No.92044

Antiarrhythmic efficacy of magnesium in single ventricular myocytes: a study using an intracellular perfusion method

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Summary

The transient inward current, I_{TI}, which underlies triggered cardiac arrhythmias, is seen in conditions of Ca^{2+} overload, such as can be produced by exposure to cardiac glycosides or low K^+ concentration. Its dependence in intracellular Ca^{2+} is well established. The proposed mechanisms are a Ca^{2+}-activated non-specific channel and an electrogenic Na-Ca exchange process. In this study effects of magnesium (Mg) on the I_{TI} were investigated in isolated guinea pig ventricular cells using the whole-cell voltage-clamp techniques. I_{TI} was induced on repolarization after a depolarizing clamp step from a holding potential (V_H) of -40～-45mV, by use of a suction-pipette containing 0.7mM Ca^{2+}. Mg^{2+} concentration of superfusing solution was 0.5mM. The amplitude of I_{TI} increased with the magnitude of preceding voltage within a rage of -45mV～+80mV, but above +80mV the current decreased. I_{TI} was also dependent on levels of V_H; when 200msec- and 100mV-depolarizing pulses from various V_Hs were applied, I_{TI} had a reverse bell-shaped voltage-dependency, showing a maximum value at -25mV. When the Mg^{2+} concentration in a suction-pipette was changed from 0mM to 2.5, 5, and 10mM, I_{TI}-persisting duration also varied. The duration was the shortest in the condition of 0mM Mg^{2+}, but lengthened with a higher concentration of Mg^{2+}. Moreover, even in the condition of zero Mg^{2+} in the pipette, the duration markedly lengthened when Mg^{2+} concentration in the superfusate was increased to 10mM. Generally I_{TI} was observed just before the cell death. This result suggested the pipette Mg^{2+} lengthened a survival time of the cell. The experiment using double suction-pipette also was conducted and supported the above data. These suggested that a mechanism underlying Mg's antiarrhythmic action is, at least, to suppress I_{TI}, possibly by decrease of intracellular free Ca^{2+} concentrations, and that its action may be done in both the outside and inside of the cell membrane.