ADVANCES IN THE MANAGEMENT OF GASTROENTERITIS

Peter Lillitos  Colin Michie  John Apps  Donald Bentley
Department of Paediatrics, Ealing Hospital, Uxbridge Road, London UB1 3HW UK

ABSTRACT

Since the 1960s oral rehydration of children suffering acute diarrhoea with specifically manufactured solutions containing salt and sugar has become more frequent globally and prevented millions of deaths from acute dehydration. This strategy was hailed as one of the major medical advances of the last century as it was estimated to prevent 90% of deaths secondary to diarrhoea in those under five years of age. Oral rehydration solutions (ORS) continue to evolve, alongside understanding of the mechanisms of enterocyte damage and recovery. Further, the application of ORS is now linked by all health professionals to preventative measures directed at limiting the spread of diarrhoeal diseases.

Key words: Oral Rehydration Solution (ORS), child, gastroenteritis, prevention

THE EVOLUTION OF ORAL REHYDRATION SOLUTIONS

Oral rehydration solutions have become the cornerstone in the treatment of diarrhoeal illness. Globally there are of approximately a billion episodes diarrhoeal illnesses annually. Although such figures are often approximations, particularly with respect to children, diarrhoea continues to result in malnutrition and death in approximately 3-5 children annually. Following successful trials in West Bengal in 1971, WHO and UNICEF made ORS widely available and by the late 1970s it was estimated that ORS was responsible for saving 500 000 lives a year.

Development of an effective ORS only followed understanding of the mechanisms of fluid-solute absorption by cells in the gut. This is largely driven by transport of sodium coupled to co-transport of small molecules such as glucose, together with some osmotic absorption and solvent drag. Diarrhoeal organisms disrupt these mechanisms and some toxins can increase chloride secretion leading to fluid loss.
Three intracellular secondary messengers (cyclic adenosine monophosphate –cAMP, cyclic guanosine monophosphate - cGMP and Ca++/protein kinase-C) have long been recognised as key mediators of this secretion; supplying extracellular glucose and sodium ensures a reduction in secretory mechanisms, limiting fluid losses. Optimal co-transport is established with ORS when the molar concentrations of glucose to sodium in these fluids is approximately one.

In the 1960s the low tech strategy of the widespread application of ORS was launched following trials in Dacca and Calcutta\textsuperscript{2}. Measurements showed that although beneficial, ORS did not reduce stool volume or shorten the length of the diarrhoeal episode. Trials of polymers other than glucose and other solutes have been relatively ineffective. The use of cereal-based ORS similar to a range of traditional remedies has shown some benefit, particularly in high output diarrhoea such as cholera. Other strategies have since been employed relating to the osmolarity of ORS. Low-osmolarity solutions (240-250 mOsml/l) have a number of advantages over higher osmolarity solutions of 311 mOsml/l as recommended by the WHO prior to 2006. A meta-analysis of 9 RCTs in 2001 demonstrated that low-osmolarity ORSs were more effective than the WHO ORS in reducing the need for unscheduled intravenous fluid therapy and stool out-put. No increased risk of hyponatraemia was seen\textsuperscript{3}. A multi-centre double-blind randomised control trial on 675 children in 2002\textsuperscript{4} reported similar findings. In 2006 the WHO switched to a low-osmolarity ORS for non-cholera associated diarrhoea on the basis that the lower concentration of the new formula allowed for quicker absorption of fluids, reducing the need for intravenous fluids and hospitalisation\textsuperscript{5}. The National Institute of Clinical Excellence (NICE)\textsuperscript{6} recommends 3 low-osmolarity ORS including Diarolyte, Diarolyte Relief and Electroade\textsuperscript{1}. (Figure 2). The British National Formulary for children\textsuperscript{7} sets out the following criteria for ORS:

- enhance the absorption of water and electrolytes
- replace the electrolyte deficit adequately and safely
- contain an alkalinising agent to counter acidosis
- be slightly hypo-osmolar (about 250 mmol/litre) to prevent the possible induction of osmotic diarrhoea
- be simple to use in hospital and at home
- be palatable and acceptable
- be readily available.

\textsuperscript{1} Rapolyte recommended in the 2009 NICE guidance has since been withdrawn from the UK market.
Figure 1: Diagram demonstrating volumes of fluid movement in the gut and coupled sodium-glucose transport across the gut lumen. (Adapted from Fig 322-1, Nelson Textbook of Pediatrics 17th Ed)

Gut Input (ml/kg/day):
Diet 100
Saliva 70
Gastric Juice 70
Pancreatic + Bile Juice 45
Total: 285ml/kg/day

Figure 2. Composition of three ORS solutions recommended by NICE.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Sodium (mmol)†</th>
<th>Potassium (mmol)†</th>
<th>Chloride (mmol)†</th>
<th>Acid neutraliser (mmol)†</th>
<th>Glucose (mmol)†</th>
<th>Net price for 6 sachet pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarolyte®</td>
<td>60</td>
<td>20</td>
<td>60</td>
<td>Citrate: 10</td>
<td>90</td>
<td>£2.25</td>
</tr>
<tr>
<td>Diarolyte Relief®</td>
<td>60</td>
<td>20</td>
<td>50</td>
<td>Citrate: 10</td>
<td></td>
<td>£2.50</td>
</tr>
<tr>
<td>Electroade®</td>
<td>50</td>
<td>20</td>
<td>40</td>
<td>Bicarbonate: 30</td>
<td>111</td>
<td>£1.33</td>
</tr>
</tbody>
</table>

† Amount of constituent present if 5 sachets of ORS reconstituted with 1 litre of water

ORS is not used as widely as one might expect in either developed or developing countries. The situation is curious as ORS is effective in the treatment of vomiting in children too, helping correct electrolyte imbalances. Traditional and alternative treatments for gastroenteritis and dehydration
persist in many situations. These range from the overzealous use of intravenous fluid therapy in hospitals in developed countries to widespread use of various over the counter preparations and flat colas in the home. Popular folk and traditional recommendations included vegetable based solutions, (e.g. carrot soup championed by Per Salender) or cereal-based fluids. There are no trial data of the same quality as that for ORS for any of these preparations and there are data that show that flat colas are less useful than ORS. The cost of ORS in some developed countries can be prohibitive for the lower socioeconomic groups living there.

Early feeding, particularly with a mixed diet containing cereal and extra protein, reduces the risk of malnutrition developing. Continuation of breast-feeding is important in infants. Although a degree of lactose intolerance results from gastroenteritis, refeeding is beneficial and the use of low lactose or soya feeds unnecessary. Significant lactose intolerance is rare unless diarrhoea persists for more than 2 weeks.

Selected probiotics (mainly Lactobacilli) have demonstrated a therapeutic role in acute diarrhoea if used in the early phase of infection and at a high concentration. Prebiotics can modify intestinal flora and interact with the immune system of the host against specific pathogens. In developing countries zinc supplementation has demonstrated a significant reduction in the duration, severity and persistence of diarrhoea. Moreover, zinc may improve immune status, intestinal permeability, epithelial and enzymatic functions as well as the transport of electrolytes. Addition of zinc supplements in addition to ORS might reduce the complications of diarrhoea worldwide, particularly in developing countries.

**GASTROENTERITIS: ASSESSMENT OF THE PATIENT**

The majority of diarrhoeal disease is the result of viral infections with rotavirus. The Health Protection Agency has valuable pages on the various agents that can be involved in outbreaks in the community, Hospital, travel or food poisoning. The risks of this illness are mainly from dehydration and malnutrition. Younger children are more vulnerable to dehydration as they have greater basal fluid and electrolyte requirements per kilogram and they are dependent on others to meet these requirements. Figure 1 shows that total fluid input into the gut (Diet + intestinal secretions) is approximately 285ml/kg/day, more than double the fluid maintenance of a child (100ml/kg/day) and therefore if gut reabsorption is impaired a child can dehydrate rapidly. A typical episode of viral gastroenteritis causes 5-7 days of diarrhoea (but can last up to 2 weeks) and 1-3 days of vomiting.

The UK guidelines from the National Institute for Clinical Excellence (NICE) provide practical advice for the assessment of the state of dehydration in a case of diarrhoeal disease together with the prescription and delivery of ORS. As the majority of gastroenteritis is viral, the recommendation is not to
send stool for culture or collect bloods for analysis unless other clinical problems manifest. For instance, a history of travel or blood in the stool should prompt a stool culture. In diagnosing gastroenteritis, the possibility of other pathologies needs to be entertained. A number of clinical signs are outlined in Figure 4 that indicate a patient may be suffering a condition other than gastroenteritis that requires other investigation and treatment. Gastrointestinal upset is seen in children and adolescents as part of sepsis syndrome and therefore if the patient is systemically unwell, consideration of a Hospital referral is important. These points are summarised in the traffic light management algorithm in Figure 5.

Figure 3. Signs to assess severity of dehydration. Red flags indicate ominous signs which could progress to towards signs of shock. Taken from NICE guideline for Diarrhea & Vomiting 2009.
Figure 4. Red-flag signs that would warrant prompt referral to hospital. Adapted and modified from NICE guidelines on diarrhoea and vomiting 2009.

<table>
<thead>
<tr>
<th>Meningism in the older child</th>
<th>Bulging fontanelle</th>
<th>Bulging fontanelle in an infant</th>
<th>Not having passed urine for &gt;12hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any signs of Shock</td>
<td>Not tolerating any oral fluids, despite oral fluid challenge</td>
<td>Bilious vomiting</td>
<td>Carers unable to cope with the child’s illness</td>
</tr>
<tr>
<td>Reduced level of consciousness</td>
<td>Fever ≥38 in a child up to 3 months</td>
<td>Bloody stool</td>
<td>Severe abdominal pain</td>
</tr>
<tr>
<td>Jitteryness/hyperreflexia/Convulsions</td>
<td>Fever ≥39 in a child over 3 months</td>
<td>Abdominal mass seen/felt</td>
<td>True projectile vomiting</td>
</tr>
<tr>
<td>Non-blanching rash</td>
<td>Tachypnoea or shortness of breath</td>
<td>Abdominal distension</td>
<td>Co-existing chronic disease increasing child’s risk of serious illness</td>
</tr>
</tbody>
</table>

**ADVICE TO PARENTS & CARERS REGARDING THE PREVENTION OF GASTROENTERITIS**

Viral gastroenteritis agents are contagious, usually viral and usually spread mainly by faeco-oral contact and to a lesser extent by airborne routes. The main method of prevention of these infections is by providing adequate sanitation facilities and ensuring hand washing with soap (liquid if possible) in warm running water followed by careful drying. Hand washing is required after going to the toilet or changing nappies, as well as prior to preparing, serving or eating food. Diarrhoeal viruses can pose a problem as they are not completely removed by hand washing. Further, a number of such viruses can survive on skin, towels and fomites for several hours. Much gastroenteritis is spread through day care and school facilities by children where many surfaces and fomites are likely to be contaminated. Children should not attend any school or other childcare facility therefore while they suffer gastroenteritis and should not go back to their school or other childcare facility until at least 48 hours after the last episode of diarrhoea or vomiting. Those who have suffered norovirus or rotavirus may excrete virus for several weeks after recovery so that careful hygiene is important. Swimming in swimming pools should be avoided for 2 weeks after the last episode of diarrhoea. Carers
need to take particular care not to spread infection too. Such strategies have been shown to limit dehydration requiring ORS in developed countries.

Figure 5: Treatment Algorithm in a child with Diarrhoea and Vomiting (adapted and modified from NICE guideline)

- Assess for dehydration
- No Clinical dehydration
  - Continue breast feeding/milk feeds
  - Encourage oral fluid intake
  - Discourage fruit juices/carbonated drinks
  - Offer ORS as supplemental fluid if at increased risk of dehydration (Box 2). As per BNFc:
    - 1 month to 1 year: 1 to 1.5 times usual feed volume
    - 1-12 years: 200ml after every loose motion
    - 12-18yrs: 200-400ml after every loose motion
  - Reassess child or advise parents to re-seek medical advice if any concerns
  - Refer if treatment failure or illness progresses
  - NB: All ORS to be given in low-osmolarity form

- Clinical Dehydration, No red-flag signs
  - 50ml/kg ORS over 4hrs in addition to maintenance amounts
  - Calculate amount and frequency of fluid for child’s carers – for ease calculate an hourly amount for 1st few hours of intervention
  - Give in small aliquots to aid absorption
  - Continue breastfeeding
  - Can give usual fluids (avoid fruit juices/carbonated drinks) if child refuses ORS
  - Reassess child to monitor progress
  - Revert to green box management once tolerating fluids and clinically hydrated after 4hrs
  - Refer if treatment failure or illness progresses

- Clinical Shock or red-flag signs
  - Refer urgently to hospital

Figure 6: Normal physiological measurements in children.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Heart Rate (beats/min)</th>
<th>Respiratory Rate (breaths/min)</th>
<th>Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>110-160</td>
<td>20-40</td>
<td>70-90</td>
</tr>
<tr>
<td>1-2</td>
<td>100-150</td>
<td>25-35</td>
<td>80-95</td>
</tr>
<tr>
<td>2-5</td>
<td>95-140</td>
<td>25-30</td>
<td>80-100</td>
</tr>
<tr>
<td>5-12</td>
<td>80-120</td>
<td>20-25</td>
<td>90-110</td>
</tr>
<tr>
<td>&gt;12</td>
<td>60-100</td>
<td>15-20</td>
<td>100-120</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

The authors would like to acknowledge the input of the junior paediatricians at Ealing Hospital in 2011 for their critical review of this manuscript.

Declarations: The authors have no commercial involvement in this subject and have no conflicts of interest to declare

REFERENCES

6. NICE clinical guideline 84: Diarrhoea and vomiting in children. April 2009
7. BNFc 2011
12. gpnotebook.co.uk – Principles of management of child with gastroenteritis