70 and over and 23.5% for the younger group⁹—a mortality ratio (about 2:1) similar to that in the present study.

Like Linn and Yurt¹⁰ we found that both synchronised DC shock and immediate defibrillation can be performed with considerable success in elderly patients, confirming the impression of Chaturvedi *et al*¹¹ that this group benefits to some extent from early treatment in a coronary care unit.

The study has shown many other similarities and a few important differences between the groups. Older patients did not give rise to more “false alarms” by their admission to the unit. Myocardial infarction, diagnosed before admission, usually by the family doctor or a deputy, was confirmed in similar proportions of both groups (elderly 58%; younger group 54%). A smaller proportion of the elderly were exerting themselves and a larger proportion were asleep at the onset of the attack, compared with younger patients, but this might have been simply a reflection of their pattern of life. Medical history was surprisingly similar in the two groups. Almost exactly half had suffered angina, quite apart from build-up and crescendo angina. More of the older people had had this for over five years. There was no appreciable difference in the proportions who had had infarcts, ischaemic attacks, pre-existing hypertension, or diabetes (table IV).

Complications related to severity and ultimate prognosis were more common in the aged. These included atrial fibrillation, atrial flutter, conduction defects, the “shock picture,” admission systolic blood pressure under 100 mm Hg, and left and right heart failure. Complications unrelated to late prognosis, such as pericarditis and other arrhythmias, showed no such increased incidence (tables V and VI).

Looking at the economics of the elderly in a coronary care unit, we found that the absence of an age bar at 70 years increased the admissions by nearly a quarter (24%) and the number of proved infarcts by just over this proportion (26%). These elderly patients have more severe infarction and death is twice as common as in those under 70. Serious complications are more prevalent, mild and reversible ones not so. The average

for monitoring time is about the same in the two groups, but when survivors only are considered the elderly spend a longer mean time in the unit and in hospital. Admitting the aged to a unit is less rewarding and necessarily entails later transfer and discharge of surviving patients, who, because of more extensive disease or for social reasons, tend to occupy general medical beds longer than younger subjects. Keeping them at home when possible, at the expense of a few lives in the mild group not saved by immediate defibrillation, may often be kinder, sounder from the psychological point of view, and beneficial therapeutically. In economic terms such a policy would contribute to coronary care unit cost-benefit efficiency by helping to ensure that these facilities are not denied to wage-earning patients. Ethical and moral considerations, however, as always, must modify admission policy, the ideal being to afford the best standards of care to all patients, irrespective of age or work potential.

We thank Miss Kathleen Scott and the nursing staff of the unit; our junior medical colleagues who contributed so much to the care of these patients and to the compilation of their clinical data; and Miss Monica Jordan, of the bioengineering department, Strathclyde University, for the computer analysis.

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Effect of atenolol on ventilatory and cardiac function in asthma

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Summary

The effects on ventilatory and cardiac function of atenolol, a new cardioselective beta-adrenoceptor blocking agent, were compared with those of practolol in a double-blind trial in 12 patients with asthma. Both drugs impaired ventilatory function—atenolol insignificantly and practolol significantly. Atenolol was if anything more cardioselective than practolol. Neither drug interfered signifi-

cantly with the bronchodilator response to inhaled isoprenaline. Atenolol is suitable for use in patients for whom practolol would formerly have been chosen because of its cardioselectivity.

Introduction

There is a risk in giving beta-blockers to asthmatics. The value of practolol for such patients has, however, been clearly shown,¹⁻³ but it is no longer available for general use.

Atenolol is a new beta-adrenoceptor blocking agent that appears from animal studies to possess a degree of cardioselectivity equivalent to that of practolol.⁴ Studies in man have confirmed that atenolol has beta-blocking properties⁵ and have shown it to be potentially useful.⁶⁻⁹ Our trial was designed to measure the effect of atenolol on ventilatory and cardiac function in patients with chronic asthma and to compare these effects with those of practolol.

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Patients and methods

Twelve patients were admitted to the study, eight men and four women with a mean age of 51.5 years (range 34-64 years). All had established chronic asthma that showed a significant degree (20%) of reversibility on administration of a beta-receptor stimulant aerosol. They were all in a stable state and no other diseases were present. Renal and hepatic functions were normal. Nine patients were using steroids and continued to do so at the same dose during the trial. Bronchodilator drugs were stopped at least 12 hours before any readings were made. No other drugs that might have influenced heart and pulmonary function were used during the study. All patients gave their informed consent, and all ethical questions were thoroughly discussed and the trial approved by the ethical committee.

The study was designed as a double-blind crossover trial in which all patients received both drugs (atenolol 100 mg, practolol 300 mg in each dose) as identical-looking tablets. The order in which the drugs were given was determined by a random code. The study occupied five days.

Day 1—In the morning the patient was seated relatively comfortably on a mechanically braked bicycle ergometer for 5-10 minutes to reach a steady state. At 0930 (time -5 minutes), peak expiratory flow rate (PEFR), forced expiratory volume in 1 second (FEV₁), resting blood pressure, and heart rate were measured. The circulatory measurements were performed before recording the respiratory values. The patient then exercised at 600 kpm/min (women 450 kpm/min) for five minutes, and the measurements were repeated at the end of the exercise (time 0) and 10, 30, and 45 minutes afterwards. At 45 minutes the patient received 1500 µg of isoprenaline sulphate by inhalation as 500 µg × 3 puffs from a pressure-packed aerosol every half minute. The cardiovascular measurements were repeated 5 minutes (at 50 minutes) and the ventilatory measurements 20 minutes (at 65 minutes) after the inhalation. PEFR and FEV₁ were measured with a Fleisch pneumotachygraph linear up to 8 l/sec. The highest of three readings was considered representative. Heart rate was measured continuously by electrocardiograms and blood pressure by mercury manometer and auscultation, taking the 4th sound (muffling) as the diastolic end point. At 2000 the patient was given the appropriate tablets marked with his number and the time.

Day 2—The patient received the second dose of tablets at 0800.

A needle was inserted in the brachial artery, and a cannula was passed through a brachial vein to the vena cava. The patient was again seated on the bicycle for 5-10 minutes to reach a steady state. At 0930 the same sequence of measurements as on day 1 was started, and additional measurements were made of cardiac output at -5, 0, 45, and 50 minutes and arterial blood gas tension at -5, 0, 45, and 65 minutes. Cardiac output was measured by dye dilution technique (Cardio-Green) and recorded on a Beckman Cardiodensimeter. Blood gas tension was determined on a Radiometer ABL 1. Blood pressure was measured through the indwelling needle in the brachial artery.

Day 3—No measurements were made and no drugs given.

Days 4 and 5—The procedures specified for days 1 and 2 were repeated, and the other drug in the patient's individual set of tablets was given.

Control values for each drug were thus obtained on the day before its administration (days 1 and 4 in the morning). Control values for cardiac output and blood gases were not obtained since another two arterial punctures would have been necessary, and only pre-exercise values were therefore registered. As stable a state as possible was ensured by keeping the patients in hospital during the study and keeping their medication unchanged as far as possible.

Student's *t* test was used for statistical evaluation.

Results

Table I shows the mean resting control values for each drug (days 1 and 4). There were no significant differences between respiratory or circulatory values.

Table II shows the differences in FEV₁, PEFR, heart rate, and blood pressures on practolol and atenolol compared with the control values. Mean FEV₁ and PEFR tended to be lower after practolol than after atenolol, but the differences were not statistically significant. After atenolol mean resting PEFR and FEV₁ were slightly lower than control values, but the differences were not statistically significant. The immediate bronchodilator response to exercise also showed some reduction. After practolol, however, all mean values for PEFR were significantly lower than the control measurements, as were most of the mean values for FEV₁. Neither drug significantly impaired the bronchodilator response to inhaled isoprenaline.

Heart rate and systolic and diastolic blood pressure at rest and after exercise were significantly reduced by both drugs. The effect of atenolol on heart rate was consistently and significantly greater than that of practolol. Its effect on blood pressure was also greater, but the differences were only occasionally significant.

Table III shows the effect of practolol and atenolol on cardiac output and blood gases. Cardiac output tended to be slightly but not significantly lower after atenolol than after practolol. Similar blood gas values were obtained after both drugs. There was a slight fall in

TABLE I—Control values (mean ± SE) at rest (days 1 and 4)

	FEV ₁ (l)	PEFR (l/min)	Heart rate (beats/min)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
Before practolol ..	1.60 ± 0.18	288 ± 31	83 ± 2.9	135 ± 5.2	85 ± 2.9
Before atenolol ..	1.57 ± 0.17	274 ± 27	88 ± 3.8	131 ± 6.9	85 ± 4.0

TABLE II—Comparison of effect of practolol and atenolol on FEV₁, PEFR, heart rate, and systolic and diastolic blood pressure. Results (mean ± SE) are expressed as differences from control values

	FEV ₁ (l)	PEFR (l/min)	Heart rate (beats/min)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
<i>At rest (5 minutes)</i>					
Practolol	-0.19 ± 0.11	-43 ± 19.2	-8 ± 3	-2 ± 6	-12 ± 3
Atenolol	-0.03 ± 0.11	-20 ± 19.5	-22 ± 3***	-9 ± 5	-16 ± 3*
<i>Exercise</i>					
Practolol	-0.27 ± 0.09	-55 ± 17.9	-29 ± 5	+2 ± 7	-12 ± 5
Atenolol	-0.19 ± 0.10	-44 ± 12.9	-33 ± 5***	-9 ± 5**	-19 ± 3
<i>At 10 minutes</i>					
Practolol	-0.27 ± 0.09	-58 ± 14.6	-7 ± 4	+15 ± 7	-9 ± 4
Atenolol	-0.20 ± 0.12	-26 ± 17.8	-12 ± 4**	-3 ± 6	-16 ± 3*
<i>At 30 minutes</i>					
Practolol	-0.31 ± 0.10	-66 ± 19.3	-6 ± 4	-7 ± 13	-18 ± 6
Atenolol	-0.25 ± 0.10	-23 ± 21.2	-13 ± 3***	-2 ± 5*	-20 ± 4
<i>At 45 minutes</i>					
Practolol	-0.26 ± 0.08	-46 ± 17.4	-8 ± 3	-6 ± 9	-16 ± 4
Atenolol	-0.20 ± 0.09	-26 ± 10.9	-18 ± 4**	-12 ± 6	-22 ± 3
<i>5 minutes after isoprenaline (at 50 minutes)</i>					
Practolol			-23 ± 5	-13 ± 7	-13 ± 5
Atenolol			-27 ± 5	-21 ± 5	-15 ± 3
<i>20 minutes after isoprenaline (at 65 minutes)</i>					
Practolol	-0.15 ± 0.09	-37 ± 16.7			
Atenolol	-0.04 ± 0.09	-11 ± 7.3			

*P < 0.05. **P < 0.01. ***P < 0.001.

TABLE III—Comparison of effect of practolol and atenolol on cardiac output (measured in only 11 patients) and blood gases. Results are means $\pm$ SE

		Cardiac output (l/min)	Paco ₂ (kPa)	Pao ₂ (kPa)
<i>At rest (5 minutes)</i>				
Practolol	..	6.66 $\pm$ 0.53	4.9 $\pm$ 0.12	11.3 $\pm$ 0.36
Atenolol	..	6.40 $\pm$ 0.48	4.8 $\pm$ 0.15	11.5 $\pm$ 0.44
<i>Exercise</i>				
Practolol	..	12.67 $\pm$ 1.16	5.2 $\pm$ 0.21	12.9 $\pm$ 0.41
Atenolol	..	11.02 $\pm$ 0.83	5.1 $\pm$ 0.16	11.9 $\pm$ 0.44
<i>At 45 minutes</i>				
Practolol	..	7.35 $\pm$ 0.72	4.7 $\pm$ 0.15	11.2 $\pm$ 0.44
Atenolol	..	6.23 $\pm$ 0.40	4.8 $\pm$ 0.11	11.2 $\pm$ 0.36
<i>5 minutes after isoprenaline (at 50 minutes)</i>				
Practolol	..	7.65 $\pm$ 0.76		
Atenolol	..	6.67 $\pm$ 0.72		
<i>20 minutes after isoprenaline (at 65 minutes)</i>				
Practolol	..		4.5 $\pm$ 0.16	10.7 $\pm$ 0.40
Atenolol	..		4.5 $\pm$ 0.09	11.5 $\pm$ 0.35

Conversion: SI to traditional units—1 kPa $\approx$ 7.5 mm Hg.

Pao₂ after isoprenaline when on practolol that was not present on atenolol, but the difference was not significant.

The pattern of variation of the values was similar in all patients.

Discussion

The cardioselectivity of practolol has recently been shown by many workers.^{1, 3, 10-12} It therefore seemed reasonable to compare the effects of a new beta-adrenergic blocking agent with those of practolol.

Marlin *et al*¹³ suggested that the bronchopulmonary effect of atenolol was intermediate to those of propranolol and practolol. Our results indicate that atenolol is at least as selective for cardiac beta-adrenoceptors as practolol. This claim can be made with some confidence since tests for blockade of cardiac beta-receptors (exercise tachycardia) and for blockade of bronchial receptors (bronchodilator response to inhaled isoprenaline) were both carried out. Cardioselectivity is a relative concept,

and, clearly, every cardioselective beta-blocker may have unwanted effects on ventilatory function. These drugs should accordingly be used with caution in patients with obstructive airways diseases.

Atenolol did not reduce FEV₁ and PEFR substantially. This confirms the findings of Åström,⁹ who gave atenolol intravenously to five patients with asthma without observing an increase in airways resistance. We observed a slight decrease in FEV₁ and PEFR after exercise, but none of the patients complained of any discomfort.

Neither atenolol nor practolol interfered significantly with the bronchodilator effect of inhaled isoprenaline. This non-interference with the effect of exogenous, and presumably endogenous, beta-agonists on bronchial smooth muscle may be one of the more clinically valuable characteristics of the selective compared with the non-selective blockers.

The dose of atenolol we used was derived from animal studies. It might have been too high compared with that of practolol as judged from the effect on the heart rate. But the fact that its effect on the airways was still small indicates that atenolol is even more cardioselective than practolol. Atenolol therefore seems to be an appropriate drug to use when practolol would formerly have been chosen because of its cardioselectivity.

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SHORT REPORTS

Hodgkin's disease presenting with hypoadrenalism

Kaplan¹ and Smithers² reported that although 8% of patients with Hodgkin's disease will be found at necropsy to have invasion of the adrenal glands, clinical evidence of hypoadrenalism is "seldom if ever recognisable during life." No such case has, in fact, been recorded, and the following report is therefore unique.

Case report

A 52-year-old woman presented in September 1974 with a three-week history of severe epigastric pain, watery diarrhoea, and vomiting. She had felt well up to eight months previously but had then noticed lassitude, anorexia, and weight loss and had bouts of abdominal pain. An appendicectomy had been performed in 1945. Excision biopsy of an enlarged tuberculous inguinal lymph node in 1970 was followed by eight months' treatment with streptomycin para-aminosalicylic acid, and isoniazid.

The patient was pale, cyanosed, and moderately dehydrated but apyrexial and normotensive (110/75 mm Hg). Her abdomen was soft with normal bowel sounds but there was some epigastric tenderness. No other abnormality was detected. Haemoglobin was 16.0 g/dl, packed cell volume 0.50 (50%), and white cell count 8.5×10^9 /l (8500/mm³). Despite evidence of dehydration, supported by a blood urea of 15 mmol/l (90 mg/100 ml), the serum Na⁺ was 121 mmol (mEq)/l, Cl⁻ 92 mmol (mEq)/l, and K⁺ 5.7 mmol (mEq)/l. Intravenous dextrose 5% and normal saline were given and she rapidly improved.

Forty-eight hours after admission her condition suddenly deteriorated and she had an epileptiform fit. Serum electrolytes suggested water intoxication, which recurred on several occasions. Pigmentation was noted in the palmar creases, and hypoadrenalism was provisionally diagnosed. A tetra-cosactrin test showed low plasma cortisol levels with an inadequate response to stimulation. There was a good clinical response to cortisone acetate 10 mg four times a day, fludrocortisone 0.2 mg daily, and Slow-K 600 mg three times a day. The electrolytes returned to normal and she was discharged.

Three weeks later she was readmitted with signs of peritonitis after the sudden onset of agonising abdominal pain. Laparotomy showed a small perforation in the jejunum distal to a neoplastic stricture, the rest of the gut being normal. The affected bowel was resected. Histologically the jejunum showed lymphocyte-depletion Hodgkin's tumour tissue (see figure) forming the floor of an annular ulcer, which had perforated. Seedling foci of Hodgkin's infiltrate were present in the lamina propria of the adjacent jejunal mucosa, which showed subtotal villous atrophy. A further perforation occurred three weeks later, and a second laparotomy showed multiple Hodgkin's tumours of the small bowel, confirmed histologically. The patient died three weeks later from pneumonia, shortly after starting combination chemotherapy.

Necropsy showed bilateral bronchopneumonia and multiple small perforations throughout the small bowel. The retroperitoneal lymph nodes were extensively enveloped by tumour which had surrounded the inferior vena cava, invading and almost obliterating the adrenal glands. The mediastinal and supraclavicular nodes were affected, and there were deposits in the thyroid and gall bladder. Histological examination confirmed the presence of lymphocyte-depletion Hodgkin's disease in all affected areas. Ante-mortem thrombus was present in the central adrenal veins, giving rise to infarction of the adrenal glands, which were surrounded and almost obliterated by tumour. The adrenals were not tuberculous and the pituitary gland was normal.