Title DISTRIBUTION OF BLOOD FLOW WITH ANESTHETICS

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Introduction: The laboratory rat has frequently been used to investigate various actions of anesthetic agents. Whether commonly used anesthetic agents produce cardiovascular effects in the rat similar to those which are known to occur in man has not been studied. The use of radioactive labelled microspheres allows for the determination of cardiac output and the distribution of blood flow before and after drug treatment. We first examined whether this technique is applicable for the study of anesthetic agents. We then used this technique to investigate three commonly used anesthetic agents and have compared these results to what is known to occur in other experimental animals and man.

Methods: 25 fasted male Wistar rats (230-400 gms) were anesthetized with diethyl ether and PE 50 tubing was inserted into the left ventricle and left femoral artery. The catheters were exteriorized and the animals allowed to awaken. The protocol then consisted of a one hour control period, a twenty minute induction period and a one hour period of stable anesthesia. Anesthesia was established with one of the following agents: halothane (H) 1.3 per cent (n=6); enflurane (E) 2.2 percent (n=6) or ketamine (K) 125 mg/kg IM (n=6). A control group (A) (n=7) was treated identically but remained unanesthetized throughout. To determine cardiac output and distribution of flow, 40,000-60,000 15 micron microspheres labelled with strontium 85 were injected through the left ventricular catheter at the end of the control period. Blood was withdrawn from the femoral artery at a constant flow rate for 70 seconds to determine cardiac output. Cerium 141 labelled microspheres were similarly injected after one hour of stable anesthesia. Arterial blood gases were also obtained at this time. The animals were then sacrificed and the organs of the body dissected out, weighed and counted in a gamma counter at the appropriate energy spectra for each isotope. Aliquots of muscle and skin were taken and counted and their contribution to body weight calculated as 18% for skin and 45% for muscle. The data were analyzed using Students's t test for unpaired data for comparisons between groups and paired data for comparisons within groups. A p value of less than .05 was taken as statistically significant

Results: Unanesthetized animals showed no differences in cardiac output, percent of cardiac output or blood flow to organs using the two different microsphere labels given 90 minutes apart. Since there were no differences found, the results for cardiac output and per cent of cardiac output for Sr and Ce were combined and compared to the awake values for the three anesthetized groups. Significant apparent differences in the awake state for lung and muscle were seen only in animals that subsequently received ketamine anesthesia. The distribution of cardiac output with the three anesthetics is summarized in the table.

PER CENT CARDIAC OUTPUT

Anesthetic Agent	A	H	E	K
% Brain	1.2	2.2*	1.4	2.0*
Heart	6.6	4.6*	3.9*	4.7
Lung	0.7	2.8	1.8	4.3
Skin	8.0	6.0	3.9	5.2
(R) Kidney	6.2	7.9*	6.7	7.2
(L) Kidney	6.4	8.3*	6.3	7.0
Muscle	53.8	17.3*	12.9*	14.2*
Liver	3.3	4.0*	4.0*	3.7
Spleen	0.6	1.4	1.3*	1.4
Stomach	1.1	.7	.6	1.5
S. intestine	10.1	15.7	9.9	11.1
L. intestine	1.6	1.9*	1.7*	1.7
C.O. (ml/min)	137	100*	126	99

mean values, SEM deleted for clarity
*p<.05 paired analysis

Halothane anesthetized animals had a fall in cardiac output from 135±13 ml/min to 100±13 ml/min. Significant increases in percent cardiac output were seen in brain, kidney, liver and large intestine while decreases were seen in heart and skeletal muscle. Enflurane anesthetized animals had no fall in cardiac output but peripheral resistance fell markedly. Significant changes in percent cardiac output were seen in heart, lung, muscle, liver spleen and large intestine. Animals anesthetized with ketamine had an insignificant fall in cardiac output and increase in flow to the brain. More interesting was the finding that microspheres that were "trapped" in the muscle from the first injection when the animals were awake, were released from muscle and skin by ketamine anesthesia and appeared in the lung.

Discussion: The microsphere technique is a reliable method to study cardiac output and distribution of blood flow in the rat with halothane and enflurane anesthesia. The cardiovascular changes induced by halothane or enflurane are similar to that which is known to occur in man. One important exception is the increase in per cent blood flow to the kidneys in the animals anesthetized with halothane. Ketamine anesthesia results in a loss of microspheres that are originally "trapped" in muscle and skin but then are found in the lung. The supposition that microspheres remain stationary once they have been "trapped" in various tissues is not supported by the experiments with ketamine anesthesia. Ketamine anesthesia results in cardiovascular changes that are not always seen in man.

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