ACADEMY OF MEDICINE (COLLEGE OF PAEDIATRICS)

CLINICAL PRACTICE GUIDELINES ON

ACUTE GASTROENTERITIS IN CHILDREN

COMMITTEE ON ACUTE GASTROENTERITIS

Chairman

1. Christopher CM Boey,
Associate Professor ,
Department of Paediatrics,
University of Malaya Medical Centre
Kuala Lumpur

Committee members (listed in alphabetical order)

2. Choo Keng Ee
Professor,
Department of Paediatrics and Child Health
Faculty of Medicine and Health Sciences
Universiti Malaysia Sarawak

3. A Jai Mohan
Consultant Paediatrician & Head
Department of Paediatrics,
Selayang Hospital,
Batu Caves

4. Michael Khor
Consultant Paediatrician,
Island Hospital,
Penang

5. Koh Chong Tuan
Consultant Paediatrician,
Island Hospital,
Penang

6. Lee Eng Lam
Consultant Paediatrician,
Subang Jaya Medical Centre
Selangor

7. Lee Way Seah
Associate Professor ,
Department of Paediatrics,
University of Malaya Medical Centre
Kuala Lumpur

8. Lim Chooi Bee
Consultant Paediatrician,
Institute of Paediatrics
Hospital Kuala Lumpur,
Kuala Lumpur

9. Noorizan Abdul Majid
Lecturer ,
Universiti Sains Malaysia
School of Medical Sciences,
Kelantan

10. Nur Atiqah
Associate Professor ,
Department of Paediatrics
Universiti Putra Malaysia
Selangor

11. Oon Meng Kar
Consultant Paediatrician ,
Klinik Kanak-Kanak Oon,
Cheras Commercial Centre,
Kuala Lumpur

This committee consists of representatives from the universities, government health service and the private sector in Malaysia.

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This document is a guide for the management of acute gastroenteritis in children and is not intended as a sole source of guidance. It is emphasised that standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as knowledge and technology advance and patterns evolve. This document is therefore not intended to replace clinical judgement or to establish a protocol for all patients with this condition. It rarely will provide the only appropriate approach to the problem. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor in the light of the clinical data presented by the child as well as the diagnostic and treatment options available.

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SUMMARY OF RECOMMENDATIONS

Three specific management issues were considered: methods of rehydration, feeding , and the use of drugs .

(i) Oral rehydration therapy is the treatment of choice in children with mild to moderate dehydration secondary to acute gastroenteritis . In severe dehydration, intravenous resuscitation and rehydration should not be delayed.

(ii) Diets appropriate to the child's age should be given as soon as is clinically possible. In general, milk-feeding should not be discontinued. This is all the more true if the infant has been breast-fed. Formula-fed infants should not have their formulas changed without good reason.

(iii) Antiemetic and anti diarrhoeal drugs are NOT recommended

(iv) Antibiotics are generally not recommended unless there are specific indications.

LITERATURE REVIEW

Background

Diarrhoeal diseases continue to be a major cause of morbidity and mortality in children in developing nations. [1, 2] In developed nations , they are an important cause of hospital admission although mortality rates may be lower. [3,4] About 9% of all hospitalisations of children younger than 5 years were reported to be a result of diarrhoea. [5]

In a study conducted at the University of Malaya Medical Centre in 1996, gastroenteritis was found to be the third most common cause of hospital admission, accounting for 6.6% of the total number of hospital admissions that year. [6] Sixty-four percent were mildly dehydrated, 10% moderately dehydrated and 3% severely dehydrated , while the rest were not dehydrated.[6] 45% had positive stool pathogens. [6] Rotavirus was the commonest viral pathogen(29%) while nontyphoidal Salmonella was the commonest bacterial pathogen(10%). [6] In 1980, acquired carbohydrate intolerance and chronic diarrhoea following acute gastroenteritis were noted in 30% and 8% respectively in children under the age of two years in Malaysia . [7] More recent data suggests that the prevalence of both carbohydrate intolerance and chronic diarrhoea is probably less than 5%. [6]

The current management of acute gastroenteritis in Malaysia is still far from ideal. In a review of the management of children before admission to hospital, it was found that 80% of them were prescribed medications, 13% were advised a change of milk formula but only 40% were prescribed glucose-electrolyte mixtures. [8] Although diarrhoea-related deaths had been found to be low (10 out of 4,689 cases) [9], significant morbidity, such as chronic diarrhoea, following acute gastroenteritis remains a problem[10]

Oral Rehydration Therapy

Oral rehydration therapy is now recognised as the treatment of choice of fluid and electrolyte losses caused by diarrhoea in children with mild to moderate dehydration. Research has shown that stool losses of water, sodium, potassium, chloride, and base must be replenished in order to ensure effective rehydration. [11-13] The discovery of coupled transport of sodium and glucose in the 1960s provides the scientific basis for oral rehydration therapy as an alternative to intravenous therapy. [14]

In addition to the obvious advantage of being cheaper and less invasive, a number of studies in recent years have shown the efficacy of oral rehydration therapy when compared with intravenous therapy. The earlier studies were conducted in patients with cholera [15,16] These were followed later by other studies that established the effectiveness of oral rehydration therapy in children with acute diarrhoea from other causes.[17-21]

A variety of oral rehydration solutions are available in Malaysia. The electrolyte concentrations of diarrhoeal stool and some of the available solutions are shown in table 1. Oral rehydration solutions must be distinguished from other popular drinks that have been wrongly used to treat dehydration caused by diarrhoea (Table 1). These drinks have low electrolyte concentrations and are hypertonic due to their high carbohydrate content. [22,23]

Cereal-based solutions containing natural polymers such as starch and simple proteins have been found to be effective in reducing diarrhoeal stool losses. [24,25] At present, cereal- or rice powder-based solutions are not available commercially in Malaysia but early refeeding has been found to give similar benefits .

Table 1 Electrolyte composition of diarrhoeal stool and some oral rehydration preparations

Liquid	Na (mmol/l)	K (mmol/l)	Cl (mmol/l)	Base (HCO3 or citrate) (mmol/l)
Cholera*				
1. Adults	140	13	104	44 -
2. Children (< 5 years)	101	27	92	32
Non-cholera*				
1. Children (< 5 years)	56	25	55	14
Oral rehydration salts**				
1. Ministry of Health preparation	56	20	56	6.7
2. Oralite (Polylab)	55	20	55	20
3. Pedialyte (Ross)	45	20	35	30
4. Infalyte(Mead Johnson)	50	25	45	30
5. Raza ORS Bicarbonate	56	20	56	20
6. DHA oral rehydration salts	90	20	80	10
7. DHA Repalyte	20	10	15	7.7
8. Servipharm Servidrat	90	20	80	30
9. Servipharm Servidrat L. S.	56	20	46	30
Fluids not suitable for oral rehydration **				
1. Cola	2	0	NA	NA
2. Apple juice	3	20	NA	0
3. Chicken broth	250	8	NA	0

* adapted from Readings on Diarrhoea. World Health Organization, Geneva, 1992
** adapted from Snyder J. The continuing evolution of oral therapy for diarrhea. Semin Pediatr Infect Dis. 1994;5:231-235

Early Feeding

Early feeding in conjunction with oral rehydration therapy can reduce stool losses as much as cereal-based solutions [26,27] Studies have shown that feeding not only does not worsen the symptoms of diarrhoea [28,29] but it can also decrease stool output. [30,31] In addition , there is also the advantage of better nutrition with early feeding. [32].

There is ongoing research on the type of food that is most suitable for feeding . No consensus is currently available on this issue , but studies suggest that certain foods such as rice, wheat, potatoes, bread, cereals, lean meats, yogurt, fruits, and vegetables, may be appropriate. [26,27,30,31]

The use of anti-diarrhoeal drugs in acute gastroenteritis

This is generally not recommended. Drugs that alter intestinal motility such as loperamide can have associated side-effects like lethargy, ileus, respiratory depression, and coma. [33-39] Death has also been reported in association with loperamide therapy. [35]. Other anti-diarrhoeal drugs such as opiate analogues or opiate and atropine are also associated with unwanted toxic side-effects.[40-43]

MANAGEMENT GUIDELINES FOR ACUTE GASTROENTERITIS

1. Indications for considering the need to admit to hospital

- Severe illness - hypovolaemic shock, lethargy, drowsiness, high fever
- Clinically detectable moderate to severe dehydration.
- Bloody diarrhoea
- Inability to retain oral feeding, even in the absence of dehydration, e.g. persistent vomiting.
- Uncertainty about the diagnosis or the state of hydration, e.g. obese child , appendicitis
- Failure of treatment, e.g. persistent or worsening diarrhoea.
- Age < 6 months old ; other diagnoses need to be considered e.g. meningitis, septicaemia., urinary tract infection
- Family unable to cope
- Associated concerns, e.g. history of previous severe diarrhoea, malnutrition, ileostomy
- Those children who are unable to come back for follow-up

Diarrhoea refers to an increase in the frequency, fluidity and volume of stool compared to normal. It is important to be aware that breast-fed infants can have motions which are loose and should not be confused with diarrhoeal stools.

2. Assessment of dehydration

The treatment of acute gastroenteritis is directed mainly by the degree of dehydration present If a reliable previous weight is available, percentage weight loss can be determined to provide an objective measure of dehydration . Capillary refill can be used to help determine the degree of dehydration. [44] If a reliable previous weight is not available, the degree of dehydration can be assessed clinically as shown in section 2.1

2.1. Degree of dehydration :

3-5% dehydration (Mild)	:	warm , normal capillary refill in the extremities normal or slightly sunken eyes dry mucous membranes thirst, oliguria. flat anterior fontanelle normal blood pressure, pulse volume, heart rate

6 - 9% dehydration (Moderate)	:	very obvious loss of skin tone and tissue turgor delayed capillary refill dry mucous membrane and sunken eyes marked thirst and oliguria (< 1 ml/kg/h) often some restlessness and apathy sunken fontanelle normal blood pressure but pulse volume may be decreased heart rate increased
10% and more dehydration (Severe)	:	all the foregoing, plus peripheral vaso-constriction (cool, mottled peripheries) thready or absent pulse, tachycardia hypotension, cyanosis, and sometimes hyperpyrexia extremely thirsty or the child may be too ill to ask for fluids anuria, acidotic breathing reduced conscious level or comatose

It is important to note that these signs may not be present in hypernatraemic dehydration. See section 3.3

2.2 Methods of Assessment

The aim is to evaluate the severity of dehydration and the cause.
Relevant aspects include:

History:	Stooling and vomiting frequency, stool consistency, stool volume , the presence of mucus and blood in the stools, urine output, weight change, presence of pyrexia, infectious disease contact.
Clinical Examination:	Vital signs including conscious level, weight change, blood pressure, temperature, pulse rate , respiratory rate; and clinical parameters as in 2.1 above.
Laboratory tests -	Full blood count, Urea and electrolytes (if more than 5% dehydration) Stool microscopy, bacteriology (culture) and viral studies; - urine specific gravity - blood gases in ill children

3. Treatment of dehydration

Oral rehydration therapy is the treatment of choice in children with mild to moderate dehydration secondary to acute gastroenteritis . It can be used effectively in the treatment of hypernatraemic, hyponatraemic and isonatraemic dehydration. Where oral rehydration solution is not immediately available, increased amounts of water should be given orally. In severe dehydration, intravenous resuscitation and rehydration should not be delayed.

3.1 Preliminary notes:

Patients with watery diarrhoea produce stools with large amounts of water, sodium, chloride, potassium and bicarbonate ions which need to be replaced. (table 1)

A child who is dehydrated as a result of diarrhoea can have a deficit of sodium up to 70-110 mmol/L . Thus, in the initial rehydration, a sodium concentration of 90 mmol/L in oral rehydration solution (ORS) would be suitable. However, in the maintenance phase, to replace continuing stool losses in which the sodium concentration is 50-60 mmol/L, an ORS containing 60 mmol/L of sodium would be safe and effective. Alternatively, to avoid the confusion of using two types of ORS, one can give ORS containing 90 mmol/L sodium together with a normal intake of water and breast milk. If ORS containing 60 mmol/L sodium alone is used, it is important to ensure that the child does not become hyponatraemic, especially if the dehydration is severe.
Ref: Readings on Diarrhoea, WHO, Geneva. 1992 [45]

3.2 Correction of Dehydration

3.2.1 No dehydration

-These children usually do not need admission to hospital.
-Breast feeding should be continued on demand
-Formula-fed babies should receive their normal feeds with extra water. Small frequent feeds via a spoon should be given especially if there is mild vomiting.
-Older children with mild diarrhoea can continue their normal diet with extra water.
-Stopping feeds for over 24 hours is not recommended as this can delay recovery and affect nutrition especially in malnourished children. (See literature review above)

3.2.2 Mild (≤5%)

- Trial of ORS 40- 60 ml/kg within 4-6 hours
- For every diarrhoea episode, replace with 10ml/kg of ORS
- Feed normally

3.2.3 Moderate (6% - 9%) dehydration

- Trial of ORS (even if hypernatraemic).
- Volume to be given: 40 - 60 ml/kg within 4 - 6 hours (12 - 16 hours if Na > 150 mmol/l)
- 10 ml/kg for each diarrhoea episode.
- Start with small frequent feeds of milk, given with a spoon.
- Hydration status should be assessed at least 4 hourly
- If not tolerating ORS (refusing, taking insufficient volumes) then try using a nasogastric tube.
- Consider intravenous therapy if oral or nasogastric therapy fail, if vomiting persists, or if there is impending shock
- The table in the intravenous section may be used as a guide to volumes.

3.2.4 Severe dehydration (>10%)

Severe dehydration results in shock and is a medical emergency, requiring intravenous fluid therapy. Intravenous fluid therapy can be divided into three components : resuscitation, correction of deficit and maintenance. Note that oral rehydration, if tolerated, can continue even when the patient is on intravenous rehydration.

(a) Resuscitation – Indicated if in shock

- Use normal saline or Ringer's lactate 20 ml/kg (do not use dextrose containing fluids) over 1 hour. However, shorter periods of administration may be required.
- Repeat if necessary until blood pressure , pulse and perfusion, return to normal
- Monitor urine output. Be alert to the possibility of acute renal failure if the perfusion and blood pressure normalises and yet, no urine is produced.

(b) Replacement of deficit

- Calculate using uncorrected weight
(e.g. An 8kg child with 5% dehydration has a deficit of 5% of 8000g or 400g of water $\Rightarrow$ 400ml of water)
- The deficit can be replaced over 12 or 24 hours together with the maintenance requirement using 0.45% saline/5% dextrose.
- If there is hypernatraemia, duration of correction of deficit is prolonged

(c) Maintenance

-For subsequent maintenance, use 0.18% saline/4.3% dextrose as shown :

age	ml/kg/24 hours
• < 3/12	150
• 3 - 6/12	120 –150
• 6 - 12/12	100 –120
• over 1 year	
first 10 kg	100ml/kg/day
second 10 kg	50ml/kg/day
subsequent kg	20 – 30ml/kg/day

Example :

10 month old child weighing 9kg is 5% dehydrated; and not tolerating oral intake

(i) *Rehydrating over 12 hours*

deficit (5% of 9000g) 5/100 x 9000 = 450ml
maintenance (at 120 ml/kg/24hr) 120 x 9 = 1080 ml/24hr, i.e.540 ml/12hr
total fluids in first 12 hours 450 + 540 = 990 ml
Rate of infusion 990/12 hr i.e 82.5 ml/hr ≈ 80 ml/hr
Give fluids as 0.45% saline/5% dextrose at 80 ml/hr for 12 hours

(ii)*Rehydrating over 24 hours*

deficit 5% of 9000g = 450ml
maintenance at 120 ml/kg/24hr = 1080 ml/24hr
total fluids in first 24 hours 450+1080 = 1530 ml
Rate of infusion 1530/24 hr = 64 ml/hr

Give fluids as 0.45% saline/5% dextrose at 64 ml/hr for 24 hours

Whichever the duration of rehydration chosen, the child's hydration status and ongoing fluid losses need to be reassessed at least 4 hourly (more often if necessary), and the fluid prescription needs to be revised accordingly.

Add **10 mmol KCl** to each **500 ml** of iv fluid after urine is passed.

Extra Na^+ is normally unnecessary, unless the serum Na^+ level is very low; i.e.: < 125 mmol/l; or the child is symptomatic.
Na^+ deficit (mmol) = (desired Na^+ level – measured Na^+ level) x 0.6 x body weight in kg.

Ongoing loss is usually not a problem except in cholera, but if profuse watery diarrhoea persists despite nil by mouth (i.e. secretary diarrhoea) replace losses with 0.45% saline/5% dextrose.

3.2.5 Acidosis

The causes of acidosis in acute gastroenteritis are multiple, including infection, dehydration, shock, starvation and gastrointestinal losses. In most cases, the acidosis is mild and improves on its own when the dehydration is corrected and with improvement of the diarrhoea. In a severely ill child or if the acidosis is severe (pH < 7.15 or serum bicarbonate level < 15 mmol/l), intravenous correction with sodium bicarbonate is indicated.

Bicarbonate required (mmol) for correction = 1/3 x base deficit x body weight (kg). Usually the blood gas is checked after ½ this amount is given before proceeding further.

3.3 Hypernatraemic dehydration

This can result from ingestion of hypertonic liquids, such as over-concentrated milk feeds or home-made solutions to which salt is added, or loss of hypotonic fluids in the stool or urine. It is more common in hot weather.

3.3.1 Definition:

Serum Na^+ > 150 mmol/l.
Frequent reassessment is needed.

3.3.2 Clinical features:

Clinical presentation is notoriously deceptive. Shock is a late and ominous sign. The usual skin criteria for diagnosing dehydration are not accurate, the skin having a characteristic doughy appearance. The anterior fontanelle is typically not sunken, and in many cases may even bulge. There is increased irritabiliy and fever may be present.

3.3.3 Resuscitation

If in shock, give normal saline 20 ml/kg intravenously over ½ to 1 hour and repeat as necessary

3.3.4 Rehydration

The aim is to reduce the sodium levels **slowly** as dramatic falls can result in cerebral oedema and convulsions. At least 48 to 72 hours is usually recommended.
The reduction in plasma Na should not exceed 10 mmol/l per 24 hours.

Oral rehydration is the method of choice and the safest.
Only if this fails is slow iv rehydration necessary.
Calculate the fluid deficit and give this together with maintenance fluids over at least 48 hours. If fluid was given to resuscitate, the amount given should be subtracted from the fluid deficit. This is particularly important in hypernatraemic dehydration to avoid giving too much fluid.

Use 1/2 normal saline (0.45%)/5% dextrose for the duration of fluid replacement. After this if the serum sodium is still over 150 mmol/l, continue using this fluid until the serum sodium is below 150 mmo/l, after which 0.18% saline/4% dextrose may be used. Rapid reduction of serum sodium by rapid rehydration with a dilute solution may cause cerebral oedema with convulsions.

Example:10 month old child weighing 9kg is 5% dehydrated and not tolerating oral fluids
Serum sodium is above 150 mmol/l

Fluid deficit = 5% of 9000g	=	450 ml
Maintenance at 120 ml/kg/24 h	=	1080 ml/24 h

To rehydrate over 48 hours, the rate of infusion should be 1/48 x (450 + 1080 + 1080) ml/hr ie 54 ml/hour

4. Feeding of infants and children with gastroenteritis

4.1 Diets appropriate to the child's age should be given as soon as is clinically possible. In general, milk-feeding should not be discontinued. This is all the more true if the infant has been breast-fed. Formula-fed infants should not have their formulas changed without good reason.

4.2 Foods such as rice, wheat, potatoes, bread, cereals, lean meats, yogurt, fruits, and vegetables, are appropriate. Avoid fatty foods and foods high in simple sugars (including soft drinks).

4.3 Low birth-weight and malnourished infants are at risk of malabsorption and further malnutrition. If normal infant formula is not tolerated, a hydrolysed formula such as pregestimil may need to be considered. Twenty four hours of oral rehydration solution or intravenous fluids may sometimes be needed prior to that.

5. Specific problems in the follow-up of patient with acute gastroenteritis

The majority of children have an uneventful recovery from acute gastroenteritis. Occasionally, the diarrhoea may become chronic (that is last over 2 weeks).

5.1 Lactose intolerance

After acute gastroenteritis infants may be temporarily unable to tolerate lactose for about a week or longer, sometimes for months. They are usually formula-fed babies less than 6 months old with infectious diarrhoea. Breast-fed babies rarely have clinically significant lactose intolerance.
The clinical features are due to the action of colonic bacteria on unabsorbed lactose, releasing gas and acid:

- persistent loose stools
- abdominal distension
- increased flatus
- perianal excoriation

The diagnosis is suggested by the history and confirmed by Clinitest or Benedict's test to detect the presence of reducing sugars(mainly lactose) in stool :

- Collect stool fluid in diapers lined with plastic. Dilute 5 drops of stool fluid with 10 drops of water in a test-tube.
- Clinitest : Add a Clinitest tablet into the resultant mixture. A colour reaction indicating over 0.5% reducing substances suggests the diagnosis.
- Benedict's Test : 5 ml of Benedict's solution is mixed with 0.5 ml of liquid stool. The resultant solution is boiled for about 5 minutes. A colour reaction indicating over 0.5% reducing substances suggests the diagnosis.

Breath hydrogen analysis can also be performed to detect lactose intolerance :

Gaseous hydrogen is produced from the fermentation of unabsorbed carbohydrates by bacteria in the gastrointestinal tract, especially the colon. Some of this hydrogen diffuses into the bloodstream and is expired through the lungs. The degree of hydrogen production can serve as an indicator of carbohydrate malabsorption.

If diarrhoea is persistent and watery (over 7-10 days) and there is evidence of lactose intolerance, a lactose-free formula may be given. The usual formula can usually be reintroduced after 3 - 4 weeks.

There is no evidence to support the indiscriminate use of lactose free formula at the onset of an episode of gastroenteritis.

5.2 Cow's milk protein and other dietary protein intolerance

Symptoms may be precipitated by the ingestion of cow's milk protein (other dietary proteins that can also cause problems include soya protein and egg protein). These symptoms may be due to immune or non-immune mechanisms. The manifestations are quite varied and include the following : acute anaphylaxis (occasional cot death),urticaria, eczema, asthma, vomiting, diarrhoea or constipation, acute colitis, occult gastrointestinal blood loss leading to iron deficiency anaemia, colicky abdominal pain.

Cow's milk protein intolerance can only be diagnosed based on thorough clinical data, ie reproducible response to withdrawal and challenge. Laboratory tests, though helpful, cannot replace a proper clinical assessment. Once the diagnosis is established, cow's milk protein should be removed from the diet and a hydrolysed formula such as pregestimil should be given. The condition usually improves with age. Most children grow out of it after the age of 1 year.

5.3 Suggested indications for referral to a paediatric gastroenterology unit

- Severe failure to thrive that is not responding to the management above
- Severe diarrhoea starting from birth
- Rectal bleeding with negative stool cultures
- Suspected inflammatory bowel disease
- Diarrhoea persisting over 2 weeks despite hydrolysed protein formula

6. Drugs In Gastroenteritis

6.1 Antibiotics

These are rarely indicated[46].
Use in:

Giardiasis - metronidazole
Amoebiasis - metronidazole
Pseudomembraneous colitis - metronidazole
Cholera - doxycycline
Typhoid – chloramphenicol, ceftriaxone
Salmonella gastroenteritis in an infant under 6 months of age *
Haemolytic uraemic syndrome (still controversial)
Hirchsprung enterocolitis
Immunocompromised children

* It has been recommended that in children under 6 months of age with acute gastroenteritis caused by non-typhoidal *Salmonella* , antibiotics should be given because of the risk of systemic infection [47]

6.2 Antiemetics

These drugs are not recommended [48].

6.3 Antidiarrhoeal drugs

These drugs are not recommended

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