The Value of Prophylactic Digitalization in Halothane Anesthesia

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THE value of prophylactic preoperative digitalization in man is not easily determined. Assessment of this form of therapy is difficult for many reasons, including the fact that patients rarely have exactly equivalent clinical conditions. Furthermore, the stresses encountered by the cardiovascular system during operations vary with different types of surgical procedures and anesthesia.

One experimental approach to the evaluation of prophylactic preoperative digitalization is the measurement of the influence of digitalization on the negative inotropic response of the dog heart to anesthetic agents. Previous studies have shown that digitalization counteracted barbiturate induced heart failure in the dog heart lung preparation [1] and in the intact dog.[2] We have demonstrated that pretreatment with digoxin protects the dog heart against the negative inotropic effect of large doses of thiopental.[3]

Halothane decreases myocardial contractility in man [4,5] and dogs.[6] The widespread use of this anesthetic agent,[7,8] the increasing employment of prophylactic preoperative digitalization,[9,10] and the demonstration that cardiac glycosides augment the contractile force of the nonfailing human [9] and dog heart,[11] suggested the following experiments in which the effect of prophylactic digitalization upon the heart contractile force response to halothane was measured.

Methods

Each of 9 mongrel dogs, (9 to 15 kg.) was given either 5 or 10 mg. of succinylcholine intravenously to facilitate endotracheal intubation. Anesthesia was then induced and maintained with halothane (0.3 to 1 per cent) and oxygen with intermittent positive pressure controlled respiration. A Heidbrink semiclosed CO_2 absorption system, a Jefferson ventilator, and a Fluotec Mark II halothane vaporizer were used. The oxygen flow was 4 liters per minute. The Fluotec had been calibrated * to assure accurate halothane vaporization. Myocardial contractile force was measured with a Walton-Brodie strain gauge arch [12] sutured to the right ventricle through a right thoracotomy incision. Femoral arterial pressure was measured with a Statham P23D transducer. Lead 2 of the electrocardiogram was recorded.

Halothane was administered in the following sequence: 0.2, 1, 0.2, and 2 per cent both before and one hour after the intravenous injection of digoxin (0.1 mg./kg.) to 6 of the 9 dogs. The changes produced by 0.2 per. cent halothane are expressed in 'Results' as the average effect obtained with two separate administrations of this concentration. Each halothane concentration was given for 15 minutes. Following the first sequence of halothane inhalation, this anesthetic agent was discontinued and only 100 per cent oxygen was administered. Digoxin was injected 12 minutes after halothane was discontinued; the administration of 100 per cent oxygen was continued until the animal regained a state of spontaneous muscular contraction without excitement. The heart contractile force and arterial pressure at this stage (20 minutes after halothane had been discontinued and 8 minutes following the digoxin injection) were used as arbitrary baselines for all measure-

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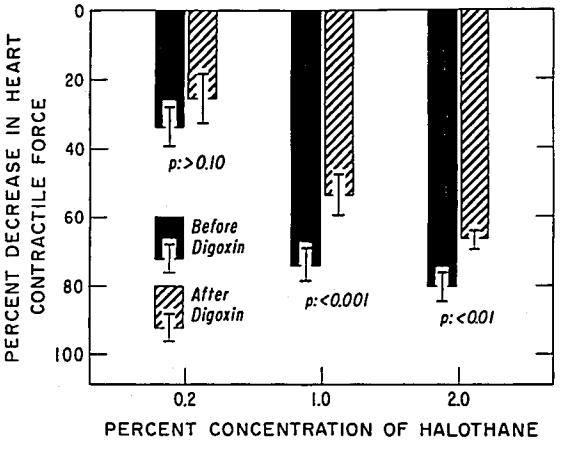

FIG. 1. The effect of halothane on heart contractile force before and after the intravenous administration of digoxin (0.1 mg./kg.). Bar values represent mean changes in 6 dogs. Standard error values are indicated by brackets.

ments. At this time the negative inotropic effect of any residual halothane should have been minimal, and the myocardial contractile force recording was observed to be higher than that of any previous or subsquent time. The succinylcholine injection, used initially for tracheal intubation, and the same concentrations of halothane which had been used for the application of the strain gauge arch and the insertion of the arterial catheter, were then repeated. The second sequence of 0.2, 1, 0.2, and 2 per cent halothane was then administered one hour after the digoxin injection.

With three dogs, the above protocol was followed exactly except that the digoxin injection was omitted. In these dogs, the inotropic and pressor effects of repeated administrations of halothane alone could be studied.

Results

The average decreases in heart contractile force produced by 0.2, 1, and 2 per cent halothane in 6 dogs prior to digitalization were 33, 73, and 80 per cent, respectively. In contrast, after digitalization, these same concentrations of halothane decreased myocardial contractile force 25, 53 and 65 per cent (fig. 1, table 1). The P values for these differences, using the paired-data t test, show that there was significantly less depression of myocardial contractile force produced by 1 and 2 per cent halothane after the administration of digoxin. No protective effect of digitalization was found at 0.2 per cent halothane.

The average decreases in mean arterial pressure produced by 0.2, 1, and 2 per cent halothane in these same dogs before digitalization were 44, 74, and 87 per cent, respectively. After digitalization, identical doses of halothane reduced the mean arterial pressure 43, 63, and 73 per cent below baseline values (fig. 2, table 2). As with the measurements of heart contractile force, these P values indicate a significant protective effect of digitalization at 1 and 2 per cent halothane, but not with 0.2 per cent.

In three dogs in which an identical protocol was followed with the exception of the digoxin administration, the second administration of 1 and 2 per cent halothane produced as much or more depression of heart contractile force and mean arterial pressure as the first halothane administration, thereby eliminating any question of halothane tachyphylaxis (tables 3 and 4).

Halothane decreased the heart rate at each concentration studied before and after the

TABLE 1. Changes in Heart Contractile Force Produced by Halothane Before and After Digoxin

Experiment No.	Baseline	Halothane Concentration											
		0.2 Per Cent				1 Per Cent				2 Per Cent			
		Before Digoxin		After Digoxin		Before Digoxin		After Digoxin		Before Digoxin		After Digoxin	
		Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change
1	25	21	−16	25	0	10	−60	17	−32	5	−80	8.5	−66
2	36	24.5	−32	28.5	−21	8	−78	14	−61	5	−86	10	−72
3	26	20	−23	19.5	−25	6	−77	13	−50	5	−80	11	−58
4	38	22.5	−41	31.5	−17	12	−68	21	−45	9	−76	14	−63
5	30	21.5	−28	20.5	−32	11	−63	15	−50	11	−63	12	−60
6	39	17	−56	18	−54	4	−90	9	−77	3	−92	11	−72
Mean percentage change ± S.E.			−33 ±5.8		−25 ±7.3		−73 ±4.0		−53 ±6.2		−80 ±4.0		−65 ±2.5
t		1.74				7.31				5.27			
P		>0.10				<0.001				<0.01			

All values, including "baseline," refer to pen deflection (mm.) produced by the strain gauge arch.

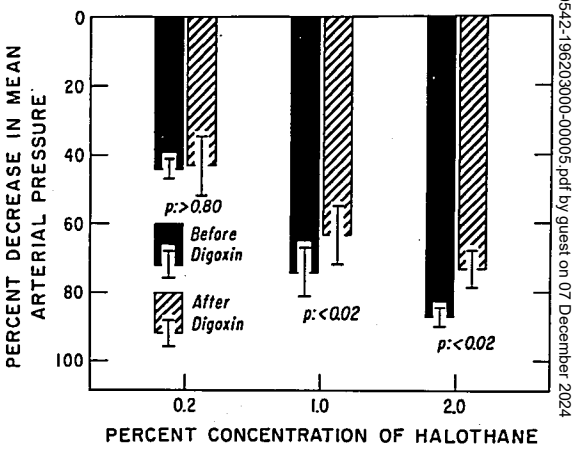

FIG. 2. The effect of halothane on mean arterial pressure before and after the intravenous administration of digoxin (0.1 mg./kg.). Bar values represent mean changes in 6 dogs. Standard errors are indicated by brackets.

TABLE 2. Changes in Mean Arterial Pressure Produced by Halothane Before and After Digoxin

Experiment No.	Baseline	Halothane Concentration											
		0.2 Per Cent				1 Per Cent				2 Per Cent			
		Before Digoxin		After Digoxin		Before Digoxin		After Digoxin		Before Digoxin		After Digoxin	
		Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change
1	149	92	−38	139	−7	80	−46	117	−22	22	−85	73	−51
2	160	72	−55	90	−44	21	−87	39	−76	17	−89	30	−81
3	150	94	−37	54	−64	27	−82	35	−77	16	−89	33	−78
4	139	73	−48	99	−29	55	−60	67	−52	33	−76	52	−63
5	154	92	−40	73	−53	36	−77	52	−66	16	−90	35	−77
6	176	92	−48	69	−61	12	−93	24	−86	9	−95	19	−89
Mean percentage change ± S.E.			−44 ±3.1		−43 ±8.8		−74 ±7.3		−63 ±9.5		−87 ±2.6		−73 ±5.6
t		0.143				3.96				3.43			
P		>0.80				<0.02				<0.02			

All values, including "baseline," refer to mm. of mercury.

administration of digoxin. The rate during 2 per cent halothane inhalation varied from 60–120 (average 93) before digoxin and from 55–100 (average 80) after digoxin. Digitalization itself decreased the heart rate in each dog.

Discussion

Advances in surgery have made it possible for operations to be performed on increasing numbers of poor risk patients. This group of patients requires anesthetic techniques that produce minimal cardiovascular depression. In this regard, the anesthesiologist is handicapped by the decrease in myocardial contractile force produced by most of the commonly used anesthetic agents.[6,14] It has recently been shown that cardiac glycosides produce an increase in contractile force of the nonfailing human heart.[9] This fact has led to the use of prophylactic preoperative digitalization in certain clinics.[9]

The present experiments have examined the effect of prophylactic digitalization upon the contractile force response of the heart to halothane. The experimental design used allowed a single anesthetic agent to be employed, the physical characteristics of which (solubility in 100 parts water = 0.345[12]) permit an effective concentration to be obtained and eliminated quickly. Furthermore, the sequences of halothane inhalation before and after digoxin were identical in both concentration and duration of administration, allowing each of the dogs in experiments 1–6 to act as its own control.

In spite of the use of identical concentrations and durations of halothane administration before and after the digoxin injection, different blood or tissue levels of halothane may have been achieved. If less tissue or blood halothane concentrations were developed during the second halothane inhalation after the digoxin injection, results similar to those which we observed might have been obtained. However, the observation that as much or more of a decrease in contractile force and arterial pressure was produced by the second administration of 1 and 2 per cent halothane in the 3 dogs in which no digoxin

TABLE 3. Changes in Heart Contractile Force Produced by Halothane Without Digoxin

Experiment No.	Baseline	Halothane Concentration											
		0.2 Per Cent				1 Per Cent				2 Per Cent			
		First Administration		Second Administration		First Administration		Second Administration		First Administration		Second Administration	
		Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change
7	34	17	−50	18.5	−46	8	−77	8	−77	6	−82	5	−85
8	33	21.5	−35	15	−55	11	−67	11	−67	9	−73	7	−79
9	31	21.5	−31	19	−39	17	−45	15	−52	12	−61	11	−65
Mean percentage change			−39		−47		−63		−65		−72		−76

This table summarizes the effects of repeated administrations of halothane on heart contractile force in dogs which received no digoxin. All values, including "baseline," refer to pen deflection (mm.) produced by the strain gauge arch.

was given (experiments 7–9), suggests that if any variation in blood or tissue halothane levels occurred, it was one of accumulation.

The findings in the present study demonstrate that the negative inotropic and hypotensive effects of halothane in the dog are lessened by the prior administration of digoxin. Furthermore, this protection occurs at clinically useful halothane concentrations. These observations support the principle of the prophylactic preoperative use of cardiac glycosides.

Summary

The inotropic (strain gauge arch), chronotropic, and pressor effects of 0.2, 1, and 2 per cent halothane have been determined in open chest dogs before and one hour after the intravenous administration of digoxin (0.1 mg./kg.). Pretreatment with digoxin significantly

TABLE 4. Changes in Mean Arterial Pressure Produced by Halothane Without Digoxin

Experiment No.	Baseline	Halothane Concentration											
		0.2 Per Cent				1 Per Cent				2 Per Cent			
		First Administration		Second Administration		First Administration		Second Administration		First Administration		Second Administration	
		Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change	Observed Value	Percentage Change
7	94	53	−44	51	−46	18	−81	18	−81	31	−67	13	−86
8	113	84	−26	72	−36	50	−56	46	−59	23	−80	23	−80
9	94	97	+3	72	−23	69	−27	56	−40	28	−70	28	−70
Mean percentage change			−22		−35		−55		−60		−72		−79

This table summarizes the effects of repeated administrations of halothane on mean arterial pressure in dogs which received no digoxin. All values, including "baseline," refer to mm. of mercury.

diminished the negative inotropic and hypotensive effects of 1 and 2 per cent halothane anesthesia.

The halothane was supplied by Ayerst Laboratories, New York, New York, and the digoxin, by Burroughs Wellcome & Company, Tuckahoe, New York.

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MEASUREMENT Anesthesia is in a state of transition from an empirical art to an exact science; this involves an increasing use of measuring equipment. Automatic pulse detectors and blood pressure followers are now available. Body temperature measurement can be derived by the application of one of two principles. A dry gas meter to which a simple mechanical differentiator has been added will soon be available to give a continuous record of the minute volume of respiration. A versatile method of gas analysis is gas chromatography. Frequent estimates during surgery of the patient's circulating blood volume should become practicable with the safe technique employing radioactive tracers which has recently been developed. (*Woolmer, R.: Measurement in Anaesthesia, Ann. Roy. Coll. Surg. Engl. 29: 226 (Oct.) 1961.*)