HALOTHANE AND PHAEOCHROMOCYTOMA

A Case Report

BY

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SUMMARY

A further instance of the successful removal of a phaeochromocytoma is reported and it is suggested that halothane, despite theoretical contraindications, may be the anaesthetic agent of choice for this procedure. The possible value of (a) prolonged pre-operative preparation with either oral phentolamine or phenoxybenzamine with or without pronethalol, (b) pre-operative blood volume studies, and (c) central venous pressure recordings during the operative procedure, should be investigated. It may be that, with these precautions, the choice of anaesthetic agent and technique will require further evaluation.

Phaeochromocytomas are tumours of the sympathetic nervous system which secrete excessive quantities of the catecholamines, adrenaline and noradrenaline, and occasionally dihydroxytryptamine and other related compounds, in varying proportions into the blood stream and the abnormalities presented by the patient can be accounted for by the known physiological effects of these amines.

Some phaeochromocytomas discharge catecholamines continuously resulting in sustained hypertension, while others do so intermittently giving rise to paroxysms of hypertension. Clinical confirmation of the diagnosis in these cases may be afforded by means of the phentolamine test (Helps, Robinson and Ross, 1955) and the demonstration of excess catecholamines in the urine (Hingerty, 1957). The phentolamine test, unfortunately, gives so many spurious positive results that some regard it as wellnigh useless (Frazer, S. C, personal communication, 1963). A small proportion of patients, however, with a secreting phaeochromocytoma are normotensive when under observation and give no history of attacks, but a histamine provocation test may provide clinical confirmation of the diagnosis (Roth and Kvale, 1945), although this test is now seldom used.

These cases are, indeed, the ones which the anaesthetist should be particularly aware of, for they may first reveal themselves during elective surgery. It has been estimated that 6–8 of every 2,000,000 patients anaesthetized in this country may have an unsuspected phaeochromocytoma (Ainley-Walker, 1962). As 90 per cent of these tumours are reputed to be benign, the majority of these patients should be completely curable. Anaesthetists should, therefore, be able to suspect the diagnosis in the first place and have that discipline of reaction necessary to avoid a fatal outcome from cerebral haemorrhage, acute pulmonary oedema or ventricular fibrillation.

Much has been written regarding the anaesthetic management of patients with phaeochromocytoma but most of the anaesthetic techniques employed have been associated with violent blood pressure swings, in spite of the aid of phentolamine.

Although concern has been expressed regarding the use of halothane in the presence of circulating catecholamines, there is no proof that this constitutes a significant hazard in man, provided adequate oxygenation and carbon dioxide elimination are ensured. Moreover, the powerful hypotensive action of halothane constitutes an effective antagonist to the hypertensive effects of the catecholamines. It was accordingly decided to use halothane as the main anaesthetic agent for the surgical removal of a proven phaeochromocytoma.
CASE REPORT

A female aged 59 was admitted to hospital on January 14, 1963, with attacks of palpitation, left frontal headache, profuse sweating, vomiting and apprehension. On admission she had cold, clammy extremities and an unrecordably low blood pressure. Her temperature was 100°F, her pulse rate was 140 beats/min, and vomiting was troublesome. An electrocardiogram at this time suggested an anterior myocardial infarct, but this was not confirmed by subsequent tracings. The abnormal record was probably due to a combination of hypotension and tachycardia (Rollason and Hough, 1959). With warmth and sedation she gradually improved but it was not until 48 hours later that her blood pressure rose to 150/100 mm Hg. Her urine contained albumin but no sugar. Her blood urea on admission was 94 mg per cent but this subsequently fell to 31 mg per cent. A chest radiograph showed no abnormality of the lungs and the cardiac shadow was at the upper limit of normal.

On January 19 she had an attack of sweating, palpitation, headache and vomiting. The pulse rate was 110 beats/min, the blood pressure 230/150 mm Hg, and the diagnosis of phaeochromocytoma was confirmed by finding large quantities of catecholamines in her urine. Intravenous pyelography and perirenal insufflation, with a mixture of 50 per cent nitrous oxide and 50 per cent oxygen supplemented with 4 per cent halothane, was then initiated in an attempt to control her hypertension. She was reassured and sedated with butobarbitone 200 mg and the foot of the bed was elevated. Operative admission

Anaesthesia was induced with a sleep dose of 125 mg of thiopentone, injected slowly, and deepening of a mixture of 50 per cent nitrous oxide and 50 per cent oxygen supplemented with 4 per cent halothane administered from a Fluotec vaporizer outside the theatre and artificial ventilation of the lungs was commenced using a Blease P.11 Pulmoflator, with a to-and-fro absorber and a Fluotec fitted outside the circuit. The Pulmoflator was set to deliver a minute volume of 14 l./min, so that hyperventilation was ensured. The patient continued to receive 50 per cent nitrous oxide and 50 per cent oxygen supplemented with 4 per cent halothane, but the total fresh gas flow was reduced to 4 l./min.

The patient was then postured in the left lateral jack-knife position. This resulted in a slight rise in blood pressure from 110/70 to 120/80 mm Hg, and a rise in pulse rate from 90 to 110 beats/min. There was no pressor response to the surgical incision and the blood pressure subsequently fell to 75/60 mm Hg, while the pulse rate remained at 110 beats/min and there were no significant e.c.g. changes.

On handling the tumour, the blood pressure rose from 75/60 to 100/70 mm Hg, and the pulse rate rose from 110 to 120 beats/min. In spite, however, of continued handling of the tumour, the blood pressure fell to 80/60 mm Hg, although the pulse rate remained at 120 beats/min, and no e.c.g. changes were observed. The halothane concentration was now reduced to 2 per cent but her blood pressure soon rose to 115/85 mm Hg, and the concentration was again increased to 4 per cent following which her blood pressure fell to 90/60 mm Hg, and her pulse rate to 110 beats/min. As successful removal of the tumour seemed imminent, the halothane concentration was reduced to 2 per cent and just prior to removal of the tumour, both halothane and nitrous oxide were discontinued and the lungs were ventilated with pure oxygen. At this point her blood pressure was 80/60 mm Hg and her pulse rate 110 beats/min, and no e.c.g. changes were evident.

After removal of the tumour, the blood pressure fell to 70/60 mm Hg, but her pulse rate remained at 110 beats/min. Five minutes later, her blood pressure rose to 80/60 mm Hg with no change in her pulse rate or e.c.g. and nitrous oxide was then reintroduced to restore the 50 per cent nitrous oxide and oxygen mixture. Her blood pressure appeared to stabilize at 85/60 mm Hg and her pulse rate was 110 beats/min. There was no reflex response or change in blood pressure, pulse rate or electrocardiogram. The patient was then transferred to the operating theatre and artificial ventilation of the lungs was commenced using a Fluotec vaporizer with a to-and-fro absorber and a Fluotec fitted outside the circuit. The Pulmoflator was set to deliver a minute volume of 14 l./min, so that hyperventilation was ensured. The patient continued to receive 50 per cent nitrous oxide and 50 per cent oxygen supplemented with 4 per cent halothane, but the total fresh gas flow was reduced to 4 l./min.

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On extubation there was no reflex spasm and on leaving the theatre (2 hours after the induction of anaesthesia) the blood pressure was 105/75 mm Hg, the pulse rate 100 beats/min, the skin was dry and the reflexes were active. She was postured in the tonsil position and the foot of the bed was elevated. Operative bleeding had been insignificant and no blood transfusion was given.

The blood pressure record during operation is illustrated in figure 1.

On her return to the ward the blood pressure was found to be 30 mm Hg systolic, although her appearance had not suggested a pressure as low as this. A noradrenaline drip was immediately started and hydrocortisone 100 mg was given intravenously. The blood
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Blood pressure record during operation.

Blood pressure then rose to 65/40 mm Hg; 15 minutes later it was 85/50 mm Hg and 35 minutes later it was 115/70 mm Hg, and did not subsequently fall below this figure. Noradrenaline and hydrocortisone were withdrawn 24 hours later, after a total of 58 mg of noradrenaline and 650 mg of hydrocortisone had been given.

Subsequent convalescence was uneventful. She was discharged fit on March 3, and has remained well since. The tumour weighed 43 g and was confirmed histologically to be a phaeochromocytoma.

DISCUSSION

This patient appeared to be in "adrenaline shock" on admission and it is of interest to note that patients with phaeochromocytoma may exhibit paroxysmal hypotension (Richmond, Frazer and Millar, 1961). This patient's pre-operative paroxysm of hypertension may have been precipitated by the effect of the premedication, but could probably have been avoided had liberal doses of phentolamine hydrochloride been given orally (Goldfien, 1963) some days prior to surgery, together with a more liberal intramuscular dose of phentolamine methanesulphonate at the time of premedication. Alternatively, it might have been prevented by giving 50 mg of phenoxybenzamine intravenously on the four pre-operative days (Robertson, 1962). On the other hand, both phentolamine and phenoxybenzamine are alpha-adrenergic blocking drugs and can produce a tachycardia, and if a tachycardia is already present the additive effects may be disturbing. This possibility may, however, be ascertained with a test dose, and if positive, beta-adrenergic blocking drugs such as propranolol (Alderlin) may be used (Dornhorst and Laurence, 1963). Occasionally a patient becomes resistant to phentolamine, when a sodium nitroprusside infusion may have to be considered (Nourok, Guinup, and Hamwi, 1963), if phenoxybenzamine is also without effect.

As patients with a phaeochromocytoma are more apprehensive than is normal, due to the stimulating effect of the catecholamines on the central nervous system, and as histamine release may precipitate a paroxysm, a good night's sleep should be ensured by administration of a barbiturate and an antihistaminic. In this case, butobarbitone and promethazine were chosen. Hyoscine is preferred to atropine because the latter is both a cardiac accelerator and a central nervous system stimulant. Methadone is preferable to pethidine or morphine, because it is less likely to cause histamine release. While promethazine is a more potent antihistaminic than the
perphenazine chosen for this case, it is not such a good anti-emetic.

Thiopentone should be injected slowly during induction to avoid sudden vasodilatation, which may precipitate a paroxysm, but in sufficient quantity to ensure unconsciousness. It can usefully be combined with hypnotic suggestion.

Relaxants are better avoided. Gallamine produces a tachycardia, tubocurarine releases histamine, and suxamethonium results in muscle fasciculations which can be violent and might precipitate a paroxysm and produce muscle pains. Using halothane as described, relaxants were unnecessary.

Intubation should be performed under deep anaesthesia to avoid a pressor response. This was quickly and successfully achieved with halothane. No violent blood pressure swings were observed during posturing of the patient or during the surgical procedure.

It is accordingly felt that halothane may be the anaesthetic of choice for this operation, for with this agent, in this case, there was:

1. No marked elevation in blood pressure.
2. No significant electrocardiographic changes.
3. No sweating.
5. Complete muscular relaxation.

It has been suggested that postoperative shock in phaeochromocytoma cases is due to a chronic decrease in blood volume resulting from the prolonged effect of vasoconstriction (Brunjes, Johns and Crane, 1960). With the release of vasoconstrictor tone at operation, the chronic reduction in blood volume is unmasked and causes oligoemic shock to appear. It is possible that oral phentolamine or intravenous phenoxycobenzamine therapy, by relaxing vasoconstrictor tone, may enable the blood volume to be restored before surgery (Johns and Brunjes, 1962). This patient received only 200 ml of normal saline during the operative procedure, and it is possible that a blood transfusion would have avoided the need for the infusion of noradrenaline postoperatively in the ward. There would, therefore, appear to be a good case for preoperative blood volume measurement and central venous pressure monitoring during operation (Sykes, 1963) in these cases.

ADDENDUM

Since this paper was written the removal of another phaeochromocytoma, occurring as an intrathoracic tumour, has been reported in which halothane was used without untoward results (Luna, Katz and Ernst, 1963).

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REFERENCES


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SOMMAIRE
L'auteur signale un nouveau cas d'enlèvement réussi d'un phéochromocytome et il exprime l'opinion que, sauf contre-indications théoriques, le halothane pourrait être l'anesthésique de choix pour cette intervention. On devrait examiner: (a) la valeur possible d'une préparation pranesthesique d'action prolongée avec de l'éther de phentolamine per os ou avec de la phenoxybenzamine avec ou sans pronethalol; (b) étudier avant l'intervention le volume sanguin; et (c) noter soigneusement la pression veineuse centrale pendant l'intervention. Il est possible que — sous réserve de ces précautions et comparaisons — le choix de l'anesthésiant et la technique à base d'halothane devraient être réévalués.

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ZUSAMMENFASSUNG
Es wird über ein weiteres Beispiel einer erfolgreichen Entfernung eines Phäochromozytoms berichtet und vorgeschlagen, daß Halothane trotz theoretischer Kontraindikationen wahrscheinlich für diesen Eingriff das Anästhetikum der Wahl ist. Der mögliche Wert einer (a) längeren präoperativen Vorbereitung mit Äther, oralem Phentolamine oder Phenoxybenzamine mit oder ohne Pronethalol, (b) von präoperativen Bestimmungen des Blutvolumens und (c) einer Registrierung des zentralen venösen Blutdruckes während des operativen Eingriffes sollte untersucht werden. Es ist durchaus möglich, daß bei Beachtung dieser Vorsichtsmaßnahmen die Wahl des Anästhetikums und der Narkosetechnik weiter überprüft werden muß.