Baclofen overdose

D. J. LIPSCOMB*
M.B., M.R.C.P.

T. J. MEREDITH†
M.A., M.R.C.P.

*Department of Medicine, Peterborough District Hospital, Peterborough PE3 6DA, and

†Poisons Unit, Guy's Hospital, London SE1 9RT

Summary

A 57-year-old woman suffering from multiple sclerosis took an estimated 1500 mg of baclofen. She became deeply unconscious with generalized flaccid muscle paralysis and absent tendon reflexes. Toxicological analysis confirmed the presence of baclofen together with small amounts of paracetamol and glutethimide. Supportive therapy, including assisted ventilation for 3 days, led to complete recovery; anticonvulsant drugs were necessary for the treatment of grand mal fits. The clinical features and treatment of baclofen overdose are discussed.

Introduction

Baclofen (Lioresal, Ciba) is widely used in the treatment of muscle spasticity. It is a lipid-soluble derivative of γ -aminobutyric acid (GABA), a naturally occurring substance which is thought to act as an inhibitory neurotransmitter in the brain. Baclofen acts principally at a spinal level to reduce muscle tone, but it is also thought to have some supraspinal activity (Koella, 1972).

There are few reports of overdose with baclofen. Two cases have been published (Paeslack, 1972; Paulson, 1976) and a further 8 patients have been reported to CIBA and the National Poisons Information Service (NPIS). These latter cases of baclofen overdose have been of a minor nature and are poorly documented. Muscle weakness, impaired consciousness and involuntary movements were commonly noted features. A published case report of severe overdosage (Paulson, 1976) describes respiratory depression which required artificial ventilation, but toxicological analysis was not performed. Now reported is the first case of baclofen overdose to be substantiated by measurements of blood concentrations of the drug.

Methods

Blood and urine samples from the patient were subjected to a toxicological screen. Glutethimide was detected and measured by the method of Flanagan and Berry (1977) and paracetamol by the method of Glynn and Kendal (1975). Serial baclofen estimations were made using the method of Degen and Riess (1976).

† Requests for reprints to Dr T. J. Meredith.

Case report

A 51-year-old woman, who had suffered from multiple sclerosis for 15 years, was prescribed baclofen 40 mg daily as part of her treatment for spastic paraplegia. One morning, she was found lying in bed unconscious and was admitted to hospital. Information given by her husband suggested that an overdose of baclofen (consisting of 152 10-mg tablets) had been taken about 2.5 hr before being found unconscious. On arrival in hospital 90 min later, she was deeply unconscious and unresponsive to painful stimuli. Respiration was depressed and the cough reflex was absent. She was intubated without resistance and ventilated; gastric lavage was performed but no tablets were returned in the lavage fluid. Further examination revealed profound hypotonia with an absence of spontaneous movement and absent limb reflexes. Pupils were pinpoint and reacted sluggishly to light. Temperature 35.0°C, pulse-rate 80/min in sinus rhythm and BP 130/80 mmHg. Three hours after admission the first of a number of grand mal fits occurred. These responded to intravenous diazepam as did a subsequent fit. Intramuscular phenobarbitone was given for further convulsions but resulted in a hypotensive episode (BP 75/0 mmHg). Elevation of the foot of the bed and increased intravenous fluids soon corrected the hypotension. Thereafter, phenobarbitone was avoided and with regular intravenous injections of diazepam (40 mg in divided doses in the first 24 hr) the fits were controlled.

At 24 hr after admission her condition was unchanged, although occasional involuntary movements of one leg were noted. She remained profoundly flaccid and showed no resistance to ventilation. However, at 30 hr after admission, the peripheral temperature suddenly fell and the extremities became blue and mottled; the core temperature rose to 38.5°C. This episode resolved in a few hours with the use of a space-blanket and increased intravenous fluids. Thereafter her condition improved steadily.

At 48 hr there were spontaneous movements of all limbs although reflexes were still absent. At 72 hr she was opening her eyes and moving her limbs to command; she was taken off the ventilator and breathed spontaneously. On the fifth day limb

FIG. 1. Plasma baclofen levels in a 57-year-old woman who took an overdose of 1500 mg of the drug (Lioresal).

reflexes had returned and, although very drowsy and weak, she was able to sit up. Steady improvement was maintained and by the ninth day she had made a full recovery and was back to her previous condition.

Toxicological analysis of blood and urine samples taken 5.5 hr after ingestion of the overdose revealed small amounts of paracetamol (85 mg/l) and glutethimide (2.3 mg/l). Analysis of subsequent plasma samples showed the presence of baclofen (Fig. 1).

Discussion

The main features of baclofen overdose result from the muscle relaxant properties of the drug which cause hypotonia muscle-weakness, and even respiratory failure in severe cases. Muscle twitching, jerking and grand mal convulsions are common in patients described in the literature (Paeslack, 1972; Paulson, 1976) and in those reported to CIBA and the NPIS. Fits persisted for 24 hr in the present patient and responded only to moderately large doses of diazepam. Convulsions were marked in one case reported to the NPIS. The patient, a 60-year-old man suffering from spinal cord compression, took an unknown quantity of alcohol together with 700 mg of baclofen; the fits responded poorly to repeated injections of diazepam and were finally controlled by a clonazepam infusion. Although respiratory depression was observed, assisted ventilation was not required and recovery was complete.

Serial plasma concentrations of baclofen measured in the patient are shown in Fig. 1. Unfortunately, specimens for baclofen levels were not obtained until the second day of admission at which time the levels were falling. In man, peak plasma levels of baclofen are achieved one to 2 hours after oral administration (0.2–0.4 mg/l following 10 mg baclofen), and the half-life for elimination of the drug is 2 to 4 hr (Faigle and Keberle, 1972). Interestingly,

the baclofen levels in the patient rose on the fifth day after admission at a time of clinical improvement. This may have been a consequence of the lipid solubility of baclofen because at no time was there evidence of an ileus. Thus, as with glutethimide and some barbiturates taken in overdose, a second peak in plasma concentration may occur when the drug is released from the body fat (Graeme, 1968).

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