THE EFFECT OF DIGOXIN PRETREATMENT ON HEART CONTRACTILE FORCE DURING THIOPENTAL INFUSION IN DOGS

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THE use of prophylactive preoperative digitalization in man has become common in some clinics. This practice assumes that the positive inotropic effect of cardiac glycosides [1, 2, 3] will protect the heart against the stresses of operation and the negative inotropic effect of certain anesthetic agents. Thiopental and other barbiturates have been shown to decrease myocardial contractile force in dogs [4] and cardiac output in man [5, 6] and dogs.[7] These effects limit the usefulness of these drugs as anesthetic agents.[8, 9] However, ouabain increases the cardiac arrest dose of pentobarbital in dogs.[10] Hence, it is important for the anesthesiologist to know if this protective effect of digitalization, shown with lethal doses of pentobarbital, is also present with anesthetic, non-lethal doses of thiopental. This paper compares the effects of thiopental on heart contractile force in control and digitalized dogs.

METHODS

Eighteen mongrel dogs with weights varying between 8.2 and 16.5 kg. were anesthetized with 100 mg./kg. of chloralose intravenously. Positive pressure respiration was maintained with room air by a Starling pump. A Walton-Brodie strain gauge arch was sutured to the right ventricle through a thoracotomy incision.[11] Femoral artery pressure was measured with a Statham P23D transducer. A continuous electrocardiogram was recorded. Thiopental was infused intravenously with a Bowman pump at a rate of 1 mg./kg./minute to 8 control and 10 previously digitalized dogs, in a total volume of less than 15 ml. Digitalization was accomplished with 0.1 mg./kg. of digoxin given intravenously between 1½ and 4½ hours prior to the thiopental infusion. Changes in myocardial contractile force were calculated as percentage changes from the average pre-infusion values.

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RESULTS

In the 8 control dogs the mean percentage changes in right ventricular contractile force produced by 15, 30, 45, and 60 mg./kg. of the thiopental infusion were −9, −33, −50, and −61 per cent, respectively (table 1). In the 10 digitalized dogs, the mean percentage changes produced by identical doses of the thiopental infusion were +3, −18, −27, and −31 per cent, respectively. The differences between the means are statistically significant at 45 and 60 mg./kg. but not at 15 and 30 mg./kg.

Figure 1 illustrates the mean percentage changes in heart contractile force during the thiopental infusions in the control and the digitalized dogs. Note that the curves for both groups are very close for doses below 30 mg./kg. However, at higher doses the

TABLE 1

MEAN PERCENTAGE CHANGES IN HEART CONTRACTILE FORCE PRODUCED BY THIOPENTAL IN CONTROL AND DIGITALIZED GROUPS, AND CORRESPONDING t AND P VALUES

Thiopental mg./kg. (minutes of infusion)	Mean Percentage Changes in Heart Contractile Force		t	P
	Control Group	Digitalized Group		
15	− 9	+ 3	1.121	$0.3 > p > 0.2$
30	−33	−18	1.441	$0.2 > p > 0.1$
45	−50	−27	2.824	$0.02 > p > 0.01$
60	−61	−31	3.585	$0.01 > p > 0.0001$

slopes of the two curves begin to change, and there are significant differences between the two curves at 45 and 60 mg./kg. of thiopental.

In 2 of 8 control dogs and 6 of 10 digitalized dogs, thiopental produced an initial rise in heart contractile force, heart rate, and arterial pressure before the characteristic effects of hypotension and decreased heart contractile force appeared (fig. 2.). These paradoxical effects have been observed by others [12] and are probably the result of catecholamine release.[13, 14]

Figure 2 illustrates the effect of thiopental on heart contractile force and arterial blood pressure in a control and a digitalized dog. Representative strips were removed from the recordings to show the progress of these two experiments at five-minute intervals during the thiopental infusion. The heart contractile force and blood pressure rose at first in both dogs. After twenty minutes (20 mg./kg. of thiopental), the contractile force and arterial pressure of the control dog began to decrease and then fell steadily throughout the rest of the infusion. In contrast, the myocardial contractile force and the arterial pressure decreased less in the digitalized dog.

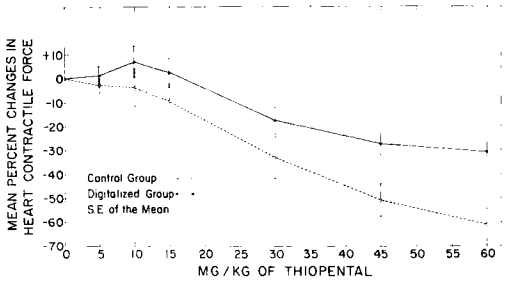

FIG. 1. Mean percentage changes in heart contractile force of the control and the digitalized groups produced by an infusion of 1 mg./kg./minute of thiopental. The abscissa represents minutes of infusion and mg./kg. of thiopental.

DISCUSSION

The value of prophylactic preoperative digitalization in man is uncertain and careful clinical trials are needed to answer this question. One aspect of this broad problem is the possible protection afforded by digitalization against the negative inotropic effect of anesthetic agents. Boniface and Brown showed that ouabain increases the cardiac arrest dose of pentobarbital in dogs.[10] Also, it is known that cardiac glycosides can counteract barbiturate-induced heart failure in the dog heart-lung preparation.[15, 16] These results indicate that prophylactic digitalization might protect the heart against decreases in myocardial contractile force induced by anesthetic doses of thiopental.

The present study demonstrates significant protection by digitalization against the negative inotropic effects of 45 and 60 mg./kg. of thiopental. These doses, which are large enough to decrease the heart contractile force of the control group by at least 50 per cent (table 1), are far greater than those used clinically. At lower doses of thiopental (15 and 30 mg./kg.), where the contractile force

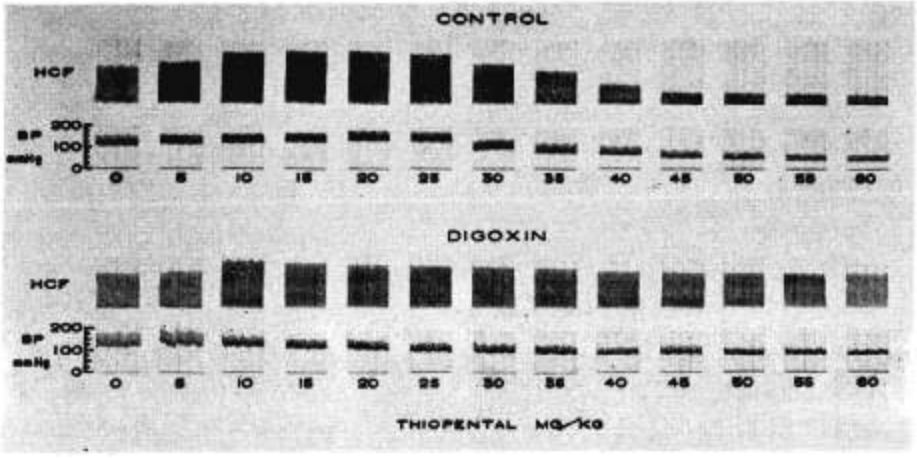

FIG. 2. The effects of an infusion of 1 mg./kg./minute of thiopental on heart contractile force and arterial blood pressure in a control dog and a digitalized dog.

values of the control group were reduced by approximately 10 and 33 per cent, digoxin did not exert a statistically significant protective effect.

The initial positive inotropic effect seen during the thiopental infusion in 6 digitalized and 2 control dogs is probably due to catecholamine release.[13, 14] This release, with its resultant positive inotropic effect, may be a significant factor in the protection seen in the digitalized dogs, even though the chi-square test does not show a clear-cut association between digitalization and effects suggestive of catecholamine release ($P > 0.10$).

Hence, the present study has established that digitalization of dogs protects against the negative inotropic effects of doses of thiopental that reduce the contractile force of the heart by at least 50 per cent, but the importance of catecholamine release in this phenomenon remains uncertain.

Summary

The effects on myocardial contractile force produced by an infusion of 1 mg./kg./minute of thiopental were observed with a strain gauge arch in 8 control and 10 digitalized dogs. The results indicate that digitalization protects against the negative inotropic effects of doses of thiopental that are large enough to reduce the contractile force by at least 50 per cent (45 and 60 mg./kg.). This protective effect was not observed with smaller doses of thiopental (15 and 30 mg./kg.).

Initial pressor, positive inotropic, and positive chronotropic effects were seen following the start of the thiopental infusion in 2 control dogs and 6 digitalized dogs. These effects, which are probably produced by catecholamine release, may contribute to the protection against thiopental seen in the digitalized dogs.

The thiopental (Pentothal) was supplied by Abbott Laboratories, North Chicago, Illinois; the digoxin (Lanoxin) by Burroughs Wellcome & Co., Tuckahoe, New York. A preliminary account of this work was presented at the Annual Meeting of the American Federation for Experimental Biology, Atlantic City, New Jersey, April 11, 1961: Fed. Proc. 20: 123, 1961.

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