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Reduced-Osmolarity Oral Rehydration Salts Solution Multicentre Trial : Implications for National Policy

Rajiv Bahl, Nita Bhandari and M.K. Bhan

ICMR Advanced Centre of Diarrhoeal Diseases Reseach, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi

Abstract. World Health Organization (WHO) recommended standard ORS solution has sodium (90 mmol/L) and glucose (111 mmol/L) almost in the ratio of 1 : 1 and a total osmolarity of 311 mmol/L. There are concerns that the sodium or glucose concentration and the overall osmolarity in the formulation is not appropriate. Therefore, the efficacy of standard and reduced-osmolarity ORS solutions in young children with acute diarrhea was evaluated in a recent WHO supervised multicentre trial conducted in India (New Delhi), Brazil, Mexico and Peru. The implications of trial results are discussed.

In non-cholera diarrhea, both the standard and reduced osmolarity ORS solutions were effective in achieving clinical rehydration. The stool output was 39% higher in the standard ORS solution group as compared to the reduced-osmolarity ORS solution group. The duration of diarrhea was 22% higher in the standard ORS solution group. The risk of requiring supplementary intravenous infusion was increased in children treated with standard ORS solution [relative risk 1.4 (0.9-2.4)]; this benefit was not observed in Indian patients due to high breast feeding rate.

The mean sodium concentration at 24 hours after admission was lower in the reduced osmolarity ORS solution group [135 (134-136) vs 138 (136-139), $p < 0.01$). The low osmolarity ORS deserves to be evaluated in adult cholera to determine its efficacy and any excess hyponatreamia. Meanwhile, it is reassuring that the WHO formulation was effective and its use was not associated with hypenatremia even in young children. Efforts must continue to be made to promote WHO-ORS while research to improve it further is welcome. **(Indian J Pediatr 1996; 63 : 473-476)**

Key words : *ORS solution; Hypenatremia; Hyponatreamia.*

The effectiveness of the oral rehydration salts (ORS) solution in diarrhea depends on the coupled active transport of sodium ions and glucose across the brush border membranes of enterocytes, which result in passive absorption of water and other electrolytes[1]. World Health Organization (WHO) recommended standard ORS solution has sodium (90 mmol/L) and glucose (111 mmol/L) almost in the ratio of 1 : 1, and a total osmolarity of 311 mmol/L. Some recent studies have reported that water absorption from solutions with osmolarity between 200 and 250 mmol/L is better than that from those isotonic with plasma[2-5]. A study from Egypt found that some children have glucose malabsorption and these children may benefit from reduction in the concentration of glucose in standard ORS solution[6]. Based on these studies it has been suggested that the sodium and glucose concentration in

Reprint requests: Dr. M.K. Bhan, Additional Professor, Division of Pediatric Gastroenterology and Nutrition, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi-110 029

TABLE 1. Composition of ORS solutions used in the multicentre trial

	Reduced-osmolarity ORS (mmol/L)	Standard ORS (mmol/L)
Glucose	84	111
Sodium	60	90
Potassium	20	20
Chloride	50	80
Citrate	10	10
Osmolarity	224	311

Reference : International Study Group on Reduced Osmolarity ORS solutions[7].

standard ORS solution should be reduced which would also decrease its total osmolarity.

The efficacy of standard and reduced-osmolarity ORS solutions in young children with acute diarrhea was evaluated in a recent multicentre trial conducted in India (New Delhi), Brazil, Mexico and Peru[7]. The composition of the two formulations is given in Table 1. Essentially, the reduced-osmolarity ORS solution had less glucose (84 mmol/L) and sodium (60 mmol/L) than the standard ORS solution. The main outcomes for which the two solutions were compared were the stool output and duration of diarrhea. The subjects were boys aged 1-24 months, who had acute non-cholera diarrhea with signs of dehydration, and with no visible blood in stools.

SALIENT FINDINGS OF THE MULTICENTRE TRIAL

Although both the solutions were effective in the treatment of dehydration, the use of reduced-osmolarity ORS solution resulted in decreased stool output, duration of diarrhea and need for supplementary intravenous infusion. The findings of the trial are summarized in Table 2.

The study has several important messages. Firstly, standard ORS solution was effective in rehydrating patients with acute diarrhea without any additional risk of hypernatremia, in patients enrolled in India. This should reassure physicians who are concerned about hypernatremia when using standard ORS solution. This trial is therefore, another endorsement of the safety and efficacy of standard ORS solution in our country. Secondly, decreasing the osmolarity of standard ORS solution significantly improved its clinical performance in the treatment of acute non-cholera diarrhea with dehydration in children. These benefits were larger in non-breastfed children.

SHOULD THE COMPOSITION OF STANDARD ORS SOLUTION BE CHANGED?

Is the size of the benefit large enough? In the multicentre trial subjects with non-cholera diarrhea, the use of reduced-osmolarity ORS solution resulted in about one-third reduction in stool output and one-fifth reduction in diarrheal duration as compared to standard ORS solution. In countries except India, the need for supplementary intravenous infusion was significantly decreased in children treated with reduced-osmolarity ORS solution; this decrease may have been due to the low breast feeding rates in the other centres. Therefore, the advantages of reduced-osmolarity ORS solution in comparison to standard ORS solution offer a distinct but modest clinical benefit.

Some of the previous studies have suggested that the use of standard ORS in newborn infants may carry a higher risk of

TABLE 2. Results of the multicentre trial of reduced-osmolarity ORS solution in non-cholera diarrhea in children

- Both the standard and reduced-osmolarity ORS solutions were effective in achieving clinical rehydration.
- The stool output was 39% higher in the standard ORS solution group as compared to the reduced-osmolarity ORS solution group.
- The duration of diarrhea was 22% higher in the standard ORS solution group.
- The risk of requiring supplementary intravenous infusion was increased in children treated with standard ORS solution in all centres [relative risk 1.4 (0.9-2.4)]. Among breastfed children, this risk was not affected by the type of ORS solution given [0.9 (0.4-2.0)]; while among the non-breastfed, it was significantly higher in the standard ORS solution group [2.0 (1.0-3.8), $p < 0.05$]. In individual centres, this risk was increased in children treated with standard ORS solution in Brazil, Mexico, and in Peru but not in India [0.6 (0.3-1.4)].
- The mean sodium concentration at 24 hours after admission was lower in the reduced-osmolarity ORS solution group [135 (134-136) vs 138 (136-139), $p < 0.01$]. This difference, although statistically significant, does not seem to be clinically important as the proportion of subjects with hyponatremia or hypernatremia were similar in the two groups.
- The proportion of children with hyponatremia during the first 24 hours of the study was slightly higher in children receiving standard ORS solution [1.3 (0.7-2.2)].

hypernatremia than formulations with lower sodium content[8] when water is not regularly given in between offerings of ORS but several other reports have suggested that if used according to guidelines, standard ORS is safe and efficacious at all ages[9]. Low osmolarity ORS would also address this concern among the community of physicians.

On the other hand, there is greater consensus that decreasing the osmolarity of standard ORS would render it safer and more efficacious for the prescription of diarrhea in the malnourished[10].

Will reduced-osmolarity ORS solution be effective in cholera? Reduced-osmolarity ORS solution has not been well evaluated in adult cholera. To contemplate a change from standard to reduced-osmolarity ORS solution, the modified ORS solution should preferably be effective in both cholera and non-cholera diarrhea so that a single formulation can be recommended. Definitive studies to examine the efficacy of reduced-osmolarity ORS solution in rehydrating patients with cholera are required; of particular concern is to ensure that it does not entail an additional risk of hyponatremia. If these trials show that reduced-osmolarity ORS solution is at least as effective as standard ORS solution in patients with cholera, it would be feasible to recommend it as the only kind of ORS solution to be used. However, if reduced-osmolarity ORS solution is less efficacious in cholera, or leads to more symptomatic hyponatremia, then the case to change the ORS solution composition will be weaker. The options in

that eventuality would be either to continue with standard ORS solution only, or to have different formulations for cholera and non-cholera diarrhea; the latter is difficult to adopt.

Conclusions

Standard ORS solution is an effective treatment for dehydration and used correctly, it should not involve any additional risk of hypernatremia in children with diarrhea of any severity. The current efforts should be directed to improve its use rates in the national programme with vigour and determination. The final decision on whether a change from the current WHO ORS to reduced-osmolarity ORS solution must await more experience of the performance of the latter in patients with cholera.

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