Abolition by Nicorandil of Spontaneous Action Potentials of the Small Atrio-Ventricular Node Preparation of the Dog

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IJIMA, T. and TAIRA, N. *Abolition by Nicorandil of Spontaneous Action Potentials of the Small Atrio-Ventricular Node Preparation of the Dog.* Tohoku J. exp. Med., 1985, **146** (4), 401-403 — Effects of carbachol and nicorandil on spontaneous action potentials were examined in the small atrio-ventricular (A-V) node preparation of the dog. Carbachol (3×10^{-6} M) definitely hyperpolarized the membrane potential and abolished the spontaneous activity. Nicorandil (3×10^{-4} M) also abolished the spontaneous activity but the membrane potential became quiescent at -65 mV, which was less negative than the maximum diastolic potential. From these results it appears that nicorandil may increase the potassium conductances but not hyperpolarize the membrane potential because the background potassium conductance is little developed in the nodal cells. — atrio-ventricular node; spontaneous action potential; carbachol; nicorandil; potassium conductance

It has been shown that acetylcholine (ACh) binds to muscarinic receptors and opens an ACh activated potassium channel in atrial and nodal cells (Sakmann et al. 1983). Nicorandil, a new coronary vasodilator, also increases potassium conductances of cardiac membranes but without mediation through muscarinic receptors (Yanagisawa and Taira 1980). Both drugs shorten the action potential duration and hyperpolarize the resting membrane potential in the atrial muscle. But hyperpolarization of the resting membrane potential is not obvious with nicorandil in cardiac Purkinje fibers (Yanagisawa and Taira 1981) and the sino-atrial node cells (Sato and Hashimoto 1984). In the present study effects of carbachol and nicorandil on spontaneous action potentials of the small atrio-ventricular (A-V) node preparation were examined to reveal the difference of the two drugs.

MATERIALS AND METHODS

Small A-V node preparations from the dog heart were prepared in the same procedure

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described previously (Iijima and Taira 1983). The preparation was superfused with Tyrode solution containing (mM): K^+ , 2.7; Na^+ , 149.3; Ca^{2+} , 1.8; Mg^{2+} , 1.0; Cl^- , 145.3; HCO_3^- , 11.9; $H_2PO_4^-$, 0.4; and dextrose, 5.5, equilibrated with 95% O_2 and 5% CO_2 . The pH of the bathing solution ranged from 7.2 to 7.4. Tissue bath temperature was maintained at $37 \pm 0.5^\circ C$. After equilibration for at least 60 min, membrane potentials were recorded with glass microelectrodes filled with 3 M KCl and having a resistance of 15–30 Mohm. Membrane potentials were displayed on an oscilloscope and photographed on 35 mm film, and also recorded with a pen-recorder.

RESULTS AND DISCUSSION

Carbachol (3×10^{-6} M) hyperpolarized the membrane potential and abolished the spontaneous activity (Fig. 1A). The maximum diastolic potential was -70 mV before the drug application (Fig. 1Aa) and the quiescent membrane potential induced by the drug was -80 mV (Fig. 1Ab). Nicorandil (3×10^{-4} M), on the other hand, also abolished the spontaneous action potential but hyperpolarization of the membrane potential was not obvious (Fig. 1B). The membrane potential

Fig. 1. Effects of carbachol (A) and nicorandil (B) on spontaneous action potentials of the small A-V node preparation of the dog. In upper traces of each panel, fast parts of the action potentials were not recorded because of low frequency response of a pen-recorder.

became stable at -65 mV (Fig. 1Bc), which was less negative than the maximum diastolic potential of -70 mV (Fig. 1Ba).

It has been reported that in atrial muscle, nicorandil (10^{-6} – 10^{-4} M) shortened the action potential duration and hyperpolarized the resting membrane potential (Yanagisawa and Taira 1980). In cardiac Purkinje fibers, nicorandil also decreased the action potential duration and produced the reduction of the slope of the slow diastolic depolarization and resulted in the decrease in the spontaneous firing rate. However, nicorandil did not change the maximum diastolic potential (about -100 mV), and abolished the action potential at -80 mV (Yanagisawa and Taira 1984). In the present study, nicorandil slowed the spontaneous firing rate and abolished the spontaneous action potential without hyperpolarizing the membrane potential more than the maximum diastolic potential of the control. These results indicate that carbachol increases the ACh activated potassium conductance in A-V nodal cells and hyperpolarize the membrane, and abolishes the spontaneous action potential. Nicorandil, however, may increase both the time-dependent and the time-independent potassium conductances but the latter is little developed in the nodal cells (Kokubun et al. 1982; Noma et al. 1984). Therefore, hyperpolarization may not be induced by nicorandil.

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