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Racecadotril

A Viewpoint by Herbert L. DuPont

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One of the great advancements in medical care has been the development of oral rehydration treatment (ORT) for the management of dehydrating diarrhoea. When properly used, ORT has reduced fatalities among children with diarrhoea in developing countries. ORT remains the mainstay of therapy for infants and children in developing countries, in any patient with the dehydrating form of diarrhoea and for all elderly patients with diarrhoea. Symptomatic therapy is an important addition to ORT for the treatment of older children and adults with nondehydrating, nondysenteric (nonbloody) diarrhoea, particularly in industrialised countries where lethal effects of diarrhoea (outside the elderly or immunocompromised) are unusual. These drugs can be used to return patients sooner to work or to school and they may improve the quality of life while on business or leisure trips.

Loperamide has been the standard symptomatic drug for therapy of acute diarrhoea. It is inexpensive and highly effective in reducing diarrhoea by up to 80% compared with untreated or placebo-treated subjects. While the drug has weak antisecretory effects, the major antidiarrhoeal mechanism involves inhibition of intestinal motility. Loperamide is not ideal in that on rare occasions it will worsen certain forms of invasive bacterial diarrhoea and it may produce post-treatment constipation.

The major mechanism of acute infectious diarrhoea is intestinal electrolyte and fluid loss mediated by microbial enterotoxins or tissue cytokines. A number of antisecretory drugs have been examined as therapeutic agents in acute diarrhoea. A selective intestinal calmodulin inhibiting drug (zaldaride) has been shown in one study of travellers' diarrhoea to be as effective as loperamide when both drugs were given in a loading dose.[1] An intestinal chloride channel blocker (Crofelemer, SP-303) was shown to decrease diarrhoea in another study in travellers with acute diarrhoea.[2] An enkephalinase inhibitor (racecadotril) has been evaluated in several studies where it shortened or decreased: 1) paediatric diarrhoea due to rotavirus and that not due to rotavirus; 2) acute diarrhoea in adults and 3) chronic HIV-associated diarrhoea in adults. Antisecretory approaches to treating diarrhoea are more physiologic than those using antimotility agents, considering the principal mechanism producing acute diarrhoea. Additional studies are needed to determine the relative safety and efficacy of the antisecretory drugs. These drugs could become the standard approach to managing diarrhoea not requiring ORT or antimicrobial agents. ▲

References

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