HAEMODYNAMIC DISTURBANCES DURING ANAESTHESIA IN A PATIENT RECEIVING CALCIUM CHANNEL BLOCKERS

A. M. GORVEN, G. M. COOPER AND C. PRYS-ROBERTS

Calcium channel blocking drugs are being used increasingly to treat cardiovascular disease; consequently more and more patients receiving these agents are presenting for surgery. Although a recent review (Prys-Roberts, 1984) highlighted some of the potential problems associated with anaesthesia and the administration of calcium channel blockers, few reports have detailed the frequency of the complications or considered whether these agents have a protective effect similar to that experienced with β-adrenoceptor antagonists. We present a case report of a patient undergoing aortic surgery who was being treated with two calcium channel blockers, nifedipine and verapamil.

CASE REPORT

A 55-year-old, 80-kg Caucasian male was admitted for elective aortic bifemoral grafting for vascular occlusive disease. He had been a heavy smoker for the previous 35 yr and was known to have been hypertensive for 25 yr. During the previous 6 yr, his antihypertensive therapy had been changed frequently because the various drugs had produced either unacceptable side-effects or inadequate therapeutic effect. Only nifedipine 20 mg twice daily controlled his arterial pressure without side effects. He was also taking verapamil 40 mg three times a day to suppress episodes of paroxysmal atrial tachycardia which had necessitated numerous hospital admissions. He had previously abandoned propranolol because it worsened his peripheral limb ischaemia. Arterial pressure on these medications averaged 150/80 mm Hg during the day before operation. Atrial fibrillation had been present for the 14 months before surgery and was evident on his preoperative ECG (80–90 beat min⁻¹, a QRS axis of +30°, left ventricular hypertrophy and evidence of a left ventricular strain pattern).

The patient received his normal morning doses of nifedipine 20 mg and verapamil 40 mg by mouth 2 h before, and premedication of papaveretum 20 mg and hyoscine 0.4 mg i.m. 1 h before surgery. On arrival in the anaesthetic room the patient was well sedated, an ECG was attached (CM5 position) and peripheral venous and brachial arterial cannulae were inserted under local anaesthesia. The arterial pressure and ECG were displayed continuously on a Hewlett-Packard monitor calibrated electronically and continuous recordings obtained (Mingograph). After pre-oxygenation, anaesthesia was induced with fentanyl 250 μg and Althesin 60 mg (as total steroid). Endotracheal intubation was facilitated by neuromuscular blockade with pancuronium 8 mg.

SUMMARY

Haemodynamic changes (supraventricular tachycardia, decreases in arterial pressure) were observed during laryngoscopy and intubation of the trachea in a patient receiving nifedipine and verapamil. Before the induced stresses of laryngoscopy and tracheal intubation, these drugs had controlled the patient’s arterial pressure and heart rate satisfactorily, and possible reasons why this was not so at the commencement of anaesthesia are discussed.
Anaesthesia was maintained with 67% nitrous oxide in oxygen, delivered by an Oxford–Penlon ventilator through a circle system without an absorber to maintain normal $P_{\text{ET}}^{\text{CO}_2}$.

The changes in systolic and diastolic arterial pressures and heart rate with events during anaesthesia and surgery are shown in Table I. Supraventricular tachycardia (144 beat min$^{-1}$) developed at laryngoscopy and intubation, was sustained for 5 min, and gradually resolved spontaneously 8 min after laryngoscopy (fig. 1). A catheter for monitoring central venous pressure was introduced via the right internal jugular vein. A second catheter was inserted to the extradural space at T8–9 and 0.5% bupivacaine 6 ml was administered and supplemented with a further 3 ml during the operation to provide intraoperative analgesia. The remainder of the anaesthetic proceeded uneventfully, there being minimal changes in heart rate and arterial pressure at cross-clamping of the aorta. At the completion of surgery, residual neuromuscular blockade was reversed, the trachea extubated and the patient transferred to the intensive care unit (ICU), 5 h after the induction of anaesthesia, awake and breathing oxygen-enriched air spontaneously by face mask.

On arrival in the ICU the patient was in some discomfort, and on reconnection of his arterial catheter to the monitoring system, his systolic arterial pressure was in excess of 360 mm Hg, a value which was confirmed by sphygmomanometry to be 300/150 mm Hg. This was controlled rapidly by the administration of 0.5% bupivacaine.
8 ml to the extradural space followed by a continuous infusion (3 ml h⁻¹) of 0.25% bupivacaine via the extradural catheter. This provided good analgesia, and heart rate and arterial pressure stabilized. The patient made an uneventful recovery, was transferred from ICU on the 2nd day after operation and discharged from hospital 10 days after operation.

**DISCUSSION**

The above report describes a patient presenting for anaesthesia and surgery while on treatment with two calcium channel blocking agents, verapamil and nifedipine, and the subsequent events. Neither of these drugs had been used in the first-line management of his hypertension and supraventricular tachycardia because numerous other agents had resulted in either an inadequate therapeutic effect or unacceptable side-effects. The hypertension and supraventricular tachycardia were well controlled during the 6 months preceding surgery, and yet continuation of this maintenance therapy was unable to prevent potentially harmful cardiovascular responses to stressful stimuli during the perioperative period. The increase in heart rate following induction and laryngoscopy was matched by a decrease in arterial pressure as left ventricular filling decreased during the shorter diastolic period. There was no response to 15° head-down tilt or to rapid i.v. infusion of 500 ml of balanced salt solution and arterial pressures only returned to pre-induction values as the heart rate decreased. The unchanged haemodynamic status at cross-clamping and on release of the clamp was predictable because the aortic disease was occlusive, rather than aneurysmal, and hence did not result in gross changes of systemic vascular resistance. In retrospect, analgesia was inadequate at the time of transfer to the ICU, and should have been corrected before the patient left the operating room.

The cardiovascular responses to laryngoscopy and pain are mediated by the sympathetic division of the autonomic nervous system and can be obtunded by the administration of β-adrenoceptor antagonists—a group of agents which are widely used in the management of hypertension and supraventricular tachycardia. In order to understand why calcium channel blockers (like β-adrenoceptor antagonists) can control hypertension and supraventricular tachycardia but (unlike β-adrenoceptor antagonists) are unable to prevent the effects of the sympathetic nervous system, the relevant physiology of calcium and the mechanisms and sites of action of the calcium channel blockers should be considered.

Calcium has a fundamental role in the processes of excitation, contraction and excitation-contraction coupling of cardiac and vascular smooth muscle. The role of Ca²⁺ during excitation is distinct from that of sodium and potassium; movement of Na⁺ through "fast channels", and the subsequent movement of Ca²⁺ through "slow channels" into the cell, contribute to the formation of the action potential. Slow channels are 100 times more selective for Ca²⁺ than for Na⁺ or K⁺ (Reuter, 1979). The respective roles of Na⁺ and Ca²⁺ in the formation of the action potential in the heart, depend on the phase of the action potential and the type of cardiac cell. In ventricular contractile cells, movement of Ca²⁺ contributes mostly to the plateau of the action potential (phase 2), but in the sinus and atrio-ventricular nodes, Ca²⁺ plays a vital role in the formation of phase 0 (Trautwein, 1973). Catecholamines increase Ca²⁺ influx through the slow inward current. Activation of β-adrenergic receptors appears not to increase the size of Ca²⁺ channels or the rate of opening or closure, but rather to recruit additional active channels through a mechanism involving cyclic AMP. These β-adrenergic-activated channels have been termed "receptor-operated" or "phosphorylation-dependent" channels, whereas those not affected by β-adrenergic stimuli but activated by mechanical or electrical stimuli are termed "voltage-dependent" channels (Morad and Maylie, 1980). Thus, there are two functional types of "slow channels" and it is predominantly at the "voltage-dependent" channels that calcium entry blockers prevent the normal Ca²⁺ influx into cells. β-Adrenergic blocking agents in turn act indirectly by neutralizing the promoter effects of catecholamines on the "receptor-operated" channels (Fleckenstein, 1977).

Cardiac muscle and vascular smooth muscle contain relatively small amounts of endoplasmic Ca²⁺ and are, therefore, more dependent on Ca²⁺ influx than is skeletal muscle (Adams and Schwartz, 1980; Morad and Maylie, 1980). Consequently, they are sensitive to the effects of the calcium channel blocking agents. The cardiovascular effects of Ca²⁺ channel blockers can be explained on the basis of selective inhibition of the transmembrane influx of Ca²⁺ at the "voltage-dependent" channels, leading to depression of...
sinus node automaticity and atrio-ventricular conduction, decreased ventricular contractility and vasodilatation of vascular smooth muscle (Reves and Kissin, 1982). Verapamil has been shown to block the “receptor-operated” channels only in vascular smooth muscle (Zelis and Flaim, 1981), but there is little evidence that such activity can block sympathetic nervous system responses in the heart. Nifedipine and verapamil are two structurally unrelated calcium channel blockers with differing effects at clinical doses on the cardiovascular system. Nifedipine exerts its main effect on vascular smooth muscle with minimal effect on the sinus and atrio-ventricular nodes. Verapamil, in contrast, affects mainly the cardiac conduction system, decreasing sinus node automaticity and prolonging conduction and refractoriness in the atrio-ventricular node, with lesser effects on vascular smooth muscle and the myocardium.

In the patient described, the normal medication of calcium channel blockers administered 2 h before surgery was unable to prevent potentially harmful cardiovascular responses to stressful stimuli. Prevention or management of these responses is further complicated by the interaction of many drugs with the calcium channel blocking agents. β-Adrenergic blocking agents are effective in controlling the cardiovascular response to laryngoscopy and intubation, but the combination of verapamil and beta-adrenergic antagonists may lead to varying degrees of atrio-ventricular conduction block, including complete heart block. The negative inotropic effects of the calcium entry blockers and β-adrenergic antagonists may result in profound hypotension, especially in patients with compromised left ventricular function (Geddes, 1983). Despite these potential hazards, verapamil has been administered i.v. to patients in sinus rhythm with ischaemic heart disease receiving β-adrenergic blocking agents by mouth without adverse effect (Kieval et al., 1982) and propranolol has been safely administered i.v., before induction of anaesthesia, to a patient receiving oral verapamil therapy (Jones, Broadbent and Adams, 1984). All patients were closely monitored and had relatively normal left ventricular function. However, further studies are required before this can be recommended as safe practice and the management of patients on calcium channel blocking agents who also have poor left ventricular function is of particular concern.

Withdrawal of calcium channel blockers before surgery risks worsening the myocardial ischaemia (Kates and Kaplan, 1983). Nevertheless, despite adequate preoperative control of hypertension and tachycardia, these doses of nifedipine and verapamil failed to block the patient’s cardiovascular response to the noxious stimuli of laryngoscopy and postoperative pain. Replacement therapy for patients who cannot take these drugs by mouth is feasible in the case of verapamil, which can be given i.v., but is more difficult in the case of nifedipine, for which no i.v. preparation is available. A recent editorial (Jones, 1984) commented that the role of the anaesthetist as a clinical physiologist and pharmacologist is perhaps no better demonstrated than in the safe management of patients on calcium channel blockers.

REFERENCES


