Editorial

ORS CONTROVERSIES AND PERSPECTIVES

ORS—Current Perspectives

A quarter century after .it was introduced to the world, ORT has indeed come a long way in a short time and is now at **a** turning point. Annually ORT saves over one million young lives a year(l). Thus, ORT is rightly considered the most important medical advance of this century(2) as it has revolutionized the treatment of diarrheal disease(3,4). Today, one in 3 children striken with diarrhea receive ORT at home resulting in the prevention of about 3000 child deaths each day. Appropriate and continued feeding during and after diarrhea can prevent malnutrition in a large number of children(l,5). Despite the propaganda for ORT, far often" it is ignored. Ironically even today more than 2 million under fives in the world's poorest neighborhoods still die every year of diarrheal dehydration or malnutrition if the episodes of diarrhea are recurrent or prolonged. In 90% patients with dehydration, it can reduce the hospital admission rate for treatment of diarrhea by atleast 50%(2,3), reduce diarrheal mortality and limit weight loss(3). In addition, ORT using the present ORS formulation is one of the least expensive health interventions(3).

Only one of ten diarrhea cases requires antibiotics as well as oral rehydration therapy. ORS sachets are widely available at no more than 10 cents (in India for approximately Rs. 5/-) and home remedies such as rice water, weak tea, butter milk or green coconut water can forestall most dehydration; yet drug treatment overwhelms ORS use in most countries. According to WHO more than $1 billion is spent each year in developing and developed countries alike on useless and often harmful antidiarrheal medicines(l).

The Oral Rehydration Solution

The glucose electrolyte solution recommended by WHO and UNICEF is prepared from a packaged mixture of glucose (20 g) and 3 salts, sodium chloride (3.5 g), sodium hydrogen carbonate (2.5 g) or more recently trisodium citrate dihydrate (2.9 g) and potassium chloride (1.5 g). This mixture (oral rehydration salt or ORS) is combined in one litre of potable water to prepafe oral rehydration solution. The molar concentration (osmolality) of the salts per litre in this ORS mixture is sodium (Na) 90 mMol, potassium (K) 20 mMol, chloride (Cl) 80 mMol, bicarbonate (HCO_3) 30 mMol, or trisodium citrate 10 mMol, and glucose 111 mMol, with the ratio of sodium to glucose not exceeding 1:1.4. This composition is based on the stool losses of sodium and other electrolytes and its similarity to plasma electrolytes. Glucose has been added as it helps in the reabsorption of sodium and water in the small intestine.

Limitations of the Present ORS Formulations

ORT with the present ORS formulations does not reduce the volume, frequency, or the duration of diarrhea(3,6). This

raises the practical problem of its acceptance since **a** major concern of mothers and health workers during diarrhea is to reduce the frequency and volume of the child's stool. This leads to a persistent desire to use anti-diarrheal drugs.

Main Issues and Controversies

In the area of ORT, the major issues or controversies- are related to the ORS and they include: (i) composition with special reference to sodium and glucose content and osmolality, *(ii)* the packaging and labelling, (*iii*) stability on storage, (iv) the effectiveness of the standard ORS versus various commercial preparations, (v) modifications by additives, coloring and flavoring agents, *(vi)* ability of mothers to learn, prepare and practice ORT at domestic level using household measures for water and ingredients, (vii) limitations of ORT, *(viii)* improved ORS formulations, cereal/food based or with chemical additives, (a) suitable fluids for different states of dehydration, *i.e.,* for rehydration and maintenance phase, *(x)* feeding during diarrhea, *(xi)* use of antidiarrheals, antimotility drugs, antiemetics, antibiotics and various combinations of individual drugs from above group; and *(xii)* health education, sanitation, training on ORT. A few of these merit closer scrutiny.

ORS Packets of Composition Different From What WHO Recommends

In India, over 40 different brands of packets are marketed and used. This has complicated the task of providing safe and effective oral rehydration to children with diarrhea. The principal concerns are related to the deviations in the concentration of glucose and sodium from that recommended by the WHO, the varying instructions for mixing and the final preparation of ORS solution.

Sodium Concentration

There is **a** general belief amongst researchers(7,8) that the WHO ORS (containing 90 mMol sodium) may be suitable only during the rehydration period and may be associated with risk of hypernatremia particularly when used in newborn period or young infants with immature kidney functions as well as during maintenance phase, when the stool sodium losses are less than those during the acute or rehydration phase.

There have been paucity of studies with standard sodium of 90 mMol/litre solution in small infants and newborn because of the potential risk of hypernatremia. However, the specific related studies(9-ll) did not reveal any long lasting hypernatremia or did not require any additional corrective measure. In order to eliminate the risk of hypernatremia using the standard WHO 90 mMol sodium Sol, the alternatives suggested are feeding the child with 2:1 of this ORS and breast milk, alternate feeds of this ORS with plain water or diluting this ORS in one and half litre of water instead of the recommended one litre of water. Whichever option is selected, it is important to remember that use of additional plain water is mandatory if standard 90 mmol sodium ORS is used in neonates and young infants to reduce the solute load. Further, during maintenance phase, the ORS intake should not exceed the stool losses(3,4,7,ll). Commercially over 15 ORS packets with low sodium concentrations ranging from 25 mMol to 60 mMol/litre are available. However, all these preparations contain more than the recommended glucose of **111** mMol/L, thereby grossly

deviating from the sodium : glucose ratio of 1:1:85 and are, therefore, not suitable.

Glucose Concentration

The optimal sodium and water reabsorption occurs in the gut lumen in presence of glucose. The recommended glucose is 20 g per liter in the form of monohydrate or dihydrate. Although the optimal sodium to glucose ratio has been suggested as 1:1.4, recently this ratio has been allowed to be raised to 1:1.85 thereby allowing low sodium with normal 2 g% glucose(12). Exceeding this concentration of 2 g% disturbs the ratio, renders the solution hyperosmolar and induces more diarrhea(3,6). In homemade solutions, the glucose is replaced by double amount (40 g) of sucrose as the latter on hydrolysis yields equal concentrations of glucose and galactose of 20g. each. Further, this glucose in improved or super ORS is replaced by a complex carbohydrate like cereal, the principal being that cereal on intraluminal digestion slowly releases glucose, thus making the glucose molecule available for the sodium ATpase pump at the intestinal brush border epithelium. The cereal based solution is hyposmolar and cereals also give additional calories to ORS. Commercially over 25-30 ORS formulas with appropriate to high glucose with varying contents of glucose ranging from 111 mMol/L to 414 mMol/L are available, thus rendering the formula hyperosmolar and aggravating diarrhea.

Stability of ORS Formulas and the Use of Trisodium Citrate

When ORS composition was formulated, sodium bicarbonate was included. However, it was realized that ORS containing sodium bicarbonate had problems with stability under the conditions of high humidity and heat found in many developing countries. Hence, sodium citrate was tried in place of sodium bicarbonate. In 8 studies in adults and older children and 5 studies in children under 3 years, the ORS citrate proved as effective as bicarbonate except that it had a longer shelf life. Inspite of its superiority in shelf life, the high cost restricts its use in developing countries where bicarbonate is still being used(4,5).

Commercial Formulas

Commercially, various ORS packets are available(13,14). Not only these packets differ in composition, but they differ in pack size, description of the contents, instructions for the preparation of oral rehydration solution and the last but not the least the price of each packet. The main controversy is, however, on the sodium and glucose content and their mutual ratio in the packet. The standard ORS packets contain the sodium of 90 mMol/L and glucose of 111 mMol/L, as per the WHO/ UNICEF$_V$ recommendations. The packets belonging to this group are Coslyte (CEF PH Ltd), Peditral 90 (Searle), Electrobion (Merc), Winhydran (Winthrop), Punarjal (FDC), Prolyte (Cipla), Emlyte (MM Labs) and Speedoral (Roussels WB). Any of these packets can be used for rehydration as well as during maintenance phase. The second group contains ORS preparations with low sodium formula ranging from 50 to 90, but with a proportion of glucose higher than the recommended and thus exceeding the sodium glucose ratio of 1:1.85. The preparations in this group are Peditral (Sparle), New Electral (ORSA-IP-FDC).

Recently, 2 rice based ORS packets Cerelyte (Raptakos Brett Ltd), and Ricelyte (FDC) are also available. ORS preparations with varied compositions have created con-

fusion in the doctors as well as consumers. The doctor who prescribes has no knowledge of the correct ORS packet and prescribes that packet which he has known because of advertisement. As these packets are available at chemists without prescription, the consumer/the patient purchases what the chemist recommends to him, the recommendation obviously depending on the commission available from the pharmaceutical firm. Thus, it is possible that due to multiple formulas, those with low sodium may be used for adults and that with normal sodium may be used for a newborn or an infant. To add to this, there has been controversial opinion amongst pediatricians on the recommendation of low sodium and normal sodium for appropriate age, *i.e.,* in favor of different formulas. The pharmaceutical industry has taken the advantage of this controversy and manufactured ORS with different compositions each varying slightly from the other. There has been debate on these controversies amongst the clinicians. To eliminate these controversies, the Government of India has given recommendations(12) which relate to various aspects of ORS. According to this, the ORS should have in mMol/L sodium between 60-90, potassium 15-25, chloride 50-80, bicarbonate 25-35 or citrate 8-12 and glucose 111 with total osmolality ranging from 200-330 and glucose/sodium ratio upto 1.85. Further, each packet must have logo suggested by the Government of India, and instructions for mixing and preparing both in written and graphic form.

Improved ORS Formula

The major limitations of WHO ORS has led to search of alternatives which if successfully evolved should have the benefits of ORS with the effect like antidiarrheal drug. Two basic approaches have been suggested(5): (*i)* cereal based(2,15-20) or (*ii*) chemical based(21-33). In the cereal based ORS, rice and many other cereals have been tried, and best results have been available with rice based ORS due to slow release of glucose in the intestine when the rice is hydrolysed. In chemical based, derivatives of proteins, fats, carbohydrates in simple forms as aminoacids have been tried. Besides being expensive, they are not very practical[1] for domestic use. Today, after many trials, rice based ORS has been proved to be the best(3,17).

Almost all controversies are getting resolved. Realization must be there that ORT is no single bullet for all issues of case management or means to cure to achieve everything. It is just a powerful means to cure and prevent rehydration. The prevention and control of diarrheal disease in children is a major challenge to health agencies of developing countries. There are unfortunately no instant remedies or short cuts and magic solutions. The problem will not be solved with crisis management strategies alone. It will be met with only if basic factors involved are also tackled adequately.

Diarrhea Treatment and Training Units (DTTU)

Realizing the need of correct treatment of diarrheal diseases and the training of medical and paramedical staff, the Government of India has established DTTUs in the public hospitals of cities and district places all over India. In addition to the treatment and training, these centres also compile statistical information and thus serve as nodal referral centre for diarrheal diseases. Such centres are already existing in Bombay, Delhi, Madras, Bangalore, Calcutta, *etc.*

Research on the various aspects of ORS will continue, but the controversies should not come in the way of successful implementation. The use of ORS both in the case management and at the public health level must meet the UNICEF goals of use of achievements of 80% ORT use for diarrheal diseases by 1995.

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