URINARY OUTPUT OF ADRENALINE AND NORADRENALINE DURING ANAESTHESIA AND SURGERY: PRELIMINARY STUDY

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SYMPATHO-ADRENAL MEDULLARY ACTIVITY during anaesthesia has been studied fluorometrically, measuring catechol amines in peripheral and adrenal vein blood.¹⁻⁵ Results of these studies indicated that light anaesthesia did not produce any significant rise in catechol amines, whereas deeper planes of anaesthesia employing ether, cyclopropane, chloroform, and vinyl ether produced significant increases in blood levels of adrenaline and noradrenaline; halothane caused little or no change; thiopentone administration resulted in no change or a decrease in blood levels. One of the investigators⁶ found decreased blood levels in deeper planes with cyclopropane and halothane.

Periodic determination of blood levels of adrenaline and noradrenaline is a useful method for relating changes in depth of anaesthesia to the output of these hormones, and it also indicates total body output. The quantity of urinary output of adrenaline and noradrenaline seems to parallel the total body output.^{7,8} Therefore, determinations of urinary output should reflect the over-all changes in total body output during anaesthesia and surgery.

METHOD

General

The urine values of adrenaline and noradrenaline were studied in fifteen patients, male and female, who were to undergo a variety of surgical procedures. Their ages ranged from seventeen to seventy-three years. Conventional pre-operative sedation (barbiturates, demerol, and atropine or scopolamine) was used. All patients were alert and co-operative. The bladder was emptied by catheterization just prior to induction, and the sample discarded. Collections were begun simultaneously with the induction of anaesthesia, and were stopped at the end of anaesthesia. Lumbar epidural analgesia, unsupplemented, was used for two procedures, and general anaesthesia was employed for the others. Technique for the latter consisted of a sleep dose of intravenous thiopentone followed by the inhalation agent and a subsequent single dose of succinylcholine to facilitate intubation. Patients were kept in light planes of anaesthesia, a succinylcholine drip was used to produce muscle relaxation when needed, and respirations were assisted or controlled to keep arterial P_{O_2} and P_{CO_2} normal. Patients were observed closely for clinical signs of sympathetic nervous system activity.

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Preparation of Urine Extracts

Urine extracts were prepared as adapted by Goodall⁷ from von Euler and Heller.^{9,10} The urine was hydrolysed, and the adrenaline and noradrenaline were selectively adsorbed on aluminum hydroxide and filtered. The precipitate was washed and redissolved with 2 N sulphuric acid. The remaining salts were precipitated out by mixing the extract with alcohol and acetone. Filtrate was concentrated in vacuo.

Biological assay. (a) Cat's blood pressure was recorded from the carotid artery, and injections of adrenaline, noradrenaline, and urinary extract were made into the femoral vein.

(b) Fowl's rectal cecum. Two to three centimeters of the hen's rectal cecum was suspended in Tyrode's solution at 39° C. Carbon dioxide 6.5 per cent in oxygen was bubbled through the solution. Injections of adrenaline, noradrenaline, and urinary extract were made into the bath, and the degree of cecal relaxation was recorded.

Computation of results. Having determined the activity ratio for adrenaline and noradrenaline by these methods, and the activity of the unknown urinary extract in terms of 1-noradrenaline, it is possible to calculate the relative amounts of adrenaline and noradrenaline in the urinary extract. The following symbols are used for such calculation:

a = 1-noradrenaline equivalents in micrograms per ml. of urine on cat's blood pressure.

A = 1-noradrenaline equivalents in micrograms per ml. of urine on hen's rectal cecum.

q = Activity ratio 1-adrenaline : 1-noradrenaline on cat's blood pressure.

Q = Activity ratio 1-adrenaline : 1-noradrenaline on hen's rectal cecum.

The amount of 1-adrenaline and 1-noradrenaline may then be calculated as follows:

$$X = \text{micrograms/ml. of adrenaline, or } (A - a)/(Q - q),$$

$$Y = \text{micrograms/ml. of noradrenaline or } A - XQ.$$

In these studies, the amount of adrenaline and noradrenaline in one ml. of urine was calculated and multiplied by total urine output for the collection period. The result was extrapolated for twenty-four hour output. Because of increased urinary output of catechol amines secondary to preoperative excitement, we compared our results with the normal urinary output of adrenaline and noradrenaline as determined by Goodall and Haynes⁷ with the same bioassay method. We used the bioassay method of catechol-amine determination because it is considered more accurate than the fluorometric or colorimetric methods,⁷⁻¹⁰ since adrenaline and noradrenaline precursors, amino acids, and other constituents are fluorometrically active.

RESULTS AND DISCUSSION

The results obtained are shown in Tables I, II, III, and IV. As seen in the tables, our average results, like the results obtained by others,¹⁻⁶ do not reveal any significant change from normal during epidural analgesia or during light

TABLE I
CYCLOPROPANE

No.	Age	Sex	Procedure	Calculated $\mu\text{g.}/24$ hours	
				adrenaline	noradrenaline
1	61	F	colectomy	11.3	21.4
2	63	F	colectomy	18.0	15.2
3	17	F	pelvic laparotomy	9.1	24.0
4	42	F	abdominal hysterectomy	1.1	21.1
5	48	F	thyroidectomy	21.6	40.4
Average normal				15.7	32.3

TABLE II
ETHER

No.	Age	Sex	Procedure	Calculated $\mu\text{g.}/24$ hours	
				adrenaline	noradrenaline
6	30	M	teeth extraction	10.1	10.7
7	71	M	gastrectomy	14.9	16.5
8	45	F	mitral valvulotomy	20.7	23.5
Average normal				15.7	32.3

TABLE III
HALOTHANE

No.	Age	Sex	Procedure	Calculated $\mu\text{g.}/24$ hours	
				adrenaline	noradrenaline
9	66	M	laparotomy	9.4	22.5
10	30	M	laminectomy	15.2	16.1
11	73	M	excision ca. of ear	18.1	27.6
12	38	F	teeth extraction	2.9	84.4
13	50	M	gastrectomy	17.2	20.5
Average normal				15.7	32.3

TABLE IV
EPIDURAL

No.	Age	Sex	Procedure	Calculated $\mu\text{g.}/24$ hours	
				adrenaline	noradrenaline
14	53	M	herniorraphy	5.5	39.9
15	46	M	herniorraphy	20.2	25.1
Average normal				15.7	32.3

anaesthesia with cyclopropane, ether, or halothane. Further investigations are necessary to determine the effects of deep anaesthesia and high arterial P_{CO_2} on urinary output of catechol amines. Because of discrepancies between the results obtained from blood levels of adrenaline and noradrenaline during deep anaesthesia by different investigators,¹⁻⁸ simultaneous determinations of blood concentrations and urinary output of catechol amines may give a better understanding of their alteration related to the depth of anaesthesia.

SUMMARY

Urinary output of adrenaline and noradrenaline was determined in fifteen surgical patients. Two received epidural analgesia and thirteen received light anaesthesia employing cyclopropane, ether, or halothane as the main agent. Results did not show a significant change from the normal urinary output of adrenaline and noradrenaline in any group.

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