Metoclopramide poisoning in children

L C K LOW AND K M GOEL

Royal Hospital for Sick Children, Glasgow

SUMMARY 15 children with metoclopramide (Maxolon) poisoning are reported. One of the 5 children accidentally poisoned developed slight extrapyramidal signs. All 10 children who experienced extrapyramidal side effects while being treated with metoclopramide had received a dose greater than that recommended by the manufacturer of 0.5 mg/kg per day. Dystonic reactions are likely to occur if the recommended dose is exceeded, but individual susceptibility to metoclopramide and the cumulative effect of repeated doses of the drug may also be important.

Metoclopramide (Maxolon), a chlorbenzamide derivative, is an antiemetic drug which has been available in the UK since 1967. It is regarded as a safe drug with few side effects and has been recommended for habitual vomiting, drug-induced vomiting, and as an adjunct to x-ray examination of the upper alimentary tract. However, alarming extrapyramidal side effects have been reported in children receiving the recommended dose, and in children who have taken the drug in excess. We have looked at a number of children who required admission to this hospital after accidental poisoning by this drug or as a result of its extrapyramidal side effects.

Patients and method

Between January 1967 and December 1978, 15 children were admitted to this hospital with metoclopramide poisoning. Most of the cases occurred during the last 5 years (Figure). The clinical details are summarised in Table 1.
Accidental poisoning group. Five children were admitted because of accidental poisoning by metoclopramide. The drug had been prescribed for other members of the family in 4 cases and in the remaining child the drug had been prescribed for the patient himself because of gastroenteritis. These 5 children were all under 4 years (range 1 year 5 months to 3 years 6 months) and the dose ingested varied between 50 and 100 mg (that is, 3·3 to 8·3 mg/kg per day). Gastric lavage was carried out within four hours of ingestion in all 5 patients. Motor restlessness and increased muscle tone in the limbs were noticed in one patient and these symptoms settled spontaneously. The other 4 children were symptom-free during their time in hospital.

Therapeutic poisoning group. During the same period, 10 children were admitted because of dystonic reaction caused by metoclopramide. The drug had been prescribed for these patients because of vomiting associated with upper respiratory infection, influenza, or gastroenteritis. Four of these children were also receiving antibiotics at the same time. These patients were older than those in the accidental poisoning group, the average age being 8 years 9 months (range 5 months to 11 years 7 months). In most of them the extrapyramidal side effects had become manifest within 36 hours of starting treatment. In one patient the symptoms began after 6 days of treatment with metoclopramide. All the patients were conscious at the time of presentation and appeared agitated. Opisthotonos, increased muscle tone in the limbs, and torticollis were the most common abnormal physical signs in these patients at admission. The other symptoms and signs are summarised in Table 2. In 4 patients these extrapyramidal signs were episodic, each episode generally lasting between 5 and 10 minutes. Apart from restlessness, the patients were symptom-free between these attacks. The dose of metoclopramide taken by these 10 patients varied between 0·9 and 1·9 mg/kg per day. In 2 patients the extrapyramidal manifestations were stopped by giving 1 mg IV benztropine, while the symptoms settled spontaneously within 12 hours in the remaining 8 patients.

Discussion
Extrapyramidal side effects are a rare complication of treatment with metoclopramide. All the patients in the present series were conscious at the time of admission and motor restlessness rather than drowsiness was observed. Opisthotonos and torticollis were the two most common extrapyramidal manifestations in our patients. In 4 of the patients in the therapeutic group the symptoms were episodic as has previously been noted.3–4 When the drug was stopped the symptoms settled spontaneously within 12 hours. We found that parenteral administration of benztropine was effective in stopping metoclopramide-induced dystonic reactions. Treatment with barbiturate has been found to be effective also.2–3 All 10 patients in the therapeutic group had received metoclopramide in a dose greater than that currently recommended by the manufacturers, 0·5 mg/kg per day (Table 1). Although it has been reported3 that children can have these side effects with the dose recommended by the manufacturer, their patients received a dose varying between 0·56 and 1·15 mg/kg per day. In the article by Witzel3 the weights of the patients were not given. If one assumes that these were average, the patients received a dose greater than that currently recommended. In other reports extrapyramidal side effects have been observed in children who were overdosed.3–4

Although it is difficult to be certain of the dose taken by the children who were accidentally poisoned by metoclopramide, no child in this series had severe dystonic reactions, despite the possibility of having taken a large quantity of the drug. Only one of them showed slight extrapyramidal signs. Two patients reported from France who had had massive overdoses recovered without any extrapyramidal signs.1 One infant experienced extrapyramidal side effects within 30 minutes of a single intramuscular injection of metoclopramide 0·7 mg/kg.4 It is therefore possible that some individuals are more susceptible to the effect of the drug than others.

Most of our patients developed symptoms within 36 hours of starting treatment with metoclopramide. Similar observations have been made by other authors and extrapyramidal manifestations have been reported between 24 and 72 hours after treatment.3–5 However, symptoms can occur as late as 120 hours as was the case in one of our patients. In one report,4 a patient developed dystonic symptoms after 7 days of treatment with metoclopramide in a dose of 0·3 mg/kg per day. Repeated doses of the drug may have

Table 2 Symptoms and signs in 10 children with metoclopramide poisoning (therapeutic group)

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>No. of patients</th>
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<tbody>
<tr>
<td>Opisthotonos</td>
<td>7</td>
</tr>
<tr>
<td>Torticollis</td>
<td>3</td>
</tr>
<tr>
<td>Increased muscle tone in limbs</td>
<td>4</td>
</tr>
<tr>
<td>Oculogyric crisis</td>
<td>2</td>
</tr>
<tr>
<td>Facial grimacing</td>
<td>3</td>
</tr>
<tr>
<td>Conjugate deviation of eyes</td>
<td>2</td>
</tr>
<tr>
<td>Diplopia</td>
<td>2</td>
</tr>
<tr>
<td>Trismus</td>
<td>1</td>
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<tr>
<td>Nystagmus</td>
<td>1</td>
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</tbody>
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a cumulative effect leading to extrapyramidal manifestations although it is known that the plasma half-life of metoclopramide is short.\(^7\)

From our observation and that of others, metoclopramide is sometimes prescribed in the treatment of trivial illness. As dystonic reactions are distressing both to the patients and their parents, greater care should be exercised by doctors when prescribing this drug for children. The dose should not exceed 0.5 mg/kg per day and prolonged use of the drug is not recommended. Extrapyramidal side effects after metoclopramide are rare and early diagnosis will depend on doctors being alert to the possibility so that unnecessary investigations can be avoided. Such reactions can be effectively stopped by administration of benzotropine 1 mg intravenously.

We thank our colleagues for permission to study patients under their care.

Q fever endocarditis in a 6-year-old child

ROBERT W A JONES AND DAVID W PITCHER

Department of Paediatrics and Department of Cardiology, Guy's Hospital, London

SUMMARY A 6-year-old boy with a congenital bicuspid aortic valve presented with finger clubbing and hypertrophic osteoarthopathy, and subsequently he developed severe hypertension. The hypertension was successfully treated by nephrectomy, at which a thrombosed myotic aneurysm of the renal artery was found. Echocardiography showed the presence of aortic valve vegetations. Blood cultures were sterile, but high antibody titres to the phase 1 and 2 antigens of Coxiella burnetii strongly suggested Q fever infection. We believe this is the first reported case of Q fever endocarditis in early childhood.

Case report

A 6-year-old boy from a rural area in Libya presented with a one-month history of polyarthritis and swelling of the fingers and toes. He had been in frequent contact with farm animals. After admission to hospital in Libya he was noted to have a heart murmur. Shortly afterwards he developed severe hypertension complicated by recurrent grand mal seizures. He was treated with a low salt diet and, after the demonstration of only one functioning kidney by intravenous urography, was transferred to Guy's Hospital for further investigation.

Examination showed pronounced finger and toe clubbing. There was also soft tissue swelling of the fingers which felt warm and podgy. A polyarthritis was present affecting the elbows, wrists, knees, and ankles; there was pronounced synovial thickening and local warmth. Systemic fever was absent. Blood pressure was 180/130 mmHg. The pulse was normal. Auscultation showed a loud ejection systolic murmur preceded by an ejection click heard maximally over the aorta. A soft early diastolic murmur was present. The liver and spleen were palpable 6 and 4 cm respectively below the costal margins. No renal bruit was heard. Neurological examination was normal.

Investigations showed: Hb 10.5 g/dl, WBC 10.3 x 10\(^9\)/l (normal differential), ESR 78 mm/1st hour, blood cultures (multiple) sterile, immunoglobulins: IgG 17 g/l (normal 8–17), IgA 1.4 g/l (normal 1.5–4.5), IgM 4.6 g/l (normal 0.45–1.45), urine microscopical examination: RBC 0.020–0.300 x 10\(^9\)/l. Electrocardiography showed left ventricular hypertrophy, chest x-ray showed slight cardomegaly (cardiothoracic ratio 1:1.8), and on fluoroscopy aortic valve calcification was seen. X-ray of the limbs

References


Correspondence to Dr K M Goel, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ.