CARDY-12

EFFECTS OF INSULIN ON TRIGGERED ACTIVITY IN HAMSTER VENTRICULAR MYOCYTES

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BACKGROUND: The mechanisms of triggered arrhythmia in heart failure likely involve triggered activity from either delayed afterdepolarizations or early afterdeoplarizations. Because insulin would increase the $[Ca^{2+}]_i$ in a failing heart, it might result in Ca^{2+} overload and induce cardiac arrhythmias. In animal models and in clinical trials, insulin had been shown to prevent ventricular arrhythmias and atrial fibrillation. The aim of the present study was to clarify the arrhythmogenic and antiarrhythmic effects of insulin on healthy and dilated myopathic (Bio 14.6) Syrian hamster ventricular myocytes (male, 32 –to 52 weeks old).

METHODS: Enzymes were used to isolate myocytes. Transient inward current (I_{ti}) was elicited at clamped potential from –40 to +40 mV for different durations ranging from 50 to 3050 ms and then repolarized to –40 mV and/or repolarization after trains of depolarizing pulses (from -40 to +40 mV for 500 ms in duration) for 20 times.

RESULTS: Exposure to insulin (1 μM) increased the amplitude of steady-state outward I_K on depolarization but reduced markedly the magnitude of I_{ti} on repolarization. Similar results were obtained in 20 hamster ventricular myocytes. However, in 3 of 23 myocytes tested, insulin increased I_{ti} on repolarization, which could be reversed by a specific inhibitor of Na^+-Ca^{2+} exchange, SEA0400. Insulin also tended to shorten AP duration and decrease the incidence of EADs. The actions of insulin were partially reversible after washout. Insulin inhibited I_{to} and increased I_k.

CONCLUSIONS: Arrhythmogenic or antiarrhythmic effects of insulin varied from one hamster ventricular myocyte to another. Effects of insulin on triggered activity depended on individual electrophysiological properties such as $I_{Ca,L}$, I_{NCX} and outward K^+ currents.

Keyword: insulin, heart failure, triggered arrhythmia