Body Surface Potential Mapping in Rats with Experimental Pulmonary Hypertension

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Abstract. *Body surface potential mapping (BSPM) was performed in female rats with pulmonary arterial hypertension (PAH) induced by a single subcutaneous injection monocrotaline (60 mg/kg body wt). Analysis of data was produced by equipotential momentous maps during ventricle depolarization. In rats with monocrotaline-induced PAH was confirmed hypertrophy of the right ventricle. It is reflected on equipotential momentous maps by a significant change of amplitudes of positive and negative extrema and increase of the duration of the first and second inversions during ventricular depolarization.*

Keywards: body surface potential mapping, pulmonary hypertension, monocrotaline

1. Introduction

Pulmonary arterial hypertension (PAH) is a clinical condition characterized by a progressive increase in pulmonary artery pressure, elevation of the pulmonary vascular resistance and overloading of the right side of the heart [1]. The increase in pulmonary resistance is caused by remodelling of pulmonary vessels, a vasoconstriction, an inflammation and thrombosis [2]. Animal models of pulmonary hypertension have contributed to our understanding of the underlying mechanisms of development this pathology [3]. The most widely used is monocrotaline-induced rat models of pulmonary arterial hypertension [4]. Monocrotaline (MCT) is a pyrrolizidine alkaloid derived from *Crotalaria spectabilis*, causes a pulmonary vascular syndrome in rats characterized by proliferative pulmonary vasculitis, PAH, and cor pulmonale [5]. In rats with MCT-induced PAH changes in heart structure were observed: considerable dilatation of the right ventricle, subendocardial fibrosis and increase in diameter of right ventricle cardiomyocytes [6]. Signs of essential hypertrophy of the right ventricle in rats with MCT-induced PAH develop on the 30^{th} -35^{th} day [7].

Diagnosis of PAH is often delayed. The routine electrocardiogram (ECG) is an inadequate screening tool of pulmonary hypertension. ECG in PAH has sensitivity (55 %) and 70 % specificity [8]. Bogy surface potential mapping (BSPM) offers considerable promise as a method that allows more comprehensive analysis of electrocardiographic information than is possible with standard ECG method [9 - 11]. A study of the development of pulmonary arterial hypertension by simulation on experimental animals will diagnose this disease at early stages.

The aim of this work was to analyze the change of amplitude-temporal characteristics of body surface potential maps in rats with experimental pulmonary hypertension during ventricular depolarization.

2. Subject and Methods

The investigation conformed to the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* (National Institutes of Health, volume 25, no 28, revised 1996).

The experiments were carried out in female Wistar rats (n = 17) weighing 200–250 g. Pulmonary hypertension was caused by a single subcutaneous injection of MCT (60 mg/kg body wt). MCT was dissolved in 1 N HCl, and the pH was adjusted to 7.4 with 1 N NaOH. Before and four weeks after an injection of the drug cardioelectrical potentials were recorded by a method of cardioelectrotopography from 64 subcutaneous needle electrodes uniformly distributed around the animal chest. During registration, the animals were anesthetized with zoletil (3.5 mg / 100 g body weight) intramuscularly. ECG signals from 64 torso and three limb electrode sites are sampled simultaneously and the data are recorded in digital format with Wilson's central terminal as reference. Analysis of data was produced by equipotential momentous maps during ventricle depolarization.

The heart ventricles were transversally sectioned by cryostat Leica CM 1510S (Germany). The right ventricle wall thickness was assessed under light microscopy.

Values given are means ± SE. Data analysis was performed with the computer-based statistical package (Statistica 6.0). Validity was defined by the Wilcoxon criterion for two dependent samples. P value < 0.05 was considered to indicate statistical significance.

3. Results

In hypertensive rats, at the initial moments of the QRS complex in the ECG in the limb leads the zone of positive cardiopotentials is situated cranially, whereas the zone of negative potentials is located caudally. During the ascending phase of the QRS complex, a shift of positive and negative zones takes place that leads to a change of their mutual location – the first inversion of cardiopotentials, as a result, the negative zone is located cranially, while the positive zone - caudally. The first inversion finishes on -3.18 ± 0.79 ms from the RII - peak that is significantly later than in the initial state (-3.65 ± 0.47 ms). In the period of time between the first and the second inversions the spatial location of the areas of positive and negative cardiopotentials doesn't change. The second inversion of cardiopotential areas finishes in the ascending phase of the SII-wave (6.08 ± 1.25 ms relative to the RII-peak) that is significantly later than in the initial state (5.33 ± 0.50 ms). As a result of the second inversion, the distribution of cardiopotentials with the area of the positive potential situated in the cranial zone, and the area of the negative potential located in the caudal zone is formed.

In rats with experimentally induced pulmonary hypertension during the depolarization, the maximum amplitude of positive and negative extrema of cardiopotentials significantly increases, the positive extremum makes 1.39 ± 0.37 mV, the negative extremum makes - 0.87 ± 0.41 mV in comparison with a control group (1.05 ± 0.38 mV; -0.61 ± 0.19 mV, respectively). The time of achievement of positive and negative extrema of their maximum values doesn't significantly differ. In hypertensive rats, the positive extremum reaches its maximum value on 0.32 ± 0.73 ms that corresponds to the moment of the R–peak in the ECG, the negative extremum on the 4.57 ± 0.62 ms after the R–peak, in the initial state it was (0.57 ± 0.40 ms; 4.11 ± 0.79 ms), respectively (Fig. 1.).

It is shown, that the thickness of right ventricle wall increased in MCT-induced rat. The maximal thickening was observed in area of pulmonary cone. The thickness of right ventricle was 1.83 ± 0.20 mm in hypertensive rats and 0.95 ± 0.11 mm in controls on the ventricle base level. It is shown, that thickening of right ventricle is due to the fibres of middle layer, that absent in control rats.

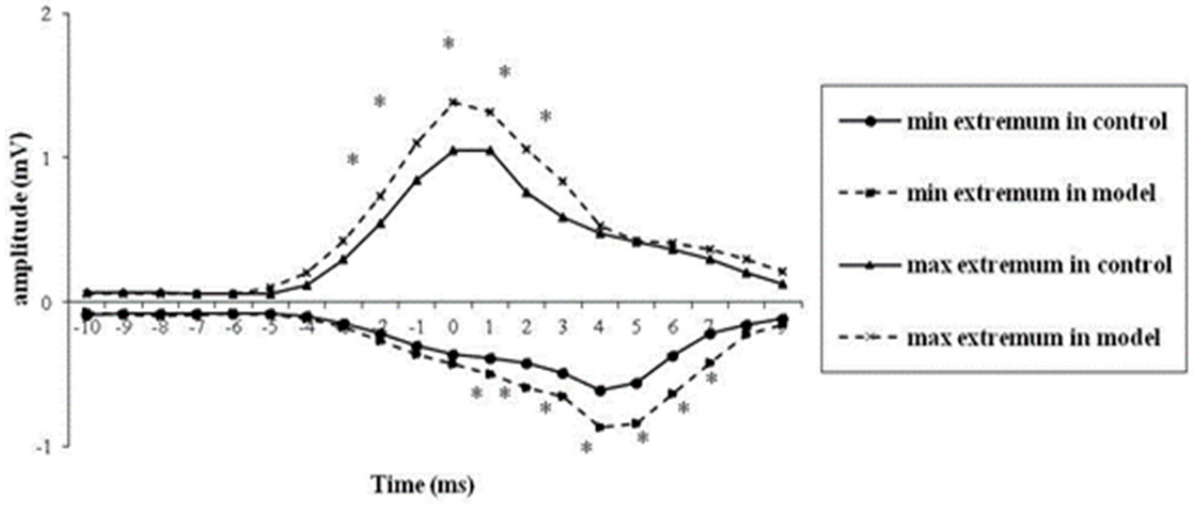

Fig.1. Amplitudes of extrema of cardioelectric field on the body surface during depolarization in rat *- differences significant relatively to the control

4. Discussion

In rats with MCT-induced pulmonary hypertension, hypertrophy of the right ventricle was observed. The thickening of the right ventricle is due to the fibres of middle layer that absent in control rats [12]. It is reflected on body surface potential maps by a significant change of amplitudes of extrema and increase of the duration of the first and second inversions during ventricular depolarization. The increased duration of ventricular depolarization is associated with right ventricular hypertrophy. The increase of the duration could be accounted for by a decline in longitudinal conduction velocity in hypertrophied myocardium [13]. It was shown, that conduction velocity of hypertrophied ventricular myocardium decreases progressively as cell diameter increases [14]. Recently, increase duration of depolarization in rat with left ventricle hypertrophy of different genesis was shown. It was connected with hypertrophy of myocardial fibres and with an increase of connective tissue volume compared to normotensive animals [15].

5. Conclusion

Right ventricular hypertrophy of the heart in monocrotaline-induced rat models of pulmonary arterial hypertension results in changes of temporal and amplitude characteristics of the body surface cardioelectric potential distribution during ventricular depolarization.

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