Improved Recovery of Neurologic Status by Oxytocin after 10-min Cardiac Arrest in Rats

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A single systemic injection of oxytocin after effective cardiopulmonary resuscitation of outbred white male and female rats exposed to 10-min cardiac arrest was conducive to a more rapid and complete neurologic recovery of animals in comparison with the control.

Key Words: *oxytocin; vasopressin; vasotocin; cardiac arrest; postresuscitation process*

Previous experiments [2] revealed that exogenous sex steroids facilitated repair processes after clinical death, thus prompting speculation about the role of reproductive neuropeptides and hormones in postresuscitation pathology and repair. In the investigation of this problem, special attention has been paid to oxytocin and its characteristics [1,8]. Increased secretion of oxytocin (OCT) and vasopressin (VP) is known to be one of the typical reactions in various kinds of stress, including terminal states [6-9]. The functional significance of the oxytocin reaction, characterized by reproductive, nootropic, and antiopioid activity, is still not quite clear, in contrast to the vasopressin reactions.

The aim of our research was to estimate the effects of oxytocin, vasopressin, and vasotocin (VT) on repair processes after 10-min cardiac arrest in rats.

MATERIALS AND METHODS

Experiments were carried out with 67 outbred white male and 30 female rats weighing 150 to 200 g. Four series of experiments were performed on animals exposed under ether anesthesia to 10-min cardiac arrest due to vascular bundle clamping [4]. The animals were resuscitated by external massage of the heart and artificial ventilation of the lungs with air [6]. The rates of vital function recovery and of neurologic deficit regress [5], and the final results of resuscitation were assessed in four variants: dead or surviving, with resolution of manifest neurologic disorders 1-3, 4-7, or 8-14 days after hypoxic aggression. Control and experimental groups were formed in each experimental series from the same batch of animals. Neuropeptides were injected subcutaneously once after effective cardiopulmonary resuscitation: to males, series I, oxytocin (Gedeon Richter), dose 5 U/kg; series IV, vasotocin (Serva), dose 0.6 mg/kg; to females, series III, oxytocin (Peptos), dose 0.6 mg/kg or (Arg^8)-vasopressin (Serva) in the same dose. To males in series II distributed into pairs with similar rates of initial function recovery oxytocin was injected at the end of the first 24 h in a dose of 6.6 U/kg. The controls were injected subcutaneously with normal saline. The results were statistically processed using variational statistics methods [3].

RESULTS

These results prompted us to use in experimental series IV with males (Ard^8)-OCT or vasotocin combining amino acid sequences OCT_{1-6} and VP_{7-9}. Vasotocin noticeably decelerated the exit from hypoxic coma, but virtually did not change animal mortality in the postresuscitation period vs. the control. The effect of oxytocin was null.

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TABLE 1. Effect of Neuropeptides on Recovery after 10-min Cardiac Arrest in Rats (mean±SEM)

Series	Experimental conditions	Recovery, min		Turning over on abdomen, h	Neurologic deficit, scores			Survivors without neurologic deficit, %			Mortality, %
		darespiration	corneal reflex		day 1	day 2	day 3	days 1-3	days 4-7	days 8-11	
I	Control (9)	6.3±0.6	27.4±3.0	2.4±0.4	13.5±1.6	7.8±1.3	3.5±0.7	11	78	11	0
	OCT (8)	7.9±1.2	24.6±1.6	2.6±0.3	7.8±1.2*	2.2±0.9*	0.2±0.2*	88*	12	0	0*
II	Control (11)	7.8±0.2	26.4±0.7	2.3±0.2	12.2±0.8	6.7±1.0	3.4±0.8	27	55	18	0
	OCT (11)					4.0±1.0	0.9±0.2*	73*	27	0	0*
III	Control (11)	7.5±0.8	45.2±1.9	2.6±0.2	25.2±2.2	16.5±3.0	7.5±2.0	18	36	18	28
	VP (10)	7.9±1.1	43.6±3.6	2.1±0.2	14.0±1.9*	8.8±1.1*	3.4±1.1	30	40	0	30
	OCT (9)	6.3±0.4	39.0±2.2*	1.9±0.2*	15.3±3.0*	6.0±1.1*	0.9±0.9*	89*	0	11	0**
IV	Control (10)	6.3±0.3	31.5±1.4	1.4±0.1	13.1±0.9	9.5±1.0	5.7±1.2	11	50	6	33
	VT (10)	6.9±0.4	30.5±2.2	2.4±0.3*	12.0±1.4	8.0±1.3	6.0±1.5	0	30	0	70

Note. One asterisk: $p<0.05$ vs. relevant control, two asterisks: $p<0.05$ in experimental series III vs. VP group and control. The number of animals is shown in parentheses.

Hence, a reproducible, unrelated to sex, positive systemic effect of oxytocin on the rate of disappearance of neurologic disorders after 10-min cardiac arrest was revealed – a model of acute polyorgan hypoxic and reoxygenation pathology with the predominant involvement of the central nervous system. Melanostatin, an OCT_{7-9} fragment, appears to play the key role in the oxytocin effect after resuscitation. The next task is to try (Phe^3)OCT with amino acid sequence VP_{1-6} and OCT_{7-9}.

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