

Role of potassium currents in the repolarization of canine left ventricular cardiomyocytes

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Potassium currents flowing during a ventricular action potential contribute to the repolarization of the cell membrane, however the exact role of each current has not been cleared yet. Although there are many studies in this topic most of them were carried out with conventional voltage-clamp technique. With this method only presumptions can be made regarding a current flowing during an action potential in reality.

The goal of our experiments were to clarify the exact role of four potassium currents (I_{to} , I_{Kr} , I_{Ks} , I_{K1}) found in canine left ventricular myocardium. For this reason, action potential clamp method has been used. Furthermore the frequency dependent properties of the currents were studied as well.

During our experiments conventional microelectrode technique, voltage-clamp and action potential clamp method in whole-cell configuration of the patch-clamp technique and mathematical modeling has been used. All of our in vitro experiments were carried out on enzymatically isolated canine left ventricular cardiomyocytes.

According to our results I_{to} is flowing only in the beginning of the action potential for about 20 ms, and is responsible for the early repolarization phase. I_{to} does not play a role in determining the length of the action potential. I_{Kr} is gradually increasing during the plateau phase, reaching its peak shortly before the maximal rate of repolarization as it were triggering the peak of I_{K1} . The I_{K1} is also active in the period of diastole but it is deactivated by the rising phase of the action potential. Later together with the gradually increasing rate of repolarization I_{K1} is becoming larger determining the maximal rate of repolarization, so thus governing the terminal repolarization. Neither I_{Kr} nor I_{K1} showed frequency dependent changes in our experiments.

We demonstrated that I_{Ks} contributes to the normal repolarization. During our measurements I_{Ks} appeared to increase together with the longer action potential duration and with the higher amplitude of the plateau phase. However our results suggest that primarily the amplitude of the plateau determines the amplitude of I_{Ks} .

We could not confirm the I_{Ks} activating effect of the L-364,373 compound previously obtained by others.

Drugs with higher effectiveness and with less proarrhythmic adverse effects can be developed by knowing the exact properties of the ionic currents establishing the action potential.

Keywords: electrophysiology, potassium current, action potential, action potential clamp, ventricular repolarization, canine cardiomyocyte, frequency dependence