Loperamide toxicity in a child after a single dose

Loperamide has been used in Britain for diarrhoea since 1975. Respiratory depression and coma may occur after overdose and have been shown to be reversible by injection of naloxone. So far as we know the first report of opioid toxicity after a single therapeutic dose was published by G L Catto, S Cass and E D McClean in the British Medical Journal in 1980.

Case report

A 15 month old girl weighing 8 kg was admitted to hospital after accidental scalding. Superficial burns covering 35% of the body area. She was hydrated with intravenous fluids, treated with flucloxacillin and penicillin, and on day 5 transferred to a plastic surgery unit for assessment. At the time she was taking fluids and had copious green watery diarrhoea. Clinical examination showed no other abnormality and she was well hydrated. Results of investigations were: haemoglobin concentration 94 g/l, urea and electrolyte values normal, stools negative for reducing sugars and culture, urine culture negative. The diagnosis was diarrhoea as a stress response to burns. On day 9 she was still having the diarrhoea, and at 1330 she was prescribed an initial 1 mg oral dose of loperamide. Fifty minutes later she was collapsed, pale, and unresponsive to pain; pulse was 120/min and respiratory rate 14/min. She had not vomited or convulsed. She was resuscitated with oxygen by Ambu bag and given 0.5 mg naloxone intravenously. By two minutes conscious level was improved and respiratory rate 30/min. Next day she was still drowsy. Blood values were: haemoglobin 87 g/l, urea and electrolytes normal, alanine aminotransferase activity 327 U/l, total protein 36 g/l, albumin 11 g/l. She was transfused 200 ml whole blood and 100 ml plasma protein fraction. Conscious level was normal on day 11. Serum alanine aminotransferase activity was 76 U/l, total protein concentration 48 g/l, and albumin concentration 18 g/l. The diagnosis was changed to cows' milk protein intolerance, as the diarrhoea resolved on withdrawal of milk.

Apart from antibiotics she received papaveretum 1·5 mg intravenously on eight occasions on days 1-3 and five doses of morphine elixir 2·5 mg on days 3-5 without ill effects. No opioids had been given within four days of the reaction to loperamide. At that time she was receiving up to 360 mg paracetamol syrup daily and had had a single dose of 200 mg chloral hydrate the previous evening.

Comment

The 1 mg dose used for this child (0·125 mg/kg) may have been greater than necessary, as the manufacturer's data sheet recommends the dose for children aged 4·8-11 mg every six hours until diarrhoea settles, and Martindale states that loperamide should not be used in the very young. Doses in clinical trials have ranged from 0·045 to 4·0 mg/kg/day with few side effects, though convulsions occurred in a 4 month old infant treated for 11 weeks, the dose being 4 mg/kg/day over the previous week, and possible ileus has been reported. These figures suggest that intragastric variation should be examined more closely, as the findings may have implications for the organisation of treatment for end stage renal failure in the National Health Service.

We thank the strategic planning group, renal interest group, and clinical and scientific services directorate of North West Thames Regional Health Authority. We are also particularly grateful to Julie Kelly for her excellent secretarial help.


(Accepted 23 February 1987)

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Insulinoma unmasked by the Cambridge diet

Hypoglycaemia is not usually a feature of adherence to very low energy diets. We describe a patient who, for the first time, developed symptoms attributable to hypoglycaemia within three days of starting the Cambridge diet and was subsequently found to have an insulinoma.

Case report

A previously fit 46 year old man (height 179 cm, weight 82 kg, body mass index 25·6) was referred to the neurology department by his general practitioner because of a history of intermittent unsteadiness, slurred speech, and intellectual impairment which began three days after he had started a self prescribed very low energy diet (the Cambridge diet; 1·38 MJ/d). His wife described how, while walking, he began to stagger and his speech became slurred. The patient described feelings of uneasiness, weakness, and intoxication. The symptoms completely resolved within 30 minutes of eating a light meal. Symptoms recurred two days later while he was still taking the Cambridge diet and again resolved after a light meal. Two days later he awoke confused and disoriented, showed signs of hypoglycaemia, and also had new onset of hypoglycaemia. Physical examination showed no abnormality and investigations for spontaneous hypoglycaemia were initiated. A random plasma glucose estimation while the patient was symptom free was 7·1 mmol/l. Next morning, after a 15 hour fast, the plasma glucose concentration was 2·6 mmol/l but unaccompanied by symptoms. The fast was continued with exercise. After 22 hours without food his responses to intellectual testing were slow and an electroencephalogram showed slowing of the a rhythm to 9 Hz during overbreathing. Intravenous injection of saline given as a control produced no change, but 25 g glucose given similarly restored his mental state and returned the a rhythm to 10 Hz. The preinjection plasma glucose concentration was 1·6 mmol/l, B-hydroxybutyrate concentration less than 0·02 mmol/l, immunoreactive insulin concentration 55 mU/l, and C-peptide concentration 3·6 ng/l. The finding of inappropriately high plasma insulin and C-peptide values and suppressed B-hydroxybutyrate concentration in the presence of hypoglycaemia was highly suggestive of insulinoma. Computed tomography showed nothing abnormal.

At laparotomy a well encapsulated tumour 1 cm in diameter was removed from the posterior aspect of the head of the pancreas. Immunohistologically the tumour contained many insulin and a few somatostatin containing cells. Recovery was uneventful. Five days postoperatively the overnight fasting plasma glucose value was 7·1 mmol/l. Immunoreactive insulin (6·7 mU/l), C peptide (3·3 ng/l), and B-hydroxybutyrate (0·12 mmol/l) concentrations were all appropriate for the...
Verapamil in atrial fibrillation in hyperthyroidism

Hyperthyroidism is a well known cause of atrial fibrillation, and until hyperthyroidism is properly controlled atrial fibrillation is often difficult to treat. Verapamil is effective in the treatment of atrial fibrillation in euthyroid patients, and we therefore tried it in the treatment of hyperthyroid patients with atrial fibrillation.

Patients, methods, and results

Nine patients were included in the study, seven women and two men, aged 52-87. On admission hyperthyroidism was confirmed in all patients by finding raised hormone concentrations, and subsequently by the absence of any thyrotrphin response to thyrotrphin releasing hormone. At the time of verapamil treatment one patient had received antithyroid treatment for one week: none of the remaining patients had received such treatment.

On admission all patients had atrial fibrillation with a heart rate of 120 beats/min or more. Six patients had cardiac failure. Details of antiarrhythmic treatment and its effects are shown in the table. Seven patients received digoxin without adequate control of heart rate, but after the addition of verapamil this was achieved in all patients. In case 4, a patient who was unresponsive to a combination of digoxin and a β blocker, the heart rate and a β blocker, the heart rate was immediately converted to sinus rhythm after intravenous verapamil. Two patients were treated with verapamil only, and both converted to sinus rhythm. One of these patients had an overt thyrotoxic crisis. In spite of this sinus rhythm was maintained with verapamil.

Verapamil caused no further deterioration of left ventricular function in any of the patients; advanced atrioventricular block was not observed.

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**Effects of antiarrhythmic treatment on nine patients with hyperthyroidism with atrial fibrillation on admission**

<table>
<thead>
<tr>
<th>Case No</th>
<th>Treatment on admission (daily dose)</th>
<th>Heart rate on admission (beats/min)</th>
<th>Initial treatment</th>
<th>Effect of initial treatment (rhythm (beats/min))</th>
<th>Verapamil dosage</th>
<th>Effect of verapamil treatment (rhythm (beats/min))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Digoxin 125 μg x 2</td>
<td>120</td>
<td>Verapamil 80 mg x 3</td>
<td>Atrial fibrillation (70)</td>
<td>80 mg x 3</td>
<td>Atrial fibrillation (70)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>160</td>
<td>Digoxin 1000 mg</td>
<td>Atrial fibrillation (160)</td>
<td>5 mg intravenously and 80 mg x 4</td>
<td>Intermittent sinus rhythm</td>
</tr>
<tr>
<td>3</td>
<td>Digoxin 65-5 μg x 2</td>
<td>160</td>
<td>Verapamil intravenously</td>
<td>Atrial fibrillation (70)</td>
<td>5 mg intravenously and by 80 mg x 3</td>
<td>Intermittent sinus rhythm</td>
</tr>
<tr>
<td>4</td>
<td>Digoxin 125 μg x 2</td>
<td>160-180</td>
<td>Practolol (drip)</td>
<td>Atrial fibrillation (160-180)</td>
<td>10 mg intravenously by</td>
<td>Sinus rhythm</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>160</td>
<td>Verapamil 5 mg intravenously</td>
<td>Atrial fibrillation (160)</td>
<td>80 mg x 3</td>
<td>Sinus rhythm</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>170-180</td>
<td>Digoxin 1000 mg</td>
<td>Atrial fibrillation (170)</td>
<td>10 mg intravenously by</td>
<td>Sinus rhythm</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>160</td>
<td>Verapamil 10 mg intravenously</td>
<td>Atrial fibrillation (100)</td>
<td>80 mg x 3</td>
<td>Sinus rhythm</td>
</tr>
<tr>
<td>8</td>
<td>Digoxin 62-5 μg x 3</td>
<td>120</td>
<td>Verapamil 80 mg x 4</td>
<td>Atrial fibrillation (100)</td>
<td>80 mg x 4</td>
<td>Atrial fibrillation (90)</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>150-160</td>
<td>Digoxin 1000 mg</td>
<td>Atrial fibrillation (140)</td>
<td>5 mg intravenously and 80 mg x 3</td>
<td>Intermittent atrial fibrillation (70)</td>
</tr>
</tbody>
</table>

**Persistent mesenteric ischaemia in a young woman**

Mesenteric ischaemia is an uncommon cause of abdominal pain, usually being considered only in older patients with vascular or haematological disease. We describe a young woman with typical symptoms in whom the condition remained undiagnosed until emergency laparotomy despite investigation by five consultants in four hospitals over 18 months. Surprisingly, she later developed recurrent pain from ischaemia despite almost total resection of the small bowel.