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LYSOPHOSPHATIDIC ACID PROLONGS ACTION POTENTIAL DURATION AND INCREASES ELECTROPHYSIOLOGICAL INSTABILITY OF ADULT RABBIT VENTRICULAR MYOCARDIUM BY AUGMENTING L-TYPE CALCIUM CURRENT

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Objectives Lysophosphatidic acid (LPA) has various actions on cardiovascular system and is widely reported to modulate multiple ion currents in non-myocardiocytes, but little is known about its electrophysiological effects on cardiac myocytes. The present experiments were designed to investigate whether LPA had electrophysiological effects on the isolated rabbit myocardial preparations.

Methods Action potentials and L-type calcium currents ($I_{Ca,L}$) were recorded in myocytes of left ventricle from 10 adult rabbits using a single-pipette whole-cell patch-clamp. Arterially perfused rabbit left ventricular preparations were used to simultaneously record transmural electrocardiogram as well as monophasic action potentials from the endocardium.

Results LPA prolonged action potential duration at 90% repolarisation (APD_{90}) in a concentration and frequency-dependent manner in the isolated rabbit ventricular myocytes. The application of extracellular LPA (10 μmol/l) increased coefficient of APD_{90} variability from (2.340.31)% to (4.680.94)% ($p<0.01$). LPA (10 μmol/l) significantly increased L-type calcium currents ($I_{Ca,L}$) density from −5.920.68 to −6.630.61 pA/pF ($p<0.05$) without altering activation or deactivation properties. In arterially perfused rabbit left ventricular wedge preparations, monophasic action potential duration (from 215.014.85 to 238.647.46 ms, $p<0.01$), QT interval (from 276.474.53 to 291.406.49 ms, $p<0.01$) and Tpeak-end (from 28.835.48 to 51.124.53 ms, $p<0.01$) were prolonged by LPA (10 μmol/l), which also significantly increased the incidence of ventricular tachycardias induced by S_1S_2 stimulation.

Conclusions We concluded that LPA prolonged APD and increased electrophysiological instability of the isolated rabbit myocardial preparations by augmenting $I_{Ca,L}$.