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ADRENERGIC AND CALCIUM REGULATION OF CONTRACTILITY OF NEONATAL RAT CARDIOMYOCYTES IN CULTURE

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The study demonstrated that activation of the adrenergic system leads to an increase in the frequency of contractions due to stimulation of bisoprolol-sensitive β_1-adrenoreceptors. In addition, neonatal cardiomyocytes demonstrated differential response to the calcium channel antagonist's verapamil and nifedipine.

KEY WORDS: neonatal cardiomyocytes, L-type calcium channels, verapamil, nifedipine, β_1-adrenoreceptors, isoproterenol, bisoprolol.

The primary cardiomyocyte culture acquired the ability to contract spontaneously on the third day of cultivation. On the fourth day, the number of spontaneously contracting cells accounted for more than 50% of the total number of cells. Therefore, our experiments were conducted on the 4th day after isolation, and data analysis was performed only on contracting cells. Cardiomyocytes were placed in a balanced Tyrode's saline solution, where the cells retained their ability to contract spontaneously. The administration of isoproterenol, a synthetic non-selective β-adrenergic agonist, led to a significant increase in the contraction frequency of cells to 179±17% (n=5) compared to the control. However, when isoproterenol and bisoprolol were used together, we observed a cell contraction frequency of 127±11% (n=5), which was close to the control values and indicated a blockade of the isoproterenol-mediated effect due to inhibition of β_1-adrenoreceptors.

The transmembrane entry of Ca^{2+} ions into cardiomyocytes is largely carried out through slow L-type calcium channels, which are activated during membrane depolarization and form an action potential plateau. Calcium antagonists belong to class IV antiarrhythmics and are capable of suppressing transmembrane Ca^{2+} ion current. In our experiments, verapamil at a concentration of 1 μM suppressed the frequency of spontaneous contractions of cardiomyocytes by 92.0±2.3% (n=10), while the same concentration of nifedipine suppressed it by only 47.6±16% (n=6). The more pronounced effect of verapamil may be associated not only with the blockade of L-type channels, but also with its ability to interact with ryanodine receptors (RyR2), reducing the release of Ca^{2+} from the sarcoplasmic reticulum [1]. Our results are consistent with the notion that verapamil reduces atrioventricular conduction and suppresses sinus node automaticity [2], whereas nifedipine and other dihydropyridines have virtually no effect on impulse conduction through the AV node.

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