Antiarrhythmic Effect of Estradiol Dipropionate in Animals of Both Sexes

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Hormonal background changes in humans are known to be associated with noticeable heart rhythm disorders, and normalization of hormonal levels with normal heart rhythm recovery [1]. Reduction of estrogen levels has been found to lead to a decrease of the number of gap junctions in the uterus [5]. The number and functional status of gap junctions in the heart determine the degree of synchronization of excitation in the myocardium and the cessation of fibrillation [2]. The object of the present research was to study the effect of exogenous estradiol dipropionate on the cardiomyocyte transmembrane potential in animals of both sexes and on the time course of fibrillation development.

MATERIALS AND METHODS

Forty-two chronic experiments were carried out on chicks of both sexes aged 1 month and 18 chronic experiments on guinea pigs of both sexes aged 2 months. All the animals were intramuscularly injected 5000-10,000 IU of estradiol dipropionate for 18-22 days until the secondary sex characters in males changed. All the experiments were carried out under hexenal anesthesia (80 mg/kg) and artificial ventilation.

Transmembrane potentials of intact heart cardiomyocytes were recorded by glass "floating" microelectrodes. Ventricular fibrillation was simulated by heart stimulation with an electrical current of 50 Hz frequency and 60 V voltage for 1 sec or by aconitine crystal application on the anterior surface of the left ventricle.

RESULTS

Measurements of resting (RP) and action potentials (AP) in control chicks and guinea pigs did not reveal sex-specific differences. The chick RP was 73.1±1.5 and AP 101.6±5.8 mV; the guinea pig RP was 91.2±2.1 and AP 102.8±1.2 mV. Estradiol dipropionate injections changed these values in female chicks and guinea pigs (71.2±2.8 and 99.8±4.4; 84.4±4.1 and 108.4±2.5 mV, respectively) and resulted in a reliable reduction of the RP in male chicks and guinea pigs (67.6±1.8 and 87.9±5.2; 78.1±2.5 and 106.1±2.3 mV, respectively).

A single electrical stimulation of the heart in control chicks resulted in spontaneous reversible ventricular fibrillation lasting 1-10 sec in 25% of male and in 64.3% of female chicks, whereas in guinea pigs of both sexes spontaneous reversible ventricular fibrillation always lasted 4-12 sec.

Spontaneous reversible ventricular fibrillation developed in 50% of male chicks with rearranged hormonal period, that is, estradiol dipropionate had a marked protective antiarrhythmic effect. Cardiomyocyte electrical activity in fibrillation did not differ from that in controls.

In guinea pigs of both sexes injected estradiol dipropionate for many days the ventricles fibrillated

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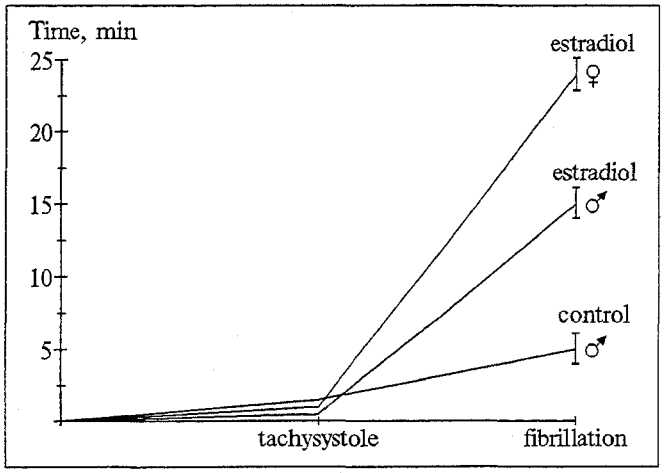

Fig. 1. Latent periods of development of tachysystole and ventricular fibrillation in the guinea pig heart.

only at the moment of electrical stimulation. A repeated stimulation induced the same response, and therefore no self-maintained regimen of spontaneous reversible ventricular fibrillation was established. The time course of aconitine arrhythmia was quite different in guinea pigs of both sexes administered estradiol dipropionate (Fig. 1). The period of tachysystole development was virtually the same in the control experimental animals, but spontaneous irreversible ventricular fibrillation, which appeared at the 5th-6th minute in controls of both sexes, was observed in males with rearranged hormonal profile at the 14th-16th minute and in 6 females at the 24th-28th minute, whereas in 3 females it did not develop at all.

Estradiol is believed to bind specifically to target uterine cell membrane receptors. A complex of secondary transmitter mechanisms is activated at the expense of conformational changes in the receptor molecule [4].

Despite the detected shifts in resting potential value, it is still unclear whether or not they result from the presence of specific receptors on the cardiomyocyte membrane. It may be assumed that estradiol dipropionate directly or indirectly influences the potassium outflow. The antiarrhythmic effect of estradiol dipropionate is due to increased cardiomyocyte electrical conjugation, since estradiol is known to lower the electrical resistance of biomembranes [3].

REFERENCES

1. D. A. Vinogradova, *Current Topics in Cardiology* [in Russian], Moscow (1970), p. 65.
2. V. I. Kobrin, G. I. Kositskii, and N. B. Khaspekova, *Kardiologiya*, **21**, № 10, 67 (1981).
3. A. N. Rossel's, *Proceedings of Reports of Postgraduates and Resident Physicians* [in Russian], Moscow (1970), p. 31.
4. P. V. Sergeev and E. N. Mineeva, Vestnik Akad. Med. Nauk SSSR, № 6, 57 (1990).
5. R. A. Bergman, *J. Cell Biol.*, **36**, 639-648 (1968).