The Effect of Cyclopropane and Halothane on the Blood Volume in Man

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THE availability of new instrumentation for the measurement of blood volume has emphasized the value of these measurements as guides for replacement therapy in patients undergoing major surgical procedures.[1, 2] Evaluation of these data requires knowledge of the effect of anesthesia on the blood volume. Information on this subject is scant because of the many variables involved in the induction of anesthesia and the lack hitherto of an accurate, repeatable and easily available method for the measurement of blood volume during anesthesia. This communication reports the red cell and plasma volume data of patients before and during cyclopropane or halothane anesthesia.

Materials and Methods

Twenty patients between the ages of 23 and 84, scheduled for elective surgery, were chosen for this study. All of the patients were recumbent for at least two hours and were given 100 mg. of pentobarbital and 0.4 mg. of atropine as premedication one hour prior to anesthesia. Ten patients received cyclopropane-oxygen and ten received halothane-nitrous oxide-oxygen anesthesia. Airway patency was assured in each case by a pharyngeal airway or endotracheal tube. Respiratory assistance was not employed. Cyclopropane and oxygen were given in a closed system with a carbon dioxide absorption circle filter. Halothane (0.7 to 2 per cent) in 2 liters each of nitrous oxide and oxygen per minute was administered in a semiclosed system with carbon dioxide absorption. No intravenous fluids were administered during the study periods.

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Blood volume measurements in each patient were based on the dilution of 1 ml. of type O Rh–Negative, human red blood cells, labeled with 30–50 microcuries of CR^{51} and 1 ml. of a 1 per cent solution of human serum albumin, labeled with 2–3 microcuries of I^{125}. These tracers were injected simultaneously into an antecubital vein, and a single sample was drawn from an antecubital vein of the opposite arm after ten minutes of mixing time. In several cases additional blood samples were taken serially up to 30 minutes after injection. The radiation characteristics of Cr^{51} and I^{125} are sufficiently dissimilar that they can be differentiated in the Volemetron * with appropriate radiation filters.[3] Accordingly, all of the blood volume measurements in this study were made by the summation of the red cell mass (RV) and the plasma volume (PV) determined independently and simultaneously. The overall body hematocrits (OBH) were calculated as follows:

$$\text{Overall body hematocrit (OBH)} = \frac{\text{Red cell volume (RV)}}{\text{Red cell volume (RV)} + \text{Plasma volume (VP)}}$$

The large vessel hematocrits (LVH) were determined in duplicate on the 8 ml. blood samples used for the blood volume measurements. These were spun at 3,000 r.p.m. for 30 minutes in an International Clinical centrifuge. The average hematocrit values of these two 8 ml. samples was multiplied by 0.96 to correct for trapped plasma. For the study of shifts of the distribution of red cells, the ratio of the overall body hematocrit (OBH) to the large vessel hematocrit (LVH) was calculated in each case.

Just before induction of anesthesia, a blood volume determination was done to serve as a control for that patient. After the patient

* A semiautomatic instrument for the measurement of blood volume manufactured by the Atomium Corp., Billerica, Mass.

had been in surgical anesthesia (plane 2, stage III) for thirty minutes as judged by clinical signs and before surgery was started, a second blood volume measurement was made.

Results

The effect of cyclopropane anesthesia on blood volume is shown in figure 1. The change in red cell mass averaged +3.9 per cent (range +12 to −1 per cent). The change in plasma volume averaged +4.1 per cent (range +21 to −5 per cent). The change in total blood volume averaged +4 per cent (range +14 to −3 per cent). A change of 4 per cent is not statistically significant because the cumulative error of the two red cell and plasma-volume determinations theoretically approaches this figure. There were no changes in blood pressure greater than 20 mm. of mercury in this group.

The effect of halothane anesthesia on blood volume is shown in figure 2. The change in red cell mass averaged +7.1 per cent (range +21 to −7 per cent). The change in plasma volume averaged +11.9 per cent (range +30 to +1 per cent). The change in total blood volume averaged +10.1 per cent (range +18 to +3 per cent). This increase was well beyond the error of the method ($P < 0.01$). An initial fall in blood pressure occurred with induction of anesthesia in each case, but the patients were normotensive before the second blood volume measurement was made.

Table 1 shows the OBH/LVH ratio for each

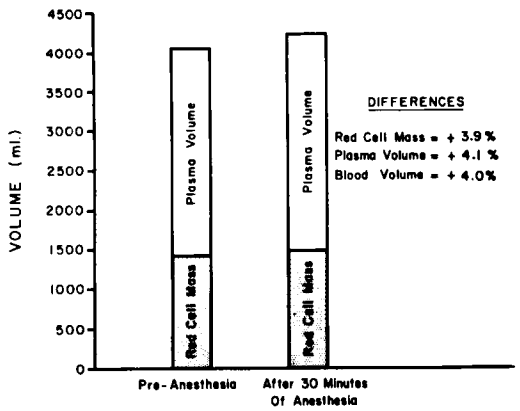

FIG. 1. The effect of cyclopropane anesthesia on blood volume (10 patients). The changes in red cell mass and plasma volume are of borderline significance.

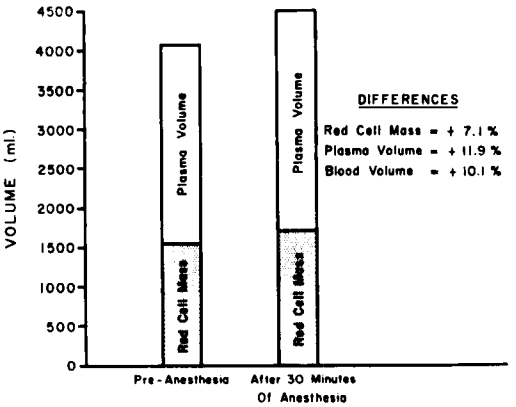

FIG. 2. The effect of halothane anesthesia on blood volume (10 patients). Both the red cell mass and the plasma volume are increased.

blood volume measurement. Although the average OBH/LVH ratio did not change appreciably (from 0.912 to 0.897 in one group and from 0.894 to 0.884 in the other group), an occasional shift of more than 10 per cent was observed in individual patients (see 3 and 19).

Discussion

The few reported clinical studies on the effect of anesthesia on blood volume differ in the anesthetic agent used, the plane and duration of anesthesia, and the methods used for the assay of the blood volume. Gibson and Branch,[4] using the Evans blue dye

TABLE 1. Overall-Body-Hematocrit/Large-Vessel-Hematocrit Ratio in 20 Patients Before and During General Anesthesia

Cyclopropane			Halothane		
Patient	Preanesthesia	After 30 minutes	Patient	Preanesthesia	After 30 minutes
1	0.870	0.825	*11*	0.935	0.965
2	0.913	0.876	*12*	0.891	0.810
3	0.953	0.848	*13*	0.844	0.942
4	0.951	0.908	*14*	0.923	0.919
5	0.851	0.911	*15*	0.872	0.872
6	0.910	0.879	*16*	0.911	0.954
7	1.110	1.100	*17*	0.904	0.889
8	0.925	0.940	*18*	0.795	0.858
9	0.844	0.885	*19*	0.912	0.787
10	0.796	0.799	*20*	0.950	0.957
			Averages		
	0.912	0.897		0.894	0.884

method, found a slight decrease in the plasma volume of six patients during the induction of ether anesthesia. Albert and co-workers,[5] using chromium-51 tagged red cells and iodine-131 labeled albumin, found a decrease in blood volume during hypotension caused by the induction of thiopental anesthesia. Price and associates,[6] using chromium-51 tagged red cells or Evans blue dye and the hematocrit values, found a 9.6 per cent decrease in plasma volume during the first 20 minutes of ether anesthesia, but a 4.9 per cent decrease after 80 minutes of ether anesthesia. No change in blood volume occurred during light cyclopropane, but an 8.8 per cent decrease in plasma volume was observed during deep cyclopropane anesthesia. This was partially attributed to the increase in intrathoracic pressure that occurred when the respirations were assisted. The plasma volume increased 3 per cent when thiopental-nitrous oxide was used by these investigators. They also observed that the changes in plasma volume were generally inversely related to changes in arterial and venous pressure.

Our findings in patients under light cyclopropane anesthesia (unassisted respirations) confirm those of Price. The 11.9 per cent increase in plasma volume observed in our patients who received halothane may be attributable to rapid shifts in plasma. However, the 7.1 per cent increase in red cell mass cannot be explained easily because similar shifts of red blood cells in and out of the circulation are not known to occur. The time allowed for mixing of the tagged cells was not a factor, because in those patients who had serial blood samples drawn for 30 minutes, equilibration with the circulating red cell mass was complete in ten minutes both before and during anesthesia. It is possible that with the increased peripheral blood flow observed under the influence of halothane,[7] capillary beds whose circulation is sluggish under normal conditions are brought into more active communication with the general circulation.

Shifts in the OBH/LVH occurred only rarely during the course of anesthesia. In two instances, the shifts were large enough to yield blood volume measurements by the single isotope method that were incorrect. Such errors as might be introduced by these shifts were avoided by the simultaneous double isotope method.

The clinical significance of the increases in blood volume observed in some of the patients is uncertain. However, the mild hypervolemia induced by halothane might be regarded as a disadvantage in patients with borderline cardiovascular reserve. In none of the cases in this study was a decrease in blood volume observed. It is, therefore, clear that hypovolemia is not responsible for the hypotension that may occur during cyclopropane or halothane anesthesia. If hypovolemia occurs during surgery, it cannot be attributed to these anesthetic agents.

Summary and Conclusions

Serial measurements of circulating plasma volume and red cell mass were made in ten patients undergoing cyclopropane anesthesia and ten patients undergoing halothane anesthesia.

The blood volumes were calculated by the summation of the red cell mass and plasma volume determined by simultaneous and independent radioisotope dilution assays.

Cyclopropane caused no significant change, while halothane caused a 10.1 per cent increase in blood volume under the conditions studied.

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