

A COMPARATIVE STUDY OF ANTIARRHYTHMIC OF PROPRANOLOL ("INDERAL") AND LIDOCAINE ON THE HEART

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INTRODUCTION

The effect of propranolol as beta-adrenergic blocking agent on the arrhythmias has been known previously (Lucchesi, Whitsitt & Stickney, 1967).

Clinical experiences have indicated the effectiveness of this drug in the treatment of cardiac arrhythmias in man (Krosnow & Barbarosh, 1968). Recent studies have indicated that the antiarrhythmic action of beta-adrenergic blocking agents (propranolol) may be related to local anesthetic or quinidine-like beside as beta-receptor inhibition (Lucchesi, Whitsitt & Stickney, 1967; Florez, Pomar & Malpartida, 1969). Lidocaine as a local anesthetic inhibits the synthesis of citrate and depresses cellular respiration. In small amounts in the blood it depresses cardiac function. During the final depressant phase there is paralysis of the muscle (Grollman, 1960).

The present study was undertaken to compare qualitatively the effects of propranolol (Inderal) as beta-blocking agent or as a local anesthetic and lidocaine as local anesthetic on arrhythmias of the heart of experimental animals induced by drugs or ligation of the anterior descending coronary artery.

MATERIALS AND METHODS

Eighteen frogs (*Bufo vulgaris*) of either sex weighing from 0,2 - 0,3 kg were prepared according to the method described by Harris (1951) for recording the heart beat.

Six cats of either sex weighing from 1.4 - 2.0 kg

were anesthetized with ether-chloralose. Doses of chloralose were 50 mg - 90 mg/kg and was given intravenously. A common carotid artery was exposed and catheterized for blood pressure and frequency recording. Arterial pressure was continuously monitored with a mercury manometer on a chart mover. An indwelling catheter in the cubital vein was used for drug injection. Ventilation was maintained with a Palmer Respirator. Paper speed was maintained at speed no. 4 of "Super 10 Recording Drum" INCO.

CATECHOLAMIN INDUCED ARRHYTHMIAS IN CATS

Doses of 100 μ g/kg of adrenalin injected intravenously at regular interval of 1 minute arrhythmias were induced. When the arrhythmia persisted for at least 5 minutes propranolol was injected at a rate of 0.4 mg/kg/min. until the sinus rhythm was restored. For one cat lidocaine solution of 4 mg/kg/min. was given during arrhythmia.

CORONARY ARTERY LIGATION IN CATS

A lateral thoracotomy was performed through the fourth or the fifth left intercostal space, ventilation being maintained by a Palmer respirator. The pericardium was excised and the anterior descending coronary was isolated, then ligation of this artery was performed. We waited until arrhythmia was produced. When the arrhythmia persisted at least for 5 minutes, propranolol at a rate of 0.4 mg/kg or lidocaine at rate of 4 mg/kg was injected until the sinus rhythm was restored.

CATECHOLAMIN INDUCED ARRHYTHMIAS IN FROGS

Adrenalin solution of 100 μ g was dropped on the frog's heart until arrhythmia was induced. When the arrhythmia persisted for at least 2 minutes the propranolol or lidocaine was dropped on the heart until arrhythmia was restored. In some frogs the drugs were given into the sinus venosus.

VENTRICULAR LIGATION IN FROGS

A ligation was performed on a part of the ventricular muscle. We waited until arrhythmia was induced. When

When the arrhythmia persisted at least for 1 minute, propranolol at a rate of 0.4 mg/cc or lidocaine at a rate of 4 mg/cc was dropped on the heart or injected into the sinus venosus until the sinus rhythm was restored.

R E S U L T S

EFFECT OF PROPRANOLOL OR LIDOCAINE UPON CATECHOLAMIN-INDUCED ARRHYTHMIAS IN CATS

The intravenous administration of catecholamin 100 μ g/kg resulted in a sustained arrhythmia in each of five cats. The administration of propranolol intravenously at a rate of 0.4 mg/kg restored normal rhythm in two of the catecholamin induced animals. The dose required to produce an initial restoration of normal sinus rhythm ranged from 2 mg/kg - 4 mg/kg. The maintenance of normal sinus rhythm had not been performed yet. The administration of 4 mg/kg killed the cat 30 minutes after propranolol administration. In one cat the administration of lidocaine intravenously had about the same effect as propranolol upon catecholamin-induced arrhythmia (Fig. 1). The cumulative doses of 30 mg/kg killed the cat about 25 minutes after administration of lidocaine.

EFFECTS OF PROPRANOLOL OR LIDOCAINE UPON ARRHYTHMIAS FOLLOWING CORONARY ARTERY LIGATION IN CATS

Spontaneous arrhythmia present in three out of four cats following ligation of the descending coronary artery 4-10 minutes after ligation. The disturbances in arrhythmias consisted of extrasystoles and irregularities in the strength of contraction. Intravenous administration of propranolol at a rate of 0.4 mg/kg/min. restored normal sinus rhythm at least 15 minutes after injection of 6 mg propranolol/kg/15 min. (in two cats). The effect of lidocaine upon arrhythmias was about the same as the effect of propranolol (in one cat) (fig. 1)

The results were summarized in TABLE 1.

EFFECT OF PROPRANOLOL OR LIDOCAINE UPON CATECHOLAMIN INDUCED ARRHYTHMIAS IN FROGS

Drops of catecholamin 100 μ g/cc resulted in a sustained tachycardia in six of nine frogs. Drops of

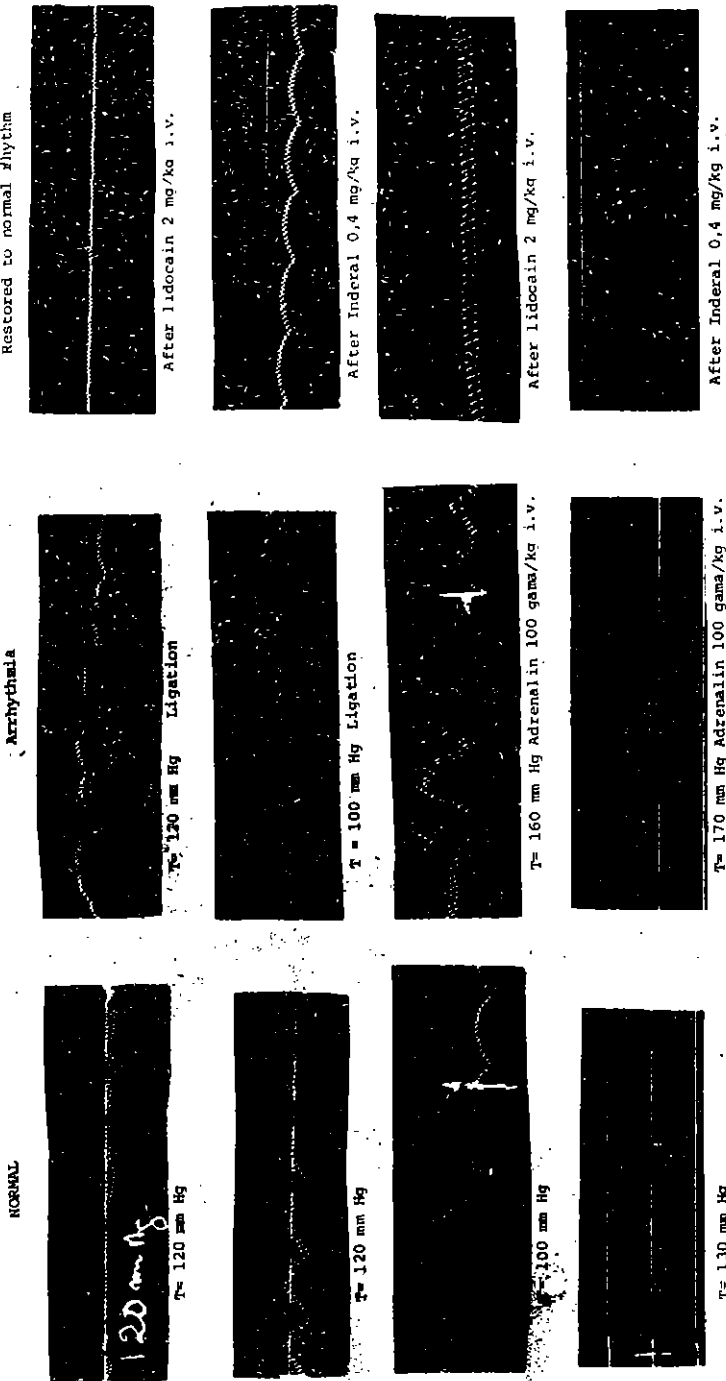


Fig. 1 The effects of propranolol and lidocaine upon arrhythmia induced by catecholamin and ligation on the anterior descending coronary artery in cats.

propranolol at a rate of 0.4 mg/cc restored normal sinus rhythm in two frogs 1 minute after dropping. Drops of lidocaine at a rate of 2 mg/cc restored normal sinus rhythm in four frogs two minutes after administration (Fig. 2). In all frogs the dropping of propranolol or lidocaine ended in stopping the heart beat shorter than the control animals.

Fig. 2

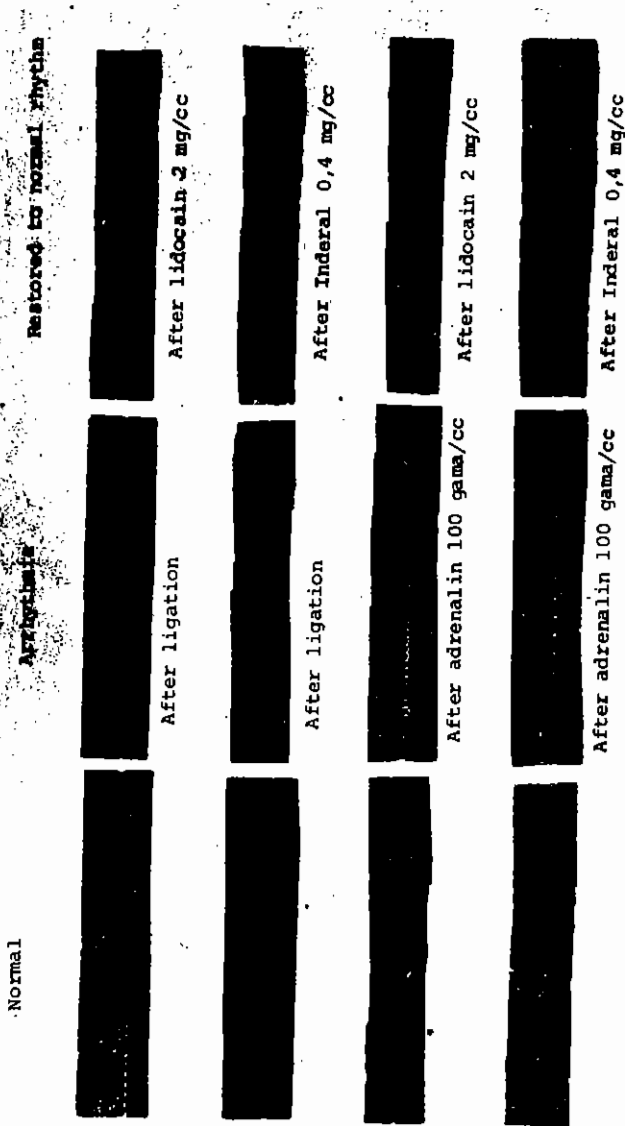


Fig. 2 : The effects of propranolol and lidocaine upon arrhythmia induced by catecholamin and ligation on a part of ventricular muscle in frogs.

TABLE 1. Effects of propranolol and lidocaine upon arrhythmia induced by catecholamin and ligation on the anterior descending coronary artery in cats.

Exp. No.	Adminis- tration of 100 gama of Catecho- lamin	Ligation on Anteri- or Descen- ding Coro- nary Ar- tery	Arrhythmias Induced by		Administra- tion of		Restora- tion to Normal Sinus Rhythm
			Cate- chola- min	'Liga- tion	0.4 mg /kg/ min.of Propra- nolol	2 mg/ kg/ min. of Li- doca- ine	
1	1		+		1		+ 1
1	1		+			1	+ 1
1		1		+		1	+ 1
3		3		(+2) (-1)	2		+ 2

EFFECT OF PROPRANOLOL OR LIDOCAINE UPON ARRHYTHMIAS FOLLOWING PARTIAL VENTRICULAR LIGATION OF THE FROG'S HEART

Spontaneous arrhythmias were present in five out of nine frogs one minute after ligation of the ventricular muscle. The disturbances in arrhythmias consisted of extrasystoles, ventricular tachycardia and irregularity in the strength of contraction. Drops of propranolol resto; red these arrhythmias into normal sinus rhythm in three frogs.

Also administration of lidocaine had almost the same effect as the effect of administration of propranolol (in 2 frogs). (Fig. 2).

Both propranolol and lidocaine killed the frogs faster than control frogs.

The results were summarized in TABLE 2.

TABLE 2. Effects of propranolol and lidocaine upon arrhythmia induced by catecholamin and ligation of a part of the ventricular muscle in frogs.

Exp. No.	Adminis- tration of 100 gama of Catecho lamin	Ligation of a part of Ventri- cular mus- cle	Arrhythmias Induced by		Administra- tion of		Resto- ration to Normal Sinus Rhythm
			Cate- chola- min	Liga- tion	0.4mg/ cc of Propra nolol	2 mg/ cc of Lidoca ine	
3	3		(+ 2) (- 1)		2		+ 2
6	6		(+ 4) (- 2)			4	+ 4
5		5		(+ 3) (- 2)	3		+ 3
4		4		(+ 2) (- 2)		2	+ 2

DISCUSSION

In the present studies arrhythmias could be induced either by catecholamin or ligation of an anterior descending coronary artery in cats and a ligation of a part of the cardiac muscle in frogs. Lucchesi, Whitsitt and Stickney (1967) induced arrhythmias by ouabain or ligation of anterior descending coronary artery in dogs.

The results not only demonstrated the ability of a beta-adrenergic receptor blocking agent to prevent the arrhythmogenic activity of the catecholamin upon the myocardium through beta-adrenergic receptor blockade, but also showed the nonspecific effect of propranolol and lidocaine upon the arrhythmias of the heart induced by ligation.

Furthermore the deleterious effect of these drugs was observed, and we still need further experiments to obtain complete data to judge which of these drugs is less dangerous to the heart.

Our interest in propranolol arose because it exerts

antiarrhythmic action (Lucchesi, Whitsitt & Stickney, 1967; Florez, Pomar & Malpartida, 1969; Davis & Tente, 1968; Whitsitt & Lucchesi, 1967) and is dangerous for the patients in whom augmented sympathetic drive is necessary for the maintenance of adequate cardiac contractility and rate (Lund-Larsen & Sivertssen, 1969). Although propranolol has been successfully used in a number of cardiac disorders, because of its tendency to produce slowing of the heart rate, impairment of myocardial contractile force (the same as our results) and blockade of the bronchial beta-receptor, great caution must be exercised when treating the patient with pronounced bradycardia, incipient cardiac failure, or bronchial asthma (Gordon & Jorgensen, 1970).

The results in this preliminary study convince us that the effect of both drugs could improve arrhythmias, but dangerous for the patient.

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SUMMARY

1. A qualitative comparison has been made of the effects of beta-adrenergic blocking agent (propranolol) and lidocaine on arrhythmias of the frogs and anesthetic cats induced by catecholamin or ligation of a part of cardiac muscle of the frogs or ligation of the anterior descending coronary artery of the cats.
2. Both propranolol and lidocaine have about the same effect upon arrhythmias.
3. The administration of propranolol 2 mg - 4 mg/kg killed the cat about 30 minutes after administration of the drug. The cumulative doses of lidocaine 30 mg/ kg killed the cat at about 25 minutes post-injection. Drops of both propranolol 0.4 mg/cc or lidocaine 2 mg/cc also stopped the heart beat of the frog shorter than the normal control animal.
4. It is concluded in this preliminary report that the

effect of propranolol or lidocaine upon arrhythmias or the deleterious effect of these drugs on the heart are about the same. But it still needs further experiments to obtain complete data to judge which of these drugs is the best for improving arrhythmias or is less dangerous to the heart.

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