risks of microbial contamination. Albumin is used due to its excellent oncotic potential and the negligible side effect profile compared to other colloids. The volume of albumin given is subtracted from the total amount of prescribed fluids to prevent excessive fluid administration. However, it has to be remembered that the patient needs to be closely monitored while on albumin infusion since they can develop features of fluid overload and pulmonary edema



Note: The commonest causes of uncorrected shock / recurrence of shock are inadequate replacement of plasma losses and occurent hemorrhage (beware of procedure related bleeds)

Fig.4. Suggested approach to a patient with severe dengue and hypotension

necessitating non-invasive or invasive positive pressure ventilation. This may happen due to the sudden influx of massive amounts of plasma into the pulmonary vasculature. The efficacy of this approach is yet to be determined by prospective studies. Fluid management in the context of dengue with renal failure, liver failure or myocarditis is complex and needs advanced hemodynamic monitoring; these children also need other supportive measures to maintain organ function.

(2) Timely identification and treatment of hemorrhage

Patients with dengue bleed almost always due to uncorrected shock.[1,4] Hence, timely recognition and treatment of shock is the most crucial step in preventing hemorrhage. Once it occurs, the most important determinant of outcome is its early recognition and control. Most often, the bleeds are internal making it difficult for clinicians to pick up, but there are pointers to suspect bleeding (Box 2).[1]

Once bleeding is identified, management consists of fresh whole blood (aliquots of 10 to 20 ml/kg) or fresh packed red blood cells (aliquots of 5 to 10 ml/kg) which restores the circulating volume, oxygen carrying capacity of blood and thus tissue oxygen delivery. Do not wait for the hematocrit to drop down further as the transfusion thresholds are much higher than in other scenarios such as sepsis.[1,4] This can be understood if one recalls the usual temporal sequence of prolonged plasma leak (with elevated hematocrit) followed by hemorrhage onset (with "normal" hematocrit - e.g. a hematocrit of 50% before bleed would have dropped only to H"40% after a bleed).

Control of large volume bleeding is multipronged and includes addressing the source of bleeding with local

Box 2. Pointers to suspect bleeding

- Normal or lower than normal hematocrit than expected for the degree of shock.
- Persistent shock despite 30 to 40 ml/kg of crystalloids/ colloids
- Life threatening hypotension
- Tachycardia rather than normal heart rates/ bradycardia which is normally expected in dengue shock
- Wider pulse pressure than expected for the degree of shock
- Abdominal distension /tenderness
- Leukocytosis rather than leucopenia
- Rising serum lactate and acidosis despite fluid resuscitation
- Worsening organ function

measures (e.g. Nasal packing in cases of profuse nasal bleed) and other supportive measures (e.g. Proton pump inhibitors in cases of gastrointestinal bleed).[4] Tranexemic acid infusion may be considered to inhibit fibrinolysis if there is no hematuria.

Transfusion of other blood components such as plasma and platelets may not be necessary unless bleeding is persistent despite fresh whole blood / packed red blood cells transfusion.[1] There is no role for prophylactic platelet transfusion unless the platelet count is less than 10,000 /cu.mm.[11] There is no role for prophylactic plasma transfusion in a non-bleeding child with or without coagulopathy. Dengue literature cautions against prophylactic platelet or plasma transfusions, since they are not only ineffective in optimising platelet counts or coagulation profile, but can significantly contribute to fluid overload and other transfusion risks including Transfusion Associated Lung Injury (TRALI).[4]

Other measures to prevent bleeding include minimising multiple pricks for blood sampling by obtaining a large bore peripheral IV cannula and heparin locking the cannulae to ensure patency. If any site is pricked but not cannulated, ensure the site is compressed by a dedicated person for atleast 10 minutes or until bleeding stops whichever is later. There have been instances of subcutaneous slow ooze from "forgotten" puncture sites leading to significant swelling of limbs and potential risk of compartment syndrome. The combination of acidosis, coagulopathy and hypothermia are considered the "Lethal triad" and worsen haemorrhage risk and hence correction of acidosis and hypothermia are important.[1] Invasive interventions are minimised unless absolutely necessary. This is applicable even to peripheral venous catheters and oro-gastric tubes (avoid nasogastric tubes, as this may induce trauma and cause torrential bleeding). Invasive procedures such as central venous catheters and arterial lines, if necessary, must be performed by experts with ultrasound guidance whenever possible.

(3) Prevention and treatment of fluid overload

Prevention: Fluid overload is the third major aspect in the management of dengue. Fluid resuscitation and maintenance therapy in dengue should be carefully planned and executed to prevent / minimize fluid overload (FO) since this is associated with longer hospital stay, invasive interventions, increased morbidity and mortality. The most common reasons for FO include over-enthusiastic administration of fluids in the febrile phase, inappropriate fluid resuscitation (volume, nature of fluids) during the critical phase, failure to recognise the transition from critical to recovery phase resulting in continuation of intravenous fluids and prophylactic transfusions of blood products.[1] Apart from these avoidable factors, inevitably, a large proportions of IV fluids used for fluid resuscitation leak from the vasculature, augmenting the extravascular fluid accumulation initiated by the disease process itself. The resultant fluid overload can present as an innocuous mild puffiness of face and generalised edema or can be dramatic causing pulmonary edema, or large volume third space collections such as pleural effusion and ascites. Pulmonary edema, especially, can occur during the recovery phase as the leaked plasma gets resorbed and returns to the vasculature. Ascites, if massive, with or without ischemic edematous gut, can cause abdominal compartment syndrome (ACS)[1,4,12] which is defined as a sustained elevation in intra-abdominal pressure (IAP) of greater than 10 mmHg associated with new or worsening organ dysfunction that can be attributed to elevated IAP.[13]

Treatment of fluid overload: Despite assiduous efforts to minimize FO, it can still occur and needs to be treated appropriately. Fluid removal can be achieved by diuretics and, if needed, by placement of abdominal drain (peritoneal dialysis catheter) or chest drain in cases of massive ascites and pleural effusions respectively.[1] Commonly used diuretics include furosemide boluses (0.5 to 1 mg/kg) and infusions (titrate infusion at doses of 0.2-0.5 mg/kg/hr, upto 1mg/kg/hr for very brief periods), with careful monitoring of perfusion and addition of potassium sparing diuretics such as spironolactone to ameliorate potassium losses induced by furosemide. However, the timing of administration of diuretics is extremely crucial; it has to be ensured that the

critical phase is no longer present, based on clinical and laboratory parameters. It is important to watch for worsening hemodynamics and if it occurs, diuretics should be discontinued and if necessary, a brief fluid bolus administered.[1] Electrolyte imbalances should be addressed appropriately. Patients with acute kidney injury may need renal replacement therapy for fluid removal.

Respiratory distress due to pulmonary edema and/or pleural effusion may warrant High Flow Nasal Cannula (HFNC) oxygen therapy or other noninvasive or invasive ventilatory support. Placement of chest drain and abdominal drain needs to be done with caution under ultrasonogram guidance and controlled fluid drainage should be carried out to prevent bleeding.[1] ACS may be treated with diuretics, abdominal drain placement and drainage of ascites and in rare instances by laparotomy and leaving the abdomen open.[13]

Electrolyte abnormalities: Electrolyte and acid- base abnormalities are common in patients with dengue as is the case with any critically illness. Asymptomatic hyponatremia is frequently seen, both due to sodium losses in the leaked plasma and possibly due to losses via the gastrointestinal tract which often gets corrected with resuscitation fluids.[4] Other metabolic abnormalities that may be encountered are hypokalemia (due to gastrointestinal losses, diuretic usage), hyperkalemia (due to acute kidney injury), hypocalcemia (due to blood products transfusion, diuretics usage), metabolic acidosis (due to hypoxia, ischemia) and hypoglycemia (due to poor oral intake, liver failure). Principles of management of these abnormalities are the same as in any other sick child. Uncorrected metabolic derangements can perpetuate shock and coagulopathy in dengue and they need to be addressed aggressively.[1,4] Prompt treatment is also warranted if there is coexistent renal failure, liver failure, myocarditis and encephalopathy.

Conclusion

Fluid management in dengue is a dynamic challenging process which involves meticulous repeated clinical assessments and precise decision making to optimise hemodynamics, prevent and recognise bleeding and to mitigate fluid overload. The key to excellent outcome is timely recognition of the need for IV fluids and prescribing them appropriately. The clinician should be careful not to be deceived by the alertness of the child in early stages of hypovolemia.

Points to Remember

- ***Spectrum of clinical presentation of dengue vary from asymptomatic infection to refractory shock, bleeding and multi-organ failure.***
- ***The cornerstone of management in hospitalised dengue patients is carefully titrated isotonic, non-dextrose containing crystalloid fluid administration based on perfusion status, blood pressure, serial hematocrit measurements and most importantly urine output.***
- ***Timely recognition and treatment of shock is the most important factor in prevention of hemorrhagic manifestations.***
- ***Suspect occult bleed in a child with persistent shock even with "normal" hematocrit and in a bleeding child, transfusion of fresh whole blood or fresh packed red blood cells may be needed early to optimise oxygen delivery.***
- ***The role of platelets and plasma infusions are very limited in a child with dengue unless he/she is bleeding.***
- ***Correction of acidosis, hypothermia and electrolyte abnormalities are as important as control of the source of bleed in a bleeding child.***
- ***Fluid overload is most often a preventable complication by rationale fluid and blood products infusion and may be treated with diuretics, non invasive or invasive positive pressure ventilation and drainage of third space collections.***
- ***Colloids may have added benefits due to their higher oncotic potential in severe dengue with refractory shock.***

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CLIPPINGS

Management and outcome of neonatal hypoglycemia.

Study analysis of data from a randomized trial of neonates (gestational age 35 to 42 weeks) at risk for hypoglycemia in the first 48 hours after birth, administration of buccal dextrose gel was associated with a greater increase in blood glucose level than placebo gel in hypoglycemic infants who were breast-fed, formula-fed, or fed expressed breast milk. Breast-fed infants were less likely to have recurrent episodes of hypoglycemia. For asymptomatic infants with hypoglycemia, buccal administration of dextrose gel 200 mg/kg followed by breast-feeding is a reasonable intervention.

Rozance PJ. Management and outcome of neonatal hypoglycaemia. Downloaded from https://www.uptodate.com/contents/management-and-outcome-of-neonatal-hypoglycemia, accessed on 3.3.2018.

NEWS AND NOTES

43rd ANNUAL CONFERENCE OF IAP – TNSC

and

32nd SOUTH ZONE CONFERENCE

Date: 9th – 12th AUGUST, 2018

Venue: Sangam Hotels, Tiruchirappalli, Tamil Nadu.

Conference Secretariat

Dr.K.Senthilkumar MD DM,

Organizing Secretary

Website: www.trypedicon2018.com

DRUG PROFILE

INTRANASAL STEROID USE IN CHILDEN

***Jeeson C Unni**
****Ranjit Baby Joseph**

Abstract: *Intranasal steroids are a group of topically acting agents that are used in various upper respiratory disease conditions with a background of respiratory allergy. Currently they are recommended as the first line agents in nasal allergy with minimal side effects. A review on the current management strategies of nasal allergy and available agents is discussed in this article.*

Keywords: *Intranasal steroids, Allergic rhinitis, Adenoid hypertrophy, Rhinosinusitis, Nasal polyp*

Intranasal steroids are widely used by pediatricians, allergy specialists and ENT surgeons for various indications. Their earliest use has been documented since 1974 and traditionally reserved for patients with severe allergic symptoms. They are found to be very potent and effective in various clinical conditions and the commonly established indications in children include allergic rhinitis, rhinosinusitis, adenoidal hypertrophy and in the treatment of nasal polyps.

There are currently seven corticosteroids available in an intranasal dosage form. These include budesonide, beclomethasone dipropionate, ciclesonide, flunisolide, fluticasone furoate and fluticasone propionate, mometasone furoate and triamcinolone acetonide. Of these ciclesonide nasal spray is not approved by British National Formulary (BNF) for the use in children.

Mechanism of action

Intranasal steroids act through various mechanisms of which, the anti-inflammatory action is the most predominant.[1] They cause profound suppressive effect on the allergic inflammatory cascade, reduce eosinophil infiltration and suppress cytokines, thus dramatically reducing the infiltration of inflammatory cells into the nasal mucosa. They also reduce the release of histamine and leukotrienes, though this may be due to a reduction in the overall number of inflammatory cells in the epithelium with fluticasone > mometasone > budesonide > beclomethasone = triamcinolone in terms of their effect. Another proposed mechanism of action is through their immunomodulatory effect. Mometasone and fluticasone have also shown the greatest inhibition of interleukins (IL4 and IL5) in T cell samples taken from healthy donors.[2] Budesonide, beclomethasone and triamcinolone also inhibit IL4 and IL5, but require higher concentrations of drug to do so. Efficacy of these agents also depends on the degree of lipophilicity (Mometasone> fluticasone > beclomethasone > budesonide > triamcinolone >flunisolide).[3] The systemic bioavailability of these drugs is as follows: mometasone furoate <1%, fluticasone propionate <1%, triamcinolone acetonide 46% and beclomethasone dipropionate 44%.[4] Hence, mometasone and fluticasone are preferred for chronic therapy in children.

Technique of delivering into the nostrils

The lining of the nose is very vascular and so the intranasal route offers an alternative to an injection to achieve a systemic effect. Some children might not like having a liquid medication squirted into the nose. Though the aim is to deliver the dose throughout the lining of the nasal cavity, including the lateral wall, in practice, less than half the dose reaches the ciliated lining of the nasal cavity. Most is lost to the anterior part of the nose and nasopharynx.[5,6] Current evidence suggests that the best spray technique involves tilting the head forward and spray with correct axis of insertion which means directing the nozzle slightly away from the midline to avoid contact with the septum.[5,7,8,9] Although evidence is limited, avoiding the septum might reduce the risk of nosebleed and may also result in a higher concentration on the areas likely to be most inflammed, because the concentration of ciliated cells is higher in the lateral nasal wall.[5] There is conflicting evidence on whether breathing in while spraying improves distribution of spray or not. Vigorously inhaling whilst spraying has no significant effect.[6] Where saline irrigation is used as an adjunctive treatment, it should be used before spraying.[10]

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Table I. Relative effectiveness of drugs for specific symptoms of allergic rhinitis

Symptom	Treatment
Ocular	LTRA+++ Oral antihistamines ++ Intranasal corticosteroids ++
Sneezing	**Intranasal corticosteroids +++** Oral antihistamines ++ Nasal antihistamines ++ Intranasal mast cell stabilizers +
Rhinorrhea (nasal discharge)	**Intranasal corticosteroids +++** Nasal antihistamines ++ + Intranasal mast cell stabilizers + Topical anticholinergics ++ Oral antihistamines ++
Congestion (nasal blockage)	**Intranasal corticosteroids +++** Intranasal decongestants ++++ Oral antihistamines + Nasal antihistamines + Oral decongestants + Intranasal mast cell stabilizers +
Itching	**Intranasal corticosteroids +++** LTRA+++ Oral antihistamines ++ Nasal antihistamines ++ Intranasal mast cell stabilizers +

Indications of intranasal steroids

Allergic rhinitis

Intranasal steroids remain the first line treatment for seasonal and perennial allergic rhinitis with very few side effects and dramatic relief in most patients. Onset of action is usually within 30 minutes. It can be given at any time of the day and not necessarily at night. There is no evidence that one drug is superior to another in the management of allergic rhinitis (Table I).[11,12] American College of Allergy, Asthma, and Immunology recommends intranasal steroids as the most effective therapy in controlling the symptoms of allergic rhinitis.[13] Children with severe and troublesome allergic rhinitis often need long-term treatment to sufficiently control their symptoms because of the chronic nature of the illness. Thus, adherence to therapy is critical to the effective management.

Airway Diseases Education and Expertise (ADEX) in pediatrics – Recommendations[14]: Second generation antihistamines are preferred for use in children. All the agents are effective but fexofenadine or levocetrizine are preferred as it cross blood brain barrier only minimally and are non-sedating. Intranasal antihistamines are not recommended in children because of the bitter taste and can cause mild somnolence. Oral decongestants are also not recommended in children, due to their systemic side effects like irritability, dizziness, headache, tremor, insomnia, tachycardia and hypertension. Intranasal decongestants are not recommended in children. Prolonged use (beyond 10 days) can cause rhinitis medicamentosa. Intranasal anticholinergic agent (Ipatropium bromide) is not routinely recommended.

Inhaled nasal steroids (INS) are the controller medications of choice. All INS are equally efficacious when used in equipotent doses and an INS/ICS with low systemic bioavailability like mometasone or fluticasone furoate at a minimum dose required to achieve symptom control should be chosen. Adverse effects of INS are negligible (Minor nasal bleed, throat discomfort), and arise mainly due to faulty technique. Technique of INS should be evaluated during each visit and most of the clinical benefit from INS/ICS is obtained at low to moderate doses. When prescribing inhaled steroids for rhinitis and asthma together, the total dose of steroid should not exceed the recommended levels. Montelukast monotherapy is inferior to INS.

Montelukast add on therapy (Montelukast + INS) for allergic rhinitis: This combination has been found efficacious in controlling total symptom score, especially night time symptoms. It does not cause psychomotor impairment as observed with cetirizine.[15]

Adenoidal hypertrophy

Intranasal steroids are useful in less severe cases. 5 out of 6 RCTs suggests that INS may significantly improve symptoms of nasal obstruction and that this may be associated with the reduction of adenoid size.[16] Evidence of long term efficacy is however limited. To have persistent symptom relief, long term maintenance therapy is needed. Further studies are required to support the use of nasal steroids as first line therapy. Although it is not yet very clear which mechanism reduce the nasal airway obstruction, the anti-inflammatory effect of steroids may reduce adenoidal and nasopharyngeal inflammation.[17]

Nasal polyp

Incidence of nasal polyps in children is 0.2-1%, whereas it can be as high as 39% in children with cystic fibrosis.[18] It is not yet clear why polyps develop preferentially in subtypes of inflammatory diseases.[19] Polyps contain degranulated mast cells infiltrated with eosinophils and high

Table II. Dosage of INS

Drugs	Dosage
Fluticasone furoate	2-12 years: 1 spray per nostril once daily (55μg), may go upto 2 sprays per nostril once daily (110μg); >12years: 2 sprays per nostril once daily
Fluticasone propionate	4-12 years: 1 spray per nostril once daily (50μg); >12years: 1-2 sprays per nostril once daily (100μg)
Mometasone furoate	2-12 years: 1 spray per nostril once daily (50μg); >12years: 2 sprays per nostril once daily (100μg)
Budesonide	Starting dose: 64μg (1 spray per nostril) once daily. Maximum dose: 128μg (2 sprays per nostril) once daily
Beclomethasone dipropionate	In children > 6years 1-2 spray in each nostril twice daily (100μg)
Triamcinolone acetonide	2-5years: 1 spray per nostril once daily (55μg); 6-11years: 1-2 sprays per nostril once daily (55μg-110μg); >12years: 2 sprays per nostril once daily (110μg)
Flunisolide	6-14years: 1 spray per nostril upto 3 times a day or 2 spray per nostril 2 times a day, not to exceed 4 sprays/day in each nostril; >14years: 2 sprays per nostril 2 times a day or may be increased to 3 times a day, maximum dose: 8 sprays/day in each nostril (400 μg/day)
Ciclesonide	2-12 years: 1-2 sprays in each nostril once daily; >12years: 2 sprays in each nostril once daily (200μg)

concentration of histamine, due to release of proinflammatory cytokines (especially interleukin-5). INS reduce rhinitis symptoms, improve nasal breathing, sense of smell, daytime cough and reduce size of polyps.[20] They are ineffective in preventing recurrences.[21] The risk of epistaxis is increased (high quality evidence).[22]

Rhinosinusitis

Studies suggest that INS are effective in management of both acute and chronic rhinosinusitis. Treatment guidelines for acute rhinosinusitis recommend the use of intranasal corticosteroids as monotherapy or adjunctive therapy.[23,24] They can be safely administered in patients without concern for systemic adverse effects.[23] It reduces the recurrence rate, decreases use of related drugs and consultations.[24] Clinicians should weigh the modest but clinically important benefits against possible minor adverse events when prescribing therapy in acute sinusitis.[25]

Dose and side effects of INS

The dosage of various INS is given in Table II. Majority of the side effects are due to the improper technique of administration. These include burning and irritation of nasal mucosa, epistaxis, head ache and light headedness. There are reports of candida infection secondary to the chronic use. Theoretically growth retardation can occur secondary to suppression of hypothalamo pituitary (HP) axis. Cataract and glaucoma are also being noted in some children. All of the above mentioned side effects are more frequent with the older agents, but several of those products have been reformulated as aqueous (AQ) preparations to reduce adverse effects. FDA recommends that all INS should carry a warning regarding the risk of growth suppression. It appears prudent to select those INS agents with minimal systemic availability to reduce the risk of growth impairment. It is also necessary to assess growth at regular intervals during treatment.

Points to Remember

- ***Intranasal steroids are the drug of choice in allergic rhinitis.***
- ***Other indications are recurrent rhinosinusitis, adenoidal hypertrophy and nasal polyps.***
- ***Systemic side effects are minimal.***
- ***Preferred drugs in children are fluticasone and mometasone.***
- ***Evidence of long-term efficacy is limited but suggests that in many children maintenance therapy is needed if symptom-relief is to persist.***

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NEWS AND NOTES

SANGAM PEDICON 2018

(Organised by IAP-MADURAI Branch)

Venue: **Hotel KODAI INTERNATIONAL, Kodaikanal**

Date: 23rd & 24th June, 2018

Contact: Dr.J.Balasubramanian (9894853726), Dr.D.Rajkumar (9789427529)

ENT

NEWBORN HEARING SCREENING - ASSESSMENT AND INTERVENTION

***Abraham K Paul**
****Vivin Abraham**
*****Rohin Abraham**

Abstract: *Congenital hearing loss is one of the most common birth defects. The incidence (1-2 cases per 200 infants) is considerably higher in infants in neonatal intensive care units. It is an established fact that detection and intervention within the first six months of life is crucial for and often associated with favourable developmental outcomes. The identification and remediation of all newborns with hearing loss before 6 months of age has now become an attainable realistic goal in almost all the developed countries. Considering the constraints in a developing country like ours, a two tier, centralized newborn hearing screening program is successfully implemented in Ernakulam District, Kerala. It is the practicability of this program that makes it relevant for replication in other cities of our country, making it a model screening program for any developing country.*

Keywords: *Disability, Hearing loss, Universal newborn hearing screening.*

Congenital hearing loss is one of the most common birth defect, with an incidence of 1 to 3 in 1000 live births.[1] This rate is comparable to that of all the metabolic disorders for which newborn screening is employed. In NICU graduates, the incidence is 1-2 per 200 infants.[2] Of all sensory disabilities in early childhood, permanent hearing impairment that originates from birth or in the neonatal period is of special interest because of its adverse consequences on speech, language, cognitive and psychosocial development and the subsequent impact on educational and vocational attainment. It is an established fact that detection and intervention within the first six months of life is crucial for and often associated with favorable developmental out comes.[3] The American Academy of Pediatrics (AAP) supports the statement of the Joint committee on Infant Hearing (1994), which endorses the goal of universal detection of hearing loss in infants before 3 months of age, with appropriate intervention no later than 6 months of age.[4] Universal detection of infant hearing loss requires universal screening of all infants. Screening by high risk registry alone (e.g. Family history of deafness) can only identify 50% of newborns with significant congenital hearing loss.[5,6] Reliance on physician observation and / or parental recognition has not been successful in the past in detecting significant hearing loss in the first year of life.

Principles and guidelines for Early Hearing Detection and Intervention (EHDI)

The goal of EHDI (Box 1) is to maximize linguistic competence and literacy development for children who are deaf or hard of hearing.[7]

The acceptable methodologies for physiologic screening include otoacoustic emissions (OAE) and auditory brainstem response (ABR), either alone or in combination. Both methodologies are noninvasive, quick (<5 minutes) and easy to perform, although each assess hearing differently. OAE measure sound waves generated by the

Box 1. Goals of EHDI

- All infants should be screened for hearing loss using a physiologic measure at no later than 1 month of age.
- All infants who do not pass the initial hearing screening and the subsequent rescreening should have appropriate audiological and medical evaluations to confirm the presence of hearing loss at no later than 3 months of age.
- All infants with confirmed hearing loss should receive early intervention services as soon as possible after diagnosis but not later than 6 months of age.

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inner ear (cochlea) in response to clicks and recorded via miniature microphones placed in the external ear canals of the infant. Although OAE screening is even quicker and easier to perform than ABR, OAE may be affected by debris or fluid in the external and middle ear, resulting in referral rates of 5% to 20% when screening is performed during the first 24 hours after birth. ABR measures the electroencephalographic waves generated in response to clicks via three electrodes pasted to the infant's scalp. ABR screening requires the infant to be in a quiet state, but it is not affected by middle or external ear debris. Referral rates <3% may be achieved when screening is performed during first 24-48 hours after birth.[7] Referral rates <4% are generally achievable with OAE combined with ABR in a two step screening system or with ABR alone.[8,9,10] "Auditory neuropathy / auditory dyssynchrony" are neural conduction disorders typically occurring in infants requiring NICU care and may not be detected by OAE testing. So, all NICU babies should undergo ABR testing.[11]

All infants, regardless of newborn hearing screening outcome, should receive ongoing monitoring for development of age appropriate auditory behaviours and communication skills. Any infant who demonstrates delayed auditory and / or communication skill development, even if he or she passed new born hearing screening, should receive an audiological evaluation to rule out hearing loss.[7] Certain high risk group for hearing loss is given in Box 2.

Box 2. High risk group for hearing loss

- Family history of hereditary childhood sensory neural hearing loss
- Craniofacial anomalies, including those with morphological abnormalities of the pinna and ear canal
- Birth weight less than 1500 grams
- Hyperbilirubinemia at a serum level requiring exchange transfusion
- Ototoxic medications including but not limited to animoglycosides
- Apgar score 0 to 4 at one minute, or 0 to 6 at five minutes
- Mechanical ventilation lasting 5 days or more
- Stigmata or other findings associated with a syndrome known to include sensorineural and / or conductive hearing loss.

Fig.1a. OAE screener

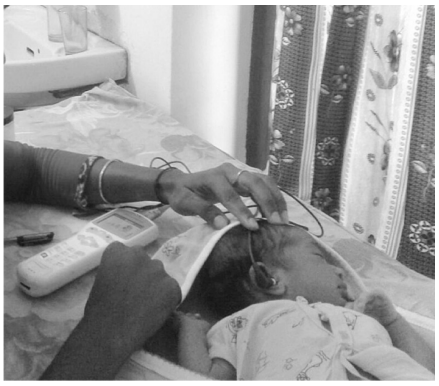

Fig.1b. Baby being screened

Ernakulam district model of newborn hearing screening

The Indian Academy of Pediatrics (IAP) Cochin Branch mooted a centralized screening facility in January 2003 initially for the 32 hospitals in Cochin City and subsequently expanded to the 78 hospitals in Ernakulam District. Screening facility operates out of Child Care Centre, which is the secretariat of IAP Cochin Branch using eight portable screening machines (Otoport Lite OAE screener) (Fig.1a and 1b).[12,13] Personnel with basic knowledge in computer and good communication skills were chosen, given training in hearing screening and also skill to gather information of high risk criteria, if any, from parents / hospital staff / hospital records. The screening personnel visits each hospital daily / alternate days / twice a week / weekly depending upon the number of births in that particular hospital. If OAE is abnormal it is repeated at 6 weeks on the 1st immunization visit. If OAE is again abnormal, ABR is done for confirmation followed by full audiological workup and remediation. All NICU babies undergo ABR testing. If any baby has abnormal ABR, detailed enquiry is made to identify and record any risk factor / factors involved.[14] Any baby missing screening before hospital discharge is called for OAE test on the first immunization visit. The program is co-ordinated by a speech and language pathologist and weekly assessment meeting is convened with the staff by the convenor, through this program. Till now 1,47,634 babies were screened and hearing loss detected in 289 babies (unpublished data).

Assessment and intervention

Every infant with confirmed hearing loss is referred for otologic and other medical evaluation. The purpose of these evaluations is to determine the etiology of hearing

loss, to identify related physical conditions and to provide recommendations for medical / surgical treatment as well as referral for other services. Essential components of medical evaluation include clinical history, family history of childhood onset permanent hearing loss, identification of syndromes associated with early or late onset permanent hearing loss, a physical examination and indicated radiologic and laboratory studies (including genetic testing). Portions of the medical evaluation, such as urine PCR for cytomegalovirus (CMV) infection, a leading cause of hearing loss, might even begin in the birth hospital, particularly for infants who spend time in the NICU.[15]

Pediatrician's role

The infant's pediatrician is responsible for monitoring the general health, development and wellbeing of the infant. In addition, he must assume responsibility to ensure that the audiological assessment is conducted on infants who do not pass screening and must initiate referrals for medical specialty evaluations to determine the etiology of the hearing loss. Because 30% to 40% of children with confirmed hearing loss will demonstrate developmental delays or other disabilities, the pediatrician should closely monitor developmental milestone and initiate referrals related to suspected disabilities.

Audiological habilitation

Most infants and children with bilateral hearing loss and many with unilateral hearing loss benefit from some form of personal amplification device.[16] Majority with mild, moderate and severe hearing loss will benefit with hearing aid fitting. Hearing aid fitting should occur within 1 month of initial confirmation of hearing loss even when additional audiological assessment is ongoing. Delay between confirmation of hearing loss and fitting of an amplification device should be minimized.[17] For infants' who are below a developmental age of 6 months, hearing aid selection will be based on physiologic measures alone. Behavioural threshold assessment with visual reinforcement audiometry should be obtained as soon as possible to crosscheck and augment physiological findings. Complementary or alternate technology, such as frequency modulation (FM) systems or cochlear implants, may be recommended as the primary and/or secondary listening device depending on the degree of the infants hearing loss, the goals of auditory rehabilitation and the infant's acoustic environments.[7]

Cochlear implantation should be given careful consideration for any child who seems to receive limited benefit from a trial with appropriately fitted hearing aid. According to US Food and Drug Administration (FDA) guidelines, infants with profound bilateral hearing loss are candidates for cochlear implantation at 12 months of age.[7] The presence of developmental conditions (e.g. developmental delay, autism) in addition to hearing loss should not, as a rule, preclude the consideration of cochlear implantation for an infant or child who is deaf. Benefit from hearing aids and cochlear implants in children with sensorineural hearing loss have also been documented. A serious complication of cochlear implants is an excessively high incidence of pneumococcal meningitis. All children receiving a cochlear implant must be vaccinated with pneumococcal vaccine. Amplification device fitting should be followed by "intervention services" (habilitative, rehabilitative or educational program) provided by an audiologist who is experienced with these procedures.

Conclusion

Hearing impairment in infants if left undetected, can negatively affect speech and language acquisition, academic achievement, social and emotional development. These negative effects can be reduced or even eliminated through early intervention at or before 6 months of age. Screening only the high risk infants is not enough as 50% of infants born with hearing loss have no known risk factors. Hence Universal Newborn Hearing Screening (UNHS) program is necessary. Considering the constraints in our country, it may not be possible to institute a UNHS strategy in every hospital - hence the concept of a centralized newborn hearing screening model of Ernakulam District covering 78 hospitals is worth replicating. It takes away the financial burden of each hospital investing for the screening equipment. This two tier screening program [the 2nd tier being auditory brainstem response (ABR) which is more expensive] is mandatory only for a selected few, making the program more practical and viable.

Neonatal hearing screening need not detect all cases of congenital hearing loss - it only provides an indication of the baby's hearing at the time of the screening. Mild hearing loss and hearing loss outside the main speech frequencies may not be detected. Hearing impairment may develop after the neonatal period and therefore, it is crucial for the pediatricians to encourage parents to continue to have their child's hearing checked. The pediatricians should maintain a high index of suspicion if there are manifestations of hearing loss such as speech and language delay. Any parental concern regarding a child's hearing should also be thoroughly investigated.

Pediatricians should take a pro-active role in developing newborn hearing screening program and in the initiation of follow-up programs to provide a continuity of care for these

infants; pediatricians should be the team leaders in the multidisciplinary approach to management of hearing impairment. They may also play a role in promoting acceptance of hearing aids, encouraging constant wearing of aids and providing information regarding early intervention services.

Points to Remember

- ***The incidence of hearing loss is 1-3 per 1000 births and 1-2 per 200 infants in NICU.***
- ***All newborns should be screened for hearing loss before discharge from hospital or at the first immunization visit.***
- ***Identification and remediation before 6 months of age is associated with near normal speech and language development.***
- ***The concept of centralized cost effective 2 tier screening protocol successfully implemented in Ernakulam District, Kerala is worth replicating.***

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RADIOLOGY

TORTICOLLIS – 2

*Vijayalakshmi G
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***Raveendran J

Cervical spine abnormalities are sometimes the cause for torticollis. These are due to structural abnormalities of the craniovertebral junction. The craniovertebral junction (CVJ) comprises the occipital condyles which articulate with the lateral masses of first cervical vertebra (C1) which in turn articulate with C2. The whole complex is so perfectly designed for flexion, extension and rotation. Excessive forward or backward translation results in subluxation. If accompanied by rotation torticollis occurs and is then called rotatory fixation. A normal coronal section of CVJ as seen in CT scan is shown in Fig.1. The occipital condyle(O) is seen articulating with the lateral mass of C1 seen as symmetric triangular structures on both sides. In children, the occipital condyles are relatively smaller and

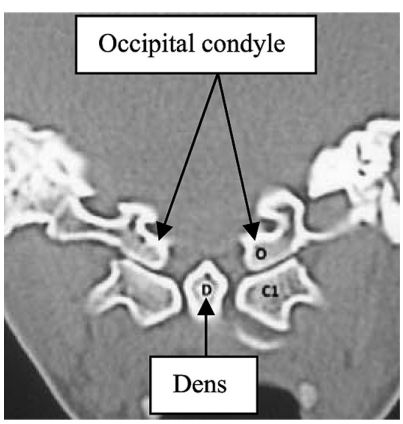

Fig.1. CT(Coronal section) - Normal atlanto-occipital joint.

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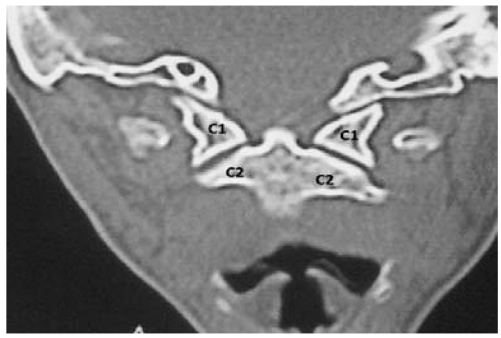

Fig.2. CT - The normal atlanto-axial joint.

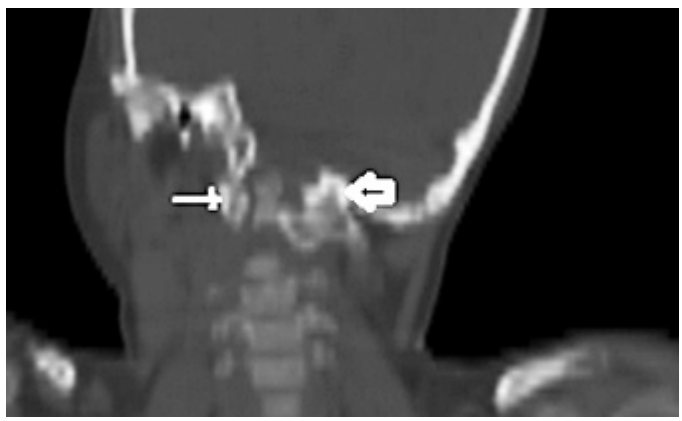

Fig.3. Atlanto-occipital assimilation(arow left)

the occipito-atlantal joints are horizontally oriented potentiating subluxation. The atlas lacks a body and instead articulates with the odontoid process in front and the relatively wide and flat laterally placed articular facets of C2 (Fig.2). The anterior arch of the atlas is not completely ossified till 5 to 8 years but the posterior arch is ossified between 3 and 5 years.

Congenital osseous abnormalities can cause torticollis as is seen in Fig.3. The triangular shaped lateral mass of C1 is seen on the right while it is not seen on the left. Instead, there is a thick occipital condyle incorporating the atlas and articulating with C2. This is occipito-atlantal fusion or occipitalisation of the atlas. The altered biomechanics predisposes to atlanto-axial joint degeneration and subluxation. The Sprengel deformity is another congenital defect where the scapula is elevated (Fig.4) and medially placed as it fails to descend from its fetal position. Cervical vertebral fusion co-exists. Often there is an osseous or

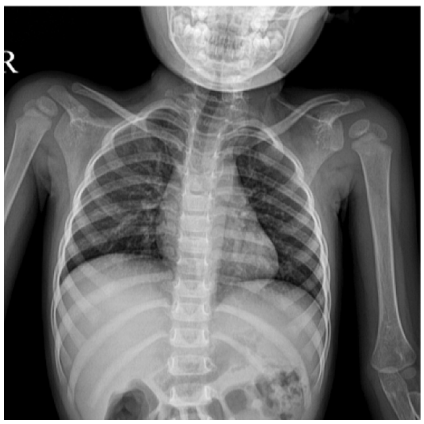

Fig.4. X-ray chest-Sprengel's shoulder. (Left)

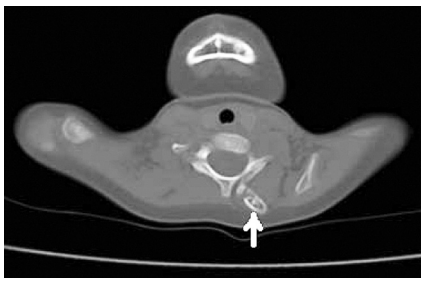

Fig.5. CT - Omovertebral bone (arrow).

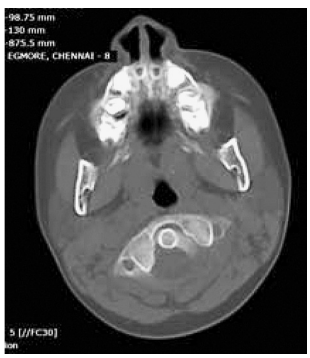

Fig. 6. Type 2 atlanto-axial dislocation.

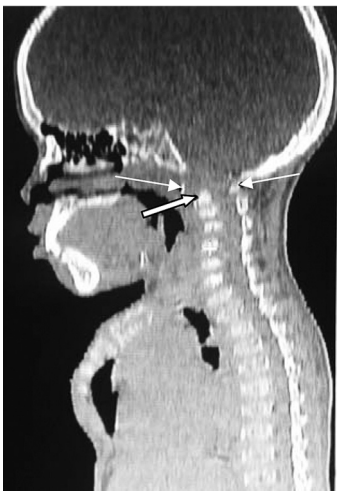

Fig. 7. Type 3 atlanto-axial dislocation. (White arrows- anterior and posterior arches of C1. open arrow- dens) Note the wide interval between C1 and dens.

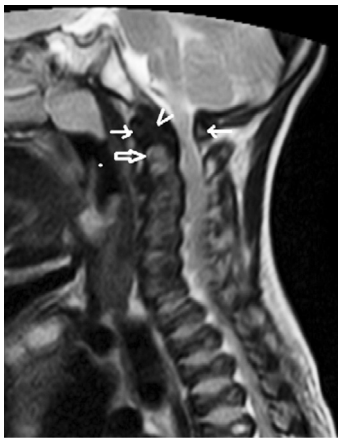

Fig. 8. Cord compression due to C1-C2 dislocation (straight arrows- C1 anterior and posterior arch. Open arrow- base of dens, arrowhead- unossified dens).

fibrous omovertebral bar (Fig.5) that anchors the scapula to one or more cervical vertebrae, C5, C6 or C7.

Two ligaments - cruciate and alar - are responsible for the integrity of the CVJ. The transverse ligament with its superior and inferior crura running to the anterior foramen magnum and body of C2 respectively constitutes the cruciate ligament. The alar ligaments arise from the lateral aspect of the dens and attach to the medial aspect of the occipital condyles inferior to the foramen magnum.

Certain conditions like skeletal dysplasias, Down'syndrome and Klippel- Feil syndrome cause laxity of these ligaments that compromise the CVJ. Laxity coupled with bony abnormalities of cervical vertebrae renders the CVJ more vulnerable to atlanto-axial instability in these patients. Children with Down's syndrome may have hypoplasia of C1 and consequent inadequate anchoring of the dens by the transverse ligament. Os odontoideum may also be present. At birth is separated from the body of the axis by cartilage which ossifies at about the age of 8. Failure of this event and the ensuing weak point causes os odontoideum and forward slipping of C1 over C2. Laxity may also be the result of some old trauma. Blood supply to the dens from the body of the axis is limited by the presence of cartilage and so a fracture through the base of the dens can cause avascular necrosis of the tip and non-union of fracture. Though an irregular lower margin of the os denotes fracture and a rounded smooth margin points to a congenital abnormality, this is difficult to ascertain in practice.

Whether CVJ abnormality is due to bony components or the supporting ligaments, the consequence is subluxation and possible spinal cord compression. The torticollis due to Grisel syndrome is rotatory fixation within the normal range of movement between the atlas and axis. This is type 1. In type 2 there is anterior slipping of the atlas with disarticulation of one lateral mass from the axis (Fig.6). The atlanto-dens interval is 3 to 5mm. Disarticulation or displacement of both lateral masses of atlas from C2 is type 3 and the atlanto-dens interval is 5mm or more (Fig.7). Type 4 is rare where there is posterior displacement of the atlas. Fortunately the cervical canal is naturally quite large so that pain in the neck precedes neurological compression. Fig.8 shows a compressive thinning of the cord with alteration in signal intensity indicating secondary myelomalacic changes.

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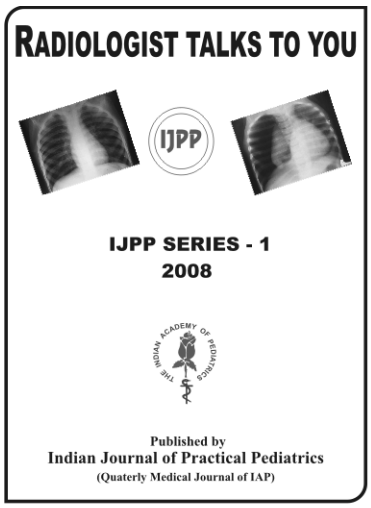

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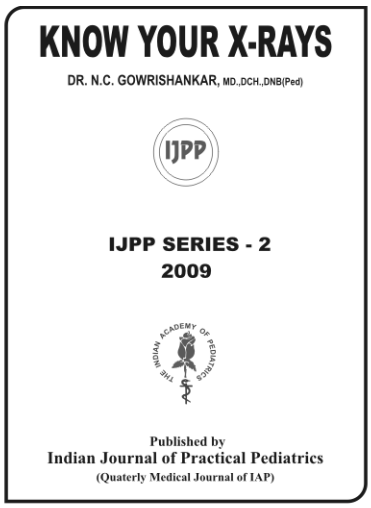

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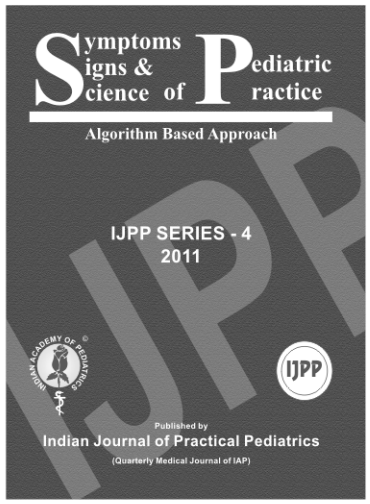

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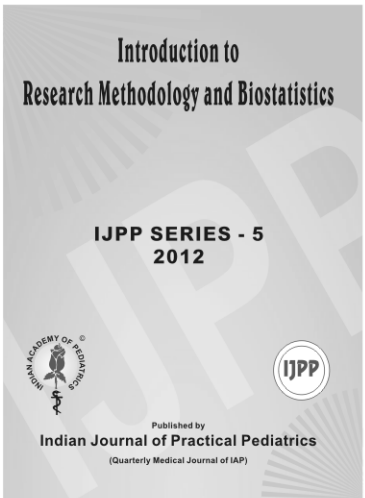

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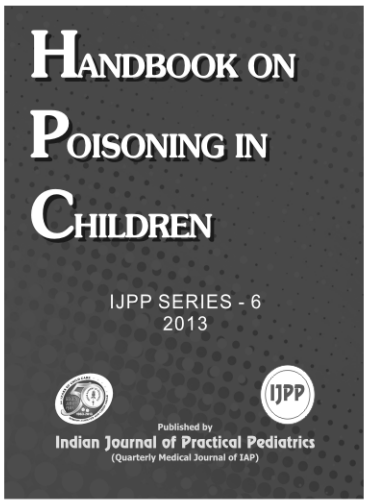

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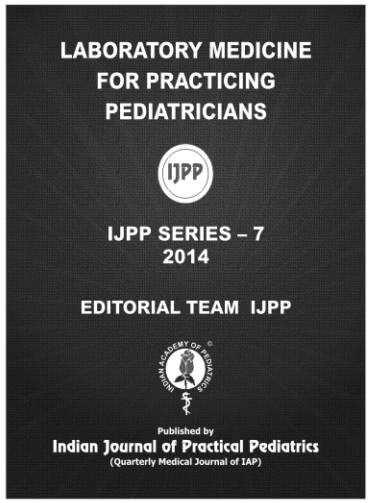

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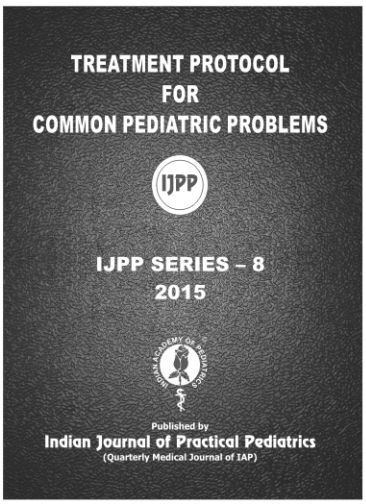

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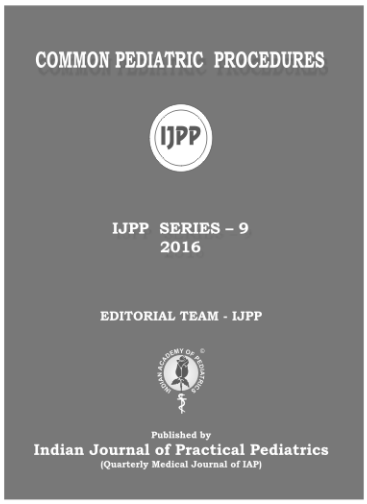

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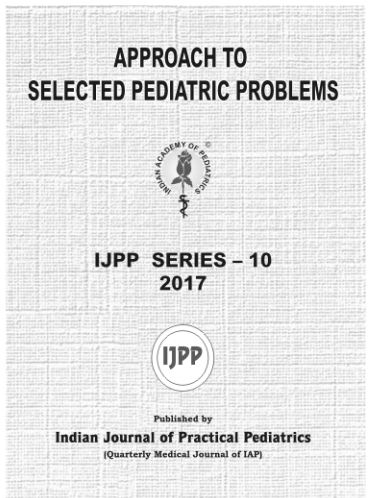

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