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Laboratory Report

Autoregulation of Renal Blood Flow during Halothane Anesthesia

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Renal blood flow, when not affected by humoral or neural influences, remains relatively constant over a wide range of renal arterial perfusion pressures. This phenomenon, referred to as "autoregulation," is an important mechanism allowing kidneys to maintain homeostasis of the internal milieu over a wide range of arterial pressures. The present study showed that 0.9 per cent halothane had no effect on autoregulation in an isolated, perfused dog kidney as renal arterial perfusion pressure was varied between 75 and 125 torr. (Key words: Kidney, blood flow, halothane; Anesthetics, volatile, halothane.)

THE KIDNEYS can maintain a constant blood flow over a wide range of perfusion pressures. This phenomenon, referred to as autoregulation, is important in renal homeostasis. General anesthesia is associated with decreased renal blood flow in the presence of increased,[1] decreased,[2] or stable blood pressures.[3] Because of these observations, it has been implied that general anesthesia interferes with autoregulation of renal blood flow,[4,5] although contrary evidence has also been reported.[6]

Because autoregulation had not been investigated during steady-state conditions with reference to concentration of anesthetic and changing neural and humoral factors, we examined the effect of halothane on autoregulation of blood flow in an isolated, perfused dog kidney during steady-state conditions.

Methods

Studies were performed in mongrel dogs weighing 17–25 kg. These dogs were fed a standard kennel ration. Food was withheld for at least 16 hours before the study, but water was permitted *ad libitum*. The donor animal was anesthetized with pentobarbital, 25 mg/kg, iv. An isolated perfused kidney was prepared as previously described.[7]

In brief, a kidney is removed from the donor dog, placed in a receptacle filled with 0.9 per cent sodium chloride maintained at 38 C, and perfused with heparinized blood from the femoral artery of a second dog (perfusion animal) (fig. 1). The perfusion animal was anesthetized with halothane in nitrogen and oxygen administered via face mask. Halothane was vaporized in a Copper Kettle vaporizer, using total gas flows of 2.5 l/min in a circle system with a carbon dioxide absorber. After the animal was anesthetized and the trachea intubated, ventilation was controlled with an Air Shields operating room ventilator. Arterial blood *p*H and P_{CO_2} were maintained at 7.40 ± 0.02 and 40 ± 5 torr, respectively. Inspired O_2 concentration was adjusted to maintain Pa_{O_2} at 100 ± 10 torr. End-expired halothane concentration was monitored continuously with an infrared analyzer (Beckman LB-2) and maintained at 0.90 ± 0.03 vol per cent. The perfusion animal received 10 mg desoxycorticosterone acetate, intramuscularly, two hours before the study to maintain a constant aldosterone effect.

The isolated kidney was perfused by heparinized blood from the perfusion animal's left femoral artery. Venous effluent from the isolated kidney flowed by gravity into a heated reservoir and was pumped back into the perfusion animal via the right femoral vein. The perfusion animal rested on an adjustable platform allowing control of perfusion pressure in the isolated kidney by raising or lowering the perfusion dog (fig. 1).

After the isolated kidney was connected to the perfusion animal (ischemia time always less than 2.0 min), the isolated kidney was allowed to stabilize for at least 60 min with a renal arterial perfusion pressure (P_{RA}) of 100 torr and venous pressure of 3 ± 1 torr. Perfusion pressure was then varied either from 75 to 100 to 125 torr or from 125 to 100 to 75 torr, with perfusion pressure maintained for 10 min. The animals were then sacrificed.

Renal blood flow (RBF) was measured using an electromagnetic flow probe (Carolina Instruments) in the renal arterial line, and by direct measurement of venous effluent rate. Arterial and venous pressure of the perfusion animal, arterial and venous pressure of the isolated kidney, and arterial blood flow to the isolated kidney were recorded on a

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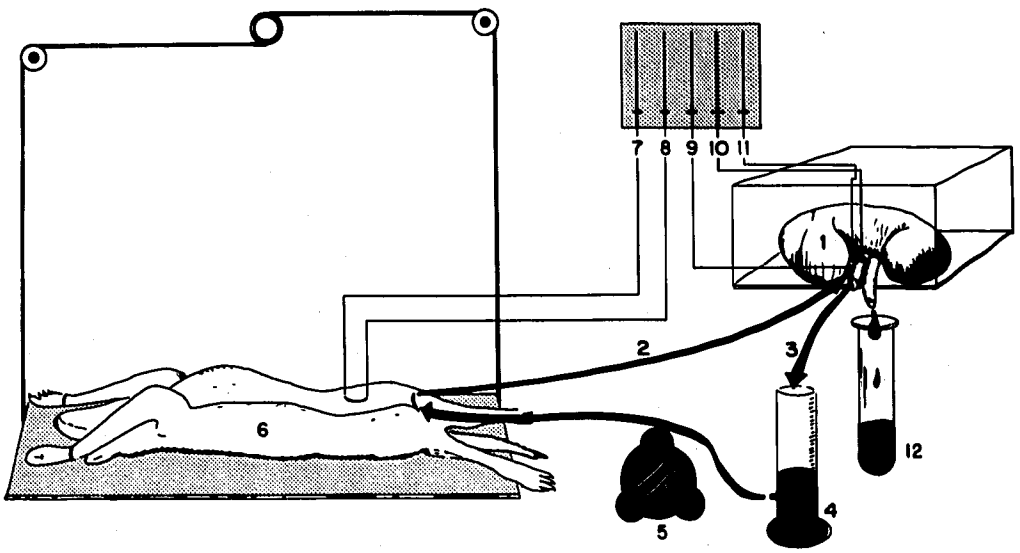

FIG. 1. Diagram of the isolated kidney preparation. The isolated kidney (1) is placed in a receptacle filled with 38 C 0.9 per cent sodium chloride. It is perfused with blood from the femoral artery (2) of a second dog. Renal venous blood (3) flows by gravity into a heated reservoir (4), from which it is pumped (5) to the femoral vein of the perfusion animal (6). The perfusion animal rests on an adjustable platform and by raising or lowering the platform with respect to the isolated kidney, renal arterial pressure in the isolated kidney can be regulated. Pressure in the femoral artery (7) and vein (8) and renal artery (9) and vein (10) are monitored with pressure transducers. Renal blood flow is measured directly from the renal vein (3) and by an electromagnetic flow probe on the renal artery (11). Urine is collected from a catheter secured in the ureter (12).

Beckman R-type dynagraph. Student's T test was used to compare blood flows at different perfusion pressures. Autoregulation indices (AI) were calculated as $\Delta RBF/\Delta P_{RA}$ (ml/min/torr).[8] Autoregulatory efficiency index (AEI) was calculated by the formula: $(RBF_2 - RBF_1)/RBF_1 \div (P_{RA_2} - P_{RA_1})/P_{RA_1}$.[9] A ratio of zero indicates perfect autoregulation, and a ratio of 1 indicates absence of autoregulation. Autoregulatory efficiency can be expressed as a percentage by subtracting AEI from 1 and multiplying by 100.

Results

Results of five experiments, representing five dogs and five isolated kidneys, are reported. Mean blood flows at 75, 100, and 125 torr were 203 ± 20, 201 ± 20, and 200 ± 23 ml/min (fig. 2), or 3.95 ± 0.35, 3.93 ± 0.30, and 3.92 ± 0.40 ml/min/g, respectively. There is no significant difference among these blood flows. Autoregulation (AI) and autoregulatory efficiency (AEI) indices are listed in table 1. When P_{RA} varied from 75 to 100 torr, AI was −0.08 ± 0.17 and AEI was −0.02 ± 0.06 (102 per cent). For a change in P_{RA} from 100 to 125 torr, AI was −0.04 ± 0.17 and AEI was −0.04 ± 0.09 (104 per cent). For the overall change in P_{RA} from 75 to 125 torr, AI was 0.06 ± 0.13, and AEI was −0.02 ± 0.05 (102 per cent).

Discussion

Autoregulation of blood flow occurs in many vascular beds, but not to the extent seen in the kidney. Moreover, the mechanisms involved with autoregulation in the kidney are more complex, not only because both afferent and efferent arterioles are involved but because of interactions among various physical and chemical factors. Among the physical factors proposed to play roles in regulation of blood flow are changes in blood viscosity secondary to pressure-dependent changes in hematocrit[10] ("plasma-skimming") and altered transmural capillary pressure brought about by pressure-dependent changes in tissue pressure.[11] One chemical substance that may be involved in autoregulation is angiotensin.[8] There is no consensus as to the exact mechanism, except that it occurs entirely within the kidney. One should keep in mind that a number of extrarenal factors also affect renal blood flow and will, in fact, play more important roles in determining renal perfusion.

Some confusion exists about the term "abolished autoregulation."[12] This term should be used only

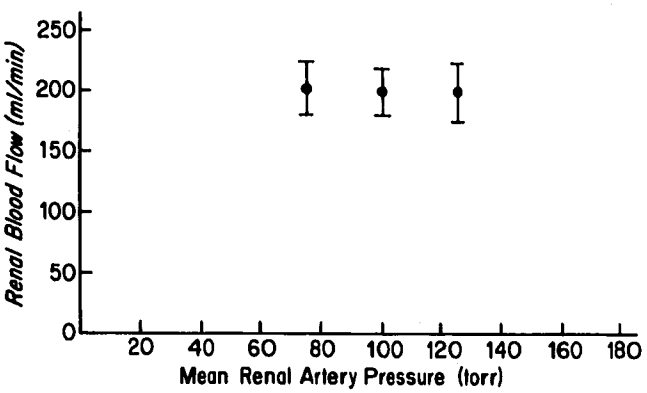

FIG. 2. Renal blood flows (mean ± SEM) at 75, 100, and 125 torr in the presence of 0.9 per cent end-expired halothane.

TABLE 1. Autoregulation and Autoregulatory Efficiency Indices and Percentage Efficiency of Autoregulation for Changes in Renal Arterial Pressures*

	Renal Arterial Pressures (P_{RA}), torr		
	Δ75–100	Δ100–125	Δ75–125
Autoregulation index (AI) (ml/min/torr)	−0.08 ± 0.17	−0.04 ± 0.17	−0.06 ± 0.13
Autoregulatory efficiency index (AEI)	−0.02 ± 0.06	−0.04 ± 0.09	−0.02 ± 0.05
Efficiency of autoregulation (per cent) (AEI%)	102	104	102

* From 75 to 100, 100 to 125, and 75 to 125 torr. Data given are means ± SEM; n = 5.

when the increase in renal resistance, which normally occurs as P_{RA} exceeds 75–80 torr, is abolished. This must be accomplished during steady-state conditions with reference to external influences (*e.g.*, renal neural activity, hormone and drug levels). It has been inferred that because RBF is diminished during general anesthesia, autoregulation is interfered with.[4] Clearly this type of observation does not meet the criteria for measuring autoregulation.

Leighton *et al.*[5] have presented data that they interpret as demonstrating impairment of renal autoregulation by methoxyflurane. In their experiments, however, blood pressure was lowered by increasing concentrations of methoxyflurane. Since anesthetic depression of renal blood flow is known to be dose-related,[13] autoregulation must be studied during steady-state conditions, which were not achieved in Leighton's study. Moreover, the concentrations of anesthetic achieved in Leighton's study are not known.

Westermark and Wåhlin[14] and Irestedt *et al.*[6] concluded that both halothane and methoxyflurane (respectively) decreased renal vascular resistance. Since the change in blood flow was less than the change in arterial pressure, they concluded that autoregulation was intact. Again, in these experiments, autoregulation was not measured during steady-state conditions.

The isolated perfused kidney technique allows one to examine autoregulation of renal blood flow during steady-state conditions. Anesthetic concentrations can be maintained constant; the kidney is isolated from direct neuronal input; and the humoral state of the perfusion animal remains constant because P_{RA} is altered mechanically. Thus, this preparation is remarkably well suited for studies of autoregulation.

Our data demonstrate that autoregulation of renal blood flow is maintained over a range of mean arterial pressures from 75 to 125 torr in the presence of 0.9 per cent end-expired halothane. If these data are also valid for man, it would indicate that the decreased renal blood flow seen during light halothane anesthesia is a result of changes in extrarenal factors influencing renal perfusion rather than impairment of the "intrinsic" autoregulatory mechanism. This conclusion may not be valid for other potent inhalation agents, higher concentrations of halothane, or wider ranges of renal perfusion pressures.

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References

1. Deutsch S, Pierce EC Jr, Vandam LD: Cyclopropane effects on renal function in normal man. ANESTHESIOLOGY 28:547–558, 1967
2. Deutsch S, Goldberg M, Stephen GM, et al: Effects of halothane anesthesia on renal function in normal man. ANESTHESIOLOGY 27:793–804, 1966
3. Deutsch S, Bastron RD, Pierce EC Jr, et al: The effects of anaesthesia with thiopentone, nitrous oxide, narcotics and neuromuscular blocking drugs on renal function in normal man. Br J Anaesth 41:807–815, 1969
4. Larson CP Jr, Mazze RI, Cooperman LH, et al: Effects of anesthetics on cerebral, renal, and splanchnic circulations. ANESTHESIOLOGY 41:169–181, 1974
5. Leighton KM, Koth B, Wenkstern BM: Autoregulation of renal blood flow: Alteration by methoxyflurane. Can Anaesth Soc J 20:173–179, 1973
6. Irestedt L, Westermark L, Wåhlin Å: Blood circulation in the kidney of the cat under methoxyflurane (Penthrane®) anaesthesia. Acta Anaesthesiol Scand 19:277–286, 1975
7. Bastron RD, Kaloyanides GJ: The effect of sodium nitroprusside on systemic hemodynamics and renal function of the dog. J Pharmacol Exp Ther 181:244–249, 1972
8. Kaloyanides GJ, Bastron RD, DiBona GF: Impaired autoregulation of blood flow and glomerular filtration rate in the isolated dog kidney depleted of renin. Circ Res 35:400–412, 1974
9. Semple SJG, de Wardener HE: Effect of increased renal venous pressure on circulation autoregulation of isolated dog kidneys. Circ Res 7:643–648, 1959
10. Pappenheimer JR, Kinter WB: Hematocrit ratio of blood within mammalian kidney and its significance for renal hemodynamics. Am J Physiol 185:377–390, 1956
11. Hinshaw LB, Day SB, Carlson CH: Tissue pressure as a causal factor in the autoregulation of blood flow in the isolated perfused kidney. Am J Physiol 197:309–312, 1959
12. Thurau K, Levine DZ: The renal circulation, The Kidney. Volume III. Edited by Rouiller C, Muller AF. New York, Academic Press, 1971, p 8
13. Miles BE, de Wardener HE, Churchill-Davidson HC, et al: The effect on the renal circulation of pentamethonium bromide during anesthesia. Clin Sci 11:73–79, 1952
14. Westermark L, Wåhlin Å: Blood circulation in the kidney of the cat under halothane anaesthesia. Acta Anaesthesiol Scand 13:185–208, 1969