haemodialysis showed a higher correlation, as it combined the effect of dose and duration of treatment.

Comment

That aluminium is implicated in dialysis encephalopathy and osteomalacic dialysis osteodystrophy has been shown convincingly in dialysis centres situated in areas with high water aluminium concentrations.^{3,4} Since the first reports an increasing number of renal units have begun to use water treatment and monitor the serum and water aluminium concentrations. With lessening of the risk of aluminium toxicity from the dialysate, attention has turned to the importance of aluminium containing phosphate binders.

We found a significant relation between the serum aluminium concentration and both the dose of aluminium hydroxide and length of time spent on dialysis. Most patients were also given aluminium hydroxide before dialysis but we were not able to analyse this. While it is still uncertain at what serum concentration bone toxicity occurs, bone aluminium content is increased in most patients receiving dialysis even with water treatment. Fifty four of the 59 patients reported on by Hodsman *et al* had raised bone aluminium concentrations despite the fact that water treatment was used by almost all of them.⁵ Thirty six of our patients had serum aluminium values above 3.0 $\mu\text{mol/l}$ (8.0 $\mu\text{g}/100\text{ ml}$). Of these, 32 were over 4.0 $\mu\text{mol/l}$ with a range of 4.0–12.3 $\mu\text{mol/l}$ (10.8–33.2 $\mu\text{g}/100\text{ ml}$). These patients were certainly at risk of developing osteomalacia, and possibly also some of those with values below 3.0 $\mu\text{mol/l}$. While no ideal phosphate binder has been described, serious consideration needs to be given to replacing aluminium hydroxide with a different compound or using smaller doses in conjunction with another agent.

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Neuroleptic malignant syndrome

The neuroleptic malignant syndrome is a rare but potentially lethal complication of neuroleptic drugs, characterised by muscular rigidity, hyperpyrexia, altered consciousness, and autonomic disturbance. Although numerous cases have been reported from France¹ and the United States,^{2,3} there has been only a single British report.⁴ We describe a further case.

Case report

A 33 year old single man presented with a paranoid psychosis which had developed insidiously over two years and deteriorated rapidly the previous month. There was no notable past psychiatric, medical, or family history. He showed both first rank symptoms of schizophrenia and features of endogenous depression. Before admission he had been taking trifluoperazine (Stelazine) 5 mg twice daily and dothiepin 75 mg twice daily.

Examination showed a tall man (193 cm) weighing 105 kg. Results of routine physical examination, full blood count, urea and electrolyte concen-

trations, liver function values, and chest x ray appearances were normal. He was treated with chlorpromazine (up to 600 mg daily) and haloperidol (up to 30 mg daily). Procyclidine 10 mg three times a day was added to counteract the extrapyramidal side effects.

The patient remained floridly psychotic and difficult to manage. Eight days after admission he appeared oversedated and the extrapyramidal side effects worsened. The neuroleptics were halved, and then stopped two days later. He developed hyperventilation, profuse sweating, dysphagia, dysarthria, tachycardia, and a labile blood pressure and his conscious level fluctuated. Plantar reflexes were intermittently extensor.

He was transferred to a medical ward, where he developed fever up to 40.2°C and neck stiffness but showed no localising neurological signs. Abnormal findings included a neutrophil leucocytosis of $17 \times 10^9/\text{l}$, abnormal liver function values (serum aspartate transaminase activity 62 U/l, lactate dehydrogenase activity 961 U/l), raised creatine phosphokinase activity (373 U/l), and raised blood urea concentration. Cerebrospinal fluid pressure was raised and protein concentration low, but otherwise the fluid was normal; an electroencephalogram was also normal. Results of viral studies were negative. The differential diagnosis was meningitis or encephalitis, and when his condition deteriorated septicaemia was considered; blood cultures, however, were sterile, and antibiotics produced no improvement. A tentative diagnosis of the neuroleptic malignant syndrome was made, and two days after transfer, and despite intensive supportive measures, he died of cardiorespiratory failure. Postmortem examination showed evidence of longstanding cardiomyopathy and a large spleen.

Comment

This patient showed all the major features of the neuroleptic malignant syndrome. The syndrome has been described in association with butyrophenones, phenothiazines, and thioxanthenes, but haloperidol and depot fluphenazines are most commonly implicated. The onset of the syndrome may be within hours of the first dose of neuroleptic or after months of drug use, and some patients have been safely re-exposed to the drug. Some reported cases show evidence of pre-existing organic brain disease, physical exhaustion, or dehydration.²

The syndrome begins with severe extrapyramidal symptoms of rigidity and akinesia together with or shortly before the development of fever and autonomic disturbance. Consciousness fluctuates from alert mutism to stupor and coma. Once started, the syndrome develops rapidly over the 24–72 hours. Respiratory failure is the commonest cause of death. There is an overall mortality of 20%,² which is higher for depot than for oral neuroleptics. There are no specific or diagnostic laboratory findings, but leucocytosis, raised creatine kinase activity, and abnormal liver function values have been reported.³ The electroencephalogram is generally normal but may show non-specific slow wave activity. Cerebrospinal fluid, isotope brain scans, CT scans, and postmortem examinations (when performed) show nothing abnormal.

Neuroleptic malignant syndrome may be misdiagnosed as encephalitis or other infectious diseases affecting the nervous system. The syndrome has been compared with acute lethal catatonia described in the preneuroleptic era, and with malignant hyperpyrexia⁵ associated with inhalational anaesthetics and depolarising muscle relaxants.

The pathogenesis of the disorder is unknown, but dopamine receptor blockade in the basal ganglia and hypothalamus has been postulated.³ There is no known specific treatment, and it is essential to stop neuroleptic medication as soon as the disorder is recognised. Then supportive measures may be effective in preventing a fatal outcome.

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