Erythromycin in neonatal postoperative intestinal dysmotility

D E Simkiss, I P Adams, U Myrdal, I W Booth

Abstract
The motilin agonist erythromycin was used successfully in four infants receiving prolonged parenteral nutrition for severe intestinal dysmotility after gastrointestinal surgery. In a further child with a neuropathic intestinal pseudo-obstruction erythromycin induced a striking small intestinal manometric response, but was without effect in a child with an intestinal myopathy.

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Erythromycin is a motilin receptor agonist.1 It induces bouts of intense motor activity in the stomach and small intestine that resemble phase III migrating motor complex activity.2 Migrating motor complexes, which occur during fasting, are episodes of phasic contractions originating in the proximal small intestine that are propagated distally, and which propel the luminal contents towards the colon.3 Erythromycin is therefore a potentially useful prokinetic drug and may be of benefit to patients with disorders of gastrointestinal motility.

We report a beneficial response to erythromycin in four infants with severe postoperative dysmotility leading to prolonged parenteral nutrition after neonatal gastrointestinal surgery. We also present small intestinal motility data from a further two patients.

CLINICAL STUDY
The table summarises the clinical details of patients 1–4. All four patients presented a problem of continuing large volume bile stained nasogastric aspirates. None of the patients responded to cisapride.

The figure shows the net nasogastric balance (enteral uptake by mouth or tube minus oral losses or nasogastric aspirates) of patients 1–4 at the time of erythromycin administration. Before erythromycin treatment the values had been constant for many weeks in each patient. Erythromycin at an antibiotic dose of 12 mg/kg every six hours was used. Intravenous lactobionate was given to patients 1 and 4, and erythromycin succinate by jejunal tube to patients 2 and 3. In each patient there was a striking improvement in the net enteral balance such that three weeks after starting erythromycin treatment all four patients were established on full bottle feeds.

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Gastration (weeks)</th>
<th>Disorder</th>
<th>Surgical intervention</th>
<th>Maximum recorded nasogastric aspirate volume (ml/day)</th>
<th>Feeding regimen at start of erythromycin treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>Jejunal atresia</td>
<td>Resection of atresia and anastomosis day 1. Two anastomotic revisions in first three months. Tapering of duodenal age 15 months</td>
<td>750</td>
<td>Parenteral nutrition and continuous jejunostomy feeds</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>Gastrochisis</td>
<td>Primary repair of defect day 1. Laparotomy and high jejunostomy age 6 weeks after necrotising enterocolitis. Resection dilated jejunum age 6 months</td>
<td>250</td>
<td>Parenteral nutrition and continuous jejunostomy feeds</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>Jejunal atresia</td>
<td>Resection and anastomosis day 1. Two anastomotic revisions in first eight weeks</td>
<td>180</td>
<td>Continuous jejunostomy feeds (recently stopped parenteral nutrition)</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>Inguinal hernia</td>
<td>Hernia reduced aged 2 weeks. Laparotomy to exclude mechanical obstruction age 3 months</td>
<td>570</td>
<td>Total parenteral nutrition</td>
</tr>
</tbody>
</table>

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Erythromycin did not alter the intracycle frequency of contractions (12/minute), but there was an increase in the mean contraction amplitude from 30 mm Hg to 40 mm Hg.

The second child with hollow visceral myopathy showed an almost flat trace during the control period. After infusion of erythromycin at 12 mg/kg (and four hours later at 60 mg/kg) there was no change.

Discussion

Erythromycin is capable of mimicking the effects of motilin in the proximal gastrointestinal tract, at least in part through its action as a motilin receptor agonist. The clinical observations in our first four patients are consistent with a useful role for erythromycin in infants with severe foregut dysmotility after gastrointestinal anomalies or surgery, or both. To our knowledge this is the first reported use of erythromycin in infants. It has been reported to correct gastric stasis in adult patients with diabetic and idiopathic gastroparesis.

Animal data suggest that the antimicrobial dose used may have been less effective than a starting dose of 1–3 mg/kg. Lower doses of this order induce premature phase III activity in dogs, which is likely to be associated with improved gastric emptying. Our manometric observations showed aboral propagation of the probe, prolonged phase III activity, and an increase in contraction pressure. The effects of erythromycin on proximal gastrointestinal motility, at least in dogs, are highly dose dependent and at high, microbially active doses (10 mg/kg), premature migrating motor complexes are not induced, although the cycle period is reduced. At supramicrobial doses (25 mg/kg) the migrating motor complex cycle period is prolonged.

We think that erythromycin is likely to have a role in the management of infants in whom delayed recovery of gastric emptying and of proximal small bowel function complicates abdominal surgery in the newborn period or early infancy. Prolonged intolerance of enteral feeding after neonatal gastrointestinal surgery is not rare, particularly after small bowel atresias or gastroschisis, and is associated with the risks of prolonged parenteral nutrition. Considerable experience with erythromycin as an antibiotic over many years suggests a high degree of safety and it therefore seems appropriate to assess this newer prokinetic role for erythromycin by a placebo controlled trial. The threshold for considering inclusion in such a trial should be relatively low, given that the drug is safe.

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