Racecadotril was effective for severe watery diarrhoea in children


**QUESTION:** In children with severe watery diarrhoea, is racecadotril (acetorphan, an enkephalinase inhibitor), as an adjunct to oral rehydration therapy, more effective than oral rehydration alone?

**Main outcome measures**

The primary outcome was 48 hour stool output. Secondary outcomes were total stool output, duration of diarrhoea, and total intake of ORS.

**Main results**

Analysis was by intention to treat. Patients who received racecadotril had a lower mean 48 hour stool output than patients who received placebo (p < 0.001) (table). The mean total stool output was lower in the racecadotril group than in the placebo group (p < 0.001) (table). More patients who received racecadotril were cured by 5 days than were patients who received placebo (p = 0.015). The total intake of ORS was lower in the racecadotril group (p < 0.001). The groups did not differ for adverse effects (10% v 7%), none of which was severe.

**Conclusion**

In children with severe watery diarrhoea, racecadotril as an adjunct to oral rehydration therapy reduced stool output, duration of diarrhoea, and intake of oral rehydration solution.

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**COMMENTARY**

Diarrhoeal dehydration is the most common killer of children. Dehydration is caused by secretion of fluids into the gut, particularly in infective diarrhoeas. Antimotility agents are not recommended because of the danger of colonisation leading to chronicity. Against this background, the promising efficacy of racecadotril, shown in the study by Salazar-Lindo et al, is welcome.

Racecadotril is an acetorphan, which acts by inhibiting intestinal enkephalinase, thus preventing the inactivation of endogenous enkephalins and reducing the secretion of water and electrolytes into the gut.1 Intestinal transit times are not altered in healthy people.2 Despite the reduction in morbidity by ORS, diarrhoea accounts for 24% of disability adjusted life years.3 Racecadotril, by controlling diarrhoea within 24–48 hours, promises to reduce this percentage further. Other studies have shown that racecadotril is better than octreotide and is effective in patients with AIDS.4 It has long been held that ORS is sufficient to treat watery diarrhoea in children. The results of the study by Salazar-Lindo et al suggest that antisecretory agents should be routinely used in acute watery diarrhoea in addition to ORS.

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**Table: Outcomes Racecadotril v placebo for severe watery diarrhoea in children**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Racecadotril</th>
<th>Placebo</th>
<th>Mean difference (95% CI)</th>
<th>Relative rate reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 hour stool output (g/kg)</td>
<td>92</td>
<td>170</td>
<td>78 (40 to 116)</td>
<td>46%</td>
</tr>
<tr>
<td>Total stool output at 5 days (g/kg)</td>
<td>157</td>
<td>331</td>
<td>174 (90 to 268)</td>
<td>53%</td>
</tr>
<tr>
<td>5 day cure rate</td>
<td>84%</td>
<td>66%</td>
<td>28% (4.9 to 59)</td>
<td>6 (4 to 29)</td>
</tr>
</tbody>
</table>

**Abbreviations defined in glossary; mean difference, RBI, NNT, and CI calculated from data in article.**

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