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Oral Rehydration Therapy for Diarrhea-Related Dehydration in The Philippines

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About the Expert

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Abbreviations used in this review:
ESPGHAN = European Society of Paediatric Gastroenterology and Nutrition
FISPGHAN =Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition
IV = intravenous
ORS = oral rehydration salts
ORT = oral rehydration therapy
RCT = randomised controlled trial
RV = Rotavirus
UNICEF = United Nations International Children's Emergency Fund
WHO = World Health Organization

This review discusses the oral treatment of dehydration associated with acute diarrhea in the Philippines and reports on the current recommendations of the World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) for such therapy. Despite the availability of a simple, effective, and affordable treatment for reducing dehydration, diarrhea remains a leading cause of mortality in many resource-limited settings in children under 5 years of age, contributing to 499,000 deaths annually.[1,2] It is imperative that both healthcare providers and caregivers appreciate the relevance of timely and appropriate oral rehydration therapy (ORT) in this group of patients.

Introduction

Diarrhea-induced dehydration is a leading cause of morbidity and mortality in the developing world, including the Philippines.[1,3-5] Among the diarrheal deaths occurring in children under 5 years old in 2016, 89.37% occurred in South Asia and sub-Saharan Africa (**Figure 1**).[6]

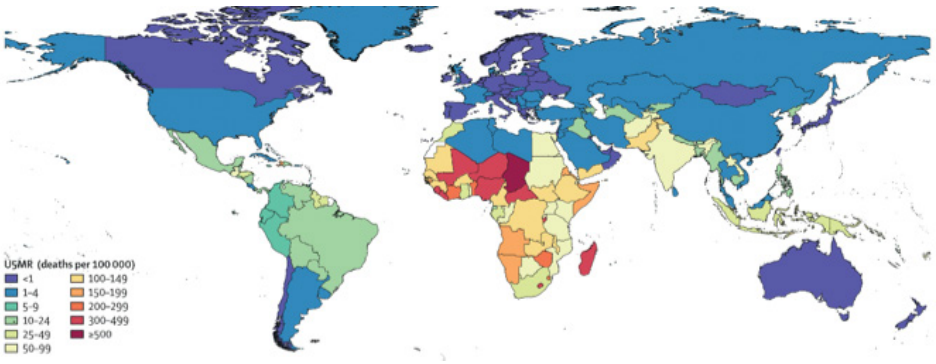


Figure 1. Worldwide distribution of diarrhea-associated mortality in children <5 years of age in 2016.[6]

In children, each episode of diarrhea potentially reduces the nutritional capacity required for growth, which may result in malnutrition; a diarrhea–malnutrition cycle then promotes further infection, and increased morbidity and mortality, particularly in young children.[1] Management of diarrhea by replenishing the lost body fluid through oral rehydration therapy (ORT) is a simple, effective, and affordable intervention that significantly reduces diarrhea-related mortality and morbidity.

In the 1970s, following the scientific breakthrough discovery of the glucose-facilitated fluid transport mechanism, WHO developed a simple, inexpensive iso-osmolar (311 mOsm/L) formulation of glucose-based oral rehydration salts (ORS) designed to correct dehydration and metabolic acidosis in the setting of acute diarrhea.[4,7] Since the introduction of ORS, the global annual mortality rate for children suffering acute diarrhea and dehydration has dropped from 5 million to 0.5 million, and ORS remains the cornerstone of therapy for dehydration secondary to acute infectious diarrhea.[4,6,7]

Despite the readily availability of ORS, mortality rates in the Philippines still remain high, with an estimated 7% of deaths due to diarrheal diseases in 2016 in children aged 1–59 months or approximately 5,000 diarrhea-associated deaths each year in this age group (13 deaths per day).[8]

Oral Rehydration Therapy for Diarrhea-Related Dehydration in The Philippines

ORS solutions

ORS solutions are designed to contain the appropriate amounts of sodium, glucose, and other electrolytes, with an osmolarity that maximizes water absorption from the gut using the principle of glucose-facilitated sodium transport (glucose enhances sodium and secondary water transport across the mucosa of the small intestine).[9] Optimal absorption of fluid from the small intestine is critically dependent on the composition of the rehydration solution; fluid absorption depends on three factors: sodium concentration, glucose concentration, and the luminal fluid osmolarity.

WHO ORS formulation

In 1975, WHO and UNICEF agreed to promote a single solution (WHO-ORS) containing: sodium 90 mmol/L; potassium 20 mmol/L; chloride 80 mmol/L; base 30 mmol/L (bicarbonate); and 2% glucose (111 mmol/L). This solution struck a compromise between the ideal solutions for different diarrheal disorders and the goal of a single formulation to simplify delivery and logistics for global use in cholera and noncholera diarrhea.[10]

Alternative ORS formulations

Alternative formulations have been investigated in order to develop an ORS formulation that would decrease stool output or have other clinical benefits, with the concern that the sodium concentration in the original formulation was too high (90 mmol/L) and was occasionally associated with hypernatremia.[11]

In 2002, WHO promoted a new low-sodium, low-glucose ORS formulation with an osmolarity of 245 mOsm/L, which was associated with reduced need for unscheduled IV therapy, decreased stool output, and less vomiting when compared with the original formulation.[11] This initiative was based on the findings of numerous studies including systematic reviews and meta-analysis of nine RCTs in children with acute diarrhea demonstrating significantly fewer unscheduled IV infusions (OR 0.61;95% CI 0.47-0.81), decreased stool output, and less frequent vomiting than in children receiving the original WHO ORS formulation (311 mOsm/L).[4,12] The low-osmolarity formulation remains the currently recommended ORS for acute diarrhea.[4]

Other organizations have also promoted lower osmolarity ORS formulations including the European Society of Paediatric Gastroenterology and Nutrition (ESPGHAN), which recommended an ORS containing 60 mmol/L of sodium and an osmolarity between 200 and 250 mOsm/L for children in developed countries who are not malnourished.[13] While the efficacy of glucose-based ORS in children with acute non-cholera diarrhea was improved by reducing sodium to 60–75 mmol/L, glucose to 75–90 mmol/L, and total osmolarity to 215–260 mOsm/L, there is insufficient evidence to differentiate between ORS solutions containing less than 75 mmol/L of sodium versus >75 mmol/L, and there are considerable programmatic and logistic advantages inherent in using a single solution around the globe for diarrhea cases at all ages.[4]

While this single ORS low-osmolarity formulation is recommended, WHO and UNICEF acknowledge a range of criteria that is acceptable for ORS formulations.[4,11] These criteria are as follows:

- The total substance concentration (including that contributed by glucose) should be within the range of 200–310 mOsm/L
- The individual substance concentration:
  - Glucose – should at least equal to that of sodium but should not exceed 111 mmoL/L
  - Sodium – should be within the range of 60–90 mmoL/L
  - Potassium – should be within the range of 15–25 mmoL/L
  - Citrate – should be within the range of 8–12 mmoL/L
  - Chloride – should be within the range of 50–80 mmoL/L

The Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN), in its 2018 publication on the universal guidelines on the treatment of acute diarrhea, also supports the use of reduced osmolarity ORS (containing 60–75 mmol/L sodium) as first-line in the treatment of acute non-cholera diarrhea for non-malnourished children and ORS containing 75 mmol/L sodium for cholera.[14]

One important facet in the treatment of dehydration is the nutritional status of the child. Because severely malnourished children experience physiologic derangements in handling fluids and electrolytes, e.g., low potassium and magnesium stores; and high total body and cellular sodium despite low serum levels and thus a greater tendency for fluid retention, a modified ORS for malnutrition (ReSoMal), with 45 mmol/L sodium and 40 mmol/L potassium, is recommended for these patients.[15,16] The FISPGHAN supports such a recommendation for severely malnourished children.[14]

Composition of rehydration solutions

Compositions of available ORS solutions and other fluids differ with regard to concentrations of electrolytes and glucose, and total osmolarity. The composition of various ORS and other fluids are shown in **Table 1**. Fruit juices and soft drinks contain minimal sodium and have excessive glucose that result in an excessively high osmolarity, which may worsen diarrhea.[9] Sports drinks have low sodium and high carbohydrate content in relation to the losses seen in diarrhea, and are therefore inappropriate as rehydration solutions.[9]

Pre-mixed ORS solutions

In an attempt to improve the uptake of ORS, a number of manufacturers have developed pre-mixed ORS solutions, some of which meet WHO criteria and have the advantage of convenience, accurate dosing, and improved taste. Pre-mixed liquid ORS solutions are less time-consuming to administer as these are ready to drink, ensuring no opportunity for errors in preparation and the subsequent final osmolarity.[10] A suitable advantage too is their availability in pre-flavored formats using sweeteners that do not significantly alter osmolarity and also offsetting the need for access to clean drinking water.[30,31] The advantage of such alternatives in the rehydration of patients with diarrhea has not yet been established.

Administration of ORS

ORS are available in three product forms: powder, tablet and liquid.[11] Powder sachets and tablets of ORS are usually made up with clean or boiled drinking water while pre-mixed liquid ORS solutions are ready-to-drink and convenient, especially in situations where clean drinking water is unavailable.[5] It is discouraged that ORS be mixed with any other liquid, except water, to ensure that the solution is within the recommended composition. If the ORS solution is not well tolerated because of the taste, and the patient is not dehydrated, it is best to advise the patient to keep drinking water and continue feeding. However, if the patient has signs of dehydration, ORS in the proper formulation is strongly recommended.

The role of zinc

Children with diarrhea receiving daily zinc supplementation have been shown to experience a significantly faster recovery from diarrhea and an 18% to 59% reduction in total stool output.[11] WHO and UNICEF endorse the use of zinc supplementation during treatment with ORS for diarrhea.[11] In countries where zinc deficiency is not prevalent, this particular recommendation is not strongly supported. The FISPGHAN recommends zinc as an adjunct to oral rehydration therapy in children older than 6 months from low-income countries or in settings where zinc deficiency is of medium to high risk. However, its efficacy is not strongly supported among well-nourished children living in high-income countries. Uniformly, for infants below 6 months old, zinc has not been demonstrated to be effective regardless of the nutritional status.[14]

Table 1. Composition of available ORS solutions and other fluids used for rehydration.[13,16-29]

Recommending Agency/Product	Carbohydrate mmol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Base* mmol/L	Osmolarity mOsm/L
WHO (acceptable range)	**At least equal to sodium, not greater than 111 mmol/L**	**Range 60-90 mmol/L**	**Range 15-25 mmol/L**	**Range 50-80 mmol/L**	**Range 8-12 mmol/L**	**Range 200-310 mOsm/L**
WHO and FISPGHAN (low-osmolarity) for non malnourished children	75	75	20	65	10	245
ESPGHAN	74-111	60	20	60	10	240
ReSoMal® for severely malnourished children	125	45	40	70	7	300
ORS in powder sachets / tablets						
Glucolyte Plus® (tab)	75	75	20	65	10	245
Hydrite® (tab)	75	75	20	65	10	245
Cholyte Plus® (sachet) with Mg, Zn, gluconate	66	50	20	40	10	247
Vivalyte® (sachet) with Vit C, Mg, Zn, sweeteners	77	40	20	44	8	293
ORS as premixed solutions						
Pedialyte® 45	139	45	20	35	10	250
Vivity Rehydrate® Apple	65	60	20	51	10	259
Vivity Rehydrate® Orange	69	60	20	51	10	244
Vivalyte® (Electrolyte Drink) with sucralose, acesulfame, artificial flavor, colorant	80	40	20	40	12	292
Fluids unsuitable for diarrhea treatment						
Apple juice	120	0.4	44	45	-	730
Gatorade®	323	20	3.2	11	-	350
Pedialyte® Mild 30 Electrolyte drink with Mg, Ca, lactate	278	30	20	30	28	501
Pocari Sweat® with Mg, Ca	400	21	5	16.5	12	388
Coca Cola Classic®**	112	1.6	-	-	13.4	650

* Citrate unless otherwise stated. ** Figures do not include electrolytes that might be present in the local water used for bottling.
Note: also includes data from commercial package inserts and labels and personal communication from Dr Juliet Sio-Aguilar.

Assessment of dehydration

Patients can be classified into three levels of dehydration (**Table 2**) based on their estimated fluid deficit as a percentage of body weight: mild dehydration (3-5%), moderate dehydration (5-10%), and severe dehydration (>10%).[32] The WHO category for some dehydration refers to mild to moderate dehydration. While the WHO criteria for the Assessment of Dehydration is still a quick and practical way of identifying patients requiring fluid replacement, the following table adapted from the National Institute for Health and Clinical Evidence (NICE) identifies the clinical features according to the likelihood of detecting significant (5%) dehydration. In systematic reviews, the first three in the list (prolonged capillary refill, abnormal skin turgor, and abnormal respiratory pattern) are more consistently associated with dehydration.[33]

Table 2. Clinical assessment of dehydration.[33]

Clinical Sign*	Mild fluid deficit	Moderate fluid deficit	Severe fluid deficit
Skin turgor	Normal	Slow	Tenting
Capillary refill	<2 sec	Increased	Increased
Respiratory pattern	Normal	Tachypneic	Deep, labored
Mucous membranes	Dry lips	Dry	Very dry, cracked
Eyes	Slightly sunken	Sunken orbits	Deeply sunken orbits
Sensorium	Alert	Irritable	Lethargic
Systolic blood pressure	Normal	Normal, orthostatic	Very low
Peripheral pulse	Slightly rapid	Rapid	Rapid, weak
Thirst	Slightly increased	Moderately increased	Very thirsty or too lethargic to indicate
Urine output	Infrequent, concentrated	Markedly decreased	Anuria

*Modified classification of dehydration from WHO Clinical Practice Guidelines on the treatment of diarrhoea, 2005; NICE Clinical Guideline on diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years, 2009; and Consensus Statements on Parenteral Fluid Therapy in Infants, Children, & Adolescents. Task Force on Fluid and Electrolyte Therapy. Philippine Pediatric Society. 2017.

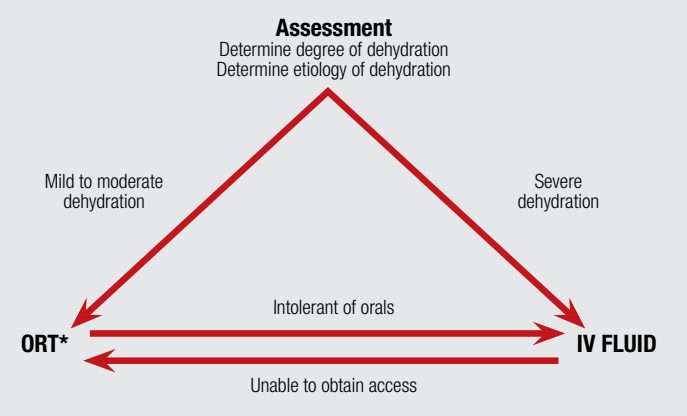
Treatment of dehydration

The majority of childhood cases of mild to moderate diarrhea-related dehydration can be successfully managed with ORT via mouth or nasogastric tube,[9,32] and this first-line treatment has been shown to be as effective and less costly than IV rehydration.[1,34] Contraindications to ORT include shock or suspected acute abdomen, paralytic ileus from hypokalemia or the use of opiates such as loperamide, and glucose malabsorption manifested as intractable diarrhea (i.e., loose or watery stools occurring 4 or more times per hour or more than 15–20 mL/kg/hour).[32] Vomiting per se is not a contraindication, unless it portends intestinal obstruction. A simple decision guide for the treatment of dehydration is shown in **Figure 2**.[35]

Successful ORT involves several phases including rehydration, maintenance and prevention of dehydration, and realimentation involving age-appropriate, unrestricted diets that should begin as soon as possible.[36]

The WHO recommendation for the treatment of dehydration is simple and effective. For mild or no dehydration, patients are to drink as much as they can to prevent dehydration. Children under 2 years old should drink ¼ to ½ cup of appropriate fluids or ORS after each vomiting and loose bowel movement; those between 2–10 years old are recommended to have at least ½ to 1 cup of ORS or any suitable fluids. For those older than 10 years, oral fluids are given as much as they can tolerate. For those with moderate dehydration, an estimated 75 mL per kg body weight given within 4 hours is recommended to treat dehydration.[32] Alternatively, small amounts of oral fluid is administered frequently, for example 0.5 mL/kg every 5 minutes with the aim of ensuring that the input exceeds the output by enough to rehydrate and then maintain hydration.[9] The overall goal is to replace the total estimated deficit in a maximum of 4 hours.[36] In severe dehydration cases, IV fluid or ORS may be delivered immediately via a nasogastric tube in situations when IV treatment is not possible. If a child with dehydration does not achieve adequate oral rehydration, they have to be admitted to hospital to receive IV rehydration.

For ongoing care, emphasis should be placed on educating caregivers on appropriate rehydration in diarrheal diseases, emphasizing that administration of water, or carbohydrate-only containing drinks, does not promote adequate fluid absorption in dehydrated individuals and that drinks with a high glucose content and unbalanced carbohydrate/sodium ratios are not suitable for rehydration as they may worsen diarrhea through osmotic mechanisms.[37]



* If intolerant of orals, a nasogastric tube may be used to administer appropriate electrolyte solutions. IV = intravenous; ORT = oral rehydration therapy

Figure 2. Decision guide for the treatment of dehydration.[35]

WHO/UNICEF recommendations for managing diarrhea in children[38]

Health care workers should:

- Advise caregivers to begin administering appropriate available home fluids immediately upon diarrhea onset
- Treat dehydration with reduced osmolarity ORS solution (or with IV electrolyte solution in children with severe dehydration)
- Emphasize continued feeding during diarrhea and increased feeding after the diarrheal episode
- Only use antibiotics when appropriate, i.e. with bloody diarrhea presumed to be due to shigellosis, and in cases of cholera. Do not administer antidiarrheal medication
- Provide children six months and older with 20 mg per day of zinc for 10–14 days if they are living in resource-limited communities. No zinc supplementation for infants under six months old
- Instruct caregivers of the requirement to increase fluids and continue feeding during future diarrheal episodes.

Issues for rehydration in the Philippines

In the Philippines, nearly five decades since the ORS scientific breakthrough, where does the country stand? Diarrheal diseases no longer ranked among the top ten causes of overall mortality in the country in 2015 but remained as the seventh leading cause of overall morbidity at 127/100,000 population. While the incidence and deaths from diarrheal diseases have steadily declined in the past decades, ORT utilization and zinc supplementation can still be improved. Based on the reports of the Field Health Service Information System of the Philippine Department of Health covering a 3-year period (2015–2017), the average ORS use in diarrhea was approximately 76% while ORS plus zinc usage in diarrhea was only 48%, with certain regions of the country faring poorly (region 11 for ORS use and region 12 for the combined ORS and zinc use).

Interestingly, the 2017 Philippine National Demographic and Health Survey found that only 6% of Filipino children under the age of 5 years developed diarrhea in the 2 weeks prior to the survey.[39] An estimated 42% of their caregivers sought advice for their children, and while 61% of those children received ORT, only 17% received ORS and zinc.[39] The use of ORT in young children appears to be on the decline in the Philippines, with a UNICEF report showing a steady decline since 2003 in the use of oral rehydration and continued feeding in children under 5 years of age.[40] Furthermore, a high knowledge of ORS (nearly 90%) does not translate to its subsequent usage.[40] Some factors that may be contributing to the underutilization of ORT in the Philippines may include the commonly reported caregiver perception that diarrhea is not a life-threatening disease and the frequently employed `wait and watch' approach, where medical attention is only sought when fever, vomiting, or severe dehydration develop.[5] Other contributing factors may include the poor palatability of ORS solutions, accessibility, ineffectiveness in stopping diarrhea, and the need to give ORS often.[31,41]

Breastfeeding remains to be a very important preventive measure against the development of diarrhea in children under 2 years.[42] Recently, the effectiveness of a monovalent RV vaccine has been underscored in the Philippines, with the study demonstrating 60% vaccine effectiveness against RV hospitalization and 65% against severe RV diarrhea.[43]

There is a clear and urgent need for caregiver education regarding the importance of ORT and zinc supplementation in children with mild-to-moderate dehydration, especially in a country where zinc deficiency is prevalent, with an emphasis on the importance of correct preparation and administration of ORS.[1]

Key measures to prevent diarrhea

WHO cites the following as key measures for the prevention of diarrhea:[44]

- Access to safe drinking water
- Use of improved sanitation
- Handwashing with soap
- Exclusive breastfeeding for the first six months of life
- Good personal and food hygiene
- Health education about how infections spread
- Rotavirus (RV) and measles vaccination.

EXPERT'S CONCLUDING COMMENTS – *Juliet Sio Aguilar*

Diarrhea continues to be a leading cause of mortality in nearly half a million children under 5 years old globally, particularly in many resource-limited settings. While significant breakthroughs have been achieved in the treatment of diarrhea through a simple oral rehydration solution introduced five decades ago, compliance to this treatment has not been in full scale. Globally, compliance to ORT in diarrhea has remained low at approximately 50% with the combined ORT and zinc usage even more dismal at around 10%.[8] Although zinc supplementation in developed countries is not as crucial as in the developing countries, this purportedly being attributed to the better zinc status in the former, the converse is however true for the resource-limited countries.

Because of the poor compliance to ORS use, attempts have been made to improve its palatability through pre-mixed preparations. Caution should be observed as not all such preparations follow the formulation as recommended by the WHO and UNICEF. Hence, in the presence of dehydration, the appropriate oral rehydration fluid is mandatory. If, however, diarrhea has just started and fluid losses are still minimal, the practice of giving any fluid is better than no fluid at all. Nonetheless, fluids that are too high in sugar and salts are to be avoided. Replacing diarrheal losses with sports drinks is strongly discouraged as these drinks are generally high in sugar and do not contain adequate amounts of sodium and potassium to replace those that are lost in diarrhea.

Reduced osmolarity ORS is currently recommended for the treatment of dehydration from diarrhea for all patients except for the severely malnourished. Instead, ReSoMal (Rehydration Solution for Malnutrition) is recommended for the treatment of dehydration in the severely malnourished.

In the Philippines, ORT usage and zinc supplementation have not been fully utilized despite a high level of awareness. The difficulty in administering ORS and misconceptions among caregivers on the use of ORS are perennial challenges that have to be addressed to promote wider compliance and better clinical outcome.

TAKE-HOME MESSAGES

- Key measures including breastfeeding, improved hygiene and sanitation, and vaccination against rotavirus and measles should be implemented for the prevention of diarrhea.
- ORT, continued feeding, and zinc supplementation are the mainstays in the treatment of diarrhea.
- WHO/UNICEF recommend the single low-osmolarity ORS formulation, but allow a range of acceptable ORS formulations.
- Most cases of diarrhea-related dehydration can be successfully treated with ORS.
- Pre-mixed liquid ORS may be a palatable and convenient option in the treatment of diarrhea, especially in situations where clean drinking water is unavailable.
- Zinc supplementation should be provided during treatment with ORS for diarrhea, particularly in resource-limited settings.

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