POTASSIUM-INDUCED AUTOMATICITY OF ISOLATED HUMAN RENAL ARTERY

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Accepted October 23, 1980

Autonomous regulation by renal arterial vessels plays an important part in maintaining a constant blood flow through the kidney. However, decisive mechanisms which account for the renal autoregulation remain to be elucidated (1). Using isolated human renal arteries, we investigated pharmacological characteristics in vitro, and compared our findings with observations in dogs.

Preparations of human renal arteries were obtained from six patients who underwent nephrectomy for tumors of the kidney (55 and 47 year old women and a 57 year old man) and ureters (73, 68 and 66 year old men). Helical strips, 2.5 mm wide and 20 mm long, were cut from a small branch (about 2.0 mm in diameter) of the renal arteries, and suspended in a muscle bath filled with Krebs-Ringer bicarbonate solution of the following composition (mM): NaCl 117.7, KCl 4.7, CaCl₂ 2.5, MgSO₄ 1.2, KH₂PO₄ 1.2, NaHCO₃ 24.4 and glucose 10.0. The solution was maintained at 37°C and continuously aerated with 95% O₂ and 5% CO₂. Under an initial or passive tension of 1.0 g, isometric tension developments were recorded on a polygraph (Nihonkohden RJG-4004) through a transducer (Nihonkohden SB-1T). The strips were allowed to equilibrate for 2 hr before each experiment. The same procedures were used in the case of dog renal arteries.

The isolated dog renal arterial strips showed no inherent or spontaneous activity. Potassium 15 mM produced a gradual increase in the tension which reached a maximum of 1050±100 mg (mean±SEM, n=10) after 10 min and persisting at the same level for more than 2 hr (Fig. 1Aa). Indomethacin 3 μg/ml, applied 30 min after administration of potassium, produced no change in the sustained tension development (Fig. 1Ab). The strips were relaxed by diltiazem 1 μg/ml (Fig. 1Ac) and the initial resting level was reverted to within 20 min. Thus, the dog renal arterial strips showed a sustained tension development in response to potassium, but there were no oscillations. In the human renal arterial strips, there were spontaneous, small oscillations with a tension from 25 mg-75 mg, under control conditions. Potassium 15 mM produced relatively rapid contractions of the strips, followed by marked oscillations with a tension from 150 mg-600 mg occurring at a rate of 4-5 times/10 min (Fig. 1Ba). In three strips, indomethacin 3 μg/ml, applied 30 min after administration of potassium, diminished the oscillations of the strips (Fig. 1Bb). Diltiazem 1 μg/ml decreased the tension and eliminated the oscillations (Fig. 1Bc). In three other preparations, the marked oscillations persisted for 2 hr, and thereafter the strips reached a steady state with the same small oscillations observed in control conditions. In these strips under a steady state, arachidonate 0.1 mg/ml produced a transient increase in
the tension, developing to the peak (about 900 mg) after 10 min and returning gradually to the initial level within 45 min (Fig. 1Ca). Along with the decline, rhythmic oscillations appeared and were gradually augmented at later times (Fig. 1Cb).

In vessels such as portal vein or vascularities of muscle and skin in human limbs, spontaneous activities have been demonstrated electrophysiologically or hemodynamically (2). We found that the renal arterial strips also have spontaneous activities in form of marked oscillations in the tension with the depolarizing action of potassium. This contrasts to findings in the dog renal arteries in which these vascular activities were lacking. The present study also showed that the oscillations in the tension of the human renal arteries can be diminished by either an inhibitor of prostaglandins biosynthesis (indomethacin) (3) or a calcium antagonist (diltiazem). The results suggest that the oscillations seen in human renal arteries may arise from production and/or activation of intramural prostaglandins and that the spontaneous activities may be related to the availability of calcium ions in the membrane of vascular smooth muscle. In biochemical studies on the human colic and/or gastric arteries, the presence of endogenous prostaglandin (prostacyclin) has been confirmed (4). The fact that arachidonate does induce oscillations of the human renal arteries further supports this view. However, it cannot be ruled out that indomethacin may have non-specific inhibitory actions on vascular smooth muscle, resulting in diminution of the oscillations in the tension of the arteries. Though the present results do not clearly explain the mechanisms
of initiation of automaticity of isolated human renal arteries, the data clearly indicate that isolated human renal arteries do exemplify contractions which have an automaticity and such findings differ from observations reported in case of dogs and rabbits (5).

REFERENCES


