ORS as compared to the standard glucose ORS in children and adults with cholera diarrhoea.[1] In the present study the initial 24-hour stool output was only 14% less in the resistant starch ORS group as compared to the standard glucose ORS group. This may well be because all the patients in this study were started on a rice-based diet promptly after rehydration in contrast to the earlier studies with rice-based ORS where early feeding was not routinely recommended.

Routine administration of antimicrobials at the beginning of the illness has been found to decrease the duration of illness to less than 48 hours and reduce stool output during the latter part of the illness. The benefits of the resistant starch solution during the later period may not have been so marked if antimicrobials had been administered at the time of enrolment and not after 24 hours. However, the study size was not adequate to give a precise estimate of the differences.

The use of short chain fatty acids to stimulate absorption of water and electrolytes in the colon during diarrhoea is important and needs to be evaluated further in a larger number of subjects.

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Efficacy of monovalent human rotavirus vaccine 89-12 in infants

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SUMMARY

Rotavirus is a major cause of acute gastroenteritis and the commonest cause of severe dehydrating diarrhoea in infants all over the world. This randomized, placebo-controlled, double-blind multicentric trial aimed to assess the safety, immunogenicity and efficacy of a live oral monovalent vaccine 89-12.[1] 89-12 is an attenuated G1 (P8) human isolate originally obtained from a rotavirus-infected infant in Cincinnati, USA. The basis for selecting this isolate was that many reports have documented the protective effects of natural infections with rotavirus subtype 89-12 against subsequent rotavirus disease and so vaccines that more closely mimic human infection would provide greater protection.

This study included 215 healthy infants between 10 and 16 weeks of age; 213 of them received an oral dose of 1 ml of vaccine (1×10^{-5} pfu) or placebo. Two such doses of vaccine or placebo were given at an interval of 6–10 weeks. They were then followed up for one rotavirus season. Immune response to rotavirus was assessed by serum and stool IgA and serum 89-12 neutralizing antibodies. The primary outcome variable (protection from rotavirus disease) was evaluated by comparing the frequencies of rotavirus gastroenteritis in an intention-to-treat analysis.

Immune response was detected in 94.4% of vaccinees. Rotavirus disease occurred in 18 of 107 placebo recipients and 2 of 108 vaccine recipients (vaccine efficacy 89%, 95% CI 65.4%–94.6%). Ten infants in the placebo group but none in the vaccine group presented for medical care. Adverse reactions were minimal, occurring only in the form of mild fever in the vaccine group (in 19% of the vaccine group and 5% of the placebo group).

COMMENT

The 89-12 rotavirus vaccine was found to be safe and immunogenic and provided a high degree of protection against rotavirus disease. The 89-12 vaccine contains only one strain and the protection offered is quite high (89%) as compared to the tetravalent rhesus rotavirus reassortant vaccine whose protection ranged from 49% in the largest American study to 68% in a Finnish study.[1,2] The immunogenicity of the vaccine was also high; 94.4% of vaccine recipients responded to vaccination as shown by serum rotavirus-specific IgA (91.4%) or neutralizing antibody (69.2%) to the G1 rotavirus strain 89-12. The immunogenicity of the tetravalent reassortant vaccine was also found to be similar in previous studies (approximately 90%)[2,3] but only 28%–31% of participants in those studies developed neutralizing antibodies to any of the four most common human serotypes G1–G4 (the most commonly circulating serotypes). The major immune response was to rhesus rotavirus. However, the correlation between serum neutralizing antibody levels and clinical protection is yet to be established and so the differences in the immune responses should be interpreted with caution.

The vaccine appears safe. Like the tetravalent vaccine, it causes mild fever (19.4%), with an incidence similar to that in the American and Finnish studies. Other side-effects are comparable to the placebo group. A potential concern is that the live vaccine virus may revert to a virulent form during replication in infected infants. Studies of nucleotide sequences are being done to compare the gene sequences in the vaccine preparation with those of unpassaged 89-12 virus and 89-12 isolates shed by vaccinated infants.

The authors concluded that the use of an attenuated human strain rather than animal rotaviruses may offer better protection because it is more closely related to human strains. Also, the use of only one strain and two doses may reduce the cost.

In India, rotavirus is detected in 5%–15% of infants with mild diarrhoea, and in 20%–40% of children with severe diarrhoea. The G serotype 9 is an important cause which is not included in the tetravalent vaccine.[3] Limited studies in developing countries sug-

gest lower vaccine efficacy, though the dose used was 10^{-4}, making a direct comparison difficult.[5,6] The postulated explanations for decreased efficacy of the tetravalent vaccine in developing countries include concurrent administration of oral polio vaccine, presence of other enteric viruses, infection with other rotavirus serotypes, micronutrient malnutrition and presence of other enteric infections.

A cause for concern are the reports of intussusception during the first few weeks after administration of the licensed tetravalent vaccine (RRV-TV). The Centers for Disease Control (CDC) have received 23 reports of intussusception after rotavirus vaccination.[6] The American Academy of Pediatrics has therefore temporarily suspended rotavirus vaccination till the results of an ongoing case–control study on intussusception after rotavirus vaccination being conducted by the CDC, are available.

The need for an effective and safe rotavirus vaccine persists. Whether a monovalent human rotavirus vaccine is better than the tetravalent rhesus vaccine needs further studies. The reports of intussusception with the rhesus vaccine have led to suspension of rotavirus vaccination and we need to wait for the CDC trial results before any firm recommendations can be made.

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