Effects of Arginine Vasopressin on Different Cardiac Arrhythmias

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It was shown that arginine vasopressin positively affects the course of cardiac arrhythmias caused by aconitine, atropine, glypine, amphetamine, and ketamine, but not by calcium chloride.

Key Words: *arginine vasopressin; cardiac arrhythmias*

Along with regulation of renal function and vascular tone, learning and memory processes, sleep, wakefulness, pain reception, and immunity, the peptide hormone arginine vasopressin (AVP) exerts strong effect on cardiac rhythm [7]. Administration of AVP causes bradycardia which can originate from direct interaction of AVP with its V1 receptors or from imbalance between adrenergic and cholinergic processes [10]. The ability to affect cardiac rhythm is a specific characteristic of antiarrhythmic drugs [4]. The aim of the present study was to investigate the AVP potential for the correction of experimental arrhythmias caused by different chemical compounds.

MATERIALS AND METHODS

Experiments were carried out on adult male albino mice (18-22 g) and rats (150-180 g). In mice, arrhythmia was induced by intravenous injection of KCl in a dose of 300 mg/kg. In rats, arrhythmias were induced by subcutaneous injection of aconitine (200 μg/kg), atropine (10 mg/kg), glypine (5 mg/kg), amphetamine (10 mg/kg), or ketamine (25 mg/kg). AVP was administered 10 min prior to arrhythmia-inducing drugs. During the experiment, rats were placed into special penal-like cages. ECG was recorded in standard lead II by subcutaneous stainless-steel electrodes connected with a RM-6000 polygraph. The data were analyzed statistically using Student's *t* test.

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RESULTS

In mice, KCl injection induced ventricular fibrillations with lethal outcome within 1 min. AVP administered in doses of 0.1, 0.01, or 0.001 mg/kg neither prevented KCl-induced death, nor prolonged the survival period.

Ten minutes after aconitine injection, all rats exhibited various types of extrasystole which lasted over 60 min. In 50% of the rats, 0.1 mg/kg AVP prevented extrasystoles and maintained the sinus rhythm. In the remaining rats AVP significantly delayed the development of extrasystole that appeared 60 min after aconitine injection.

Ten minutes after administration of atropine, amphetamine, or ketamine, sinus tachycardia of varying degree was observed for over 60 min. AVP in a dose of 0.01 mg/kg postponed and in a dose of 0.1 mg/kg prevented atropine-induced tachycardia. It also slowed down heart rate, and as a result, 10 min after atropine injection bradycardia developed instead of tachycardia. AVP significantly shortened the effects of glypine, a muscarinic cholinergic receptor blocker. With the preceding AVP administration glypine-induced sinus tachycardia lasted only 10 min.

AVP in a dose of 0.1 mg/kg completely prevented amphetamine-induced tachycardia and slowed down heart rate.

In AVP-treated rats, ketamine failed to produce tachycardia; sinus bradycardia was observed during the entire observation period (Table 1).

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TABLE 1. Effects of Arginine Vasopressin on Cardiac Arrhythmias ($M \pm m$)

Group	Baseline HR	Time after injection		
		10	30	60
Saline (n=12)	448±15	435±18 (97±4)	417±13 (93±3)	413±10 (92±2)
Atropine, 10 mg/kg (n=6)	447±26	532±5 (119±1)*	512±9 (115±2)*	502±6 (112±1)
Atropine, 10 mg/kg+AVP, 0.1 mg/kg (n=6)	498±19	288±19 (58±6)*	432±34 (87±7)	510±24 (102±5)
Atropine, 10 mg/kg+AVP, 0.01 mg/kg (n=6)	452±9	378±13 (84±3)*	498±11 (110±2)*	526±6 (116±1)*
Glypine, 5 mg/kg (n=9)	447±9	546±8 (122±2)*	530±8 (119±2)*	518±5 (116±1)*
Glypine, 5 mg/kg+AVP, 0.01 mg/kg (n=6)	471±21	548±7 (116±1)*	438±28 (93±6)	422±35 (90±7)
Amphetamine, 10 mg/kg (n=6)	340±17	365±22 (107±6)	450±34 (132±10)*	510±39 (150±11)*
Amphetamine, 10 mg/kg+AVP, 0.1 mg/kg (n=6)	396±18	272±25 (69±6)*	314±37 (79±9)*	370±48 (93±12)
Ketamine, 25 mg/kg (n=6)	410±21	490±10 (120±2)*	467±28 (114±7)	457±11 (111±3)
Ketamine, 25 mg/kg+AVP, 0.1 mg/kg (n=6)	380±18	320±14 (84±4)*	312±11 (82±3)*	307±16 (81±4)*

Note. Figures in parentheses show the percentage of baseline HR (100%); * p=0.05 compared with the baseline value.

Thus, AVP has no effect on KCl-induced fatal arrhythmia, but reduced or prevented cardiac rhythm disturbances caused by aconitine, atropine, glypine, amphetamine, and ketamine. The absence of positive effects of AVP on KCl-induced arrhythmia is probably due to its ability to elevate the cytosolic calcium concentration [9]. The antiaconitine effect of AVP is probably associated with its regulatory influence on the conductivity of myocardial Na^+ channels [8] disturbed by aconitine [3]. AVP also prevents other effects of cholinolytics [13]. Through specific receptors AVP regulates the transmission in cholinergic synapses by modulating presynaptic acetylcholine release and depolarizing the postsynaptic membrane [12]. AVP releases cholinoreceptors from competitive antagonists via a yet unknown mechanism [13].

The mechanism underlying the positive effects of AVP on arrhythmias induced by amphetamine and ketamine probably involves synthesis and release of noradrenaline and dopamine and the interaction of biogenic amines with specific receptors in different brain structures [1,2]. AVP is known to exert dose-dependent up and down regulation of these processes. It should be noted that all proarrhythmic drugs used in this study can be considered as chemical stresses; therefore, the positive effects of AVP can also be explained by its regulatory function in stress and shock [5,6]. Interestingly, pronounced changes were observed in vasopressin secretion during chemically induced stress [11]. The role of AVP in stress consists in tonic regulation of the sympathetic nervous system, particularly of its central parts [14]. This effect is mediated predominantly by V1 receptors [15].

Thus, optimization of the activity of central sympathetic structures can also contribute to the positive effects of AVP on drug-induced arrhythmias. It is interesting to study the effect of cardiovascular AVP derivatives [5] on cardiac arrhythmias.

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