Lesson of the Week

Near-fatal bronchospasm after oral nadolol in a young asthmatic and response to ventilation with halothane

JUNE M RAINE, M G PALAZZO, J H KERR, P SLEIGHT

It is well recognised that the use of beta-blockers in patients with asthma may be hazardous, but it is not widely known that it may be fatal. We report on a patient with asthma who had an acute bronchospasm that was nearly fatal after taking one dose of nadolol, a long-acting non-cardioselective beta-blocker.¹

Case report

On routine medical examination a 23-year-old music teacher was hypertensive (blood pressure 160/110 mm Hg). She had a history of childhood asthma, with three brief hospital admissions at 17 years of age that had been precipitated by a chest infection. There were no known allergens, and she controlled a tendency to wheeze after exercise by inhaling salbutamol, and required three puffs a day on average. After seven months' treatment with a diuretic her diastolic pressures remained between 90 and 100 mm Hg, and her general practitioner then prescribed nadolol 80 mg daily.

She took the first tablet early on a Sunday morning and shortly afterwards complained that she felt unwell. She then collapsed, suffered a respiratory arrest in the ambulance, and was pulseless. The ambulance crew intubated her, ventilated her manually, and gave external cardiac massage. On arrival in casualty she was making spontaneous respiratory efforts but was centrally cyanosed with a marked wheeze. Her pulse was 80 per minute, inappropriately slow, and she had over 50 mm Hg of paradox. The pupils were widely dilated but reacted slowly to light. The left plantar response was extensor, the right equivocal. Blood gases on manual intermittent positive pressure ventilation and oxygen were: P_{O_2} 12.7 kPa (95 mm Hg), P_{CO_2} 8.46 kPa (64 mm Hg), and pH 7.15.

She was transferred to the intensive therapy unit where she was put on a Servo ventilator. She was started on intravenous aminophylline 250 mg immediately, then 75 mg/h; hydrocortisone 500 mg immediately, then 50 mg/h; and salbutamol 20 mg/h; and on nebulised salbutamol 10 mg every three hours. With a tidal volume of 600 to 800 ml and a respiratory rate of 13-15/min, P_{CO_2} remained at 6-7 kPa (45-53 mm Hg) and pH around 7.3. To achieve this, peak inspiratory airway pressures of 80 cm of water were generated, and she rapidly developed gross surgical emphysema. As she had taken a beta-adrenergic blocker, an isoprenaline infusion was also started, but despite large doses titrated to produce a tachycardia of 120/min the bronchospasm did not relent. After 12 hours a trial of halothane

Giving a beta-blocker to a patient with apparently mild asthma may cause immediate and near-fatal bronchospasm

The effective dynamic compliance (tidal volume (corrected) divided by peak inspiration airway pressure) in an asthmatic patient nearly doubled when she was given halothane.

1% in 100% oxygen was started in an attempt to reduce the surgical emphysema and possibly to lessen bronchospasm.² Within two hours both peak inspiratory airway pressures and P_{CO_2} fell, and the effective dynamic "compliance" almost doubled (figure), at a time when a significant plasma level of nadolol (half life 24 hours) would still be predicted.¹ Intermittent periods off halothane during the next 18 hours resulted in a rapid rise in airway pressures from 40 to 80 cm H₂O. Halothane was continued for 38 hours in decreasing concentrations.

Fifty hours after admission she was weaned from the ventilator and extubated, but she remained unconscious for another four days. She was distressingly restless, and an intravenous infusion of chlormethiazole was given to sedate her. A computed tomographic scan showed no localised cerebral lesion, and there was no obvious improvement after intravenous mannitol and dexamethasone. It is unclear whether this period of unconsciousness was related to the initial hypoxic episode or to her subsequent treatment. On the 6th day she recovered consciousness quite suddenly and communicated with simple sentences. She suffered memory loss for the three days before admission and complained of difficulty with fine movements of the hands, although this has improved steadily.

Her mild hypertension (diastolic blood pressure 100-110 mm Hg) reappeared during recovery, and was treated with hydrala-

Cardiac Department, John Radcliffe Hospital, Headington, Oxford OX3 9DU

JUNE M RAINE, MSC, MRCP, senior house officer in medicine
M G PALAZZO, MB, MRCP, senior house officer in anaesthetics
J H KERR, DM, FFARCS, consultant anaesthetist
P SLEIGHT, MD, FRCP, professor of cardiovascular medicine

zine, which caused a tachycardia, and then methyldopa. Although she was apparently a "mild" asthmatic, subsequent serial measurements of peak flow rate through the day showed a diurnal variation with a consistent early morning dip from 400 l/min to 100-180 l/min, a recognised pattern in some asthmatic patients.³

Discussion

Near-fatal bronchospasm has recently been reported after the accidental ingestion of a single dose of oxprenolol,⁴ although there was a fairly prompt response to conventional intensive therapy. In our patient, however, similar treatment with the addition of large doses of isoprenaline was ineffective, and an appreciable improvement occurred only when halothane was introduced after 12 hours of active therapy. Although halothane has been credited with a beta-2 agonist effect it probably produced bronchodilatation by a direct effect on bronchial smooth muscle.²

This case emphasises the danger of giving beta-blockers to patients with a history of asthma. Some patients whose asthma is in remission may show only minimal changes in peak flow even after taking a non-cardioselective beta-blocker.⁵ Nevertheless, the usual response is a fall in peak flow, which is significantly less with cardioselective drugs than non-cardioselective ones. Cardioselective beta-blockers also permit a bronchodilator response whereas non-selective ones do not.⁶ Thus if beta-blockers are considered essential treatment for a patient with asthma a cardioselective agent should be used,⁶ and treatment should preferably be started under medical observation,

monitoring peak flow for at least two to three hours with bronchodilators available.

There is clearly a worrying lack of awareness of the selectivity or otherwise of currently available beta-blocking drugs. We suggest that in view of the near-fatal outcome of our patient greater attention should be drawn to this point, particularly when new preparations are introduced. The trend towards once-daily dosage with long-acting beta-blockers is an additional hazard in patients such as ours whose medication may be taken at the time when peak flow is at its lowest and the consequences of added bronchospasm most serious.

We are grateful to Dr M K Benson for valuable criticism of the manuscript.

References

- ¹ Hitzenger G. Initial experience with a new long-acting beta-blocker, nadolol, in hypertensive patients. *J Int Med Res* 1979;**7**:33-8.
- ² Aviado D. Regulation of bronchodilator tone during anesthesia. *Anesthesiology* 1975;**42**:68-80.
- ³ Turner-Warwick M. On observing patterns of airflow obstruction in chronic asthma. *Br J Dis Chest* 1977;**71**:73-86.
- ⁴ Williams IP, Millard FJC. Severe asthma after inadvertent ingestion of oxprenolol. *Thorax* 1980;**35**:160.
- ⁵ Benson MK, Berril WT, Sterling GM, *et al.* Cardioselective and non-cardioselective beta-blockers in reversible obstructive airways disease. *Postgrad Med J* 1977;**53**, suppl 3:143-8.
- ⁶ Kumana CR, Martin GE. Selectivity of beta-adrenoceptor agonists and antagonists. In: Turner P, Shank DG, eds. *Recent advances in clinical pharmacology*. Edinburgh and London: Churchill Livingstone, 1978: 33-54.

(Accepted 26 November 1980)

Musings of a Dean

A post-Christmas carol

"What's Christmas time," asked Scrooge, "... but a time for paying bills without money; a time for finding yourself a year older, and not an hour richer; a time for balancing your books and having every item in 'em through a round dozen of months presented dead against you?" Never a more pertinent question for deans, or for vice-chancellors for that matter—and not just at Christmas.

Few people realise how difficult University accounting has become. It used to be possible to plan in five-year periods. Not so now, partly, of course, because of inflation and salary explosion. The financial year begins without knowledge of the year's budget; indeed it may be several months before the figure is announced. Even then there is no undertaking that wage rises, over which the University has no control because they are arrived at by national bargaining, will be reimbursed; indeed it becomes progressively less likely that they will. Responsible, well-judged budgeting is impossible: astrologers, soothsayers, and fortune-tellers would do as well as accountants and better than deans.

As if this were not enough the University Grants Committee (UGC) (which does its best in a hard world) has recently notified universities that they may expect a reduction in recurrent grant for 1981-2 of 3½% as a result of government cuts and almost as much again as a result of new policies for overseas

students. Most of an institution's grant is committed to salaries, and inevitably staff-student ratios and technical support must diminish.

Collapse of the dual-support system

A university's salvation in a competitive world might reasonably be seen to lie in attracting increasing outside funds for research—"soft" money. Soft it may be in the sense that it is the padding in the research of any active department but it is in no way a soft touch. The securing of outside grants is one essential of the dual support system: the UGC grant to universities is intended to provide academic staff salaries and the basic laboratory accommodation (optimistically termed the "well-found" laboratory); grants from research councils and other bodies are expected to provide selective support for specific research projects.

Many faculties and colleges (and medical schools figure high in the list) have been most successful in attracting steadily increasing outside support while their UGC-funding has been static or has actually declined in real terms. Unfortunately, success in attracting new resources has carried with it the seeds of its own destruction. The "well-found" laboratory has not