Physiological Institute of the University of Freiburg i. Br., Germany

Effects of changes in frequency on guinea pig ventricular action potential duration and on QT interval under different experimental conditions

L. v. Savigny, S. Hohnloser, and H. Antoni

(Received February 25, 1981)

Summary

Isolated perfused guinea pig hearts (Langendorff preparation) were arrested by carbachol (0.1–0.2 mg/l) and electrically stimulated in the region of the AV-conducting system. The QT interval was determined by means of extracellular electrodes at different driving frequencies. Separate experiments were performed on papillary muscles from the right ventricle to measure the duration of the transmembrane action potential under comparable conditions.

At 35 °C (K⁺ 5.4 mmol/l) increasing the frequency of stimulation (range 12–120/min) caused the action potential duration (APD) to decrease to a greater extent than the QT interval. Stepwise rising of the external K⁺ concentration up to 16.2 mmol/l produced a nearly parallel shift of the APD-frequency relation to lower values. Again, the QT interval was less affected by increasing the external K⁺ concentration than the APD. Stepwise reduction of the temperature down to 20 °C prolonged the APD as well as the QT interval, the effects being more pronounced at lower than at higher stimulation frequencies. Under all examined experimental conditions, the APD proved to be markedly shorter than the QT interval even when the latter is diminished by the duration of QRS.

The results suggest that no close relation exists between the APD and the QT interval. The observed divergencies may be due to functional differences among various parts of the ventricles.

Key words: guinea pig heart, papillary muscle, QT interval, action potential duration, frequency-duration relation, potassium concentration, temperature.

Introduction

In recent years the growing interest in cardiac arrhythmias due to reentry has also attracted increasing attention to the factor which mainly determine the length of a propagated wave of excitation, namely its conduction velocity and the duration of the excitatory process. This latter parameter may considerably change under different conditions and thus exert a decisive influence on the development of those arrhythmias. Alterations of the ionic composition of the extracellular fluid as well as changes in temperature or in beating frequency are known to affect the duration of cardiac excitation. In isolated myocardial preparations the influence of the stimulation frequency on the duration of the action
potential has been studied by different investigators in much detail (6, 7, 13, 15, 25). However, less studies have been concerned with the effects of various experimental conditions on this relationship (23). Similarly, little is known about the connections between the action potential duration of isolated myocardial preparations and the corresponding excitatory phenomena of the whole heart.

The present studies are dealing at first with the influence of changes of the external potassium concentration (Ke) or of the temperature on the frequency-duration relation of the action potential. Subsequently the duration of ventricular excitation in the whole heart, as expressed by the QT interval, is compared with the data obtained in the isolated myocardium. The investigations show that considerable effects on the frequency-duration relation of the action potential are exerted by the examined conditions. However, no close correlation could be found between the QT interval of the whole heart and the duration of the cellular action potential measured in the isolated papillary muscle.

**Methods**

For the studies in the isolated myocardium, papillary muscles from the right ventricle of guinea pigs (250–300 g) were used. Muscles with a diameter up to 1 mm were mounted in the perfusion chamber and allowed to incubate for 45 minutes at a stimulation frequency of 30/min. A modified Tyrode's solution (pH 7.36) was used containing in mmol/l: Na⁺ 149.3; K⁺ 2.7; Ca⁡⁺⁺ 2.0; Cl⁻ 143.7; HCO₃⁻ 11.9; H₂PO₄⁻ 0.4; glucose 10.0. In some experiments Ke was increased up to 16.2 mmol/l by adding solid KCl. The solutions were gassed with 97 % O₂ and 3 % CO₂ and brought to the desired temperature (35 °C–20 °C) immediately before entering the bath.

Action potentials were recorded by means of conventional glass microelectrodes filled with 3 mol/l KCl. Oscillographic traces of action potentials were photographed and evaluated by projection of the records upon a calibration grid. The duration of the action potential was measured at the levels of 50 % and 90 % repolarization (APD₅₀; APD₉₀). Only those recordings were considered in which constant impalement of the microelectrode was maintained throughout the whole experimental procedure. Following changes in frequency, the registrations were started when the steady state was attained (after about 2 minutes).

The studies in the whole heart were performed in isolated perfused guinea pig hearts (Langendorff's preparation). The perfusion fluid was composed as follows (in mmol/l): Na⁺ 148.6; K⁺ 5.4; Ca⁡⁺⁺ 2.5; Cl⁻ 132.9; HCO₃⁻ 24.9; H₂PO₄⁻ 1.2; glucose 5.5; Na-pyruvate 2.0. Higher potassium concentrations were obtained by adding KCl. The stock solutions were equilibrated with 95 % O₂ and 5 % CO₂ (pH 7.4) and heated up to achieve the desired temperature immediately before entering the heart. The perfusion temperature was controlled at the point where the solution left the preparation. The gradient of temperature across the preparation was minimized by thermal isolation of the chamber. Coronary flow was continuously measured during the whole experiment. At a perfusion pressure of 7.98 kPa (60 mmHg) the flow amounted to 2.5–6.5 ml/min. After suspending the heart at the perfusion cannula, the preparation was allowed to equilibrate for about 10 to 15 minutes.

In order to drive the heart over a wide range of frequencies without interference by spontaneous activity, supraventricular pacemakers were arrested by adding carbachol (0.1–0.2 mg/l) to the perfusion fluid. The stimulation electrodes consisted of thin glass-coated silver wires and were impaled at the av-boundary. In any case, QT-measurements were performed at a given frequency not before the steady state had been achieved. Electrical activity was recovered via AgAgCl₂-electrodes.