normal conditions are not involved in the regulation of coronary vascular tone. Other investigators have reached the same conclusion [10, 12]. However, it is possible that conditions in vitro are not sufficiently adequate for the study of the effect of PG on coronary vascular tone.

The results of this investigation showed that only if indomethacin is injected in vivo is an intensification of noradrenalin-induced injury observed, although PG biosynthesis is inhibited by administration of indomethacin both in vivo and in vitro. Inhibition of PG biosynthesis evidently affects certain processes of regulation of cardiac metabolism at the whole body level. Indications have recently appeared that PG regulate synaptic neurotransmission and may affect processes of secretion and uptake of catecholamines by the heart [1, 3, 4]. Disturbance of one of these processes probably leads in this case to an increase in the sensitivity of the heart to noradrenalin injury in vitro.

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EFFECT OF LITHIUM PREPARATIONS ON CARDIAC ARRHYTHMIAS DUE TO STROPHANTHIN*

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The efficacy of lithium preparations in psychiatric practice is linked with the ability of lithium to inhibit activity of the central adrenergic apparatus [2, 3, 6, 13, 14]. Autonomic imbalance, in the genesis of which an important role is played by activation of the sympathetic nervous system, can lead as we know to disturbances of cardiac rhythm [5]. One example of disturbances of this sort is the arrhythmias induced by administration of large doses of cardiac glycosides. According to observations made by various workers, the genesis

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TABLE 1. Effects of Lithium Hydroxybutyrate on Strophanthin-Induced Arrhythmias in Animals with Divided Carotid-Sinus, Aortic, and Vagus Nerves

Expt. No.	Initial values		Strophanthin						Lithium hydroxybutyrate					
	BP, mm Hg	HR, beats/min	dose, μg/kg	time of start of admin., min	BP, mm Hg	HR, beats/min	character of change in rhythm	SA, % of initial level	dose, μg/kg	time of start of admin., min	BP, mm Hg	HR, beats/min	character of change in rhythm	SA, % of initial level
1	170/130	185	109	2	160/120	218	VES	+10	400	35 sec	70/40	196	CIVR, AVD	—57
				3	105/75	220	IVR	+4		4 min	70/40	182	IVR, AVD	—53
							AVD		400	2 min	120/65	128	SR	—93
2	180/140	186	95	1	140/105	230	VES	+17	400	30 sec	→0	350	VF	+70
			110	1,5	140/105	250	CVT	—7		5 min	120/65	180	IVR, AVD	—64
							AVD			8 min	120/65	176	SR	—64
3	140/80	213	62	1	140/90	218	IVR, AVD	+20	400	30 sec	65/35	188	SR	—40
4	110/70	160	96	1	170/120	172	IVR, AVD	+33	400	1 min	120/60	160	SR	—33

Legend. VES) Ventricular extrasystoles, IVR) idioventricular rhythm, AVD) atrioventricular dissociation, CVT) chaotic ventricular tachycardia, CIVR) chaotic idioventricular rhythm, SR) sinus rhythm, VF) ventricular fibrillation.

of these arrhythmias is based on central sympathetic hyperactivity, one manifestation of which is increased activity of the cardiac sympathetic nerves [4, 5, 8, 10].

The object of this investigation was to study the effects of lithium on arrhythmias due to strophanthin.

EXPERIMENTAL METHOD

Experiments were carried out on 15 cats weighing 2.0-3.3 kg anesthetized with chloralose (30 mg/kg) and urethane (500 mg/kg) intravenously.

The animals were divided into three groups. Group 1 consisted of five intact cats. The vagus nerves of the animals of group 2 (six cats) were divided in the neck (together with the cervical sympathetic and aortic nerves) 30-60 min before administration of strophanthin. Preliminary division of the carotid-sinus, aortic, and vagus nerves was performed on the animals of group 3 (four cats). To prevent any sharp increase in sympathetic activity (SA), which could lead to the onset of arrhythmias, each successive division was carried out after a sufficiently long interval for SA and the arterial blood pressure (BP) to become stabilized. Completeness of denervation of the carotid sinus zones was verified by the absence of any significant increase in BP in response to bilateral compression of the common carotid arteries.

The right inferior cardiac nerve was exposed close to the stellate ganglion, after preliminary removal of the first two ribs without disturbing the integrity of the pleura, and, without dividing the nerve, it was placed on bipolar platinum electrodes. To prevent displacements of the nerve relative to the electrode that could arise as a result of respiration, pneumothorax was induced distally to the 4th rib. Drying of the nerve was prevented with warm mineral oil. The animals were immobilized with succinyl choline (150 μg/kg injected intravenously during 1 min) and artificially ventilated. The respiratory volume was established in accordance with body weight by means of nomograms [7]. The rectal temperature was maintained at 36-38°C. BP was recorded by an electromanometer through a polyethylene catheter introduced into the femoral artery. Potentials of the sympathetic nerves, their mean intensity, BP, and the ECG in standard II and thoracic leads were recorded on an RM-86 polygraph (Nihon Kohden, Japan).

Cardiac arrhythmias were induced by intravenous injection of a 0.005% solution of strophanthin K. Strophanthin was injected in different doses (from 7 to 36 μg/kg per injection) at different intervals (3-10 min), depending on the state of the cardiac activity, starting with a dose of 33-77 μg/kg. The dose causing stable ventricular disturbances of rhythm was taken to be the arrhythmogenic dose. Lithium chloride (200 mg/kg) and lithium hydroxybutyrate (150, 200, or 400 mg/kg) were injected intravenously as 10% solutions.

EXPERIMENTAL RESULTS

After receiving strophanthin the animals of all three groups developed ventricular extrasystoles, which subsequently changed into an idioventricular rhythm or ventricular tachycardia, against the background of atrioventricular dissociation (AVD). Later an infrequent idioventricular rhythm or chaotic ventricular tachycardia and ventricular fibrillation developed.

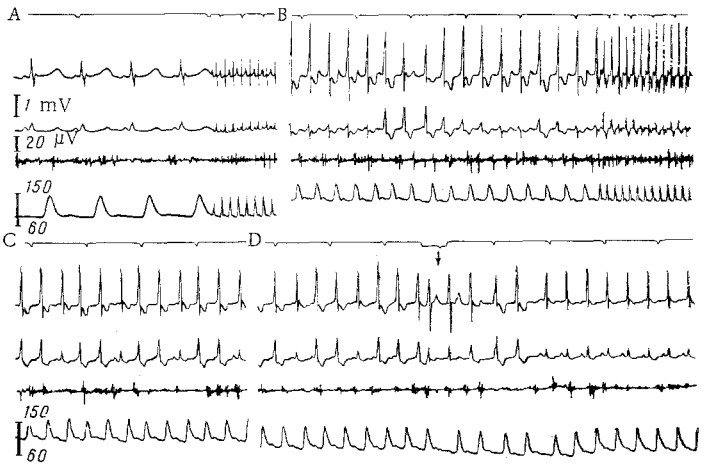

Fig. 1. Antiarrhythmic effect of lithium hydroxybutyrate on vagotomized cat with denervated baroreceptor zones. A) Before administration of strophanthin; B) after strophanthin (96 μg/kg); C) 20 sec after beginning of administration of lithium hydroxybutyrate (400 mg/kg); D) 30 sec after beginning of administration of lithium hydroxybutyrate (end of administration indicated by arrow). Traces denote, from top to bottom: time marker (1 sec), ECG in thoracic lead and lead II, SA, and BP (mm Hg).

In the animals of group 1 SA diminished in the course of strophanthin administration, in four cases gradually. In one experiment, before the beginning of ventricular extrasystoles a decrease was observed in SA, followed by a small increase during the transition to an idioventricular rhythm. The heart rate (HR) fell gradually without any correlation with the values of BP. By the time of onset of the idioventricular rhythm SA in all animals of this group was lower than initially. Arrhythmogenic doses of strophanthin in this group amounted to 90-120 μg/kg. SA of all the cats fell sharply after injection of lithium chloride. The maximum fall in activity was recorded 1 min after the beginning of injection of the compound, and it was accompanied by a marked decrease in BP and HR (except in one case, in which HR was almost doubled). The antiarrhythmic effect of lithium was not manifested in this series of experiments.

The arrhythmogenic doses of strophanthin in the animals of group 2 varied from 38 to 84 μg/kg. A gradual decrease in SA was observed in four cases. In one experiment SA rose initially, but 1 min after the onset of an idioventricular rhythm it fell below its initial level, and in one case it rose only during the period of transition from ventricular extrasystoles to an idioventricular rhythm. No significant changes in HR and BP took place. By the beginning of administration of the lithium compounds SA was thus depressed below its initial level in five cats and elevated in one. After administration of lithium chloride or hydroxybutyrate to all animals a marked decrease in SA was observed (in two experiments after a short increase). No general tendency was observed for the decrease in HR and BP. The sinus rhythm was restored in one case, when lithium chloride was injected against the background of ventricular extrasystoles of trigeminal type.

In the animals of group 3 the arrhythmogenic doses of strophanthin were 62-102 μg kg. In the course of its administration a gradual increase in SA and HR was observed until the development of ventricular extrasystoles or an idioventricular rhythm (Table 1). In experiments Nos. 1 and 2, by the time of development of an idioventricular rhythm or of chaotic ventricular tachycardia, some decrease in activity took place (below the initial level in experiment No. 2). No stable and significant changes in BP, correlating with the changes in SA, were observed. By the beginning of administration of lithium hydroxybutyrate, SA was significantly higher than initially in three cats and a little depressed in one. After administration of the compound all animals showed a marked decrease in SA with the appearance of a sinus rhythm. In two experiments the sinus rhythm was restored by the end of the first minute of administration of lithium hydroxybutyrate (Fig. 1); at the same time both HR and BP fell. In another two animals, evidently because of the further development of glycoside poisoning, a chaotic idioventricular rhythm or ventricular fibrillation developed (in experiments Nos. 1 and 2, respectively). BP fell sharply in both cats. The sinus rhythm was restored 6-8 min after the beginning of administration of lithium hydroxybutyrate (in experiment No. 1 the compound was given twice). BP by this time had risen, although it did not reach its initial level.

As the results show, in the animals of the first two groups ventricular arrhythmias after administration of strophanthin developed in conjunction with depression of SA. This is in agreement with data showing the ability of glycosides to increase the sensitivity of baroreceptors of the carotid sinus reflexogenic zones and to induce a vagotonic effect [5, 9, 12]. The latter is evidently not a significant factor in the genesis of strophanthin arrhythmias, for similar disturbances of rhythm also arose in animals with divided vagus nerves. It can be tentatively suggested that an important role in the genesis of the arrhythmias was played by the effect of strophanthin directly on the heart. The data described above disagree to some extent with the results of experiments [4, 5, 9] in which ouabain, in doses inducing ventricular arrhythmias, increased SA. The disagreements noted above may perhaps be connected with the use of different forms of cardiac glycosides. In the animals of group 3 administration of strophanthin caused an increase in SA and quickening of the cardiac rhythm. It can be concluded from these particular features that the arrhythmias in the animals of this group were attributable mainly to intensification of SA.

Lithium had no significant effect on arrhythmias in the cats of the first two groups, although it reduced SA in the cardiac nerves. In the animals of group 3 it had an antiarrhythmic effect, simultaneously depressing activity in the cardiac nerves. According to the results of other investigations, lithium preparations either shortened the duration of ventricular arrhythmias caused by strophanthin [11] or abolished them [1]. The results suggest that an important role in the mechanisms of the antiarrhythmic action of lithium is played by its depressant effect on the adrenergic system and, in particular, on the extracardiac apparatus. This action of lithium compounds (and, in particular, of lithium hydroxybutyrate) may be of very great importance in clinical practice for the treatment of arrhythmias associated with increased tone of the sympathetic nervous system.

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