Recovery after massive MAOI overdose complicated by malignant hyperpyrexia, treated with chlorpromazine

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A PATIENT is reported who fully recovered after a massive overdose with a monoamine oxidase inhibitor (MAOI) drug, despite the occurrence of hyperpyrexia, parturition and acute renal failure. The hyperpyrexia, although resistant to cooling, responded rapidly to intravenous chlorpromazine and fluids.

Case history

A 27-year-old housewife, 7 months pregnant, with a previous history of depression treated by ECT, took ten tablets of diazepam without ill-effect. At noon 4 days later she was admitted for an overdose of fifty tablets (0.5 g) of tranlycypamine taken 1½ hr earlier. Her normal blood pressure was 120/70 mmHg, and pulse 84/min.

On admission her blood pressure was 150/100, pulse 160/min and temperature 102° F (39° C). She was restless, drowsy, sweating, and had muscle contractions resembling rigors. Gastric lavage produced a good but unmeasured return. An hour later she was cyanosed, dyspnoeic, and the muscles of her limbs were in tonic spasm. She was given 100 mg of chlorpromazine i.m. A quarter of an hour later she suffered the first of five cardiac arrests, each responding rapidly to external massage, with return to sinus rhythm. The pulse quickened, the blood pressure fell (60/0), and ventricular tachycardia preceded each arrest. However, 5 hr later, her rhythm had stabilized to sinus tachycardia of 130/min., and her blood pressure to 90/50, after 600 mg of i.v. hydrocortisone, 10 mg of glucagon i.v., and bicarbonate, lignocaine and isoprenaline in a 5% dextrose drip. But her temperature remained 106° F (P.R.), despite the use of ice, wet sheets and a fan. Her pupils were fixed and dilated and there was intense fasciculation of all groups of muscles, producing rigidity from head to toe. Her feet were markedly plantar flexed. Although her respiration was satisfactory she was given oxygen.

More chlorpromazine (70 mg in 3 hr) was given intravenously, together with bicarbonate and large doses of hydrocortisone. Her temperature fell to 102° F, with improvement in her skin, which became

warm, dry and pink. The temperature rose when the fan was switched off for a few minutes, but fell on restarting it. Glucagon (5 mg i.v.) did not improve her hypotension.

Some 24 hr after taking the tranlycypromine she was breathing well, had a palpable pulse (sinus rhythm, 100/min, BP 60/0 Hg), but muscle tremor and rigidity persisted. Her pharyngeal and eyelash reflexes had returned and she made occasional spontaneous grimaces. Plantar responses remained flexor. During the second day moderate uterine contractions were felt; her chest X-ray showed evidence of pulmonary oedema, and she had passed only 270 ml of urine since admission despite hydration, Dextran 40 and mannitol. At about the fortieth hour she appeared to be conscious and opened her eyes on request. Muscle spasm remained severe, blood pressure was 80/0 and pulse was 80/min. At 78 hr low forceps were applied and a macerated foetus delivered.

Acute renal failure was treated by peritoneal dialysis. She suffered two episodes of pulmonary embolism and developed signs of a deep venous thrombosis in her right calf, for which she was heparinized. Other complications included pressure necrosis of the right heel with a bilateral contractural foot drop, worse on the right. A pressure sore also developed on her occiput. Twenty-one days after admission a diuresis started and over the following 3 weeks her blood urea fell from 230 to 27 mg/100 ml. Bilateral selective renal arteriograms had shown no significant abnormality save for lack of density in the nephrogram phase. Renal size was normal. She also became anaemic (8.9 g%), but her haemoglobin rose with oral iron and free diet to 11.4 g%. Her visual acuity and intellect were unimpaired and there was no change in her personality. There were no residual neurological abnormalities, nor was there evidence of myopathy.

Discussion

Some features of this case may be of interest. On admission the patient said that she had also taken five tablets of imipramine, but after recovery

she denied doing so. The combination of imipramine and an MAOI is known to cause hyperpyrexia whether taken in excessive or normal dosages (Stanley & Pal, 1964). She was overhydrated during the first 48 hr, and chest X-rays showed pulmonary oedema which cleared rapidly after dialysis. Her hypotension might be explained either by myocardial depression following arrest, or by the action of tranlycypromine. Sixty milligrams given over a day is considered to be a large dose capable of hypotensive effects similar to those of sympathetic blockade. Possibly the chlorpromazine injection was responsible, in conjunction with the waning effects of her diazepam overdose. The duration of the muscle spasm was remarkably long, and its persistence after the hypothermic effect of chlorpromazine intravenously might suggest that the latter's main site of action was not on the muscles.

Chlorpromazine seems the ideal drug to use for hyperpyrexia. Macgraith (1966) states that it may be used in intravenous doses of 25–50 mg together with physical cooling, and suggests that it is especially useful in restless patients, or those who have had convulsions. In animals it is one of the most potent drugs in lowering a normal body temperature, or antagonizing a pyrexial response (Paton & Payne, 1968). It is known to aid induction of hypothermia in humans, and has been used to lower body temperature in thyroid crisis (Ibbertson, 1967). It has been recommended as being of use in hypothermic patients who are rewarmed too quickly (Bloch, 1967), and is thought to predispose to the development of hypothermia in the elderly and in swimmers, by inhibiting shivering. Smith (1968) suggests that repeated half-hourly doses (0.2 mg/kg) may be used to lower high fever and control shivering. It is thought to act on the hypothalamic heat control centre producing a central hypothermic effect. In moderate doses it controls the muscle spasm of tetanus and the spasticity of some neurological conditions. It has an alpha-blocking action, producing hypotension and peripheral vasodilatation, and it blocks response to adrenalin considerably

more than noradrenalin. It has a quinidine-like action on the heart and protects against arrhythmias.

Wood-Smith & Stewart (1964) stress that unless active cooling is employed the fall in temperature is minimal. This was confirmed in the case reported here, when the temperature rose after turning off the fan.

Review of the literature suggests that while chlorpromazine is of value in high fevers, it is often not tried even in fatal cases of hyperpyrexia. The nature and definition of malignant hyperpyrexia and the way in which chlorpromazine may work in overcoming the resistance to cooling so often present in severe cases has been discussed (Robertson, 1970). The case reported here suggests that MAOI overdose need not be fatal if complications can be treated as they arise, and that chlorpromazine should be used in cases of resistant hyperpyrexia.

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