ROLE OF 5-HYDROXYTRYPTAMINE IN ATRIAL ARRHYTHMIAS—AN EXPERIMENTAL STUDY IN DOGS

By

B.R. MADAN, N.K. KHANNA, J.L. GODHWANI AND V.K. PENDSE

Department of Pharmacology, S.P. Medical College, Bikaner

5-HT level in the atrium and the ventricle is increased during ventricular ectopic tachycardia following 2-stage ligation of the anterior descending branch of the left coronary artery (12). This work has been further extended to determine the changes in 5-HT content of the heart during the occurrence of experimental atrial arrhythmias and consequent to their termination by quinidine.

MATERIALS AND METHODS

36 healthy mongrel dogs of either sex weighing between 9.5 *kg* and 18.5 *kg* were anaesthetized with pentobarbital sodium (30 *mg/kg* i.v.). Artificial respiration was instituted and chest was opened to expose the heart. Animals were divided into six groups for carrying out the following procedures :

Group I—Controls. The dogs were not subjected to any procedure.

Group II—Quinidine sulphate was administered in doses of 10 *mg/kg* i.v.

Group III—Atrial arrhythmia was produced by topical application of 0.05 per cent aconitine nitrate to the sino-atrial node (11,17).

Group IV—After the aconitine-induced arrhythmia had lasted for 10 minutes, quinidine sulphate, 10 *mg/kg* i.v. was administered. This produced reversion to normal sinus rhythm.

Group V—Long-lasting atrial flutter was produced by crushing a portion of the right atrium followed by electrical stimulation according to the method of Rosenblueth and Garcia Ramos (16) which has been described in detail in a previous communication (1).

Group VI—After the flutter had been established, quinidine sulphate, 10 *mg/kg* i.v., was administered which resulted in the abrupt restoration of normal sinus rhythm.

After the completion of each procedure, the left atrium and a portion of the apex of the ventricle were excised for extraction of 5-HT with acetone according to the method of Barlet (2). The 5-HT content of the extract was determined by using the rat fundus preparation of Vane (19).

RESULTS

The mean control 5-HT content in the atrium and the ventricle was 2.9 *ng/gm* and 2.8 *ng/gm* respectively. It was reduced significantly following the administration of quindine sulphate, 10 *mg/kg* i.v. During the occurrence of aconitine-induced atrial arrhythmia and injury-stimulation-induced atrial flutter, there was a statistically significant increase in the 5-HT content of the atrium and the ventricle. The elevated 5-HT level registered a fall either below the normal level or to a level slightly higher than the control values when the arrhythmias were terminated by quinidine sulphate. The results are summarized in Table I.

TABLE I

5-HT content of the dog's myocardium (ng/gm of fresh tissue)

Group	Procedure	No. of animals	Atrium			Ventricle		
			Mean	*±S.E.*	*P* value*	*Mean*	*±S.E.*	*P* value*
I	Control	8	2.9	±0.7	..	2.8	±0.6	..
II	Quinidine treated dogs	5	0.4	±0.1	<0.001	0.6	±0.1	<0.02
III	Aconitine-induced atrial arrhythmia	8	8.0	±0.8	<0.01	14.6	±1.4	<0.001
IV	Reversion of aconitine induced atrial arrhythmia by quinidine	5	0.6	±0.6	<0.001	1.0	±1.0	<0.001
V	Injury-cum-electrical stimulation induced atrial flutter	5	26.1	±6.6	<0.02	29.7	±3.3	<0.001
VI	Reversion of atrial flutter by quinidine	5	4.8	±2.4	<0.02	4.3	±1.5	<0.001

* 'P' value of group II, III and V was compared with group I ; that of group IV with group III; that of VI with group V.

DISCUSSION

When the present observations are considered together with the findings obtained in the previous study (12), it is inferred that 5-HT content of all portions of the heart is increased during the occurrence of both atrial and ventricular arrhythmias; and it is decreased following treatment with quinidine. Although the exact manner in which 5-HT is involved in the production of cardiac arrhythmias and in the antiarrhythmic action of quinidine cannot be defined clearly in the present state of our knowledge, the work done by other investigators provides an indirect and circumstantial evidence regarding its role in arrhythmias.

5-HT is known to exert stimulatory effect on the heart (10). Since this cardiac action is abolished by previous reserpinization (8) and by beta-adrenergic blocking agents(7), it was hypothesised that the excitatory effects of 5-HT on the heart are mediated through adrenergic mechanism (9). In support of this, it was observed that intravenous administration of 5-HT increased the noradrenaline content (biological determinations) of the coronary venous effluent (6). Noradrenaline has often been implicated in the initiation and perpetuation of disturbances of the rate and rhythm of the heart (5, 13, 18). Evidence is thus adduced to show that the arrhythmogenic action of 5-HT may be exerted by the liberation of catecholamines.

Another explanation for the role of 5-HT in arrhythmias may be found in its electrophysiological properties. 5-HT has a depolarizing action on the cell membrane (20) and it is known that depolarization is accompanied by increased entry of calcium in the cell (3). Augmentation of the lipid-facilitated transport of calcium across the cardiac cell membrane favours the production of cardiac arrhythmias (14, 15). It may thus be possible that 5-HT favours the production of arrhythmias by stimulating the calcium transport activity.

Since the elevated level of 5-HT in the heart falls to nearly normal values when the arrhythmias are reverted to normal sinus rhythm, it appears that the antiarrhythmic action of quinidine is exerted by causing a decrease in the 5-HT content of the heart. No attempt has been made in this work to elucidate the mechanism by which such a decrease occurs. It may be attributed to reduced synthesis or augmented degradation of 5-HT by enzymes which are normally present in the heart (4).

SUMMARY

5-HT content of the dog's atrium and ventricle has been estimated during the occurrence of aconitine-induced atrial arrhythmia and atrial flutter produced by injury-stimulation procedure. Results indicate that 5-HT content of the heart increases significantly during atrial arrhythmias and falls to nearly normal values when the sinus rhythm is restored by quinidine. In the light of observations made previously, it is suggested that : (*i*) 5-HT favours the production of cardiac arrhythmias through adrenergic mechanisms and/or by stimulating calcium transport activity; and (*ii*) antiarrhythmic action of quinidine may be exerted by reducing the 5-HT content of the heart.

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