

MODERN PHARMACOTHERAPY OF ACUTE DIARRHEA

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Mortality from acute diarrhea is overall globally declining but remains high. Most estimates have diarrhea as the second cause of childhood mortality, with 18% of the 10.6 million yearly deaths in children younger than age 5 years.

Despite a progressive reduction in global diarrheal disease mortality over the past 2 decades, diarrhea morbidity in published reports from 1990-2000 slightly increased worldwide compared with previous reports. The vast majority of diarrhea-associated infant deaths were reported in 2005-2007, with 86% of deaths occurring among low-birthweight (< 2500 g) infants.

Furthermore, in countries in which the toll of diarrhea is highest, poverty also adds an enormous additional burden, and long-term consequences of the vicious cycle of enteric infections, diarrhea, and malnutrition are devastating.

Viral diarrhea is most common in young children. Rotavirus and adenovirus are particularly prevalent in children younger than 2 years. Astrovirus and norovirus usually infect children younger than 5 years. *Yersinia enterocolitis* typically infects children younger than 1 year, and the *Aeromonas* organism is a significant cause of diarrhea in young children.

Pharmacotherapy of dehydration due to diarrhea includes the following:

Minimal or no dehydration: rehydration therapy - not applicable. Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode.

Mild-to-moderate dehydration: rehydration therapy - oral rehydration solution (50-100 mL/kg over 3-4 h). Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode.

Severe dehydration: rehydration therapy - intravenous lactated Ringer solution or normal saline (20 mL/kg until perfusion and mental status improve), followed by

100 mL/kg oral rehydration solution over 4 hours or 5% dextrose (half normal saline) intravenously at twice maintenance fluid rates. Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode. If unable to drink, administer through nasogastric tube or intravenously administer 5% dextrose (one fourth normal saline) with 20 mEq/L potassium chloride.

Not all commercial oral rehydration therapy formulas promote optimal absorption of electrolytes, water, and nutrients. The ideal solution has a low osmolarity (210-250) and a sodium content of 50-60 mmol/L. Administer maintenance fluids plus replacement of losses. Administer small amounts of fluid at frequent intervals to minimize discomfort and vomiting. Oral rehydration is now universally recommended to be completed within 4 hours.

The following probiotics showed benefit in treatment of acute diarrhea in meta-analyses of randomized controlled trials: *Lactobacillus GG* (I, A) and *S. boulardii* (II, B).

The addition of zinc to oral rehydration solution has been proven effective in children with acute diarrhea in developing countries and is recommended by the World Health Organisation.

At completion of hydration, resumption of feeding is strongly recommended. In fact, many studies convincingly demonstrate that early refeeding hastens recovery. Also, robust evidence suggests that, in the vast majority of episodes of acute diarrhea, refeeding can be accomplished without the use of any special (eg, lactose-free or soy-based) formulas.

Clinical trials found that the vaccines prevented 74-78% of all rotavirus gastroenteritis cases, nearly all severe rotavirus gastroenteritis cases, and nearly all hospitalizations. Rotarix protects against rotavirus gastroenteritis caused by G1, G3, G4, and G9 strains and is administered as a 2-dose series in infants aged 6-24 wk.

With the help of vaccination and early started rehydration therapy it is possible to reduce mortality and to control the morbidity level. Of course there are many other issues such as quality of drinking water in developing countries and its supply to population which could be improved as well.