Selected Summaries

Search For Super ORS

[International Study Group of Reduced Osmolarity ORS Solutions. Multicentre evaluation of reduced osmolarity oral rehydration salts solution. Lancet 1995, 345 : 282-285.]

This multicentre study was designed to compare the clinical efficacy of reduced-osmolarity ORS and standard ORS solutions in children with acute diarrhea. The double-blind trial was conducted in four developing countries Brazil, India, Mexico and Peru. Four hundred and forty seven boys aged 1-24 months, admitted to hospitals with acute diarrhea and signs of dehydration, were randomly assigned either standard ORS (n=223; sodium 60 mmol, potassium 20 mmol, chloride 50 mmol, citrate 10 mmol, glucose 84 mmol arid osmolarity 224 mmol/L solution. Total stool output was 39% greater, total ORS intake 18% greater, and duration of diarrhea 22% longer in the standard ORS group than in the reduced-osmolarity ORS group. The risk of requiring intravenous infusion after completion of the initial oral rehydration was greater in children given standard ORS solution than in those given reduced-osmolarity ORS solution in three of the four countries (all-country relative risk 1.4). This relative risk (RR) was significantly increased only in non-breastfed children (RR-2.0 $p<0.05$). In breastfed children, the RR of requiring intravenous infusion was not affected by the ORS solution (RR-0.9). The mean sodium concentration 24 h after admission was significantly lower in the reduced-osmolarity ORS group than in the standard ORS group (135 vs 138 rnmol/L; $p<0.01$).

It was concluded that treatment with reduced-osmolarity ORS solution decreased mean stool output and mean duration of diarrhea in comparison to the standard ORS solution. These findings support the use of reduced-osmolarity ORS solution in children with acute non-cholera diarrhea in developing countries. However, further studies are needed to find the best formulation and whether such a solution would be satisfactory for the treatment of cholera.

[Sack RB, Castrellon J, Sera ED, *Goepp J, Burns B, Croll J, Tseng P, Reid R, Carrizo H, Santpsham M. Hydrolyzed lactalbumin-based' oral rehydration solution for acute diarrhea in infants. Ada Pediatr 1994, 83: 819-824.]*

Studies in animals and humans have shown that water soluble organic molecules, such as amino acids (glycine), dipeptides and tripeptide, enhance the absorption of sodium and water in the small intestine. Alanine-bases ORS has also been found to significantly reduce stool output in older children and adults with cholera. Further studies have shown that hydrolyzed whey protein containing amino acids of different amounts improved sodium absorption more than an equivalent mixture of amino acids and thereby decreased stool losses. The present study was, therefore, designed to evaluate in infants with acute diarrhea, the safety and efficacy of

three oral rehydration solutions (ORS) which had the same concentrations of electrolytes (with sodium 60 mmol/l, potassium 20 mmol/l, chloride 50 mmol/1 but different substracts of proteins and carbohydrates. One solution (LAD-ORS) contained hydrolyzed lactalbumin (LAD) with maltodextrin and sucrose (LAD 4 g/l, maltodextrin 60 g/l, sucrose 20 g/1, osmolarity 302 mosm/1 and energy 336 kcal/1), a second (MS-ORS) was identical but without LAD (Osmolarity 298 mosm/1, energy 320 kcal/1), and a third (G-ORS) was glucose ORS (glucose 20 g/1, osmolarity 260 mosm/1, energy 80 kcal/1). The three solutions were compared in a double-blind, randomized trial in 74 hospitalized well-nourished children in Panama and the United States.

All three oral rehydration solutions were equally efficacious and safe in these children, 54% of whom were infected with rotavirus. There was no suggestion that hydrolyzed lactalbumin or maltodextrin provided any advantage over glucose-ORS in terms of stool output or in duration of diarrhea. The average weight gain from admission to discharge was greater in LAD-ORS group and least in the G-ORS group. The group receiving MS-ORS was intermediate in weight gain and not significantly different from the G-ORS group. Only at the time of resolution was the weight gain of the LAD-ORS group significantly greater than that of MS-ORS group. At the two week follow up, however, there was no significant difference between the three groups when compared to discharge weight. An increase in weight gain temporarily during the therapy could not be readily explained. It was concluded that all the three solutions are equally effective in the therapy of acute dehydrating diarrhea in infants.

Comments

Oral rehydration therapy (ORT) with standard glucose electrolyte ORS (WHO/Unicef) has proved safe and effective for treating patients of all ages, suffering from dehydration due to diarrhea of any etiology provided they are able to drink and the dehydration is not severe. However, the primary concern of the parents, which is often shared by pediatricians, is to see that diarrhea stops. This leads to a persistent desire to use antidiarrheal drugs. Therefore, an 'improved ORS' is desired which: *(a)* reduces stool volume, *(b)* shortens duration of diarrhea, (c) reduces the failure rate of ORT in the presence of high purging, and *(d)* provides nutritional benefit by permitting early and effective feeding(l). As early as 1970 Nalin *et al.(2)* observed a significant reduction in stool volume and duration of diarrhea in patients suffering from acute watery diarrhea due to Vibrio cholera 01 or enterotoxigenic Escherichia coli by addition of glycine to WHO-ORS. However, later clinical trials did not support this view. During the last two decades efficacy and use of other formulations containing L-alanine, L-glutamine, rice based and maltodextrin based ORS formulations have been evaluated. Results of these clinical trials have concluded that rice based ORS (50 g/1) is superior to WHO-ORS for patients with cholera. However, the WHO-ORS is equally effective as rice based ORS for treating children with acute non-cholera diarrhea when feeding is resumed promptly following rehydration, as has been consistently recommended by WHO. Maltodextrin-based ORS formula-

tions (50 g/1) and WHO-ORS appear to be equally effective for treating children with acute non-cholera diarrhea. Aminoacid containing ORS formulations have been shown to be beneficial only in cholera and are not recommended for either non-cholera diarrhea or cholera since they are more expensive. Even for cholera cases, they have no advantage over rice based ORS(3). It seems that most of these formulations have been only partly successful in reducing the failure rate of ORT with WHO-ORS in the presence of high purging, *e.g.,* cholera. However, there has been no significant breakthrough in identifying a 'Super ORS' for children with non-cholera diarrhea.

Sack *et al.* (Summary 2), have carried the search one step further by evaluating hydrolyzed lactalbumin-based oral rehydration solution (LAD-ORS) specifically in acute noncholera diarrhea in children. LAD-ORS was expected to fare better than amino acid based ORS but like the earlier studies no beneficial effect over WHO-ORS was observed with this new formulation. It is possible that LAD-ORS used in this study had a higher osmolarity (approximately 40 mosm/1) than G-ORS which could have masked a possible reduction in stool volume. Greater energy offered by LAD-ORS (336 Kcal/l) may have an apparent however, benefit, particularly in malnourished children. However, since the study population included all well nourished children, this aspect has not been explored by the authors. Moreover, since the weight gain with LAD-ORS was temporary and no significant difference was noted in the discharge weight, the benefit does not seem to be real.

Lately the focus has shifted to a low osmolarity ORS with some modifications in glucose and sodium contents(4,5) or even offering a diluted WHO-ORS(6). This approach has been guided by the assumption that standard ORS (osmolarity 311 mosm/1), being slightly hypertonic, causes a net flow of water from extracellular fluid in to the gut, which in some children may not be fully absorbed probably because of transiently impaired absorption of glucose.

The results of the International Study Group on Reduced Osmolarity ORS Solutions (Summary 1) are quite encouraging. However, these need to interpreted very carefully since there has been no dramatic reduction in the duration of diarrhea. In standard ORS group, the duration of diarrhea ranged from 37-46 hours in comparison to reduced osmolarity group in whom it ranged from 30-39 hours. The difference even though statistically significant may not practically offer an appreciable clinical advantage. The other important observation in this study is that the mean serum sodium cocentration at 24 hours was significantly lower ($p<0.02$) in children receiving the reduced osmolarity ORS but the range of serum sodium levels did not exceed the normal limits even in the standard ORS group. This observation indirectly addresses the concern of many of us who prefer a lower sodium concentration of ORS (as has been advocated in developed countries where most of the young children are well nourished and fewer are breastfed) because of risk of hypernatremia with standard ORS solution. It is also reassuring that the relative risk of development or worsening of hyponatremia was not increased in children given the reduced osmolarity ORS solution.

Hypertonicity of standard ORS solution, which is believed to be responsible for osmotic diarrhea in some young children, can be easily and reliably avoided by lowering the osmolarity of the ORS solution as has been highlighted by this study. However, the adverse effect of standard ORS can also be prevented by giving additional water to children treated with standard ORS solution and breastfeeding in younger infants. Therefore, one wonders whether reduced osmolarity ORS, with a marginal reduction in duration of diarrhea by couple of hours, qualifies to be an 'improved ORS.'

The search for a 'super ORS' is still on. At the moment the standard glucose electrolyte solution remains the most economic, safe and effective solution for oral rehydration in non-cholera diarrhea in children.

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