OXYGEN LEVELS AND HAEMODYNAMICS DURING ANAESTHESIA WITH NITROUS OXIDE, THIOPENTAL, AND CURARE*

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ADVOCATES of certain anaesthetic regimens often stress the apparently superior cardiopulmonary performance with specific agents and techniques. Such claims are usually difficult to support or to refute because of the scarcity of quantitative data from truly comparable clinical situations in which the anaesthetic regimen is the only major variable. This situation is due in part to the de-emphasis of clinical studies during the current expansion of anaesthesia research efforts. In addition, it is ordinarily very difficult to have available for study a reproducible clinical situation in which there is opportunity to vary only the anaesthetic agent. When such a situation became available through the interest and co-operation of a surgical colleague, we set out to determine whether certain anaesthetic regimens were inherently superior to others in terms of cardiopulmonary performance. When the need for information regarding the effects of anaesthesia on metabolism became apparent, the studies were appropriately expanded. The present study of oxygen levels and haemodynamics during anaesthesia with nitrous oxide, thiopental, and curare has been preceded by similar studies during anaesthesia with ether, halothane, and methoxyflurane.¹⁻³

MATERIAL AND METHODS

Ten adults were studied during operation for varicose veins. All received pentobarbital (100 mg.) at two hours and meperidine (50 to 100 mg.) and atropine sulfate (0.4 mg.) at one hour before induction of anaesthesia with thiopental (125 to 350 mg.) and intubation with the aid of succinylcholine (40 to 60 mg.). Anaesthesia was maintained with a 6 L./min. flow of N₂O and O₂. The flow of O₂ was adjusted via the Beckman O₂ Analyzer, Model #D-2, as required to maintain the inspired Po₂ at approximately 160 mm. Hg (Patients 1 and 2) or 210 mm. Hg (all other cases). Manual hyperventilation was used with a semi-closed, circle CO₂ absorption system. Mean airway pressure was approximately 3 mm. Hg. Curare (d-tubocurarine chloride) was given after intubation (20 to 30 mg.) and each 20 minutes thereafter (3 mg.). Thiopental was given in amounts of 50 to 100 mg. as required to maintain a clinically satisfactory state of anaesthesia and suitable working conditions for the surgeon. The total amount of thiopental required to achieve this state varied from 450 to 1,800 mg. and is listed for the individual patients in Table I. Intravenous fluids (5% glucose

*Mayo Clinic and Mayo Foundation: Section of Anaesthesiology. Read at the meeting of the Canadian Anaesthetists' Society, Montreal, Quebec, June 25 to 30, 1967. This investigation was supported in part by Research Grant H-4881 from the National Institutes of Health, Public Health Service.

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TABLE I
HAEMODYNAMICS DURING N₂O, THIOPENTAL, AND CURARE ANAESTHESIA

Patient	Age	Hour	Total thiopental (mg.)	Oesophageal temperature (°C)	Mean arterial pressure (mm. Hg)	Cardiac output (L./min./m. ²)	Heart rate (beats/min.)	Stroke volume (ml./beat/m. ²)	Right atrial pressure (mm. Hg)
1	54	2	825	35.0	106	1.6	82	20	7
		3	925	35.0	107	1.5	87	18	6
2	48	2	375	37.0	100	1.5	55	27	9
		3	450	36.0	96	1.6	56	29	9
3	33	2	450	36.5	89	2.3	73	31	10
		3	725	36.1	81	2.8	73	39	7
4	49	2	650	35.9	80	2.2	65	33	8
		3	1000	35.7	77	2.3	72	32	8
5	69	2	500	35.5	110	1.6	93	18	12
		3	725	35.7	107	1.4	88	16	10
6	38	2	900	35.0	89	2.8	128	22	11
		3	1175	34.9	89	2.5	115	22	11
7	35	2	1375	36.9	120	2.9	69	42	10
		3	1800	36.9	115	3.1	71	44	9
8	47	2	700	35.7	120	2.9	64	46	11
		3	1000	35.6	123	2.9	63	46	13
9	64	2	750	34.4	125	1.2	84	15	10
		3	900	34.3	135	1.1	91	12	13
10	48	2	900	35.9	87	2.1	61	35	8
		3	975	35.4	73	1.8	59	31	7

in 0.2% saline) were given at a rate of 2 ml./kg. per hour. Measurements included oesophageal temperature (thermistor); arterial blood pH, P_{CO_2} , and PO_2 (electrodes); O_2 saturation (reflexion oximetry); haemoglobin concentration (cyanmethaemoglobin); cardiac output (indocyanine green, dye dilution); and arterial and right atrial pressures (strain gauge). In all known respects, the clinical situation studied and the methods used were similar to those of the previous studies during ether, halothane, or methoxyflurane anaesthesia.¹⁻³

The first hour of anaesthesia was occupied with establishing arterial (Teflon needle) and right atrial (catheter advanced from antecubital vein, electrocardiographic localization) sampling and steady anaesthetic and surgical conditions. Observations were then made at consecutive 15-minute intervals during a two-hour period. At the completion of these studies, measurements were repeated five minutes after 125 mg. of thiopental were administered (six patients).

RESULTS

The haemodynamic and blood gas values observed in each of ten patients during the second and third hours of N_2O , thiopental, and curare anaesthesia are listed in Tables I and II. Considerable variation existed in individual total thiopental requirements (450 to 1,800 mg.) and cardiac output values (1.1 to 3.1 L./min./m.²). Low values of cardiac output for individuals tended to be associated with low total amounts of thiopental administered (Fig. 1). Values for right atrial O_2 saturation were fairly normal (66 to 74%) in the majority of individuals (six patients) in association with cardiac outputs of 1.8 L./min./m.² and

FIGURE 1. Average values for cardiac output and total thiopental administered for each of ten patients (individuals are indicated by the numbers used in the text). Note the lack of association of low cardiac output values with high total amounts of thiopental.

TABLE II
BLOOD GAS AND ACID-BASE VALUES DURING N₂O, THIOPENTAL, AND CURARE ANAESTHESIA

Patient	Hour	Inspired		Arterial				Right atrial O ₂ saturation (%)	
		Po ₂ (mm. Hg)	pH	PCO ₂ (mm. Hg)	Po ₂ (mm. Hg)	O ₂ saturation (%)	Haemoglobin (gm./100 ml.)		Buffer-base (mEq./L.)
1	2	160	7.57	23	87	96	13.0	48	63
	3	160	7.53	24	81	95	12.7	46	56
2	2	160	7.61	21	76	95	13.2	49	62
	3	160	7.60	20	76	94	13.4	48	65
3	2	200	7.67	17	142	99	12.1	49	66
	3	197	7.70	16	142	99	12.5	49	70
4	2	200	7.67	16	94	98	12.2	48	—
	3	200	7.66	16	93	97	11.9	48	—
5	2	210	7.54	23	78	96	13.1	46	63
	3	215	7.55	23	72	96	13.2	47	59
6	2	212	7.63	18	77	95	12.5	48	69
	3	218	7.65	18	99	97	12.9	49	70
7	2	205	7.55	24	123	96	13.8	48	72
	3	211	7.57	22	120	97	13.9	47	70
8	2	210	7.69	18	111	98	13.5	51	67
	3	210	7.68	18	130	98	13.4	51	74
9	2	214	7.58	22	130	97	12.5	48	54
	3	203	7.58	22	125	98	12.6	48	36
10	2	213	7.63	16	110	98	13.8	45	70
	3	218	7.60	16	126	98	13.8	45	76

greater (Fig. 2). Abnormally low right atrial O_2 saturations (65% and lower) were noted in patients 1, 2, 5, and 9 in association with abnormally low cardiac outputs (1.6 L./min./m.² and lower). A careful study of the other observations available failed to reveal the basis of the distinctly impaired cardiac performance common to these four individuals. The reduced cardiac output was not characteristically associated with a lowered or elevated arterial pressure, heart rate, or stroke volume (Table I and Fig. 3).

The arterial blood acid-base status was similar for all (Table II) with elevated pH, lowered PCO_2 , and fairly normal buffer-base values (uncompensated respiratory alkalosis). Arterial PO_2 values varied considerably among patients without an apparent relation to age, inspired PO_2 , degree of hyperventilation, haemodynamics, or passage of time. The described differences among individuals in haemodynamic and blood-gas values remained fairly constant throughout the two hours of observation. For the group as a whole, significant change in circulatory system function with time did not occur (Table III). Cardiac output and arterial pressure were characteristically unchanged five minutes after thiopental (125 mg.), despite the presence of an increase in heart rate and reduction in stroke volume (Table IV). In comparison with other anaesthetic regimens studied,

FIGURE 2. Average values for right atrial O_2 saturation and cardiac output in nine patients. The hatched lines indicate the lower limits of normal. Note the good agreement between abnormally low cardiac output values and right atrial O_2 saturation values in patients 1, 2, 5, and 9.

FIGURE 3. Average values for arterial pressure and cardiac output for each of ten patients. Note particularly that arterial blood pressure was not characteristically low in the four individuals (1, 2, 5, and 9) who had demonstrated abnormally low cardiac outputs.

N₂O-thiopental-curare anaesthesia appears to be associated with a cardiac output midway between the greater value in ether anaesthesia and the lesser values for halothane or methoxyflurane use (Table V).

DISCUSSION

These findings indicate that an anaesthetic regimen based on thiopental, N₂O, and curare is neither particularly desirable nor remarkably undesirable in the clinical situation studied. Favourable findings include comparatively high average values for cardiac output and arterial pressure, stability of individual haemodynamic and blood-gas values, and the absence of significant change in buffer-base values. Unfavourable findings are believed limited to the abnormally low cardiac output and right atrial O₂ saturation values in four of the ten individuals studied.

It seems unlikely, however, that the low cardiac output values in these four patients are related solely to myocardial depressant effects of thiopental, and

TABLE III
HAEMODYNAMICS* DURING THIOPENTAL, N₂O, AND CURARE ANAESTHESIA PERIOD (15 MINUTES EACH)

Measure	1	2	3	4	5	6	7	8	9
Cardiac output (L./min./m. ²)	2.10 (0.18)	2.14 (0.21)	2.14 (0.16)	2.09 (0.21)	2.05 (0.24)	2.11 (0.27)	2.13 (0.21)	2.11 (0.22)	2.03 (0.22)
Mean arterial pressure (mm. Hg)	103 (5)	105 (5)	103 (5)	103 (6)	99 (5)	100 (6)	101 (7)	104 (9)	95 (6)
Mean right atrial pressure (mm. Hg)	10 (1)	9 (1)	9 (1)	10 (1)	10 (1)	9 (1)	10 (1)	9 (1)	9 (1)
Systemic vascular resistance (dynes sec. cm. ⁻⁵)	2200 (300)	2300 (300)	2100 (200)	2300 (400)	2300 (400)	2300 (400)	2200 (300)	2300 (400)	2300 (400)
Stroke volume (ml./beat/m. ²)	28 (3)	29 (3)	29 (3)	29 (3)	29 (4)	29 (4)	28 (3)	29 (4)	29 (4)
Heart rate (beats/min.)	79 (7)	78 (7)	77 (7)	77 (7)	77 (7)	76 (6)	81 (7)	79 (6)	73 (6)

*Mean value (SE) in ten individuals for each period.

TABLE IV
HAEMODYNAMICS BEFORE AND FIVE MINUTES AFTER 125 MG. OF THIOPENTAL

Patient	Situation	Cardiac output (L./min./m. ²)	Heart rate (beats/min.)	Stroke volume (ml./beat/m. ²)	Mean arterial pressure (mm. Hg)	Systemic vascular resistance (dynes sec. cm. ⁻⁵)	Mean right atrial pressure (mm. Hg)
3	before after	2.7 2.8	72 81	38 34	85 88	1400 1400	7 8
4	before after	2.1 2.0	75 87	28 23	79 64	1500 1300	8 6
5	before after	1.4 1.4	85 100	16 14	105 98	3200 2900	9 10
6	before after	2.7 2.6	110 130	24 20	87 89	1400 1500	10 10
7	before after	2.7 3.0	63 78	43 38	113 117	1900 1800	10 9
8	before after	3.0 2.5	60 63	49 39	120 129	1700 2200	13 12

TABLE V
COMPARATIVE HAEMODYNAMICS*

	Mean (SE)			
	Thiopental and curare	Ethyl ether 2-3%	Halothane 0.8%	Methoxyflurane 0.5%
Cardiac output (L./min./m. ²)	2.10 (0.07)	2.39 (0.06)	1.91 (0.06)	1.78 (0.03)
Mean arterial pressure (mm. Hg.)	102 (2)	94 (1)	81 (2)	82 (3)
Right atrial pressure (mm. Hg.)	9 (0.2)	8 (0.4)	11 (0.4)	9 (0.3)
Stroke volume (ml./beat/m. ²)	29 (1)	34 (1)	30 (1)	27 (1)
Heart rate (beats/min.)	77 (2)	71 (1)	64 (1)	67 (1)

*With each regimen, the respired gas mixture contained 60-70 per cent N₂O.

for two reasons. Firstly, in this series of ten patients, the degree of depression of cardiac output was not apparently directly related to total thiopental dosage (Fig. 1). In fact, although high cardiac output values were not associated with low total amounts of thiopental, low values for cardiac output were frequently associated with low total amounts of thiopental. Secondly, administration of 125 mg. of thiopental was followed by a reduction of stroke volume, but generally cardiac output was maintained by means of an increase in heart rate (Table IV). These findings are consistent with previous demonstrations of direct myocardial depressant properties of thiopental in heart-lung studies⁴ but are in conflict with reports of progressive reduction in cardiac output with increased depth of thiopental anaesthesia in man.⁵ Failure to demonstrate a clear, direct effect of thiopental on cardiac output in the present studies is believed to be due, in major part, to the low total amounts of thiopental administered. However, it may be that, as suggested by one reviewer, moderate surgical levels of thiopental anaesthesia do not cause myocardial depression in normal human subjects.⁶

The present study and others in the series¹⁻³ rely heavily on cardiac output values in the ultimate appraisal of relative effects of a particular anaesthesia regimen on the circulatory system during anaesthesia and operation. In addition, the rate of metabolic consumption of O₂ and the arterial O₂ content have been measured in several situations in order to permit the evaluation of circulatory system adequacy in terms of the O₂ system. In this context, values for right atrial O₂ saturation have been demonstrated to be useful as an index of the relationship of cardiac output, O₂ consumption, and arterial O₂ content.^{7,8} For example, a reduction in cardiac output without change in O₂ consumption rate or arterial O₂ content would necessarily be accompanied by a reduction in the value for right atrial O₂ saturation. In this approach, care must be taken to remember that only the whole-body situation is considered without knowledge of events in individual organs, tissues, or cells, that variations of haemoglobin concentration can be at times an important consideration, and that values for right atrial O₂ saturation may not be identical with those obtained with a true sample of mixed venous blood (pulmonary artery).

Despite these limitations and reservations, values for right atrial O_2 saturation have considerable immediate usefulness in the rapid evaluation of a clinical situation. For example, during the present study, it was known in the operating room that four patients (1, 2, 5, and 9) had low values for right atrial O_2 saturation and that, therefore, a disparity in cardiac output, arterial O_2 content, and metabolic requirements must exist. After the dye-dilution curves were processed and cardiac output values were calculated, it was established that an abnormally low cardiac output existed in each of these patients. In this situation, blood pressure measurements and pulse rate determinations were remarkably unrevealing (Table I). From this and other experiences, we believe that the values for right atrial O_2 saturation offer to the clinical anaesthetist a convenient and handy tool for rapid evaluation of adequacy of cardiopulmonary performance.

SUMMARY

Haemodynamic and blood gas studies have been carried out in ten patients during anaesthesia with N_2O , thiopental, and curare and during operations for varicose veins. Similar observations have been made previously during anaesthesia with ether, halothane, or methoxyflurane in the same clinical situation. With N_2O , thiopental, and curare, average values for cardiac output were somewhat lower than those observed during anaesthesia with ether but were somewhat higher than with halothane or methoxyflurane. Abnormally low values for cardiac output were noted in four of the ten patients, but these low values could not be ascribed to overdosage of thiopental. Values for right atrial O_2 saturation were demonstrated to be useful indices of the interrelationships of cardiac output, arterial O_2 content, and rate of metabolic consumption of O_2 .

RÉSUMÉ

On a fait des études de l'hémodynamique et des gaz du sang chez dix malades durant l'anesthésie au N_2O , pentothal et curare et durant des opérations pour cure de varices. Auparavant, on avait fait des observations semblables dans des circonstances identiques mais dont l'anesthésie était pratiquée à l'éther, à l'halothane ou au méthoxyflurane. Durant l'anesthésie au protoxyde-pentothal-curare, la moyenne de débit cardiaque était quelque peu inférieure à celle qu'on a observée durant l'anesthésie à l'éther, mais supérieure à celle des cas d'halothane ou de méthoxyflurane. Quatre des dix malades ont présenté un débit cardiaque considérablement abaissé, mais ces anomalies ne pouvaient être imputées à un surdosage de pentothal. On a démontré que le taux de saturation d'oxygène dans l'oreillette droite est un indice utile des rapports entre le débit cardiaque, le contenu d'oxygène artériel, et le taux de consommation métabolique d'oxygène.

ACKNOWLEDGMENTS

Our thanks to Dr. T. T. Myers, Section of Peripheral Vein Surgery, for making these studies possible, and to Henrietta Cranston and James Milde for technical assistance.

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