The mechanisms of antiarrhythmic efficacy of magnesium ions in isolated ventricular cells

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Summary

Despite magnesium ions (Mg)'s widespread use for antiarrhythmic purposes, little is known concerning its antiarrhythmic mechanisms. We, therefore, examined Mg effects on delayed afterdepolarization (DAD), early afterdepolarization (EAD), triggered activity (TA) and aftercontraction (AC), using isolated ventricular cells and/or ventricular papillary muscle. In the experiments using the multicellular preparation, ACs were measured, with the use of strain gauge. ACs were induced in isolated rat papillary muscle superfused with low K^+ (0.5 mM) medium, after a train stimulation (2-5 Hz, 10-30 beats). In the experiments of cardiac myocytes, the effects of Mg on transient inward current (TI), which is responsible for DAD, were studied using whole-cell voltage-clamp method applied on isolated ventricular cells from guinea pig. And action potentials were also induced by current clamp (10 ms) and the effects of Mg on DAD, EAD and TA were examined. TI, DAD, EAD and TA were induced by use of pipette solution with high Ca^{2+} (0.7 mM) and low EGTA (0.1 mM). Moreover, Mg effects on the intracellular Ca^{2+} concentration were measured in neonatal rat ventricular cells, by means of Ca^{2+}-indicator dye fura-2. We found: 1) In the rat papillary muscle, 10 mM Mg inhibited ACs, although 5 mM Mg failed to inhibit them; 2) In cardiac myocytes, 5 mM Mg was unable to inhibit DAD, EAD and TA, however, 10 mM of the ions inhibited them completely; 3) The amplitude and frequency of TI were significantly reduced in the presence of 10 mM Mg (e.g. amplitude of first TI: 307±224 pA to 54±22 pA; amplitude of second TI: 203±30 pA to 30±10 pA; frequency: 5.9±1.7 Hz to 4.8±1.3 Hz); 4) Mg (10 mM) inhibited Ca transient responsible for DAD and/or TA. These results show that the antiarrhythmic activities of Mg may reflect a decrease in Ca^{2+} influx via Ca^{2+} channels, an impairment of Ca^{2+} sequestration, a blockade of non-specific cation channels, and/or a blockade of Na^+-Ca^{2+} exchanger, alone or in combination.