observed without specific treatment. Once the effects wore off she was given oral chlorpromazine 50 mg three times a day.

Interestingly, after this episode her behaviour was improved. Electroencephalography and a brain scan showed no focus of epilepsy.

Comment

Adverse effects of high dose depot neuroleptic injections have been reported,[1] but the *Index Medicus* contains no report after dosage as high as in the present case.

This case shows that fluphenazine decanoate is fairly safe in overdosage. The perplexing factor was the delay in occurrence of toxic effects till three to four weeks later, which then lasted for one month. Pharmacokinetic studies[2] show that each injection of fluphenazine is followed by a rapid rise in plasma concentration of the drug to a maximum at one to eight hours, which over the next 12-36 hours falls to a value slightly above that before the injection and remains stable until the next injection. Hence the maximum toxic effects would be expected to occur within the first few days after overdose. A possible explanation for the delay may be the effect of very high blood concentrations of the drug on neurotransmitters other than dopamine—for example, an anticholinergic effect would balance out the parkinsonian effects; and not until the drug concentration fell to a more usual value would the toxic effects start to appear.

The improved behaviour of this patient after overdosage may suggest a possible therapeutic effect of megadosage fluphenazine in cases refractory to more usual dosages. This has been reported before: McClelland *et al* found that a regimen of 250 mg a week appeared more effective than 12·5 mg a week and did not produce greater side effects.[3] Further research is needed.

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Continuous electroencephalographic recording to detect seizures in paralysed newborn babies

A muscle relaxant is often given to abolish spontaneous respiratory activity in babies who require artificial ventilation. Paralysis abolishes the clinical signs of neurological complications, particularly seizure activity, which may follow hypoxic brain damage, hypercapnia, or other biochemical abnormality. Some studies have suggested that repeated seizures lead to permanent neurological sequelae.[1 2] We report seizure activity, detected by a new method of continuous electroencephalographic monitoring, in three babies paralysed while receiving intensive care. This technique permitted prompt diagnosis and rapid assessment of anticonvulsant treatment.

Patients, methods, and results

The table gives the clinical details of the three babies studied. In each case a continuous record of the electroencephalogram, electrocardiogram, and respiration (transthoracic impedance) was made on to a small four channel, battery powered tape recorder (Medilog 4-24 recorder; Oxford Medical Systems, Abingdon, Oxfordshire). Recording was started as soon as possible after paralysis was induced and continued until the neuromuscular blockade was stopped. Standard electrodes were used to obtain bipolar frontoparietal records of the electroencephalogram on the right and left. To reduce artefact from movement the electrodes and miniaturised preamplifiers (HDX-82; Oxford Medical Systems) were attached to the scalp by collodion. The skin electrode impedance was less than 5 kΩ and the frequency response 0·5-100 Hz. The electrocardiogram and transthoracic impedance were recorded from electrodes on the chest wall.

Data obtained over 24 hours were recorded on to a standard C120 cassette tape and analysed by replay through a visual display unit (PMD12 Virgo special; Oxford Medical Systems) at 60 times the recorded speed. Each tape was reviewed at intervals that were determined by the findings—that is, after anticonvulsant treatment or after a change in the clinical condition of the baby.

Seizure activity was recorded in the three babies (table). Continuous recording of the data did not interfere with intensive care, and no more than 10% of any tape was obscured by artefact. There were no complications, regular ultrasound scanning of the brain through the anterior fontanelle was possible, and the major part of the scalp remained available for intravenous cannulas.

Comment

Sick newborn babies are at risk of neurological disorder after perinatal asphyxia, intracerebral haemorrhage, metabolic disturbance, or meningitis. The incidence of clinical seizures is as high as 3%,[3] but muscle relaxation prevents seizures being diagnosed. Studies in animals have shown that repeated seizures in the neonatal period adversely affect brain growth and result in permanent neurological sequelae, even when hypoxaemia is avoided.[1 2] Seizures may be the presenting sign of a neurological disorder that requires investigation and treatment, and early diagnosis and control of the seizures may improve the prognosis. The American National Collaborative Perinatal Project found that cerebral palsy and mental retardation were related to the duration of the longest seizure.[4] In addition, children were 55-70 times more likely to have cerebral palsy or mental retardation if they had had neonatal seizures.[4]

Diagnosis of seizures in paralysed babies depends on electroencephalography, but intermittent recordings are unreliable. Continuous recording with conventional apparatus is impractical, but this new method detects all seizure activity throughout the period of paralysis. Seizure activity was recorded in all three babies but would not have been diagnosed without continuous monitoring. The monitoring also permitted an assessment of the efficacy of anticonvulsant treatment.

Motor end plate blockade in very sick newborn babies prevents a clinical assessment of the neurological state of babies who are at high risk of brain damage. Continuous electroencephalographic monitoring may disclose abnormalities and lead to appropriate investigation and early effective control of seizure activity.

Clinical details and results of electroencephalographic monitoring

Case No	Sex	Gestation (weeks)	Birth weight (g)	Clinical details	Duration of electroencephalographic monitoring (h)	Clinical signs of seizure before paralysis	Electroencephalographic findings	Results of other investigations
1	M	40	3800	Severe birth asphyxia, aspiration of meconium, pulmonary hypertension	48	None	Left sided paroxysmal rhythmical 8–9 Hz "α like" activity; right sided suppression	
2	M	41	2930	Severe birth asphyxia, aspiration of meconium, pulmonary hypertension	72	None	Left sided paroxysmal burst of rhythmical 10–11 Hz "α like" activity	Computed tomography: infarcted left hemisphere
3	M	26	1200	Severe hyaline membrane disease, recurrent pneumothorax, intraventricular haemorrhage	72	Multifocal clonic jerks	Right and left synchronous paroxysmal bursts of rhythmical sharp waves 1–3 Hz of long duration	Ultrasonography: intraventricular haemorrhage

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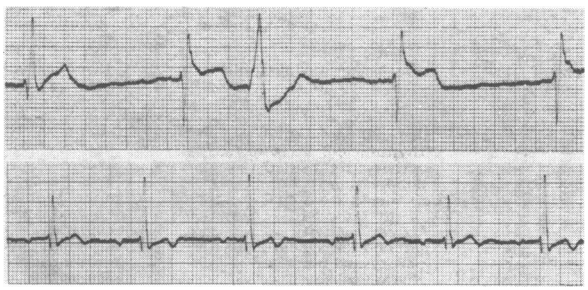
Cardiac complications of carbamazepine intoxication: treatment by haemoperfusion

Although carbamazepine is widely prescribed for epilepsy and trigeminal neuralgia, it rarely seems to be taken in overdosage. Manifestations of severe acute poisoning include sinus tachycardia, ataxia, convulsions, coma and respiratory depression.[1-4] First degree atrioventricular block has also been noted[1 2] but has not been well documented. We describe a case of acute carbamazepine intoxication complicated by severe myocardial depression with bradycardia, conduction defects, hypotension, and oliguria. There was no improvement with conservative management, but the patient recovered after charcoal haemoperfusion.

Case report

A 50 year old man with no history of heart disease was admitted in deep coma 12 hours after apparent ingestion of 20 g carbamazepine. There was no response to any stimulation, the pupils were fixed and dilated, and there was divergent strabismus. Respiratory rate was 14/min, blood pressure 85/60 mm Hg, and pulse rate 52/min; an electrocardiogram showed first degree atrioventricular block (P-R interval 0·28 s) with normal QRS and QT_c intervals. Gastric aspiration and lavage were carried out after endotracheal intubation. There were no haematological or biochemical abnormalities, and the plasma carbamazepine concentration (enzyme multiplied immunoassay technique) was 62 mg/l (261 μmol/l).

Arterial blood gas analysis showed acute respiratory acidosis, and assisted ventilation was required for six hours. His condition deteriorated further with peripheral circulatory failure, oliguria (urine flow 10 ml/h), hypotension (systolic blood pressure 50 mm Hg), and an irregular and slow pulse. Electrocardiography showed loss of P waves, occasional ventricular ectopic beats, and prolongation of the QRS interval (figure). Intravenous atropine (1·2 mg) and glucagon (15 mg) had no effect, and after infusion of a litre of plasma protein solution the central venous pressure remained raised at 14 cm of water. Dopamine (5 μg/kg/min) was infused; the heart rate rose to 67/min and the blood pressure to 110/70 mm Hg, and the urine output increased.



Electrocardiogram monitor traces shortly after admission (top) and after haemoperfusion (bottom).

Forty hours after admission he was still deeply unconscious and continuous inotropic support was required to maintain the pulse rate, blood pressure, and urine flow. Electrocardiographic appearances were essentially unchanged. Charcoal haemoperfusion was therefore carried out (Haemacol, flow rate 200 ml/min) in an attempt to remove the carbamazepine. Haemoperfusion was stopped after five hours, at which time he was extubated and responded to verbal commands. Dopamine was no longer required, and electrocardiography showed sinus rhythm, first degree atrioventricular block (P-R interval 0·26 s) and normal QRS and QT_c intervals. During haemoperfusion the plasma carbamazepine concentration fell from 31 to 15 mg/l (131 to 63 μmol/l) and the initial clearance across the column was 174 ml/min. At two and five hours, however, the clearance had fallen to 80 ml/min and the estimated total amount of drug removed was less than 1 g.

The following day the electrocardiogram was within normal limits. The patient remained confused and ataxic for a further four days and was subsequently transferred to a psychiatric ward.

Comment

Such profound and prolonged myocardial depression with bradycardia, conduction defects, hypotension, and oliguria has not been reported previously after carbamazepine overdosage despite similar drug concentrations in some patients.[3 4] Depressed atrioventricular conduction with complete heart block has occurred, however, with therapeutic use of carbamazepine,[5] and there seems to be great individual variation in response to the drug's cardiac effects. As in other reports,[1 4] haemoperfusion was moderately effective in removing carbamazepine and the fall in drug concentration in our patient was associated with considerable electrocardiographic and clinical improvement.

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SOPEWORT, OR BRUISEWORT. The roots creep under ground far and near, with many joints therein, of a brown colour on the outside and yellowish within, shooting forth in divers places weak round stalks, full of joints, set with two leaves a-piece at every one of them on a contrary side, which are ribbed somewhat like to plantain, and fashioned like the common field white campion leaves, seldom having any branches from the sides of the stalks, but set with flowers at the top, standing in long husks like the wild campions, made of five leaves a-piece, round at the ends, and dented in the middle, of a rose colour, almost white, sometimes deeper, sometimes paler; of a reasonable scent. It grows wild in many low and wet grounds of this land, by brooks and the sides of running waters. It flowers usually in July, and so continues all August, and part of September, before they be quite spent.

Venus owns it. The country people in divers places do use to bruise the leaves of Sopewort, and lay it to their fingers, hands or legs, when they are cut, to heal them up again. Some make great boast thereof, that it is diuretical to provoke urine, and thereby to expel gravel and the stone in the reins or kidneys, and do also account it singularly good to void hydropical waters: and they no less extol it to perform an absolute cure in the French pox, more than either sarsaparilla, guiacum, or China can do; which, how true it is, I leave others to judge. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)