Novel and non-toxic treatment for night terrors

Bryan Lask

Department of
Psychological Medicine,
Great Ormond Street
Hospital for Sick Children,
London WC1N 3JH
Bryan Lask, FRCPsych,
consultant psychiatrist

Night terrors (*pavor nocturnus*) are characterised by screaming, extreme distress, autonomic arousal, and increased body movements (sometimes including sleepwalking).¹ They affect about 3% of children,² often occurring every night. The episodes arise in slow wave sleep (stages 3 and 4), most commonly within two hours of falling asleep.^{1,2} The child cannot be comforted or woken and has no memory of the episodes the next day. There is rarely evidence of an associated psychiatric disorder, and the attacks are thought to represent a fault in slow wave sleep.^{1,2}

A wide range of drugs has been suggested as treatment, including bromazepam, diazepam, midazolam, and imipramine.^{3,4} As there is no firm evidence that they are effective and potential side effects must be a cause for concern non-pharmacological measures should be tried first. Behavioural alteration of the sleep pattern has not previously been described.

Patients, methods, and results

Nineteen successive children (age range 5-13, mean 8.7, 11 boys eight girls) referred to the department of psychological medicine for treatment of night terrors were found to have no physical abnormalities and no psychiatric disorder. Electroencephalographic recordings either yielded normal results or showed non-specific changes. All except one of the children were of average or above average intelligence. The terrors had lasted for between four and 37 months, with a mean of eight months, and generally occurred four to five nights a week.

Each child was treated as follows: parents were asked to note for five successive nights at what time the episodes occurred, and whether there were signs of

autonomic arousal, such as sweating, tachycardia, or increased movements. They were then instructed to wake their child fully 10-15 minutes before the terror occurred or, if this was too difficult to specify, when autonomic arousal was noted. After four to five minutes the child was allowed to return to sleep. The parents were told to stop waking up their children when the terrors had stopped. No other instructions were given.

In each case the night terrors stopped within a week of starting treatment. In three cases terrors returned four to seven weeks later but were completely eliminated by restoration of treatment for a further week. At follow up one year later there had been no further relapses. One boy aged 9 had developed intermittent headaches for which no organic cause could be found but which were eliminated by relaxation twice a day. A girl of 11 had developed a phobia about school four months after treatment was started. This was satisfactorily treated with the help of her parents in a gradual return to school over three weeks. There was no evidence of psychological disturbance or of development of other symptoms in the other children.

Comment

Although the condition is benign and usually resolves within a few years, treatment is indicated because of the intense distress experienced by parents and children and the dangers of sleepwalking. The successful elimination of night terrors by behavioural alteration of the sleep pattern shows that treatment with drugs, which has not been proved to be effective, is unnecessary. Interruption of faulty slow wave sleep seems to cause reversion to a normal sleep pattern and resolution of the disorder. This technique may also be used for sleepwalking alone.

- 1 Matthews B, Oakey M. Triumph over terror. *Br Med J* 1986;292:203.
- 2 Fenwick P. Murdering while asleep. *Br Med J* 1986;293:574-5.
- 3 Vela A, Dobladez M, Ramos M, et al. Action of bromazepam on sleep of children with night terrors. *Pharmatherapeutica* 1982;3:247-58.
- 4 Popoviciu L, Corlariu O. Efficacy and safety of midazolam in the treatment of night terrors in children. *Br J Clin Pharmacol* 1983;16:975-1025.
- 5 Weissbluth M. Is drug treatment of night terror warranted? *Am J Dis Child* 1984;138:1087.

(Accepted 28 April 1988)

Severe reaction to diphosphonate: implications for treatment of Paget's disease

A T Elliott, T Murray, R M Mackie,
J A Hunter

Western Infirmary,
Glasgow G11 6NT
A T Elliott, PhD, top grade
physicist, department of
clinical physics and
bioengineering
T Murray, MPS, principal
pharmacist

University of Glasgow,
Glasgow
R M Mackie, FRCP, professor
of dermatology

Gartnavel General
Hospital, Glasgow
J A Hunter, MRCP,
consultant physician

Correspondence to:
Dr Elliott.

We report a potentially life threatening allergic reaction to sodium medronate, a component of the radiopharmaceutical most widely used for bone scanning. Sodium medronate is a diphosphonate, congeners of which are being used to treat Paget's disease.

Case report

A 47 year old woman who did not have a history of allergy was referred for a bone scan to assess the spread of psoriatic arthritis. Some 12-24 hours after administration of the radiopharmaceutical (Medronate II, Amersham International) an acute episode of vasculitis and erythema multiforme developed. At the time of the injection her skin had been clear, and exacerbation of psoriasis was ruled out. Over the next seven days her condition worsened and she had painful inflamed lesions over 80% of her body, but her domestic circum-

stances precluded admission to hospital. Accordingly, she was treated with a topical corticosteroid (clobetasol propionate twice daily) and seen every second day for two weeks. Her condition responded slowly, requiring treatment for four weeks.

The radiopharmaceutical had been prepared from a multidose phial, from which doses for seven other patients were drawn; none of these other patients developed a reaction. Tests for pyrogens and for sterility yielded negative results, and the manufacturer's quality control records did not show any abnormality. The scans obtained two to three hours after injection showed a normal biodistribution of the radiopharmaceutical in all eight patients, with no uptake in the thyroid. Hypersensitivity to sodium medronate was diagnosed on the basis of the symptoms and their time course.

Comment

Adverse reactions to radioactive diphosphonates, though rare, are the most common type of reactions in nuclear medicine in the United Kingdom, with an incidence of 4.50/100 000.¹ The medical assessor of the British Institute of Radiology, to whom adverse reactions to radiopharmaceuticals are reported, states that most reactions to diphosphonates are reactions to sodium medronate (D Keeling, personal com-

munication). They present typically as macropapular erythematous rashes, though dermatographism, nausea, vertigo, and malaise have also been reported. The reactions commonly develop several hours after administration of the radiopharmaceutical and may last up to 48 hours. These localised reactions are considered to be minor, and only one other severe systemic reaction has been described; in that case rechallenge by skin testing proved a causal relation.² We thought that rechallenge was unwise in our case given the severity of the reaction.

Diphosphonates are present in several radiopharmaceuticals other than those used for bone scanning; examples are agents for labelling red cells (Amerscan Stannous Agent, Amersham International) and imaging the liver (Microlite, Du Pont (United Kingdom)). Alternative agents should thus be used for patients known or suspected to be sensitive to diphosphonates; bone scanning may be done with pyrophosphates. In addition, hypersensitivity reactions may occur in patients with Paget's disease being treated with

therapeutic concentrations of diphosphonates. The radiopharmaceutical that we injected contained only 0.5 mg diphosphonate, whereas single therapeutic doses are in the range 15-30 mg^{3,4} and are administered by intravenous infusion over less than two hours. We therefore suggest that skin testing for sensitivity be considered when pharmaceuticals containing diphosphonates are used therapeutically and it would not compromise management of the patient.

- 1 Keeling D, Sampson CB. Adverse reactions to radiopharmaceuticals: incidence, reporting, symptoms, treatment. *Nuklearmedizin* 1986;23 (suppl):478-82.
- 2 Ramos-Gabatin A, Orzel JA, Maloney TR, Murnane JE, Borchert RD. Severe systemic reaction to diphosphonate bone imaging agents: skin testing to predict allergic response and a safe alternative agent. *J Nucl Med* 1986;27: 1432-5.
- 3 Ralston SH, Alzaid AA, Gardner MD, Boyle IT. Treatment of cancer associated hypercalcaemia with combined aminohydroxypropylidene diphosphonate and calcitonin. *Br Med J* 1986;292:1549-50.
- 4 Cardwell B, Harris AL. Single high dose aminohydroxypropylidene diphosphonate infusions to treat cancer-associated hypercalcaemia. *Lancet* 1986;i: 165-6.

(Accepted 15 April 1988)

Plasmapheresis: a rational treatment for fulminant acute pancreatitis?

M Larvin, M R J Lansdown, M J McMahon, A G Chalmers, J H Turney, A M Brownjohn

The General Infirmary at Leeds, Leeds LS1 3EX
M Larvin, FRCS, pancreatic research fellow
M R J Lansdown, FRCS, lecturer in surgery
M J McMahon, FRCS, senior lecturer, university department of surgery
A G Chalmers, FRCP, consultant radiologist
J H Turney, MRCP, consultant physician
A M Brownjohn, FRCP, consultant physician, regional renal unit

Correspondence to: Mr McMahon.

Roughly 5-10% of attacks of acute pancreatitis prove fatal. Death usually results from fulminant multiorgan failure, with activation of complement, kinin, fibrinolytic, and coagulation cascades, which may be triggered by pancreatic proteases liberated into the circulation. α_2 Macroglobulin, functionally the most important plasma antiprotease, binds proteases irreversibly, forming a complex of around 800 000 daltons. The active site of the protease remains free, so that the complexes retain the ability to hydrolyse peptides. Conformational changes in α_2 macroglobulin trigger phagocytosis by the reticuloendothelial system, clearing complexes from the circulation with a half life of about 10 minutes in health. We recently showed that clearance is impaired in severe pancreatitis,¹ possibly because the reticuloendothelial system is overwhelmed in a manner similar to that which occurs in severe sepsis.

Plasmapheresis is a logical means to aid the reticuloendothelial system and we describe its use in two patients with fulminant acute pancreatitis.

Case reports

Case 1—A 68 year old man developed respiratory and renal failure 72 hours after admission to hospital with severe gall stone pancreatitis (Ranson score 8).² Ventilation and haemodialysis were begun and the pulmonary capillary wedge pressure monitored. CT angiography showed peripancreatic necrosis. Four days after admission he developed severe fever, tachycardia, hypotension, and peripheral vasodilatation. He continued to deteriorate despite antibiotics and plasmapheresis was performed through femoral arterial and venous cannulas. A 2.8 litre exchange was completed with a Curesis plasma separator (3×10^6 dalton filter; Organon Teknika, Cambridge, United Kingdom), replacing filtrate with an equivalent volume of fresh frozen plasma. Vital signs stabilised and the fever decreased (figure). The APACHE II score, which summates abnormalities in 12 physiological variables,³ fell from 33 to 27. Five days later

he deteriorated again, and CT guided aspiration yielded infected peripancreatic debris. Debridement was carried out at laparotomy but failed to influence progressive multiorgan failure, and the patient died 18 days after admission.

Case 2—A 33 year old man was transferred to this hospital four days after admission elsewhere for severe acute alcoholic pancreatitis (Ranson score 6).² He developed a severe toxic confusional state and gross hypoxia (P_{aO_2} 4.7 kPa; F_{IO_2} air). CT angiography