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RISK OF MYOCARDIAL ISCHAEMIA DURING ANAESTHESIA IN TREATED AND UNTREATED HYPERTENSIVE PATIENTS

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SUMMARY

Hypertensive patients were monitored for myocardial ischaemia during anaesthesia and surgery with the V5 lead of a standard electrocardiograph. Myocardial ischaemia was detected in 11 of 39 untreated hypertensive patients and in four of seven receiving therapy with a diuretic, but in none of 44 receiving atenolol. Fourteen of the atenolol-treated patients were receiving the drug on a long-term basis and the remaining 30 were treated acutely only on the morning of surgery. When myocardial ischaemia was observed, it was always associated with noxious stimulation and tachycardia, but a conspicuous increase in arterial pressure was not usually present. We conclude that myocardial ischaemia is prevalent during anaesthesia in untreated hypertensive patients, and that pretreatment with atenolol, but not diuretics, provides prophylaxis.

Hypertension increases the risk of myocardial ischaemia during anaesthesia [1, 2] and antihypertensive therapy reduces that risk [3]. This study was undertaken to corroborate the studies of Prys-Roberts and his colleagues, and to determine if the type of antihypertensive therapy influences either the incidence of myocardial ischaemia or the vital signs seen during anaesthesia and surgery.

Diuretics and β-adrenoceptor antagonists are prescribed commonly for the treatment of hypertension. In this study we have compared untreated, chronically treated and acutely treated patients.

PATIENTS AND METHODS

With the approval of the Central Oxford Research Ethics Committee, 90 mildly to moderately hypertensive surgical patients were studied. Sixty-nine were not receiving antihypertensive therapy; at least three measurements of arterial pressure on the day before surgery were between 160/90 and 200/100 mm Hg. With their informed consent, 30 of these untreated hypertensive patients were allocated randomly to receive a single 50-mg tablet of atenolol by mouth 2 h before induction of anaesthesia. Patients suffering from heart block, heart failure or asthma were excluded. Fourteen other patients with a history of hypertension were receiving atenolol 50 or 100 mg per day for a prolonged period including the day of operation. Seven additional patients were receiving chronic diuretic antihypertensive therapy (chlorothiazide-3, furosemide-2, spironolactone-1, chlorthalidone-1) up to the day of operation. These chronically treated patients were receiving only one antihypertensive drug. No patient had a history of overt coronary heart disease or a preoperative electrocardiogram indicating left ventricular hypertrophy and strain or left bundle branch block.

The decision to proceed with anaesthesia and operation was left to the discretion of independent clinicians who selected an appropriate premedication and anaesthetic. Opioids, benzodiazepines and vagolytic drugs were prescribed

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frequently as premedication. Those who did not receive opioid premedication were given fentanyl during induction of anaesthesia, which was with thiopentone or etomidate; a myoneural blocker was administered to facilitate tracheal intubation. Halothane was the volatile agent used most commonly, but nitrous oxide with opioid supplementation and enflurane were also frequently administered. All patients underwent major surgery, which varied in duration, and those patients who had long procedures usually received additional opioid before emergence.

In the anaesthetic room, operating theatre and recovery area a V5 lead of the electrocardiogram was displayed continuously, and calibrated paper strip recordings were obtained during induction, tracheal intubation, the early phase of surgery, other intraoperative stressful periods, emergence, extubation of the trachea and at any time the vital signs changed significantly or myocardial ischaemia was seen on the monitor. Subsequently, these electrocardiographic recordings were interpreted by a cardiologist who was unaware of the patient's group or therapy. The diagnosis of myocardial ischaemia was based upon the appearance of new ST-segment depression of at least 1 mV with a horizontal or downsloping configuration (fig. 1). Heart rate and arterial pressure were measured and recorded every 1 min by a non-invasive Datascope Accutorr system.

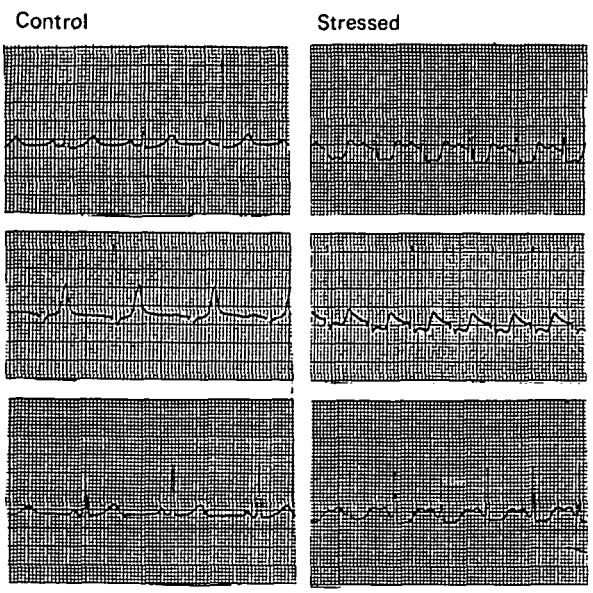

FIG. 1. Electrocardiographic records from three different patients before and during ischaemia.

Venous blood samples (5 ml) were obtained from the patients medicated with atenolol just before induction of anaesthesia and again upon entry to the recovery area. After centrifugation, the supernatant was frozen and the plasma concentration determined at a later date by gas–liquid chromatography [4]. Categorical data were evaluated by chi-square analysis, and numerical comparisons performed by analysis of variance and unpaired t tests which were corrected for inequalities of variance as described by Bonferroni. $P < 0.05$ was considered significant.

RESULTS

Myocardial ischaemia was detected in 11 of 39 untreated control patients, in four of seven treated with diuretics and in none receiving atenolol. Those patients who were either untreated or treated with a diuretic demonstrated significantly more myocardial ischaemia than the atenolol-medicated patients ($P < 0.001$), even though their risk factors and demographic characteristics were not significantly different.

All ischaemic episodes took place during stimulation of great intensity such as intubation of the trachea or emergence from anaesthesia. With one exception, all were self-limited and of short duration, and no patient suffered a perioperative myocardial infarct. Tachycardia was present during all of these episodes, heart rate reaching a mean (SEM) of 119 (3) beat min^{-1} at those times. Patients who did not develop myocardial ischaemia during intubation or emergence (and excluding those who received atenolol) were found to have a slower concurrent mean heart rate of only 93 (3) beat min^{-1} ($P < 0.05$). In contrast, a conspicuous increase in arterial pressure did not usually accompany the development of ischaemia. During ischaemic episodes the associated mean systolic arterial pressure was 192 (11) mm Hg, which was not significantly different from that found during tracheal intubation or emergence in patients who did not receive atenolol or develop ischaemia (179 (13) mm Hg).

Ventricular extrasystoles were observed during intubation or emergence in seven untreated patients and in two receiving diuretic therapy, But ectopic beats were not seen in patients treated with atenolol ($P < 0.001$). Episodes of bradycardia, defined as at least 1 min with heart rate of less than 45 beat min^{-1}, were noted only in patients medicated with atenolol. The incidence

TABLE I. *Measurements of arterial pressure and heart rate (mean (SEM)). Significant changes (P < 0.05) from measurement *on day before operation; †before induction*

	Day before operation	Before induction	Tracheal intubation	Emergence
Systolic arterial pressure (mm Hg)				
Untreated	169 (3)	161 (3)	179 (5)†	182 (6)†
Diuretic	166 (6)	173 (7)	178 (11)	191 (7)†
Chronic atenolol	158 (4)	147 (5)	171 (9)†	164 (7)†
Acute atenolol	168 (3)	135 (4)*	140 (5)	144 (6)
Diastolic arterial pressure (mm Hg)				
Untreated	89 (1)	87 (2)	98 (3)†	100 (3)†
Diuretic	85 (3)	84 (4)	94 (5)†	101 (7)†
Chronic atenolol	94 (2)	80 (4)*	99 (5)†	94 (3)†
Acute atenolol	92 (1)	80 (2)*	91 (4)†	88 (2)†
Heat rate (beat min^{-1})				
Untreated	79 (2)	78 (3)	99 (3)†	100 (2)†
Diuretic	77 (5)	86 (6)	102 (5)†	104 (7)†
Chronic atenolol	65 (3)	58 (2)	81 (2)†	79 (2)†
Acute atenolol	78 (2)	60 (2)*	72 (2)†	71 (2)†

of bradycardia was 30% in these atenolol-treated patients, and thus it occurred more frequently than in the other groups ($P < 0.001$). Hypotension, defined as a persistent systolic arterial pressure of less than 70 mm Hg, occurred on induction of anaesthesia in two untreated patients, in one receiving diuretic therapy and in four who had received atenolol. However, this apparent difference between groups was not significant. Moreover, neither hypotension nor bradycardia were associated with myocardial ischaemia.

Arterial pressure was similar in all four groups on the day before surgery. In the group receiving chronic atenolol therapy, heart rate was slower ($P < 0.05$) (table I). In the operating theatre before the induction of anaesthesia, the patients who had received either chronic or acute atenolol treatment had slower heart rates and lower arterial pressures than the others ($P < 0.05$). During tracheal intubation and emergence from anaesthesia, heart rate and arterial pressure increased in almost every patient. However, patients acutely treated with atenolol demonstrated the most attenuation of vital signs and thus the lowest peaks ($P < 0.05$); those receiving chronic atenolol therapy had slower heart rates than the untreated or diuretic-treated patients ($P < 0.05$), even though arterial pressures were not significantly different.

The therapeutic plasma concentration for atenolol varies between 200 and 5000 ng ml^{-1} [5]. The patients in this study who received acute atenolol treatment had a mean plasma concentration of 324 (54) ng ml^{-1} just before induction and a plasma concentration of 321 (40) ng ml^{-1} shortly after emergence. Those receiving chronic atenolol therapy had concentrations of 439 (93) and 302 (78) ng ml^{-1}, respectively.

DISCUSSION

Despite advances in recognition and therapy, hypertension remains a major cause of death and disability from coronary, cerebral and renovascular disease. Anaesthetic risk also is increased by hypertension [6], as these patients are more likely to exhibit substantial fluctuations in haemodynamic state [1, 3, 7], myocardial ischaemia [1, 2, 7] and perioperative myocardial reinfarction [8] than normotensive control patients. Chronic antihypertensive therapy tends to stabilize arterial pressure and to decrease the incidence of ischaemia during anaesthesia [1, 3, 7]. However, as the present study shows, not all therapy is equally protective.

β-Adrenoceptor antagonists competitively inhibit sympathetic adrenergic overactivity and thereby suppress increases in arterial pressure,

heart rate and myocardial oxygen consumption. Blunting the hyperdynamic response to stress during anaesthesia is responsible for the reduced incidence of myocardial ischaemia and arrhythmias [3]. Various beta-blockers and different routes of administration have proved effective in the operating room. Atenolol has been used to attenuate arrhythmias during fibreoptic bronchoscopy [9], but these patients were pretreated for 3 days before surgery. In this study prophylaxis agonist both ischaemia and arrhythmia was achieved equally well with either chronic atenolol therapy or a single dose of the smallest commercially available tablet, taken 2 h before surgery.

Atenolol is absorbed rapidly following oral administration and the plasma concentration is sustained for a minimum of 12 h thereafter [10]. When ambulatory patients receive beta-blockers for the first time, bradycardia and postural hypotension are not uncommon [11]; we believe this observation provides a possible explanation for why the acutely pretreated patients in this study had lower arterial pressures and slower heart rates during anaesthesia than those receiving chronic atenolol therapy.

All beta-blockers slow heart rate, but atropine 1 mg i.v. produced an increase in the heart rate of our patients. Atenolol is a cardioselective or beta-1 adrenoceptor antagonist, but its specificity diminishes as the dose increases [12]. Although not statistically more prevalent in the atenolol-treated groups in this study, hypotension may well occur as a result of the unopposed beta-2 vasodilator action of the drug, its inhibition of plasma renin activity, negative inotropic effect and additive interaction with potent anaesthetics. Nevertheless, the hypertensive patient behaves in a more labile fashion during anaesthesia, and it is not possible from our data to determine if atenolol contributed to any of the observed hypotension.

Diuretics are the most commonly prescribed antihypertensive therapy. However, recent reports indicate that hypertensive patients controlled with diuretics may show a higher incidence of both myocardial infarction and sudden death than those treated with other forms of therapy [13–16]. Although the group of patients in this study who were receiving diuretic antihypertensive therapy was small, it appears that these drugs provided little if any protection against stress-induced myocardial ischaemia. Moreover, arterial pressure and heart rate during anaesthesia were not different from those seen in the untreated control group. We postulate that the failure of the diuretics to provide protection may be related to two actions: first, diuretics decrease blood volume [17] and increase circulating concentrations of vasoactive substances [18–21], leading to increased cardiovascular lability; second, many diuretics cause greater extracellular than intracellular depletion of potassium [22] and thus increase the tendency to ventricular ectopic activity [23, 24].

Another form of antihypertensive therapy which has been advocated recently for perioperative use is clonidine by mouth [25, 26]. This drug acts centrally to reduce sympathetic outflow and thereby decreases plasma catecholamine and aldosterone concentrations and renin activity.

The principal conclusions to be drawn from this study are:

(1) Untreated hypertensive patients are at considerable risk of developing myocardial ischaemia during anaesthesia.

(2) Ischaemia occurs during stressful stimulation and is accompanied by tachycardia.

(3) Antihypertensive therapy with diuretics does not protect anaesthetized patients against the risk of ischaemia.

(4) β-Adrenergic blockade with atenolol appears to protect, whether taken before operation on a chronic basis or given acutely as a single, small, oral dose on the day of operation.

(5) Beta-blocker prophylaxis produces a slower heart rate during anaesthesia and operation and may induce hypotension.

(6) If beta-blocker prophylaxis is used, anaesthesia and surgery can probably be undertaken with safety in the mildly or moderately hypertensive patient.

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