Studies on Potassium Induced Coronary Dilation in the Isolated Guinea Pig Heart *

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Summary. Changes of coronary flow in the isolated perfused spontaneously beating guinea pig heart were induced by elevation of potassium concentration in the perfusion medium (4–16 meq/l). Potassium caused a dose-dependent transient increase of diastolic coronary inflow. The response was inhibited by ouabain (1.4 x 10⁻⁷ M) or reduced temperature. Rubidium ions elicited almost identical vasodilator effects which were also inhibited by ouabain.

Autoregulation of coronary flow, reactive hyperemia, and hypoxic coronary dilation were not significantly altered in the presence of ouabain.

The results support the hypothesis that potassium as well as rubidium cause vasodilation by activating a Na⁺, K⁺-ATPase. On the other hand, they do not favour the view of an essential involvement of potassium ions in local regulation of coronary flow under the conditions studied.

Key words: Na⁺, K⁺-ATPase — Ouabain — Rubidium — Vasodilation — Autoregulation — Reactive hyperemia.

INTRODUCTION
Small increases in extracellular potassium concentration reduce the vascular resistance in heart and skeletal muscle [15] and also cause a dilation of pial and ear arteries [18, 16]. In skeletal muscle such dilator responses can be inhibited by ouabain [10]. Similar inhibitory effects of the glycoside were reported for the potassium induced relaxation of isolated facial [13] and cerebral artery strips [29]. Since cardiac glycosides are known to inhibit the Na⁺, K⁺-ATPase [26, 23] as well as the Na⁺-pump [22, 26, 23], it has been suggested that potassium causes vasodilation by stimulating a Na⁺, K⁺-ATPase operating as an electrogenic Na⁺-pump, which induces hyperpolarization and thus relaxation of the vascular smooth muscle cell [10, 2, 13, 29]. To our knowledge studies have not been reported which were designed to determine whether a similar mechanism is also responsible for potassium vasodilation in the heart. Experiments were therefore performed on the isolated perfused guinea pig heart to evaluate the influence of ouabain and temperature on potassium induced alterations of coronary flow. The effects of ouabain on the coronary responses to rubidium ions, ischemia, hypoxia, and changes in perfusion pressure were also studied.

MATERIALS AND METHODS
All chemicals purchased from E. Merck AG, Darmstadt, were of highest available purity.

Isolated guinea pig hearts were perfused according to Langendorff in a non-recirculating system at constant pressure (75 cm H₂O). The preparation was described in detail in an earlier communication [9]. The perfusion medium (38°C), equilibrated with 95% O₂ - 5% CO₂, pH 7.41 – 7.45, was a modified Krebs-Ringer-bicarbonate solution of the following composition (mM): NaCl 119.7, KCl 4.7, KH₂PO₄ 1.2, CaCl₂ 1.25, MgSO₄ 0.3, NaHCO₃ 24.9, glucose 5.5, pyruvate 2.0. The addition of pyruvate to the perfusate has been shown to stabilize the isolated heart with respect to energy metabolism and coronary reactivity [9].

Coronary phasic and mean inflow were measured with a flow transducer of 1.5 mm inner diameter (In Vivo Metric Systems), which was located in the aortic cannula and calibrated in connection with an electromagnetic flowmeter (M 4000, Statham). The electronic damping system of the flowmeter was eliminated in order to record rapid changes of coronary inflow during systole and diastole. A flaccid rubber balloon filled with saline, coupled to a pressure transducer (P 23 Db, Statham), was placed in the left ventricle to measure isovolumetric ventricular pressure. Heart rate was counted electronically from the ventricular pressure pulses.

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All recordings were accomplished with a Dynograph, Type 504, Beckman. Oxygenated (95% O₂—5% CO₂) isotonic NaCl, KCl or RbCl solutions were infused by machine (Unita, Braun-Melsungen) into the perfusion line close to the aortic cannula at a slow rate (0.1—0.5 ml/min). Aliquots of an ouabain stock solution (1 mg/ml, dissolved in 0.9% NaCl and ethanol 1:1, v/v) were added to the perfusate in the reservoir. The solvent itself had no measurable effect on the K⁺- or Rb⁺-induced coronary flow change or on ventricular function.

Autoregulation of coronary flow was elicited by rapid, step-wise increases in perfusion pressure. Reactive hyperemia was measured following release of coronary inflow occlusions of 10 and 40 s. Coronary responses to hypoxia were induced by equilibrating the perfusate with 30% O₂—5% CO₂—65% N₂.

RESULTS

a) Effects of Ouabain on Coronary Flow Responses to Potassium and Rubidium. Changes of coronary flow induced by minor increases (approx. 4—16 meq/l) of the potassium concentration in the perfusion medium are shown in Figure 1. The flow responses in the control period were dose-dependent and transient. The increases of flow were associated with large decreases in peak systolic pressure, whereas diastolic ventricular pressure was much less affected. The elevation of peak coronary inflow during diastole could therefore be taken as a measure for the dilator effect of potassium ions [11]. Ten to 15 min after the addition of ouabain to the perfusate (final concentration 1.4 x 10⁻⁷ M) the dilator responses induced by potassium were found to be markedly smaller or completely abolished (Fig. 1, right side). This inhibitory effect was shown to be partially reversible during subsequent perfusion for 20 min with ouabain-free medium.

In additional experiments it could be demonstrated that reduction of perfusate temperature from 38°C to 26°C also strongly and reversibly antagonized the