Renal Function During Anesthesia and Surgery

1. The Effects of Halothane Anesthesia

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THE current widespread use of halothane (Fluothane) anesthesia warrants studies of its effects on renal function in man. In dogs, Blackmore found that 2 per cent halothane decreased glomerular filtration rate (GFR) and renal plasma flow (RPF). These values approached control levels when the concentration of anesthetic drug was decreased.[1] Urine flow was decreased and potassium excretion was increased at all depths of anesthesia. The present study was performed to define the renal effects of halothane anesthesia in man, and to compare it to several of the other commonly used anesthetic agents.

Methods

Six male surgical patients with normal renal function were selected for study. They were prepared in a manner in common use today, *i.e.*, nothing was allowed by mouth after midnight of the day preceding surgery, and only small quantities of fluids were administered during the operative procedure itself. Premedication, consisting of 10 mg. of morphine sulfate and 0.4 mg. of scopolamine hydrobromide was given, intramuscularly, at 7 A.M. on the morning of operation. At this time an intravenous drip of 5 per cent glucose in water was begun at a rate of 30–50 ml./hour, to continue throughout the study. Inulin and para-aminohippuric acid (PAH) were administered by the constant infusion method, to measure GFR and as an index of RPF, respectively. Renal clearances were performed in the routine manner[2] utilizing air washouts through an indwelling urethral catheter. Studies were initiated one hour after the administration of premedication, and ended thirty minutes after the completion of operation. Two to four urine collections were made prior to induction and at each level of anesthesia. Clearances were determined at delivered halothane concentrations of 0.5–1.0 per cent (light anesthesia) and 1.2–3.0 per cent (deep anesthesia). In each subject halothane concentrations were alternated between light and deep levels at least twice during the procedure. Equilibration periods of 20 to 30 minutes were allowed between collection periods when the concentration of halothane was changed. Collection intervals of 15 to 30 minutes were used to insure obtaining at least 10 ml. of urine for each clearance determination.

Anesthesia. The anesthetic technique consisted of halothane-oxygen anesthesia utilizing a semiclosed circle system with a Heidbrink 550 carbon dioxide absorber. Oxygen, at a flow rate of 4 liters per minute, was passed through a Mark II Fluotec, adapted according to Lowe,[3] for vaporization of the halothane. No supplementary anesthetic agents were employed. Anesthesia was induced by increasing the halothane concentration to 3.0–3.5 per cent within several breaths. After a period of from five to ten minutes, 30–50 mg. of succinylcholine was given intravenously and endotracheal intubation was accomplished. Pulmonary ventilation was controlled with a Bird Mark IV controller-assister and a Mark VII respirator, manually adjusted to maintain arterial P_{CO_2} in the physiologic range. Blood pressure was obtained with a standard sphygmomanometer. Arterial *p*H and P_{CO_2} were measured by the Astrup technique.[4] ECG lead 2 was monitored throughout the procedure on a Corbin-Farnsworth Duotrace Car-

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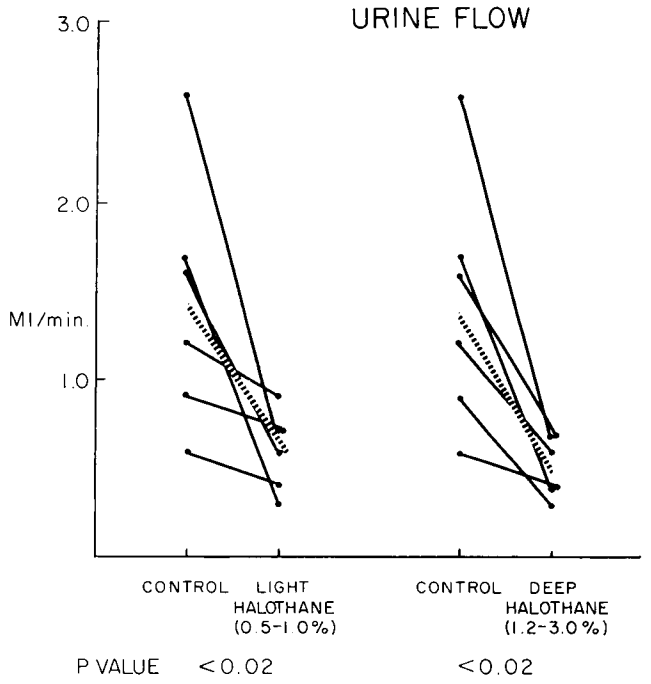

FIG. 1. Individual urine flow rates. The broken line represents the mean for the group.

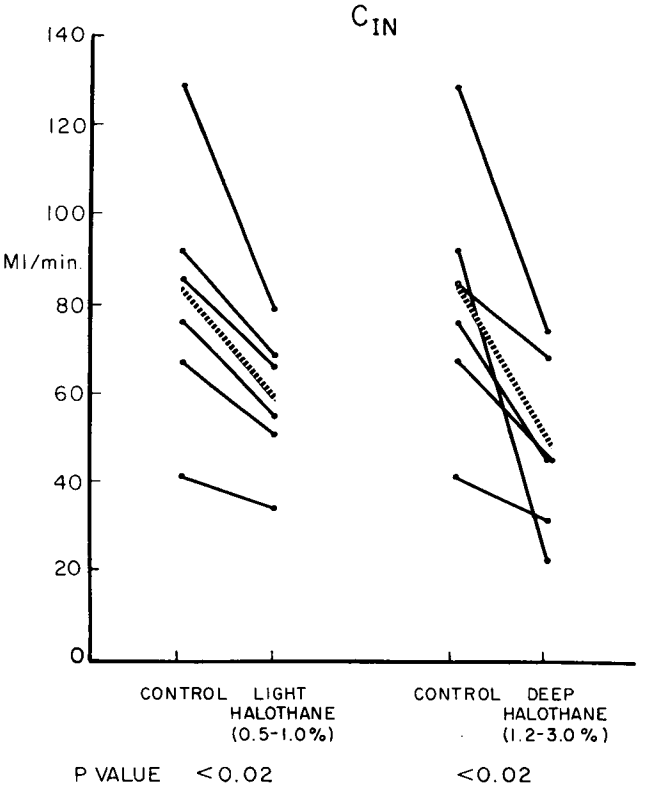

FIG. 2. Individual inulin clearance (C_{In})—glomerular filtration rate. The broken line represents the mean for the group.

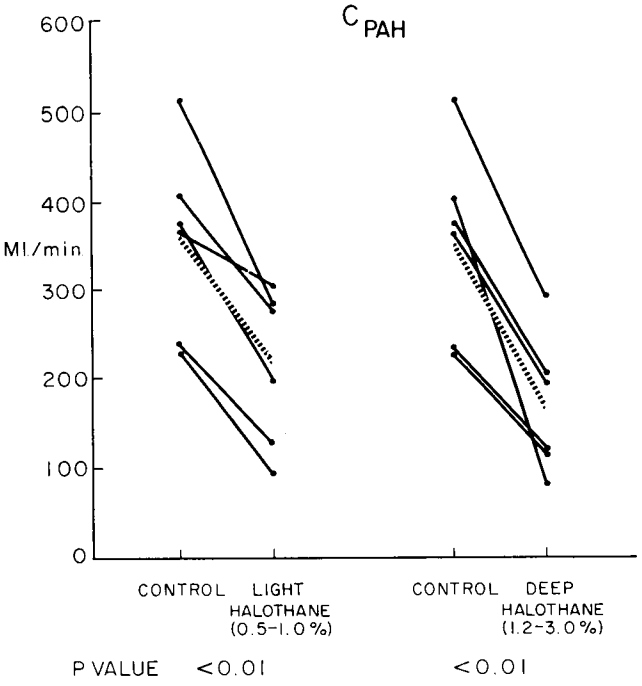

FIG. 3. Individual para-aminohippuric acid clearance (C_{PAH})—renal plasma flow. The broken line represents the mean for the group.

dioscope. Pulse and respiratory rate were counted directly.

Results

Urine flow, clearances of inulin and PAH, and sodium excretion were depressed consistently in all subjects with no apparent differences between light and deep anesthesia (figs. 1–3, table 1). Urine flow and sodium excretion showed the greatest changes, each falling to 43 per cent of control values with light anesthesia; 36 per cent with deep anesthesia. Inulin clearances fell to 72 per cent and 56 per cent, while PAH clearances fell to 60 per cent and 48 per cent, with light and deep halothane, respectively (table 1). Filtration fractions though increased were not significantly elevated. Potassium excretion was variable at all halothane depths.

Changes in mean blood pressure during light anesthesia were variable, while there was

TABLE 1. Renal Function Under Halothane Anesthesia

	Control*	Halothane (per cent)						Average Halothane
		0.5–1.0			1.2–3.0			
			% of Control	*P* Value		% of Control	*P* Value	% of Control
Urine flow (ml./min.)	1.4	0.6	43	<0.02	0.5	36	<0.02	40
C_{In}† (ml./min.)	82	59	72	<0.02	48	56	<0.02	64
C_{PAH}† (ml./min.)	353	213	60	<0.01	168	48	<0.01	54
Filt. fract. (%)	23	30	130	<0.05	29	126	>0.05	128
Na excret. (μEq./minute)	113	49	43	<0.01	41	36	<0.01	40
K excretion (μEq./minute)	53	62	117	<0.10	57	108	>0.10	113

* Morphine sulfate—10 mg., scopolomine—0.4 mg., intramuscularly.
† Corrected to B.S.A. of 1.73 m².

TABLE 2. Individual Results of Studies With Halothane Anesthesia

Patient	Procedure	Age (years)	Mean Blood Pressure (mm. Hg)	Urine Flow (ml./min.)	C_{In}* (ml./min.)	C_{PAH}* (ml./min.)	Filt. Fract. %	U_{Na} (μEq./l.)	U_K (μEq./l.)
1. Control	Lt. inguinal herniorrhaphy	32	90	2.6	76	374	20	64	51
Lt. Annes.			97	0.7	55	193	28	79	38
Deep Anes.			81	0.7	45	206	22	86	42
2. Control	Acromioclavicular joint reconstruction	25	88	1.2	85	363	23	132	46
Lt. Anes.			90	0.9	66	301	22	94	110
Deep Anes.			81	0.6	68	193	35	42	94
3. Control	Bankhart procedure for dislocated shoulder	26	85	1.7	41	228	18	123	20
Lt. Anes.			82	0.3	34	93	37	23	33
Deep Anes.			80	0.4	31	115	27	40	36
4. Control	Putti-Platt procedure for dislocated shoulder	25	80	1.6	129	511	25	134	104
Lt. Anes.			89	0.6	79	286	28	38	68
Deep Anes.			76	0.7	74	293	25	35	97
5. Control	Meniscectomy Lt. knee	25	74	0.9	92	407	23	47	57
Lt. Anes.			74	0.7	68	275	25	22	84
Deep Anes.			70	0.3	22	83	26	9	11
6. Control	Removal of loose bodies. Lt. knee	21	76	0.6	67	233	29	79	42
Lt. Anes.			76	0.4	51	129	40	37	36
Deep Anes.			70	0.4	45	117	39	36	60
Mean—Control		26	82	1.4	82	353	23	113	53
Lt. Anes.			85	0.6	59	213	30	49	62
Deep Anes.			76	0.5	48	168	29	41	57

* Corrected to B.S.A. of 1.73 m^2.
C_{In} = Inulin clearance.
C_{PAH} = Para-aminohippuric acid clearance.

only a slight drop in blood pressure with deep halothane anesthesia (table 2).

Discussion

Halothane anesthesia causes depression of renal function comparable to that produced by other general anesthetic agents in premedicated patients. There was no relation between the duration of anesthesia and the degree of depression noted. In fact, parameters of renal function were essentially the same at similar depths of anesthesia during collections performed several hours apart. Since the surgical procedures performed did not directly involve the genitourinary tract or its blood supply, no additional depression of renal function was noted during the operation itself.

Previous studies have reported the renal effects of cyclopropane, ether, and thiopental (table 3).[5-7] Because of the different conditions which prevailed at each study, *i.e.*, premedication, depth of anesthesia, fluids administered, methods of collection, etc., a detailed comparison of results cannot be made. However, there are certain similarities in the studies which should be brought out. There appears to be little difference among the effects of ether, thiopental, cyclopropane and halothane. All cause considerable depression of renal function which affects urine flow and sodium excretion to a greater extent than GFR and RPF. With each agent the filtration fraction is increased suggesting some degree of increased intrarenal efferent arteriolar constriction as at least one common site of action. Cyclopropane and ether differ from the other two in their more marked depressant effects on RPF, filtration fraction and sodium excretion. These differences may be explained by the increased catecholamine production asso-

ciated with the administration of these agents, causing further efferent arteriolar constriction.[8]

Multiple factors have been implicated in attempting to explain the effects of general anesthesia on renal function. These include the secretion of antidiuretic hormone (ADH), aldosterone, and catecholamines;[9-11] decreased cardiac output, systemic and renal blood pressure, and peripheral resistance;[12-17] peripheral shunting of systemic blood volume with renal vasoconstriction,[18] and changes in body temperature and acid-base balance.[19-20] We have thought that all of the changes noted during anesthesia may be secondary to the fall in GFR and RPF alone. Several investigators have demonstrated that changes in GFR of as little as 30 per cent can produce exactly these changes in sodium and water excretion.[21-23] Further evidence to this effect has been accumulated in unilateral renal disease.[24-25] Here, the profound decrease of sodium and water excretion on the ischemic side (associated with smaller reductions of GFR and RPF) serves as the diagnostic test for this condition.[26]

Changes in sodium and water excretion in unilateral renal disease are reversible by the infusion of saline or hypertonic mannitol.[27] Recently we have collected data on a number of patients who received hypotonic saline prior to the administration of halothane anesthesia. In these patients the usual depression of renal function seen during surgery was significantly ameliorated.[28] Another group of patients with only one functional kidney did well during urologic surgery with prophylactic mannitol diuresis.[29] Mannitol has also been used successfully in the prevention of postoperative oliguria and renal failure associated with aneurysmectomy of the abdominal aorta.[30] The use of saline or hypertonic mannitol infusion during operation may serve to counteract the decreases in GFR and RPF primarily by increasing cardiac output and plasma volume, and also by decreasing intrarenal efferent arteriolar resistance.[31]

Summary

Measurements of urine volume, clearances of para-aminohippuric acid and inulin, filtration fraction, and sodium and potassium excretion were performed in six patients with normal renal function undergoing elective surgery. Studies were performed prior to induction and at light and deep levels of anesthesia. Halothane was the only anesthetic agent used.

Results indicated that halothane is comparable to thiopental in its depressant effects on renal function, and is somewhat superior to ether and cyclopropane. The changes in urine volume and sodium excretion during general anesthesia may be due solely to the fall in glomerular filtration rate and renal plasma flow. It is suggested that these changes may be reversed by the prophylactic administration of saline or hypertonic mannitol.

TABLE 3. Comparison of the Renal Effects of Cyclopropane, Ether, Thiopental, and Halothane

Author	Agent	Percentage of Control			
		Volume	GFR	RPF	Sodium Excretion
Habif	Cyclopropane	30	53	37	11
Miles	Cyclopropane	—	52	44	—
Burnett	Cyclopropane	—	52	31	—
Habif	Ether	29	55	48	28
Miles	Ether	—	45	33	—
Burnett	Ether	—	39	21	—
Habif	Thiopental	29	67	61	18
Mazze	Halothane	40	64	54	40

GFR = Glomerular filtration rate.
RPF = Renal plasma flow.

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