

OVERVIEW PAPER

RICE-BASED ORAL REHYDRATION

HASAN SHAREEF AHMED AND ABDUL MAJID MOLLA¹

*International Centre for Diarrhoeal Disease Research, Bangladesh, G P O Box 128, Dhaka 1000,
Bangladesh; ¹Department of Paediatrics, The Aga Khan University Hospital, Stadium Road,
P O Box 3500, Karachi 5, Pakistan*

Introduction

Diarrhoeal disease is the greatest cause of infant mortality in the developing world (1). In 1980, for example, it killed an estimated 5 million children aged less than 5 – equivalent to one every six seconds (2). In addition, diarrhoea is a leading cause of malnutrition in childhood.

Eliminating diarrhoeal disease can be expensive largely because prevention depends on safe water supplies as well as improved sanitation and hygiene. Diarrhoeal diseases caused by bacteria, viruses and parasites are injurious but need not necessarily be lethal: death results mainly from the loss of essential water and electrolytes from the body and can often be prevented if the patient can be rehydrated promptly and effectively.

The time between the onset of diarrhoea and death is often short – a matter of few hours or at most a few days. In a poorly nourished and diseased population, by the time a severely dehydrated patient is admitted to hospital – assuming the family can afford the transportation and hospital care – it may already be too late for rehydration, even if given intravenously. In this situation, oral rehydration solution (ORS) – a mixture of salts, sugar, and water – has been a scientific breakthrough, and is now successfully used worldwide to treat diarrhoea. ORS acts to correct an electrolyte imbalance and replace lost fluids. In spite of the fact that this excellent treatment for diarrhoea is now widely

available, ORS is still used very little in countries where diarrhoea is a major health problem (3-5). There are probably two major reasons for this. The standard glucose-ORS does not reduce diarrhoea in terms of stool output or its duration (3,37). Thus ORS fails to convince mothers to continue using it. Also in some countries, even if packets of ORS are available, they may be prohibitively expensive.

During the last three decades ORS has been gradually improved and scientists have been trying to develop a cheaper, more easily prepared formula. Researchers at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) have developed a new rice-based ORS with distinct advantages over the WHO-recommended glucose-based ORS. In this new ORS, glucose or sucrose is replaced by rice powder (6).

Developing ORS

As long ago as 1949, scientists recommended a solution of salts and glucose in water as an orally administered treatment for diarrhoea (7-9). In 1953, ORS was successfully used to treat cholera in an epidemic in Calcutta, India (8), but it was not until 1964 that more interest was shown (10). Since 1968, the Cholera Research Laboratory (CRL), which subsequently became the ICDDR,B, has carried out many clinical trials as well as field research to test different formulae for ORS (11-14). These trials have improved ORS, with emphasis on its practical use and benefits as an oral treatment. Research in this field has shown that the coupled trans-

Correspondence and reprint requests should be addressed to: Hasan Shareef Ahmed.

port of glucose and sodium remains intact during acute diarrhoea, and that glucose carries water and sodium across the intestinal epithelium (15, 16). This glucose-mediated sodium transport is the basis of oral rehydration therapy (ORT).

The discovery that sodium transport and glucose transport in the small intestine are coupled, so that glucose facilitates the absorption of solutes and water, was described in the *Lancet* as potentially the most important medical advance of this century (17). Studies have shown that a solution of glucose and electrolytes administered orally can replace intravenous fluids for treating cholera, a disease which can cause severe purging. ORS has proved equally useful in treating enterotoxigenic *Escherichia coli* enteritis and other forms of infectious watery diarrhoea (18, 19).

Glucose is expensive and not easily available in many of the less developed countries where diarrhoea is most common. However sucrose, a major constituent of cane-sugar, a common crop in tropical countries, has proved to be a successful alternative in the ORS formula (12, 13). A solution of salt, cane-sugar, and water can be easily and cheaply prepared in the home and has been recommended worldwide by the World Health Organization (WHO).

The United Nations Children's Fund (UNICEF) have recommended an ORS formula of 3.5 g of sodium chloride, 2.5 g of sodium bicarbonate, 1.5 g of potassium chloride, and 20 g of glucose in one litre of clean drinking water. The salts are often available as dry packets and once dissolved in water should be consumed within 12 hours because of bacterial contamination.

In 1980, the ICDDR,B performed a clinical trial to examine the efficacy of ORS using common salt and molasses. Both the ingredients are commonly available in Bangladesh, where it is known as *lobon-gur* solution. The study was carried out on 50 adult patients with moderate dehydration due to diarrhoea of various causes (14). The results indicated that the *lobon-gur* solution was not only efficient in restoring lost fluids, but its taste was also acceptable. After further field research, this solution has been advocated by other institutions to treat mild or moderate dehydration when glucose or sucrose is not available. The composition currently re-

commended is a pinch of salt, a fistful of molasses, and a half litre of clean drinking water. This solution can be easily prepared at home.

Further research has continued to simplify the ORS formula, reduce its cost, and provide nourishment during diarrhoea. The use of chicken soup with glucose or cereal starch was suggested for treating diarrhoea in 1977 (20). The cereal starch is converted to glucose in the small intestine. In another study, the weak starch solution which forms when rice is boiled in water was found to be better in some respects than the glucose-electrolyte solution for treating diarrhoea (21). ORS made with this "rice water" was found to be more effective in reducing the number of stools than glucose ORS, while its lower osmolarity reduced the risk of osmotically induced diarrhoea and vomiting (21). However, its use in infantile gastroenteritis needs further research. Although there may be problems in administering electrolyte solutions to infants with diarrhoea and there are dangers of bacterial contamination, rice water is sterile when freshly prepared and is widely available wherever rice is a staple food. Rice water has also been used as a traditional treatment for diarrhoea in many parts of Asia (22), so it is likely to be the basis of an acceptable treatment. Several studies have shown rice water to be a superior treatment to glucose ORS (21-24). One of these studies was conducted in Thailand and had a success rate of 94% in patients treated with rice water and salt (24). These findings have stimulated a search for new and better oral rehydration solutions based on rice and other easily available and cheap dietary staples.

Soaked rice with added salt and sugar has been a traditional dietary treatment for diarrhoea in Bangladesh and many other developing countries for centuries (6). Until recently little attention has been paid to this fact by scientists, although there are biochemical reasons why it could be an effective treatment. The starch found in rice, cereals, and some fruits and vegetables consists of polymers of glucose. Even during diarrhoea the starch-digesting enzyme amylase is present in large amounts in the upper intestine, so starch is broken down rapidly into glucose, thereby providing carrier molecules where they are needed most, and without any of the "osmotic penalty" which results if the quantity of glucose is increased in ORS (25). The

result is the development of a new cereal-based ORS in which rice powder replaces glucose or sucrose (6,26).

Scientists at the ICDDR,B found that "the proportions of successfully treated patients in the rice powder group were 80% for cholera patients and 88% for *E. coli* patients - not different from those in patients receiving the sucrose-electrolyte solution" (6). In subsequent studies on adults it was demonstrated that rice ORS reduces stool output by 50%, reduces the need for ORS by 40%, and reduces vomiting by 60%. Rice ORS has three practical advantages. First, it is cheaper and is more readily available in poor households than glucose or sucrose. Secondly, it is a familiar food, so it may be more acceptable as a component of a treatment for diarrhoea. Thirdly, field studies have shown that rice ORS maintains and even improves nutritional status during illness (27). These studies suggest that rice ORS is an efficient and safe rehydration fluid which can be given orally during acute diarrhoea (6,27). Research is continuing at the ICDDR,B to examine whether rice ORS is as effective for treating infants as adults.

Composition and preparation

The composition of the rice ORS developed at the ICDDR,B is sodium chloride 3.5 g, sodium bicarbonate 2.5 g, potassium chloride 1.5 g, rice powder 50.0 g and a little more than 1.0

litre of clean drinking water. The rice powder is prepared by grinding dry rice and is packaged separately from the electrolytes. To prepare the solution, the rice powder is first dissolved in water and boiled for about 5 to 7 minutes to make a homogenous mixture. The solution must be stirred while being boiled otherwise rice flour may clump at the bottom of the pot. When the solution is cool, the electrolytes are added and mixed. Once prepared, this solution remains good for use in Bangladesh for up to 8-10 hours in summer and for 12-14 hours in winter. Rice ORS should be given to patients as long as diarrhoea lasts but plain water and food should also be given as usual.

The following table shows the composition of three oral rehydration solutions now commonly used in Bangladesh.

How it works

Rice starch is rapidly hydrolysed by pancreatic amylase to glucose, maltose, maltotriose, and branched dextrans (28). The oligosaccharides are further hydrolysed to glucose by the maltases of the brush border enterocytes (29). Even a one-month-old infant can digest and absorb a large amount of rice starch (30).

Rice starch contains two different polyglucoses, amylose and amylopectin. Rice contains 7-10% protein and negligible electrolytes (31). Rice protein contains glycine (30-36 mg/100 g of rice), an amino acid which has been shown to

COMPOSITION OF VARIOUS ORAL REHYDRATION SOLUTIONS (ORS)

Components	Rice-based ORS	WHO-recommended ORS	<i>Lobon-gur</i> ORS
Sodium chloride	3.5 g	3.5 g	A 3-finger pinch
Sodium bicarbonate	2.5 g	2.5 g	—
Potassium chloride	1.5 g	1.5 g	—
Rice powder	50.0 g	—	—
Glucose	—	20.0 g	—
Molasses	—	—	A fist-full
Clean drinking water	1.0 l	1.0 l	0.5 l

promote the transport of sodium from the intestinal lumen (32).

The digestion of rice powder in the intestinal lumen liberates glucose slowly without causing an osmolar load. It is possible therefore to give a greater quantity of rice powder without causing an osmolar drag of fluid from the vascular space into the gut lumen (6). Diarrhoea appears to have no effect on the intestinal enzymes which hydrolyse rice powder (6).

The effectiveness of rice ORS can be assessed by measuring the rate of purging, the rate of gain in body weight, serum specific gravity, urine output, and the post-hydrolysis sugar content of the stools.

Practical trials of rice ORS

In Calcutta, India, in a controlled trial, one of the first rice-based electrolyte solutions was evaluated in a group of infants and young children aged between 3 months and 5 years with moderate or severe dehydration due to acute diarrhoea. In this study, 50 g of precooked rice powder replaced 20 g of glucose in preparing one litre of solution. The results were compared with a matched control group receiving the glucose-electrolyte solution recommended by the WHO. The rice ORS was found to be more effective than the glucose ORS: there was an appreciably lower rate of stool output, a shorter duration of diarrhoea, and a smaller intake of ORS (26).

These findings have been confirmed, both in adults and in children with acute diarrhoea, at the ICDDR,B (6). In addition, rice ORS was found to correct an electrolyte abnormality, including both moderate and severe acidosis. The same study also found that treating diarrhoea with rice ORS required less supervision by the nursing staff and physicians than did the sucrose-electrolyte solution. Moreover, cholera patients with severe diarrhoea could eat a full meal of rice without adversely affecting the character of the stools.

Subsequent studies have shown that in patients with *V. cholerae* or *E. coli* diarrhoea, carbohydrate absorption is less hampered than the absorption of other nutrients. Even during infections with invasive organisms such as rotavirus and *Shigella*, the absorption of carbohydrate is not significantly impaired (33).

In another study of rice ORS in Calcutta, the control group received the standard WHO-recommended ORS with glucose. One of the two study groups received the same solution with added glycine, while the other received rice ORS in which 50 g of popped rice powder was used in each litre of rice ORS solution. Both experimental groups showed a significant reduction when compared with the control group as follows: in their stool output, by 49% and 50% respectively; in their mean duration of diarrhoea, by 30% in each group; and in the volume of ORS consumed, by 33% and 43% respectively. A series of animal and human studies are in progress to define the optimum composition of a 'super ORS' (34).

Another study at the ICDDR,B showed that even the highest concentration of rice powder so far tested in ORS (80 g/l) can be drunk by patients and is highly effective. At this concentration, rice ORS provides four times more energy than the standard glucose ORS (35).

The efficacy of rice ORS was calculated in another ICDDR,B study by giving two groups rice ORS or the WHO-recommended glucose ORS. Patients treated with rice ORS consumed 50% less solution than the group given the WHO-recommended ORS, and their stool output and vomiting were reduced by 50% and 75% respectively. The gain in body weight was similar in both groups. The energy balance during the first 24 hours was significantly higher in the rice ORS group. The development of an energy-dense ORS to provide extra energy during treatment for diarrhoea can serve as a tool for effectively interrupting the diarrhoea-malnutrition cycle (36), although the main energy source should be the usual diet.

In a study in Chandpur, Bangladesh, rural mothers were able, after proper training, to prepare rice-salt ORS quite easily and use it to treat diarrhoea. Mothers considered that this method would increase the use of ORT at home level (37). Rice ORS was also found to be more effective in a recent ICDDR,B field study which compares between WHO-recommended ORS and rice ORS (A. Bari, Personal Communication).

The studies described above indicate that rice ORS has some significant advantages over glucose or sucrose ORS, with no adverse effects noted so far. It provides more nutrients and

energy during illness and it reduces stool output, vomiting, and the duration of diarrhoea. Rice ORS appears to be superior to the extensively tested glucose-electrolyte solution, until now the most effective oral rehydration solution developed so far.

But rice ORS does have problems. Bacteria may grow quickly if the prepared solutions remain unused for a long time in a warm environment. At the ICDDR,B it was found that rice ORS, once prepared, remains good at ambient temperature for use for only between 8 and 12 hours.

Advantages

To sum up, rice ORS has the following advantages over other electrolyte solutions :

1. Rice is cheaper and more easily available than glucose or sucrose. It is consumed by 60% of the world's population as their dietary staple and this familiarity is likely to make it acceptable as a component of ORS.
2. Treating diarrhoea with rice ORS is safe. Since no adverse effects have yet been detected the patient can consume larger amounts of rice ORS than glucose ORS. It thus provides extra nutrition for malnourished patients.
3. In hospitals giving rice ORS, little supervision by nursing staff and physicians is required.
4. Even very young children can digest and absorb a large amount of rice starch, as amylase and most of the disaccharidases are fully developed at birth.
5. Treatment with rice ORS when compared with other forms of ORS shortens the duration of diarrhoea, reduces the volume of stool produced, reduces vomiting, and reduces the consumption of rehydration fluid.

Disadvantages

The few disadvantages of rice ORS – the reasons why it is not yet in mass use – can be summarised as follows :

1. To some patients rice ORS is hard to drink because it is a thick gruel, and patients often do not want to eat thick or solid food during

diarrhoea. There is a possibility then that some patients will not consume enough rice ORS to rehydrate sufficiently.

2. Bacterial growth and fermentation of the prepared solution may reduce its useful life to only a few hours, particularly in hot and humid conditions. Under the worst conditions, a rice-based oral solution may become useless after only 8 or 10 hours, compared with 12 hours for standard ORS.
3. Rice powder needs to be cooked before preparing the solution. Cooking may be a problem in some rural areas where fuel is in short supply.

Conclusion

Rice ORS is still undergoing clinical and field trials although the ICDDR,B has been using rice ORS in its diarrhoea treatment centre for the last two years. The further simplification of its formula is necessary so that people can make it easily at home and preserve it for a longer time once it has been prepared.

Acknowledgements

We would like to thank Mr. Ian Montagnes, Project Coordinator, International Rice Research Institute, Los Baños, Philippines for his editorial help and guidance. We also thank Mr. M. Shamsul Islam Khan, Head, Library and Publication Branch, ICDDR,B for encouraging us to write this review.

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