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CATECHOLAMINE RESPONSES DURING ANAESTHESIA FOR PHAEOCHROMOCYTOMA

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SUMMARY

Plasma catecholamine concentrations were measured, at frequent intervals, in a 40-yr-old female patient undergoing resection of a phaeochromocytoma under enflurane anaesthesia. Measurements before operation revealed that the tumour secreted predominantly noradrenaline and during surgery the plasma concentration of the hormone increased markedly (180 pmol ml^{-1}; normal range 1.5–3.0 pmol ml^{-1}). Plasma adrenaline concentrations increased markedly only at endotracheal intubation and in the period immediately after operation.

Phaeochromocytoma is a rare condition occuring in 0.4–2% of patients with arterial hypertension. The management of this condition during surgery presents many problems for the anaesthetist unless adequate preparation is undertaken.

Circulating catecholamine concentrations are increased and further increases (resulting in dangerous hypertension or arrhythmia) may occur during provocative manoeuvres, such as palpation of the tumour, surgical dissection and the administration of certain pharmacological agents. Diagnosis is confirmed by the demonstration of increased concentrations of the catecholamines and their metabolites in 24-h collections of urine.

Some controversy exists regarding the perioperative management of such patients. There is general agreement (Ross et al., 1967; Brown, 1980) that alpha-blockade before operation is associated with greater cardiovascular stability during operation, but there is less agreement on the necessity for concomitant beta-blockade in the absence of severe tachycardia or arrhythmias (Desmonts et al., 1977). In some centres, labetalol (a mixed α and β blocker) is now recommended as the sole agent before surgery.

Various pharmacological agents have been recommended to control fluctuations in arterial pressure during operation. These include phentolamine (Brown, 1980), sodium nitroprusside (Daggett, Verner and Carruthers, 1978), labetalol (Kaufman, 1979) and halothane (Etsten and Shimosata, 1965).

However, halothane sensitizes the myocardium to the arrhythmogenic effects of catecholamines, a feature which is less notable with enflurane. This theoretical advantage of enflurane was noted in three previous case reports (Kopriva and Eltringham, 1974; Oritz and Diaz, 1975; Kreul, Dauchot and Anton, 1976), in which the frequency of arrhythmia during surgery was low.

We report a case managed successfully by the use of α-blockade before operation, the continous use of enflurane during surgery and with the occasional administration of phentolamine. The changes in plasma catecholamine concentrations throughout the perioperative period were studied, the concentrations being determined using high pressure liquid chromatography (Fell, Achola and Smith, 1982), based upon the technique of Hjemdahl, Daleskog and Kahan (1979).

CASE REPORT

A 40-yr-old housewife was admitted to a psychiatric unit for treatment of an anxiety state, and found to be markedly hypertensive. Fourteen years previously, severe toxaemia had accompanied her first pregnancy, necessitating early Caesarean section. She gave a history of headaches and anxiousness over the previous 8 yr, but had recently developed blurred vision, palpitations and attacks of panic. Mild left-sided abdominal pain had been present for 2 yr.

Examination revealed a slim, anxious lady. Arterial pressure was 200/108 mm Hg (standing), 192/90 mm Hg (sitting). A left subcostal mass was palpated, but this did not reproduce her symptoms. An ultrasound scan revealed a 7-cm mass above the

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left kidney, and the IVP was normal. A 24-h urine collection showed a grossly increased noradrenaline concentration (11 400 nmol/24 h (normal range 120–500 nmol/24 h)), with moderately increased adrenaline (585 nmol/24 h (normal range 30–190 nmol/24 h)). Urinary VMA was 110 μmol/24 h (normal range 8–38 μmol/24 h) and HVA was also present, indicating some secretion of dopamine. Plasma noradrenaline concentration was 30 pmol ml^{-1} (normal range 1.5–3.0 pmol ml^{-1}), whilst plasma adrenaline concentration was 0.4 pmol ml^{-1} (within the normal range of 0.2–0.5 pmol ml^{-1}). These results suggested that the tumour secreted predominantly noradrenaline.

Before operation, a central venous catheter was inserted and alpha-blockade effected using an infusion of phenoxybenzamine 0.5 mg kg^{-1} i.v. given over 3 h, on each of the three days immediately preceding surgery. The central venous pressure was maintained in the normal range by infusions of plasma protein fraction and packed red cells. Since compensatory tachycardia did not occur, and plasma adrenaline concentrations remained within normal limits, beta-blockade was not used. Arterial pressure became less labile and the diastolic pressure settled at approximately 90 mm Hg.

Operative management

Premedication consisted of lorazepam 4 mg and droperidol 2.5 mg, 2 h before operation. The radial artery was cannulated and large i.v. cannulae inserted, under local anaesthesia, before the induction of anaesthesia. Arterial pressure was 190/100 mm Hg, and heart rate 115 beat min^{-1}. As a result of this tachycardia relative to her previously stable heart rate and because β-blockers obtund the well-known hypertensive response to laryngoscopy and endotracheal intubation, practolol 10 mg was administered i.v. immediately before induction of anaesthesia, which was accomplished with thiopentone 3–4 mg kg^{-1}. Suxamethonium 1 mg kg^{-1} was administered to facilitate endotracheal intubation. Tubocurarine was used to obtain neuromuscular blockade and anaesthesia maintained with a mixture of 60% nitrous oxide in oxygen with increments of fentanyl. The inspired concentration of enflurane was adjusted throughout the operation according to variations in arterial pressure. The administration of phentolamine was necessary on only four occasions, which corresponded with vigorous manipulation of the tumour. No arrhythmias were noted, with the exception of sinus tachycardia.

Blood samples were obtained from the CVP catheter at specific stages for measurement of plasma catecholamine concentrations.

A large mass 9 cm × 7.5 × 8 cm, separate from the kidney but adherent to the pancreas, was removed from the left suprarenal area. Blood 3000 ml and colloid 2500 ml were required throughout the procedure to maintain blood volume.

Changes in catecholamine concentrations

A dramatic increase in plasma noradrenaline concentration occurred during endotracheal intubation, to approximately 50 times the upper limit of the normal range (fig. 1). Plasma adrenaline concentrations increased by a modest extent at this stage to 3 pmol ml^{-1}, a magnitude of response which is seen in normal patients undergoing endotracheal intubation (Fell, Vater and Smith, 1983).

The increase in arterial pressure noted at this stage (fig. 1) was unimpressive and ill-sustained, reflecting the efficacy of alpha-blockade.

With successive palpation of the tumour, arterial pressure increased gradually to 205/140 mm Hg, necessitating the administration of phentolamine, which produced an abrupt decrease in pressure. During the palpation, plasma noradrenaline concentration increased to a very high value (fig. 1), but following removal of the tumour, decreased to moderate values in association with a decrease in arterial pressure. No infusion of pressor agent was required following the removal of the tumour.

Adrenaline concentrations remained within the normal range during surgery and this was reflected by the relatively stable heart rate. However, plasma adrenaline concentration increased markedly following endotracheal extubation and awakening from anaesthesia, a period when the patient was cold and in pain. One hour later, following rewarming and adequate analgesia, adrenaline concentrations decreased. It is interesting that heart rate changed little during the periods of hypertension when the CVP was stable and when the plasma concentration of noradrenaline, but not that of adrenaline, had increased. However, there appeared to be an association between tachycardia and a decrease in CVP during transient periods of heavy blood loss, suggesting reflex responses from volume receptors. However, periods of severe hypertension were not associated with transient decreases in heart rate, and it is postulated that baroreceptor mechanisms may have been obtunded by enflurane.

Peripheral venous blood samples obtained 10

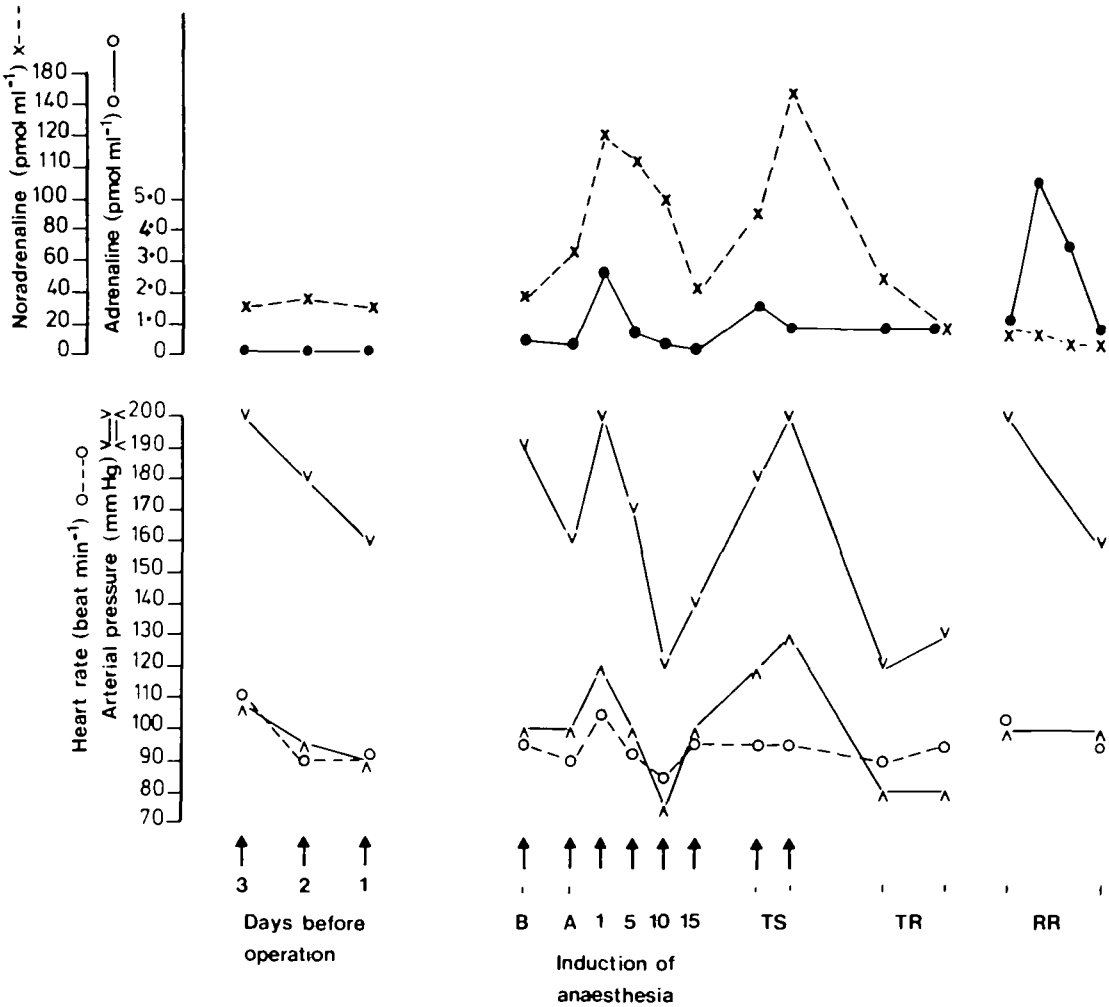

FIG. 1. Measurements obtained before, during and following operation. From above downwards, plasma noradrenaline concentrations X--X, plasma adrenaline concentrations ●——●, systolic arterial pressure V——V, heart rate O---O, diastolic arterial pressure Λ——Λ. B = before induction; A = after induction; 1–15 = minutes after induction; TS = tumour squeeze; TR = tumour removed; RR = recovery room.

days after the operation revealed a marginally increased plasma noradrenaline concentration of 7.0 pmol ml^{-1}, with the plasma adrenaline concentration slightly above the upper limit of normal (0.9 pmol ml^{-1}). Arterial pressure was 150/90 mm Hg.

The patient made a relatively uneventful recovery after operation.

DISCUSSION

It is notable that the arterial pressure responses of this patient correlated well with the changes in plasma noradrenaline concentration. In addition, the patient's plasma adrenaline concentrations and responses were within the normal range and (despite an increased 24-h urine value) this was reflected by the lack of clinical signs of excessive β-adrenergic activity.

It is known that, in patients with phaeochromocytoma exhibiting paroxysmal hypertension, normal plasma catecholamine concentrations may be demonstrated during periods of normotension

(Hamberger et al., 1981). However, increases in hormonal concentrations occur in those patients with sustained hypertension, as in the present patient, or may be provoked by various manoeuvres (Hamberger et al., 1981). Since measurement of plasma catecholamine concentrations may be obtained relatively quickly using HPLC (which is an accurate, relatively inexpensive technique with a sensitivity approaching that of radioenzymatic assays), it is suggested that the use of this technique defines the extent of secretion of adrenaline and noradrenaline and may improve clinical assessment of the relative degree of α and β blockade required before, and during, operation.

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REPONSES DES CATECHOLAMINES AU COURS DE L'ANESTHESIE POUR PHEOCHROMOCYTOME

RESUME

Les concentrations plasmatiques de catécholamines ont été mesurées, à intervales rapprochés, chez une patiente de 40 ans subissant l'ablation d'un phéochromocytome sous anesthésie à l'enflurane. Les mesures pré-opératoires avaient révélé que la tumeur sécrétait surtout de la noradrénaline et au cours de l'acte chirurgical la concentration plasmatique de cette hormone a aumgenté de façon marquée (180 pmol ml^{-1}; valeurs normales: 1,5–3 pmol ml^{-1}). Les concentrations plasmatiques d'adrénaline n'augmentaient de façon marquée que lors de l'intubation endotrachéale et dans la période post-opératoire immédiate.

KATECHOLAMINAUSSCHÜTTUNG WÄHREND DER NARKOSE BEI PHÄOCHROMOZYTOM

ZUSAMMENFASSUNG

Bei einer 40 Jahre alten Patientin wurden während der Resektion eines Phäochromozytomes unter Enfluranenarkose in häufigen Intervallen die Katecholamin-Plasmaspiegel gemessen. Die präoperativen Messungen ergaben, daß der Tumor vor allem Noradrenalin ausschüttet. Während der Operation stieg die Plasmakonzentration des Hormons deutlich an (180 pmol ml^{-1}; Normalbereich 1,5–3,0 pmol ml^{-1}). Der Adrenalin-Plasmaspiegel war nur während der endotrachealen Intubation und in der unmittelbaren postoperativen Periode deutlich erhöht.

RESPUESTAS DE LA CATECOLAMINA DURANTE LA ANESTESIA PARA FEOCROMACITOMA

SUMARIO

Se midieron a intervalos frecuentes las concentraciones de catecolamina en el plasma de una paciente de 40 años sometida a una resección de un feocromacitoma bajo anestesia por enflurano. Las mediciones realizadas antes de la operación revelaron que el tumor secretaba, con predominancia, noradrenalina y durante la cirujía, la concentración en el plasma de la hormona aumentó notablemente (180 pmol ml^{-1}; gama normal 1,5–3,0 pmol ml^{-1}). Las concentraciones de adrenalina en el plasma aumentaron notablemente únicamente al momento de la intubación endotraqueal y en el periodo inmediatamente después de la operación.