The contractility of venous vascular smooth muscle in spontaneously hypertensive or renal hypertensive rats

Die Kontraktilität venöser Gefäßmuskeln von spontan hypertensiven oder renal hypertensiven Ratten

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With 4 figures and 3 tables

Summary

The influence of arterial hypertension on the contractility of venous smooth muscle was studied by using force-velocity relations derived from the isolated tetanized portal vein of spontaneously hypertensive (SHR) or renal hypertensive rats (RHR). The results were compared with those obtained from corresponding normotensive rats (NR).

The portal vein contractility of SHR was determined by the analysis of either a single isometric contraction or of a number of afterloaded isotonic contractions. The series elasticity needed to calculate the shortening velocity of the contractile element was found to be greater in SHR than in NR. Both the isometric and the isotonic force-velocity relations were shifted similarly by the spontaneous hypertension. The maximum rate in tension increase was greater by a factor of 1.4 and the force generation was increased by a factor of 1.5 as compared with the results obtained from the NR. The velocity of shortening of the unloaded preparation remained constant, which indicates that the turnover rate of the myosin linkages, i.e. the elementary process of contraction, was unchanged (the so-called polytropic effect). The augmentation in force generation is probably caused by a recruitment process induced by an increase in the intracellular calcium level.

In RHR a slight increase in the force generation of the portal vein from 15.6 ± 1.1 mN to 18.4 ± 1.0 mN was seen in rats which had been submitted to a period of arterial hypertension of about 20 weeks. The speed of isotonic shortening extrapolated to zero load was considerably reduced from 0.86 ± 0.03 ML/s to 0.61 ± 0.09 ML/s (P < 0.0025); this is the so-called tachytropie effect.

The results revealed a different influence on the elementary process of vascular smooth muscle contraction for both types of arterial hypertension. The dynamics of the cycling myosin linkages were only affected by renal hypertension whereas with spontaneous hypertension the dynamics remained constant.

During arterial hypertension the variation of the contractility of the vascular smooth muscle may take the form of a change in the extent of force generation and/or in the velocity of shortening. The mechanisms responsible for the intracellular calcium release and changes in the structure of the vessel wall might be potential agents in causing arterial hypertension. The following were discussed as possible factors: the responsiveness to vasoactive drugs (5, 30, 4, 7, 31), changes in the excitability (11) or in the spontaneous automaticity (6, 31), changes in the structure of the vessel wall (6, 31, 20), failures in nervous control processes (3).
Besides these effects an alteration of the contractile machinery itself may be involved in the pathogenesis of arterial hypertension. An insight into the dynamics of contractile protein movement can be obtained through analyzing the muscle contraction by means of force-velocity relations. The peak force generation $T_0$ of a maximally activated muscle is related to the number of cycling cross-bridges. The maximum shortening velocity of the unloaded preparation $V_{\text{max}}$ is an index of the speed of cross-bridge movement (2, 15). $T_0$ and $V_{\text{max}}$ are the intercepts of Hill’s hyperbola with the tension-axis and the velocity-axis, respectively. Basically, both values can be changed independently of each other and therefore polytropic and tachytropic effects (25) can be distinguished. Polytropic effects were observed in the vascular smooth muscle of the portal vein when the extracellular calcium level was altered within the range of pCa 2.0 and 3.2, when the concentration of extracellular hydrogen-ions was varied between pH 8.0 and 6.8 or when one added noradrenaline (10, 25). Tachytropic effects do not seem to be essential from the physiological aspect since they are only seen to occur when the temperature is altered (26) or when the pH-values are below 6.8 (25). In experimental hyperthyreosis the hormone thyroxine induces an increase in both the force and the velocity of the portal vein contraction so that polytropic as well as tachytropic effects occur (21). The elementary process of myosin cycling can therefore be affected by the variation of the bath temperature, pH values below 6.8 and by addition of thyroxine. Thus, a relative constancy in the dynamics of the cross-bridge movement of vascular smooth muscle can only be expected under physiological conditions. In the following the intrinsic speed of shortening of the rat portal vein was studied under those pathophysiological conditions found in spontaneous or renal hypertension. In the case of the portal vein a direct influence of high blood pressure on the vessel wall can be excluded as this vessel is not exposed. Therefore the changes observed in the dynamics must have been induced by unknown factors.

The elementary process of portal vein contraction will be analyzed by two methods which require either a single isometric contraction (17) or a number of afterloaded isotonic contractions (26). Furthermore, not only the dynamics of the contractile elements but also the behaviour of elastic elements was studied with the use of a method already published by Peiper et al. (24) as a varied extensibility in the portal vein of spontaneously hypertensive rats had been demonstrated by Greenberg and Bohr (6).

**Methods**

Rats of both sexes were slightly anaesthetized with ether and bled before their vena mesenterica-portal vein was removed. The isolated preparation was placed in a circulating Tyrode’s solution (NaCl 132.2; KCl 4.8; CaCl$_2$ 2.5; MgCl$_2$ 0.5; NaHCO$_3$ 11.9; NaH$_2$PO$_4$ 0.36; glucose 5.05; pyruvate 2.0 mM; aerated with 95% $O_2$ and 5% $CO_2$; pH 7.3; 37 °C). The portal vein was tetanized in an electric field induced by 50 Hz ac, 6 volts, applied through platinum plate electrodes. The preload of the 78 preparations tested averaged $2.4 \pm 0.3$ mN ($\bar{x} \pm s_x$).

The mean arterial blood pressure was determined throughout the period of hypertension by recording the maximum of cuff pulses obtained from the rat’s tail;