Antiarrhythmic Effects of Allapinin in Neurogenic Atrial Fibrillation

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Antiarrhythmic effect of allapinin under conditions of neurogenic atrial fibrillation includes a vagolytic effect, which consists in inhibition of the synchronizing and tonic components of the vagal chronotropic influence.

Key Words: *vagus nerve*; *neurogenic atrial fibrillation*; *allapinin*; *antiarrhythmic effect*; *vagolytic effect*

The antiarrhythmic drugs allapinin (AP, lappaconitine hydrobromide [5]) exhibits a pronounced antiarrhythmic effect in the aconitine- and barium chloride-induced arrhythmias, as well as in arrhythmia evoked by frequent stimulation of the myocardial atria and ventricles [3,8,9].

Although AP has been used in cardiology practice for a long time [1,7,8], interpretation of its pharmacological effects so far is still in controversy. According to conventional classification [11], AP belongs to the class I of antiarrhythmic drugs [5,6]. More detailed characterization of this drug within the class is complicated.

In view of this, the aim of this work was to study the antiarrhythmic effect of AP in neurogenic atrial fibrillation (NAF).

MATERIALS AND METHODS

Experiments were performed on 9 cats weighing 2.5-4.5 kg narcotized with intraperitoneal Chloralose and Nembutal (75 and 15 mg/kg) and artificially ventilated; the body temperature was maintained at 37°C. Methods of modeling and analysis of NAF were described previously [2,10]. AP was injected intravenously in a dose of 0.5 mg/kg.

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The results were statistically analysed by Student's *t* test.

RESULTS

Injection of AP did not alter cardiac automaticity, atrial excitability, and atrioventricular conduction, but slightly inhibited sinoatrial conduction 30-60 min postinfusion (Table 1, Fig. 1).

At the same time, AP exhibited pronounced vagolytic activity (Table 1), which consisted in a persistent elevation of vagus excitability threshold and suppression of the synchronizing and tonic components of vagal the chronotropic influence 5 min postinjection. The vagolytic effect persisted throughout the observation period.

Injection of AP reduced the duration of NAF.

Thus, antifibrillation effect of AP is primarily due to its vagolytic activity. This is of special interest, since little attention is traditionally focused on this effect of AP, although the presence of a neurotropic component in the pharmacological effect of AP cannot be excluded [4,9].

Our findings are consistent with the hypothesis [10] that the mechanism underlying atrial tachyarrhythmia is premature repolarization of cardiomyocytes, which brings about the conditions for spontaneous membrane depolarization. This repolarization occurs when two or more arrhythmogenic factors act together reducing the interval between the inward and

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TABLE 1. Effect of AP on Heart Function and Atrial Fibrillation During Vagus Nerve (VN) Stimulation in Cats ($M\pm m$, n=9)

Parameters	Initial values	Time postinjection, min			
		5	30	60	120
Baseline *P-P* interval, msec	370.0±6.4	373.3±5.7 (100.8)	373.3±6.0 (100.8)	373.3±5.5 (100.8)	371.1±4.5 (100.2)
VN excitation threshold, V	0.32±0.02	0.40±0.03* (125)	0.42±0.02* (131.2)	0.39±0.02* (121.8)	0.40±0.03* (125)
Components of the VN chronotropic effect, msec					
synchronising	277.7±19.4	183.3±21.9* (66)	147.7±11.5* (53.1)	173.3±17.2* (62.4)	192.2±22.5* (69.2)
tonic	103.3±7.4	85.5±7.4* (82.7)	78.8±4.5* (76.2)	83.3±7.6* (80.6)	93.3±12.9 (90.3)
Atrial excitation threshold, V	0.50±0.05	0.51±0.04 (102)	0.60±0.06 (120)	0.56±0.06 (112)	0.54±0.06 (108)
Effective refractory period of the myocardium, msec	131.6±5.4	133.8±5.2 (101.6)	134.4±3.9 (102.1)	127.7±5.1 (97)	131.1±4.5 (99.6)
Sinoatrial conduction time, msec	27.3±2.5	28.4±2.0 (104)	34.2±2.9* (125.2)	34.4±2.5* (126)	33.3±3.5 (121.9)
P-Q interval, msec	64.8±2.6	68.8±3.6 (106.1)	68.8±3.8 (106.1)	68.8±3.9 (106.1)	67.1±3.9 (103.5)
Duration of atrial fibrillation, sec	173.8±14.3	98.8±18.8* (56.8)	73.8±15.5* (42.4)	77.7±11.3* (44.7)	91.2±13.0* (52.4)

Note. Percentage is given in parentheses; *p<0.05 compared with the initial values (100%).

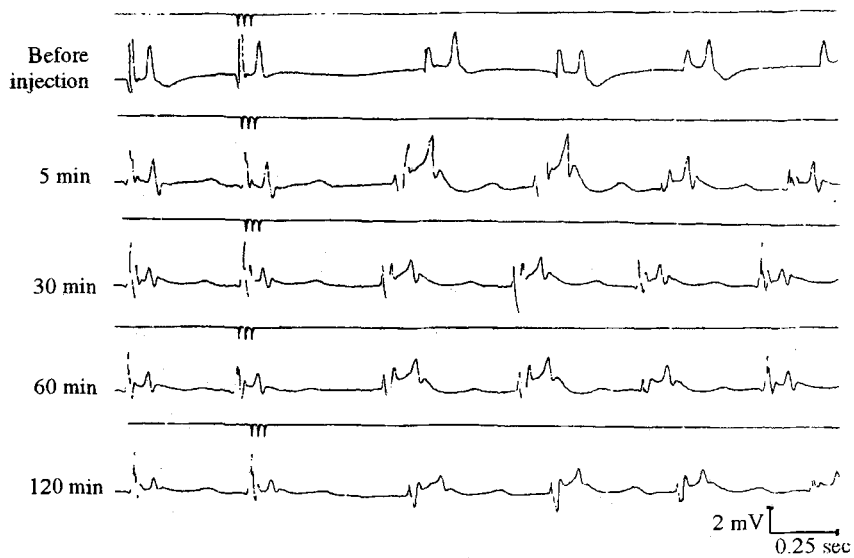

Fig. 1. Vagolytic effect of allapinin on the vagal chronotropic effect during stimulation with a single burst synchronized with the *P* wave. Each fragment presents a record of vagus nerve stimulation (3 pulses, 2 msec, 40 Hz, 6 thresholds) and intraatrial ECG (the first and second peaks correspond to *P* and *R* waves, respectively).

outward ionic currents. In our experiments rhythmic stimulation of the vagus nerve (20-40 Hz) acted as arrhythmogenic factors reducing the effective refractory period to 40 msec or less, while extrasystole additionally shortened this interval. This facilitates autoexcitation of the contractile myocardium, which can be considered as an extrasystole transforming into self-exciting autorhythmic activity. Vagolytic drugs, in particular, AP effectively suppress NAF under these conditions.

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