THE CARDIOVASCULAR EFFECTS OF HALOTHANE

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WITH the increasing use of electrical equipment in the anesthesia area, there has arisen a need for a potent, nonexplosive, inhalation anesthetic agent. In addition to these properties, halothane (Fluothane) possesses the advantages of rapid induction with minimal metabolic disturbances. Because hypotension and peripheral vascular collapse have been associated with halothane anesthesia, this study was undertaken to elucidate its effects on the cardiovascular system. Although other significant studies have been reported in this connection, the present study differs in some particulars such as the additional recording of aortic flow rates.[1]

Hypotension may occur with anesthesia when (1) the force of contraction of the myocardium is depressed, resulting in a depression in stroke volume; (2) when heart rate is inadequate to maintain sufficient cardiac output; (3) when peripheral vasodilatation is excessive; (4) when a significant decrease in blood volume is not compensated. Such depressant effects on the cardiovascular system may be due to direct effects of the anesthetic or secondary to depressant effects on the neurohumoral mechanism responsible for homeostasis.

METHODS

Animal Studies. The animal experiments were conducted in 18 healthy mongrel dogs weighing 8 to 13 kg. Anesthesia was induced with 4 liters nitrous oxide and 2 liters oxygen through a Fluotec vaporizer with a 3 per cent halothane setting through a semiclosed system. Following tracheal intubation, ventilation was controlled by means of a positive pressure Harvard respirator at a constant rate and volume required to produce adequate lung expansion. This tidal volume was usually 20 to 25 ml. per kilogram with a respiratory rate of 12 per minute. After the establishment of experimental conditions, the animals were maintained on 4 liters of nitrous oxide and 2 liters of oxygen until a control state of analgesia was obtained, at which time the halothane studies were undertaken. Arterial blood pressure (BP) was recorded via a femoral artery from an indwelling polyethylene cannula inserted to the level of the descending aorta. Pressure changes were measured with a Statham transducer. A second polyethylene catheter for drug injection was placed in the inferior vena cava via a femoral vein. The chest was opened in the midline, and a Walton-Brodie strain gauge arch was sutured directly to the right ventricle.[2-5] The strip of myocardium between the two feet of the arch was stretched to 30–35 per cent above end-diastolic length. The ventricular contractile force (CF) changes which were measured and recorded have been shown to be due primarily to humoral and neurogenic changes.[3, 4] Myocardial adjustments secondary to hemodynamic changes were insignificant because of the fixed initial length of the muscle segment. Aortic blood flow was measured with a Kiger-Dennard square wave electromagnetic flowmeter,[6, 7] inserted around the ascending aorta just distal to the coronary ostia. Contractile force, blood pressure, and aortic blood flow changes were recorded by a Sanborn polyvisagraph. Peripheral resistance was determined by dividing the mean aortic blood pressure by the aortic blood flow.[8] Sympathetic blockade was produced according to the technique of Brewster and associates[9] but modified to the extent that 0.05 per cent tetracaine was used in place of 0.5 per cent procaine. Following a lumbar laminectomy, three polyethylene catheters were inserted into the epidural space to the first and eighth thoracic and first sacral levels. Ten cubic centimeters of tetracaine was administered into all three catheters at twenty-minute intervals until there

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was no further sympathetic stimulation or sympathetic depression following repeat doses of the drug. Total body perfusion was controlled by extracorporeal circulation with cardiopulmonary bypass, utilizing a Kay-Cross disc oxygenator. In the procedure the heart and lung circulation was separated from the peripheral circulation. The quantity of blood traversing all or part of the heart and pulmonary circulation was limited to coronary flow and bronchial artery flow. The cannulation procedure for the extracorporeal circulation experiments has been described.[10]

Clinical. Ten patients scheduled for elective pulmonary surgery with no known heart disease were studied in this project. They were lightly premedicated with an opiate and belladonna drug. Anesthesia was induced with thiopental, the patients' tracheas intubated following relaxation with succinylcholine, and anesthesia was maintained with 2 liters nitrous oxide and 2 liters oxygen flows in a semiclosed system. Respirations were controlled with a Jefferson ventilator at a constant rate and volume as determined by a Radford normogram. Relaxation was maintained with a succinylcholine drip until the study was begun. None of the patients in this series had any postoperative recall of the surgical experience. Control levels of arterial blood pressure and pulse were similar to those obtained preoperatively. Blood pressure was recorded from a percutaneous cannulation of the radial artery with a Statham transducer. The electrocardiogram (EKG) and electroencephalogram (EEG) were recorded. The chest and pericardium were opened, and a Walton-Brodie strain gauge arch was sutured directly to the right ventricle in a similar manner as described in the animal studies. Following the establishment of control recordings, halothane administration was begun and continued until no further depth could be achieved without endangering the patient. Recordings were made on either a Grass or Sanborn polyvisagraph.

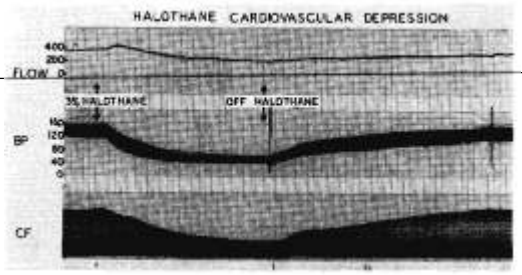

FIG. 1. Typical effects of halothane on aortic blood flow (Flow), arterial blood pressure (BP), and right ventricular contractile force (CF).

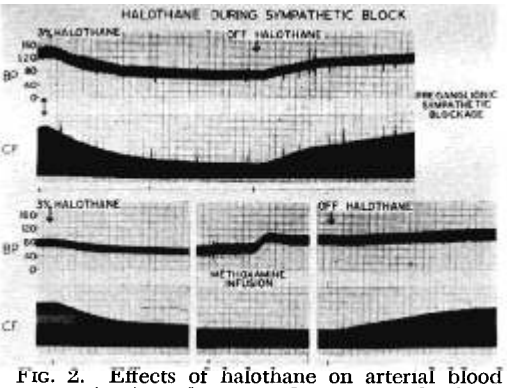

FIG. 2. Effects of halothane on arterial blood pressure (BP) and ventricular contractile force (CF) before and after preganglionic sympathetic blockade. Lower tracing represents the effects of halothane on these parameters following sympathetic blockade. Note that methoxamine infusion only produced an increment in blood pressure.

RESULTS

Animal Studies. The cardiovascular effect of halothane was determined in 8 experiments. Figure 1 is typical of these results. Following the administration of halothane, there is a marked decrease in blood pressure and ventricular contractile force, the average decrease being 59 per cent for blood pressure and 61 per cent for ventricular contractile force. There is a transient increment in aortic blood flow which is attributed to a decrease in peripheral resistance during light anesthesia.

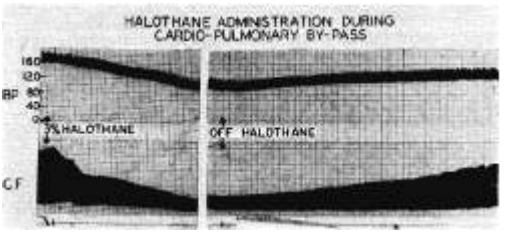

FIG. 3. This experiment, as in figures 1 and 2, illustrates typical effects of halothane on the cardiovascular system in open chest animals.

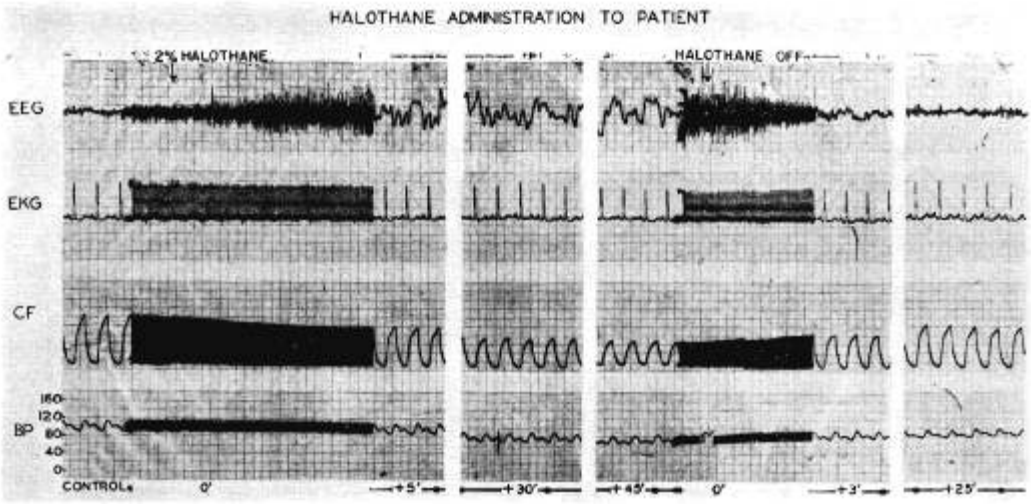

FIG. 4. Halothane administration to a patient monitoring right fronto-occipital electroencephalogram (EEG), electrocardiogram (EKG), ventricular contractile force (CF), and arterial blood pressure (BP).

Progressive hypotension and cardiac depression were accompanied by a 45 per cent decrease in aortic blood flow. This indicates that the decrement in blood pressure (59 per cent) is due primarily to the decreased cardiac output (45 per cent) and to a lesser degree to the decrease in peripheral resistance (25 per cent).

The hypotension produced with halothane anesthesia has been associated with possible ganglionic blocking properties of this agent. Figure 2 illustrates the results of 5 experiments in which halothane was administered prior to and during preganglionic sympathetic blockade. Myocardial contractile force decreased markedly during halothane administration following sympathetic blockade. This indicates a direct myocardial depression by this agent. The fall in blood pressure parallels the reduction in contractile force. Therefore, it appears that the myocardial depression contributes significantly to the occurrence of hypotension. Since increments in blood pressure and therefore coronary perfusion pressure have been shown to increase coronary flow,[11, 12] the vasopressor drug, methoxamine (Vasoxyl), was administered. With the increase in coronary perfusion pressure, there was still no increment in myocardial contraction, which demonstrates the myocardial depression was not a secondary effect of hypotension.

In 5 experiments, halothane was administered during cardiopulmonary bypass. In this group of dogs, anesthesia was induced with thiopental and maintained with a nitrous oxide-oxygen-halothane mixture. During bypass, 3 per cent halothane was administered directly into the disc oxygenator with a 97-3 per cent oxygen-CO_2 mixture through a Fluotec vaporizer. Figure 3 illustrates these results. The effects were similar to those occurring in animals with intact circulation—a marked depression of both contractile force and blood pressure occurred. In several of these experiments, blood pressure was maintained close to control levels during halothane administration by increasing total body perfusion. There was still a marked myocardial depression which again demonstrates the cardiac depression is not secondary to hypotension.

Patient Results. Ventricular contractile force, electroencephalogram, electrocardiogram, and arterial blood pressure changes were recorded during thoracotomy in 8 patients. These results are typified in figure 4. With deep halothane anesthesia, which produced predominantly slow frequency electroencephalographic waves (1 cps-100 mv.), contractile force was depressed approximately 55 per cent of control, and mean arterial blood pressure was reduced by 30–40 mm. of mercury in this series of patients. The electrocardiogram showed a slight but insignificant brady-

cardia (5 per cent). As anesthesia is deepened, contractile force and blood pressure are depressed in a parallel manner. When the agent is discontinued, there is a rapid return to control levels.

Figure 5 represents graded increments in halothane administration as observed in 2 patients. No significant depression of contractile force or blood pressure was noted until the halothane concentration reached 1.2 per cent.

Discussion

The response in the animals with intact innervation and the animals with preganglionic sympathetic blockage were closely similar in rate of development of myocardial depression, total depression, and rate of recovery. These changes indicate that the sympathetic nervous system is not significantly involved in the cardiovascular response to halothane. Administration of methoxamine during deep anesthesia increased peripheral resistance and blood pressure, but decreased cardiac output and had no appreciable effect on ventricular contractile force. Atropine increased heart rate, cardiac output and blood pressure, but blood pressure failed to return to light anesthesia levels. Atropine had little effect on the direct myocardial depressant effects of halothane. The cardiac output following atropine frequently exceeded that obtained at light anesthesia levels. This was largely a reflection of the increase in heart rate.

In all of these studies, depression in contractile force paralleled depression of blood pressure. Bloodwell *et al.*, in a generally similar study, reported occasional instances in which myocardial depression persisted after pressure had returned to control levels. As reported in another study,[13] there is no significant increase in catechol amines with deep halothane anesthesia. Price[13] has suggested a reduced effectiveness of norepinephrine as the sympathetic mediator in the presence of halothane. This would decrease the patient's ability to compensate for depressive effects of this agent on the cardiovascular system.

Studies by Nayler[15] on the isolated cardiac preparation indicate that halothane depressed myocardial contractility, reduced the rate of oxygen utilization, lowered the useful work output, and resulted in a reduced cardiac efficiency. Severinghaus and Cullen[16] noted significant depression in cardiac output and blood pressure with concentrations of 1.5 per cent halothane. Etsten and Li[17] attributed hypotension occurring with less than 2 per cent inspired halothane to peripheral vasodi-

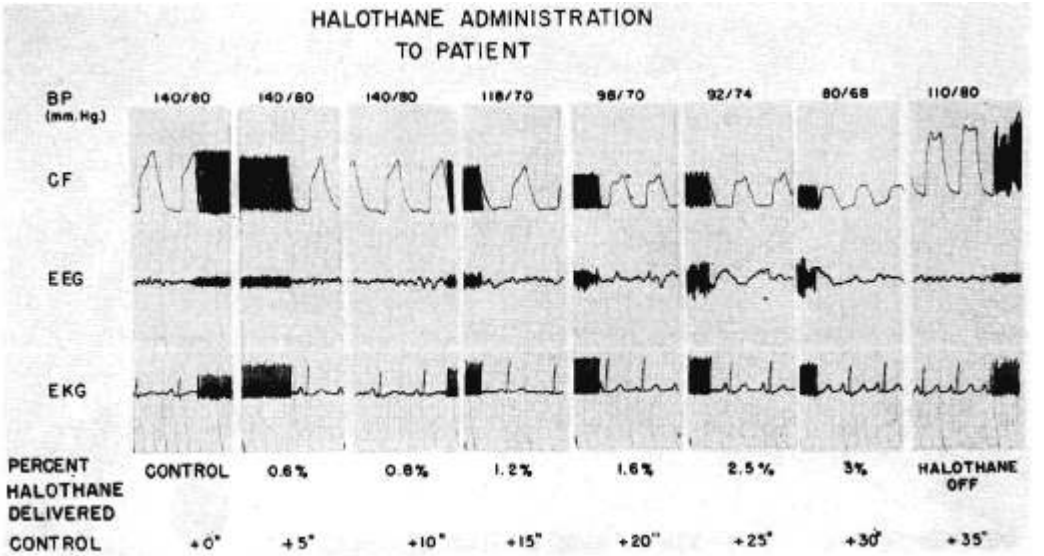

Fig. 5. Graded increments in halothane administration to a patient. Ascultatory blood pressure (BP), ventricular contractile force (CF), electroencephalogram (EEG), and electrocardiogram (EKG) are recorded.

lation and that occurring with a concentration greater than 2 per cent to myocardial depression. Dobkin [18] states that severe hypotension is usually avoided when halothane is administered in concentrations of less than 1 per cent. In this study, depression of contractile force and blood pressure was observed with concentrations of 1.2 per cent halothane. It may be contemplated that if higher concentrations are used for induction, high blood levels may be obtained rapidly with pronounced depression of contractile force and alarming hypotension.

This property of halothane is not unique as all inhalation anesthetics are capable of producing cardiovascular depression.[5, 13, 18] However, the potency of halothane and probable depression of compensatory neurohumoral influences predisposes to cardiovascular depression. Although we cannot conclude that tissue ischemia exists with hypotension, as pointed out by Price,[18] hypotension can undoubtedly cause tissue ischemia, and is usually considered undesirable. In a light plane of halothane anesthesia, accomplished with an inspired concentration of less than 1 per cent, severe cardiovascular depression is unusual, both clinically and experimentally.

Summary

The effects of halothane inhalation on the cardiovascular system were studied in 18 mongrel dogs and 10 patients scheduled for elective pulmonary surgery. Contractile force, blood pressure, and cardiac output were depressed in a parallel degree with increasing depth of anesthesia. The reduction in cardiac output and blood pressure is attributed primarily to the direct depressant effect of halothane on the the myocardium.

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