Acute poisoning with maprotiline hydrochloride

Concern has been expressed about the increasing number of deaths from overdosage with tricyclic antidepressants.1 In recent years there has been a proliferation of such compounds but whether any one has particular advantages over another in therapeutic dosage, far less overdosage, is doubtful. More recently tetracyclic compounds, such as maprotiline hydrochloride (Ludomid; CIBA) have become available for the treatment of depression. Self-poisoning with maprotiline in two patients has already been reported,2 and further cases will inevitably occur. Information on acute poisoning with this drug is limited, however, and we report six cases of overdosage treated by us in 1976.

Patients

Each of the six patients (four women, two men) obtained his overdose from the manufacturer’s blister packs, each of which contains 14–75 mg tablets. The important clinical features of acute poisoning were depression of consciousness, convulsions, and urinary retention followed by a variable period of confusion, disorientation, agitation, and visual hallucinations during recovery (table). Each patient underwent gastric aspiration and lavage. None required endotracheal intubation or assisted ventilation, and none was hypotensive. Cardiac monitoring was carried out in five patients, and though three had a sinus tachycardia no dysrythmia or conduction defect was noted. None of the patients was epileptic. The duration of coma was measured from admission to hospital till the patient could obey a simple verbal command. The duration of delirium in unconscious patients was measured from the time of regaining consciousness. Every patient recovered completely.

Comment

The effects of maprotiline poisoning on two patients have been reported.3 4 Both had convulsions but only one had impaired consciousness, and in neither was there urinary retention or delirium. The clinical features of maprotiline poisoning are clearly no different from those encountered in overdosage with tricyclic antidepressants, and are presumably due to anticholinergic effects. In the first half of 1976 we treated 126 patients with tricyclic antidepressant poisoning and found that 91 (72%) were unconscious, 7 (6%) had convulsions, 47 (37%) urinary retention, and 19 (15%) delirium during recovery. Though experience with maprotiline overdose is small, comparison of the two types of poisoning suggests that delirium and convulsions are commoner with maprotiline. The latter, particularly, could have an important influence on mortality. Several deaths are recorded.5 4

Disturbances of cardiac rhythm and conduction after maprotiline poisoning have been reported only by the manufacturers.4 Even in the case of poisoning with tricyclic antidepressants they are by no means as common as the reports suggest (5 (4%) of our 126 patients). All our patients with maprotiline poisoning survived with supportive measures alone. In view of the anticholinergic nature of some of the clinical features, physostigmine salicylate might be valuable for desperately ill patients, but would have to be used with great caution because it may precipitate fits. Haemodialysis, forced diuresis, and haemoperfusion would be unlikely to remove therapeutically effective quantities of drug. A recent review of maprotiline in therapeutic doses5 concluded that it had no obvious advantages over established antidepressives. Unfortunately the same conclusion may be valid for maprotiline in overdosage.


(Accepted 2 March 1977)

Regional Poisoning Treatment Centre, The Royal Infirmary, Edinburgh EH12 9YW
J PARK, BSc, MRCP, registrar
A T PROUDFOOT, BSc, FRCP ED, consultant physician

Plasmapheresis in systemic lupus erythematosus

We describe here the findings in two patients from a group we treated with various forms of plasmapheresis. In these two cases the effects of substituting plasma protein fraction (PPF) or fresh-frozen plasma (FFP) were compared.

Case reports

In both patients bound C1q and IgG in immune complexes were estimated after precipitation from serum by 2% polyethylene glycol. Results were expressed as a percentage of total serum C1q or IgG. Plasmapheresis, using the Haemonetics cell separator Model 30, exchanged 2-5 litres of plasma daily.

CASE 1

This 24-year-old girl had had lupus nephritis for 18 months. After episodes of thrombocytopenia, alopeica, and polyarthritis she deteriorated with pleuritic pains, recurrent pleural effusions, rash over face and arms, vomiting, and hypertension of 200/120 mm Hg. Daily azathioprine 150 mg and prednisolone 40 mg did not control her symptoms.

Investigations—Proteinuria averaged 12 g daily, with plasma creatinine at 167 μmol/l (1.9 mg/100 ml). Antinuclear factor (ANF) was positive to 1/320. DNA binding (Amersham) was raised at 33 units/ml. Many immune complexes were present, 2-5% of total IgG was present in complexes, and all detectable C1q was bound. Total complement (CH50) was always below 20%, of normal.

Results—Six plasmaphereses in three weeks with PPF relieved her rash

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Stated ingested dose (g)</th>
<th>Depth of coma</th>
<th>Duration of coma (h)</th>
<th>Convulsions (No)</th>
<th>Urinary retention</th>
<th>Approximate duration of delirium (h)</th>
<th>Other drugs ingested</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>28</td>
<td>0.75</td>
<td>Conscious</td>
<td>6</td>
<td>2</td>
<td>No</td>
<td>12</td>
<td>Ethanol</td>
</tr>
<tr>
<td>F</td>
<td>27</td>
<td>0.95</td>
<td>Conscious</td>
<td>2</td>
<td>2</td>
<td>No</td>
<td>48</td>
<td>None</td>
</tr>
<tr>
<td>F</td>
<td>28</td>
<td>2.25</td>
<td>Conscious</td>
<td>2</td>
<td>2</td>
<td>No</td>
<td>30</td>
<td>Ethanol</td>
</tr>
<tr>
<td>F</td>
<td>44</td>
<td>3.2</td>
<td>Unconscious; maximal response to pain</td>
<td>6</td>
<td>2</td>
<td>Yes</td>
<td>48</td>
<td>Paracetamol</td>
</tr>
<tr>
<td>M</td>
<td>31</td>
<td>2.25</td>
<td>Unconscious; maximal response to pain</td>
<td>12</td>
<td>2</td>
<td>Yes</td>
<td>30</td>
<td>Ethanol</td>
</tr>
<tr>
<td>M</td>
<td>24</td>
<td>3.2</td>
<td>Unconscious; maximal response to pain</td>
<td>14</td>
<td>2</td>
<td>Yes</td>
<td>30</td>
<td>Ethanol; diazepam</td>
</tr>
</tbody>
</table>
and pleuritic and joint symptoms. Proteinuria fell from 13 to 8 g in 24 hours, but immune complex levels rose again within hours of each session. CH₄₈ fell, but later recovered. Free C1q did not appear. She relapsed after eight weeks, and two plasmaphereses were performed with FFP to increase serum complement. Immune complex levels now continued to fall for several days after exchange, with a substantial rise in CH₄₈ and free C1q and a decrease in proteinuria to 2.5 g/24 hours. Eight more exchanges with FFP were used for the third relapse 10 weeks later. This produced a lasting rise in CH₄₈, persisting free C1q, and normal levels of complexes. Her hypertension had been resistant to treatment and two months later she died suddenly in hypertensive heart failure.

**CASE 2**

This 55-year-old housewife with systemic lupus erythematosus described 10 years of polyarthritis, severe malaise, Raynaud’s syndrome, and facial rashes with photosensitivity. Simple anti-inflammatory agents and prednisolone 10 mg daily were not effective in relieving her joint symptoms.

**Investigations**—ANF gave a peripheral pattern at 1/320. DNA binding was raised at 32 units/ml. LE cells were present, with a sheep cell agglutination titre of 1/128. Radiographs showed erosive polyarthritis. Circulating immune complexes were present in large quantities, 20% of total IgG being in complexes.

![Graph showing plasma concentration and clinical symptoms over time](image)

**Results**—Five initial exchanges with PPF produced only modest results (see figure). Pain and walking time improved, but malaise, morning stiffness, and grip strength were not affected. Complement declined, and complexes decreased transiently. Three weeks later four exchanges with FFP were much more effective. Morning stiffness disappeared within three weeks. Walking time became near optimal. Grip strength and wellbeing greatly increased. Complement levels returned to normal and immune complex levels fell and remained normal for two months. Malaise returned after one month and arthritis after three months.

**Comment**

The mechanism of benefit from plasmapheresis is probably multifactorial, the removal of reactants in PPF exchanges being augmented by the addition of factors in FFP exchanges. It seems logical to add complement when there is a relative deficiency, since complement is thought to be implicated in immune complex clearance.

Although definite conclusions cannot be drawn from the evidence of only two cases, we have presented these cases in the hope that further work will discriminate between the materials used to substitute for plasma and take note of differences in effect.

This continuing study is funded by the Sir Jules Thorn Foundation.


(Submitted 11 March 1977)

Department of Haematology, University College Hospital, and Department of Experimental Pathology, St Mary's Hospital, London

C J Morar, BSC, MRCP, senior medical registrar
H F Parry, MB, CHB, research registrar
J O'M Volbray, MRCP, consultant immunologist
J D M Richards, MD, consultant haematologist
A H Goldstone, MRCP, MRCPATH, consultant haematologist

---

**Rectouterine fistulation in Crohn's disease**

Fistulation is a frequent complication of Crohn's disease, the reported incidence varying between 15 and 48%. Small bowel fistulae outnumbering those from the large bowel by roughly 3 to 1. Most large bowel fistulae tend to reach the exterior via the vagina, the incidence of rectovaginal fistulae being 5 to 14%. Rectouterine fistulation in Crohn's disease has not been described.

**Case History**

A 23-year-old woman originally presented to a gynaecologist in 1964 with a pelvic mass. At laparotomy this was found to "originate from the bowel," but no definitive procedure was performed. A further laparotomy was undertaken in 1965 after twelve months' ill health, when Crohn's disease of the terminal ileum and sigmoid colon was found. The terminal ileum was resected with end-to-end anastomosis and sigmoid colectomy performed with formation of a terminal left iliac fossa colostomy. Alimentary continuity was re-established in 1968 by colorectal anastomosis, there being no evidence of active Crohn's disease at laparotomy. The patient remained well until 1973, when an anal fistula developed after incision of an ischiorectal abscess, and in March 1974 she developed a faecalulent vaginal discharge but refused investigation or treatment. Nevertheless, in April 1976 after five months'...