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Oral Rehydration Therapy for Diarrhea-Related Dehydration in Indonesia

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About the Expert

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Professor Yati Soenarto has been called the mother of modern pediatrics in Indonesia. Since graduating in Medicine from Universitas Gadjah Mada (UGM) Indonesia, she has pursued a quest to improve the health of the nation's children and build pediatric capacity in the country's medical workforce. Her post-graduate training has spanned Indonesia; Vriye Universiteit, Amsterdam; The Royal Children's Hospital, Melbourne; University of Toronto; and Harvard Medical School, Boston. She has been Professor of Pediatrics at Universitas Gadjah Mada (UGM) in Yogyakarta since 2007 and was formerly Head of the Department of Pediatrics.

In 2015 the University of Melbourne awarded her a Doctor of Medical Science (Honoris Causa).

Prof. Dr. Yati Soenarto is the recipient of the Bakrie Award, an award given to Indonesian scientists who care about the progress of the nation to appreciate their development and progress in terms of freedom, culture, and sciences in Indonesia. For decades, she has worked to reduce the mortality and morbidity rates in young children.

Abbreviations used in this review:
ESPGHAN = European Society of Paediatric Gastroenterology and Nutrition
IV = intravenous
ORS = oral rehydration salts
ORT = oral rehydration therapy
RCT = randomised controlled trial
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 Indonesia and reports on the current World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) recommendations for such therapy. Despite this effective, simple and affordable treatment for reducing diarrhea-related dehydration, it remains a leading cause of death in developing countries in children under 5 years of age.[1-3] It is imperative that both healthcare providers and caregivers understand the importance of timely and appropriate oral rehydration therapy (ORT) in this group of patients.[2]

Introduction

Diarrhea-induced dehydration is a leading cause of morbidity and mortality in the developing world and is especially problematic in South-East Asian countries, including Indonesia.[1-4] Of the deaths occurring in children <5 years of age in 2016 as a result of diarrhea, 89.37% occurred in South Asia and sub-Saharan Africa.[4] According to WHO data published in 2011, diarrhea was responsible for 18% of childhood deaths in low-income countries (**Figure 1**).[5] In children, each episode of diarrhea reduces nutrition required for growth, resulting in undernutrition and a diarrhea-undernutrition cycle that promotes further infection and increased morbidity and mortality, particularly in young children (**Figure 2**).[6]

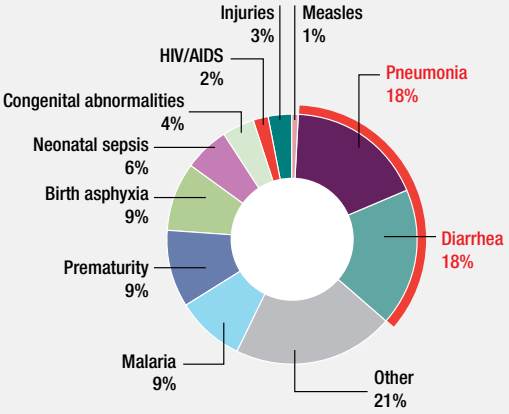

Figure 1. Causes of child deaths in low-income countries.[5]

Figure 2. The cycle between diarrhea and undernutrition.[6]

Management of diarrhea by replenishing the lost body fluid through oral rehydration therapy (ORT) is a simple, affordable, and effective intervention that significantly reduces diarrhea-related mortality and morbidity.[1] In the 1970s, WHO developed a simple, inexpensive iso-osmotic (311 mOsm/L) formulation of glucose-based oral rehydration salts (ORS) designed to correct dehydration and metabolic acidosis in the setting of acute diarrhea.[3,7] 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.[3,4,7] In Indonesia, a 2012 national survey revealed that 14% of children under the age of 5 years had experienced diarrhea in the prior 2 weeks and that 65% of those children were taken to a healthcare provider.[8] The survey also revealed that while 9 out of 10 mothers reported knowledge of ORS, only 39% of children suffering diarrhea received ORS (or a prepackaged liquid).[8]

Oral Rehydration Therapy for Diarrhea-Related Dehydration in Indonesia

ORS solutions

ORS solutions are designed to contain the appropriate amount of sodium, glucose and other electrolytes, with appropriate osmolarity to maximise 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 upper 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 disorders and the goal of a single formulation to simplify delivery and logistics for global use in cholera and non-cholera diarrheas.[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 concerns that the original ORS sodium concentration 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 a number of studies including a meta-analysis of nine RCTs in children with acute diarrhea showing 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).[3,12] The low-osmolarity formulation (**Table 1**) remains the currently recommended ORS for acute diarrhea.[3]

Other organisations have also promoted lower osmolarity ORS formulations including the European Society of Paediatric Gastroenterology and Nutrition, which recommended an ORS containing 60 mmol/L of sodium with an osmolarity between 200 and 250 mOsm/L for children in developed countries who are not malnourished.[13] However, as the WHO 2002 Consensus meeting emphasised, 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 to 260 mOsm/L there was 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.[3]

While this single ORS low-osmolarity formulation is recommended, WHO and UNICEF acknowledge that there is a range of criteria for acceptable ORS formulations.[3,11]

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 ORSs and other fluids are shown in **Table 1**. Fruit juices and soft drinks contain minimal sodium and have excessive glucose that results in excessive osmolarity, which may worsen diarrhea.[9] Sports drinks have varying sodium and carbohydrate levels, and are therefore inappropriate as rehydration solutions.[9]

Table 1. Composition of available ORS solutions and other fluids used for rehydration[13-18]

Product	Carbohydrate mmol/L	(g/L**)	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Citrate 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 (low-osmolarity)	75	(13.5g)	75	20	65	30	245
ESPGHAN (European formula)	74-111	(16g)	60	20	60	10	240
Pedialyte®	139	(25g)	45	20	35	10	250
Dehidralyte®	75	(13.5g)	75	20	65	10	245
Vivity Rehydrate® Apple	65	(30g)	60	20	51	10	259
Vivity Rehydrate® Orange	69	(30g)	60	20	51	10	244
Electral®	75	(13.5g)	75	20	65	10	245
Beverages not appropriate for diarrhea treatment							
Coca Cola classic*®	622	(112g)	1.6	N/A	N/A	13.4	650
Gatorade®	322	(58.3g)	20	3.2	11	N/A	350
Apple juice	666	(120g)	0.4	44	45	N/A	730
Pocari Sweat®	400	(72g)	21	5	16.5	12	388

*figures do not include electrolytes that might be present in local water used for bottling

**carbohydrate g/l shown in blue font in brackets

Adapted from King (MMWR) 2003 and Sandhu 2001 and also includes data from commercial package inserts and labels.

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.[16] WHO and UNICEF endorse the use of zinc supplementation for 10-14 days during treatment with ORS for diarrhea.[21]

Pre-mixed ORS solutions

In an attempt to improve the uptake of ORS, a number of manufacturers have developed pre-mixed ORS solutions, which meet WHO criteria and have the advantage of convenience, accurate dosing and improved taste. Pre-made liquid ORS solutions are less time consuming to prepare and have the advantage over sachets of not requiring interpretation of instructions for their preparation, ensuring no opportunity for errors in preparation and subsequent final osmolarity.[14] Other major advantages of such commercially prepared ORS solutions are their availability in pre-flavoured formats using sweeteners that do not significantly alter their osmolarity, and the fact that they do not require access to clean drinking water by the caregiver.[22,23]

Administration of ORS

ORS are produced in three dosage forms: powder, tablet and liquid.[16] Powder sachets of ORS are usually made up in clean or boiled drinking water. Pre-made liquid ORS solutions are an effective, convenient and safe option, especially in situations where clean drinking water is unavailable, and caregivers often prefer such formulations.[2] ORS may be formulated with fruit juice to improve the taste, but the final product should be within the recommended osmolarity range (200-310 (mOsm/L).[24]

Assessment and treatment of diarrhea-related dehydration in children

The majority of childhood cases of mild-to-moderate diarrhea-related dehydration can be successfully managed with ORT via mouth or nasogastric tube, and this first-line treatment has been shown to be as effective, more straightforward, and less costly than IV rehydration.[1,9,25] Contraindications to ORT include shock or suspected acute abdomen, but vomiting is not a contraindication.

The flow chart in **Figure 3** outlines the WHO assessment and treatment (Plans A, B and C) of diarrhea-related dehydration in children.[26]

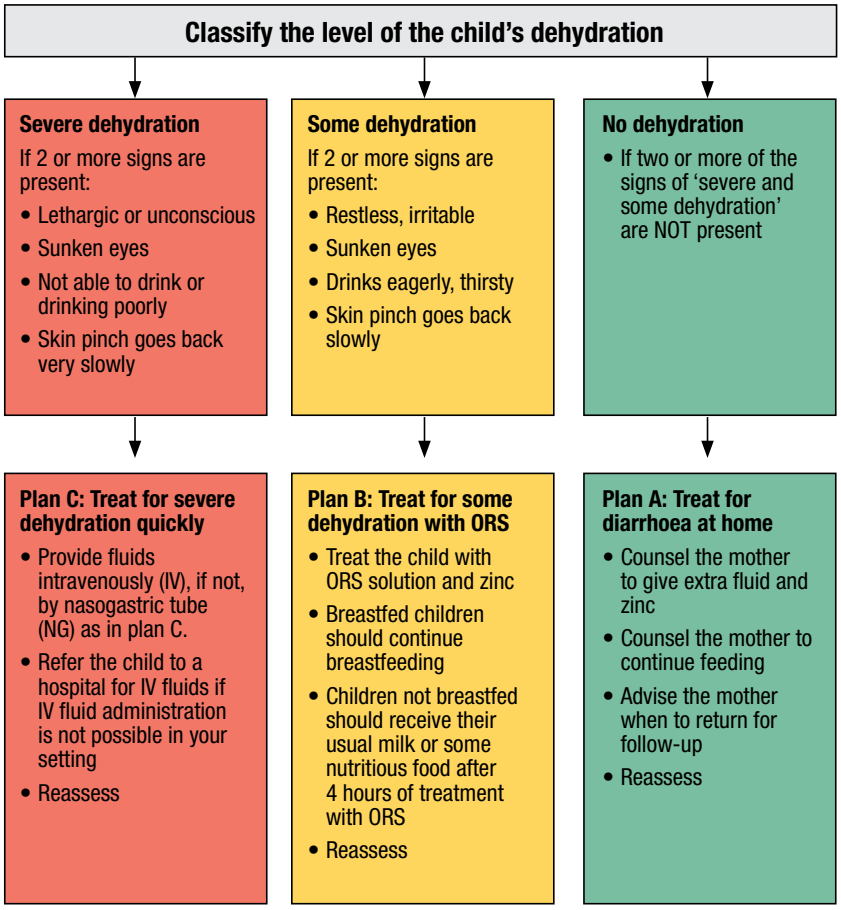

Figure 3. Assessment and treatment options for children with diarrhea-associated dehydration.[26]

Plan A (for when 'no dehydration' is present) involves giving as much extra fluid as the child will take.[26] It is especially important to give ORS to use at home when the child has been treated with Plan B or Plan C during their healthcare visit, and when the child cannot return to a clinic if the diarrhea gets worse.[26] The amount of fluid administered should equal 50-100 mL after each loose stool in children up to 2 years of age, and 100-200 mL in those ≥2 years of age. This should be administered via frequent small sips and should be continued until the diarrhea stops.

Plan B (for when 'some dehydration' is present) involves the administration of recommended amounts of ORS over a 4-hour period as shown in **Table 2.**[26] If the child desires more ORS than is suggested, give more. This should be administered via frequent small sips and should be continued for 4 hours. After 4 hours the child should be reassessed and classified for dehydration (**Figure 3**) and the appropriate plan selected.

Table 2. Approximate amount of ORS solution to give in the first 4 hours in children with some dehydration[26]

Age[1]	Up to 4 months	4 -12 months	12 -24 months	2 - 5 years
Weight in kg	<4	6 to <10	10 to <12	12 to <20
Fluid in ML	200–450	450–800	800–960	960–1600

[1] Use the patient's age only when the weight is unknown. The approximate amount of ORS required (in mL) can also be calculated by multiplying the patient's weight (in kg) times 75

Plan C (for when 'severe dehydration' is present) involves administering IV fluids immediately if possible and having the child consume ORS while the drip is set up if they are able to drink (otherwise when they are able to drink, administer ORS at a rate of 5 mL/kg/hour). If it is not possible to administer IV fluids, ORS may be administered via a nasogastric tube (or by mouth) at a rate of 20 mL/kg/hour for 6 hours (total 120 mL/kg). After 6 hours, the child should be reassessed and classified for dehydration (**Figure 3**) and the appropriate plan selected. Urgent referral to hospital for IV therapy may be required in severe cases.

For ongoing care, emphasis should be placed on educating caregivers on appropriate rehydration in diarrheal diseases explaining 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.[27]

Issues for rehydration in Indonesia

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, is considered a major reason for the poor uptake of ORS in developing countries.[2] Other contributing factors include the poor palatability of some ORS solutions, cost and accessibility.[21]

A survey of Indonesian General Practitioners revealed that approximately 46% prescribed ORS for the treatment of children with diarrhea and only 25% prescribed both zinc and ORS.[28] Zinc is only available over-the-counter in Indonesia, and is prescribed for at least 10 days. Rotavirus surveillance data conducted in several Indonesian hospitals has shown that the use of zinc in children

under five years of age is increasing whereas the use of antibiotics is decreasing (unpublished data, Soenarto et al).

An Indonesian study has revealed that only 23.7% of mothers correctly prepared ORS, and none exhibited fully correct administration practices.[29] Furthermore, a study from West Java indicated that the primary factors impacting ORS use were mothers' knowledge of the signs of dehydration and their ability to satisfactorily prepare and administer ORS.[30]

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, with an emphasis on the importance of correct preparation and administration of ORS.[1]

Key measures to prevent diarrhea

WHO cite the following as key measures for the prevention of diarrhea:[31]

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

EXPERT'S CONCLUDING COMMENTS

When ORS (oral rehydration solution) was introduced in Indonesia, most children refused; however, reformulations have helped to improve palatability. Since then, several studies were conducted using home fluid solutions such as: rice based solution, soup, boiled guava leaves solution, etc. This local wisdom represents a great wealth of medicinal knowledge and provides an avenue for a combination of treatments with evidence-based medicine.

Sucrose is not available in most areas in this country. In place of sucrose, most Indonesian communities use rock sugar, java sugar, rice sugar and coconut sugar, which are established as safe and effective feeding solutions. In collaboration with researchers in agriculture technology, we developed alternative sugar products to replace the use of sucrose. These innovations have made ORS more acceptable, affordable and palatable, especially in rural areas and in traditional communities.

More education is needed to make ORS more acceptable with these home fluid based solutions, which are also considered as early and rapid (re)feeding treatment and are very important in combating and preventing malnutrition caused by diarrhea disease.

Rotavirus was traditionally the highest cause of diarrhea in Indonesian children under 5 years (60%). Vomiting occurs significantly more often in Rotavirus diarrhea compared to non-Rotavirus diarrhea. This dilemma makes children more difficult to rehydrate by oral solutions, whereas a nasogastric tube can even cause more vomiting. This emphasizes the importance of starting rehydration as early as possible. Even more importantly, Rotavirus vaccination programs should be made available in neonatal care as a proven prevention of diarrhea disease for infants and children <5 years, particularly in Rotavirus endemic areas.

It is our hope that more researchers will continue our innovative efforts to promote Rotavirus vaccination programs in their respective countries and explore their local wisdom for global solutions.

TAKE-HOME MESSAGES

- Key measures including improved hygiene and sanitation, and vaccination for rotavirus should be implemented for the prevention of diarrhea
- Dehydration should be prevented and treated in children with diarrhea by administering an appropriate ORS solution
- WHO/UNICEF recommend the single low-osmolarity ORS formulation, but acknowledge that there is a range of acceptable ORS formulations
- Most cases of diarrhea-related dehydration can be successfully treated with ORS
- Zinc supplementation should be provided for a duration of 10-14 days in children and infants receiving ORS for diarrhea
- Pre-made liquid ORS solutions may be an effective, palatable and convenient option, especially in situations where clean drinking water is unavailable.

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