EPIDURAL BLOCKADE AND CIRCULATING CATECHOL AMINE LEVELS IN A CHILD WITH PHAEOCHROMOCYTOMA

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THIS REPORT concerns the management of a child in whom transperitoneal excision of an adrenal medullary tumour was performed under a combination of continuous epidural blockade and supplementary light general anaesthesia. The epidural block provided abdominal relaxation with operative and postoperative analgesia, while the upper level of analgesia was carried high enough to ensure total sympathetic blockade. An attempt was made to assess the effects of this anaesthetic technique on the circulating blood levels of adrenalin and nor-adrenalin during operation. The data obtained includes that from analysis of pre and postoperative plasma samples and of adrenal venous blood before tumour removal. The findings will be presented and discussed here.

CASE REPORT

This 8-year-old boy (height 47 in, weight 47 lb) was admitted to hospital with a 7-day history of paroxysmal headache, cold sweats, and three convulsive seizures. Blood pressure was 195/170, heart rate 160, cerebrospinal fluid and urine examinations were normal, B.M.R. was +22 per cent, sugar tolerance was diminished.

A phaeochromocytoma was diagnosed and preoperative treatment with phentolamine ("Regitine") started forthwith. Oral doses of 50 mg three hourly were required to reduce and maintain blood pressure at about 140/90. Samples of peripheral venous blood were withdrawn for analysis of plasma adrenalin and noradrenalin concentration, five days and one day preoperatively. The results are illustrated in Table I.

ANAESTHETIC MANAGEMENT

The last oral dose of phentolamine (50 mg.) was given at 3.00 A.M. on the day of operation, the effects were expected to last for about four hours. Between 7.15 and 8.15 A.M. 3 mg of the drug were given by slow intravenous infusion, but none thereafter. At 8.00 A.M. the child was brought to the operating room asleep, following heavy premedication with pentobarbital 60 mg two and a half hours before, and Demerol 25 mg with hyoscine gr. 1/150 one hour before. Light anaesthesia was induced with nitrous oxide, oxygen, and thiopental. An epidural catheter was then inserted between the first and second lumbar spines. It was estimated that 24 ml. of Xylocaine solution would be required to produce epidural analgesia up to the segmental level T₁ C₈, with total sympathetic blockade (1). Twenty minutes after injection of 19 ml. of 1.4 per cent Xylocaine, skin analgesia was present to T₄, the block was therefore extended by injecting a further 10 ml. In the meantime the trachea was intubated and a gastric tube

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passed during brief succinylcholine paralysis (20 mg.). General anaesthesia was continued with nitrous oxide and oxygen in the proportion 5.3, apnoea being maintained by manual hyperventilation.

Several blood samples were withdrawn during the preparatory period before surgery (Samples 1-3, Table I and Fig 1) Sample 4 was withdrawn as the surgical incision was made, fifty minutes after the first epidural injection of Xylocaine.

TABLE I
PLASMA CATECHOL AMINE LEVELS

Sample	Period	Noradrenalin $\mu\text{g/L}$	Adrenalin $\mu\text{g/L}$
Preoperative	5 days before operation	14.4	2.6
	1 day before operation	10.1	5.9
Sample I	Immediately after induction of anaesthesia	50.8	—
Sample II	12 minutes after induction	65.3	—
Sample III	30 minutes after inducing epidural block to T ₄	60.6	—
Sample IV	10 minutes after extending epidural block to C ₈	31.4	—
Sample V	During manipulation of tumour	95.7	—
Sample VI	From adrenal vein before tumour removal	602.2 $\mu\text{g/ml}$	3.1 $\mu\text{g/ml}$
Postoperative	6 days after operation	0.42 $\mu\text{g/L}$	0.42 $\mu\text{g/L}$
Excised tumour (assayed by Dr B. G. Benfey)		1470 $\mu\text{g/g}$	4.14 $\mu\text{g/gm}$

FIGURE 1. Anaesthetic chart of 8-year-old boy undergoing excision of phaeochromocytoma. Epidural injections of 1.4% Xylocaine are shown as vertical columns. Samples of peripheral venous blood were taken at S₁, S₂, S₃, S₄, S₅. Methedrine 10 mg. was given intravenously at M.

A left adrenal medullary tumour weighing 26 grams was removed through a transverse abdominal incision. The operative course was smooth, apart from two

periods when the blood pressure changed sharply (see Fig. 1) During manipulation of the tumour blood pressure increased to 185/125 mm, and the peripheral venous plasma concentration of noradrenalin rose to the highest estimated level, 95 microg. per litre (Sample V, Table I).

No adrenalin could be detected in any of the five blood samples withdrawn during anaesthesia. The hypotension which occurred following removal of the tumour was partly corrected by an infusion of noradrenalin (2-20 μ g. per minute), supported later by methyl amphetamine methedrine 10 mg., which produced a sharp increase to normotensive levels. Thereafter blood pressure remained at about 125/85 with an infusion rate of 2-3 μ g. of noradrenalin per minute.

The patient was awake as the last stitches were being tied, when analgesia was present to the level of the sixth cervical segment. The noradrenalin infusion was stopped one hour postoperatively, no further pressor drugs being required. Postoperative analgesia was maintained for the next twelve hours by injecting 10 ml. of 0.8 per cent Xylocaine through the epidural catheter every 90 minutes.

The subsequent postoperative course was smooth. Heart rate was 160 per minute for 15 hours, 140 per minute for the next 8 hour period, finally declining to 90-110 over the next 3 days. A sample of peripheral venous blood withdrawn on the sixth day after operation showed "normal" low values of noradrenalin and adrenalin (Table I). The patient was discharged in excellent condition, with a blood pressure of 120/80, on the eleventh postoperative day.

DISCUSSION

The fluorimetric method used in this study for plasma catechol amine estimations enables adrenalin and noradrenalin to be determined separately (2). The peripheral venous plasma levels in normal resting subjects are less than 0.5 μ g. per litre for each amine. Analysis of the two preoperative samples withdrawn from this patient (total circulating catechol amines 17.0 and 16.0 μ g. per litre respectively), and the findings from a case previously reported (3) illustrate the value of plasma estimations in confirming the diagnosis of suspected adrenal medullary tumours.

A study of the literature suggests that choice of anaesthetic technique for patients with phaeochromocytoma is usually based on individual experience and preference, rather than on a firm foundation of applied pharmacology. Many agents have been successfully employed, against any one of which some theoretical objections can be raised. Thus, although ether has been used extensively and successfully (4, 5), it is nevertheless a powerful adrenal medullary stimulant in animals (6), and might be expected to increase circulating catechol amines to undesirably high levels. Cyclopropane incurs a serious risk of ventricular arrhythmias in the presence of high concentrations of adrenalin or noradrenalin (7), and yet it has been used successfully (8). Spinal block has its advocates (9, 10), although interference with circulatory control might appear to make it a dangerous choice in the presence of phaeochromocytoma (4, 5). Thus, practical

success has been obtained with a variety of methods, each of which could be labelled as theoretically objectionable, confirming the statement of Apgar and Papper that "the relationship between mortality and morbidity and anaesthetic agent or technique cannot be clearly defined from the data available" (4).

The formation, methylation and discharge of catechol amines in the normal adrenal medulla may be intimately related to splanchnic nervous control (11), but factors governing the activity of adrenal medullary tumours are poorly understood. It is usually assumed that the discharge of pressor amines from a phaeochromocytoma is dependent on mechanical or humoral factors rather than direct nervous control through the splanchnic outflow. In this patient, the relative depression of circulating noradrenalin to the lowest operative level at Sample 4 may have been due to the 50-minute period of induced sympathetic blockade. Nevertheless, the persistently high levels of noradrenalin seem to imply that efferent nervous control of the adrenal medullary tumour was relatively unimportant in this case. The obvious influence of mechanical compression is reflected in the highest circulating noradrenalin levels occurring during manipulation of the tumour area. This is an expected finding, which has been noted by one of us in a previous case (3). The enormous concentration of noradrenalin in adrenal venous blood just before removal of the tumour (600 μg per millilitre) illustrates the extraordinary tolerance shown by these patients to blood levels far beyond the physiological range.

The physiological meaning of such high levels is difficult to determine, for above a certain limit additional increases in pressor amine concentration fail to produce further significant rises of blood pressure. It has been shown that the response of blood pressure to infused adrenalin or noradrenalin follows a hyperbolic curve, so that at a certain blood concentration the arterial pressure curve flattens out to a maximum beyond which further doses of pressor amine produce little effect (12). The circulating noradrenalin concentrations found at operation in this patient were almost certainly well above this level. Moreover, high circulating levels of adrenalin or noradrenalin can produce ganglionic blockade and vasodilation (13, 14, 15), so that with concentrations of this order it is difficult to assess the significance of blood pressure in relation to changing levels of noradrenalin. Thus any attempt to relate the effect of a particular anaesthetic technique to levels of circulating catechol amines so far beyond the physiological range could be of academic rather than practical importance.

In spite of greatly increased plasma concentrations of noradrenalin during operation, epidural blockade was accompanied by levels of blood pressure lower than those observed in the preoperative period before phentolamine was started. In this case, therefore, total sympathetic blockade did not appear to produce the augmentation of pressor response to circulating vasoactive amines that has been reported previously (16, 17).

From a clinical viewpoint the operative and postoperative course in this child was impressively smooth. The use of continuous epidural blockade, in conjunction with light general anaesthesia, is recommended as a suitable anaesthetic technique for patients with adrenal medullary tumours.

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RÉSUMÉ

En enlevant un phéochromocytoma du côté gauche, chez un enfant de huit ans, on a fait disparaître une hypertension considérable. Comme mode d'anesthésie pour permettre cette opération, on a associé du pentothal, du protoxyde d'azote et de l'oxygène, et une analgésie épidurale continue atteignant la huitième cervicale. L'état du malade, au cours de l'opération et des suites opératoires, est demeuré satisfaisant.

Avant, pendant et après l'opération, nous avons fait le dosage des catécholamines plasmatiques pour juger de l'influence d'un blocage sympathique total sur les quantités de noradrénaline circulante. Après l'induction de l'anesthésie générale, en comparaison avec les taux préopératoires, la quantité de noradrénaline circulante a quadruplé et même, après le blocage sympathique total, la concentration des catécholamines sériques est demeurée double de ce qu'elle était avant l'opération. Il nous a semblé que, au cours de l'opération, de façon générale, la tension artérielle est demeurée indépendante du taux absolu de catécholamines, car elle est restée plus basse qu'on aurait pu s'attendre de la trouver étant donné la haute concentration de noradrénaline circulante qui existait. Toutefois, les augmentations et les chutes de tension artérielle ont suivi, en général, les modifications de concentration de catécholamines. Nous faisons l'interprétation de ces résultats.

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