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COMPARATIVE STUDY OF THE INFLUENCE OF UREA ON NORADRENALINE CONTRACTION IN ENDOTHELIUM-DENUDED AND ENDOTHELIUM-CONTAINING RINGS OF RAT AORTA

N.Temnyalov

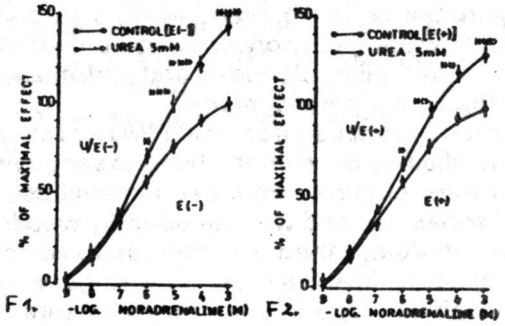
Department of Pharmacology, Varna

During the last decade many data show that the endothelial cells help to co-control the tone of the underlying vascular smooth muscle by releasing vasoactive factors. The first demonstration that the presence of endothelium can augment, rather than depress, noradrenaline contractions of isolated blood vessels has been shown with arachidonic acid(3). The augmentation was not observed in preparations in which the endothelium had been removed mechanically. Depression of selective and nonselective adrenergic agonist by spontaneously released endothelium-derived relaxing factor(s) is confirmed in several groups of investigators(2, 5, 6). It is already accepted that in physiological circumstances the release of relaxing factors (nitric oxide, PG I_2 and endothelium-derived hyperpolarizing factor) appears to predominate(8).

The main purpose of the present work is to compare the influence of urea in physiological concentration on noradrenaline contraction on both - endothelium-denuded and endothelium-containing vascular preparations in a parallel study.

Thoracic aortas were taken from male Wistar rats weighing 300-330 g body mass, killed by blow on the head exsanguined. Up to four rings 3 mm long were obtained from each animal used:one was intact for a control series; second was denuded by wooden stick - both for simultaneous recording; third was denuded and fourth - intact - for a light microscopic investigation. The rings were suspended under isometric regimen (Ugo Basile - Italy pressure transducer) in organ baths, filled with 10 ml Krebs-Henseleit solution, aerated with 95% O_2-5% CO_2 gas mixture and allowed to equilibrate for 90 min. At the end of this period cumulative concentration-response curves to noradrenaline 10^{-9} - 10^{-3} mol/l (expressed as final molar concentrations in chambers) were obtained. Increases in tension are expressed as percentage of maximal effect of adequate control before and after 15 min exposure time of urea 5 mmol/l, without washing out. Statistical evaluation of data(Mean ± S.E.M.) was done by Student's t-test for paired observations.

It is clear that when urea acts on denuded ring the noradrenaline contractions are more augmented(fig.1) than in endothelium-containing ring(fig.2). The enhancement of adrenergic contractions are above EC_{50} in both cases. It is to be underlined that the maximal effect of noradrenaline is only significantly higher in denuded rings in comprasion with intact ones. As related to urea effect in endothelium-conteining rings we assume a calcium entry pathway through voltage gated calcium channels(1,9) together with a noncompetitive increase of alpha-adrenoceptor sensitivity(9). However, the presence of EDRF(s) counteracts this urea influence in physiological conditions. Therefore in denuded rings it is logic to wait a more expressed augmentation of noradrenaline contractions, because the homeostasis is distroyed and new pathophysiological conditions exist (2,3,5,6,8). Recently it has been shown that "endothelial cells lack a fully functional urea cycle but can convert L-citruline to arginin - a prerequisite for the release of EDRF"(4). In this aspect we agree that "the reality of the physiological modulation of vascular tone is one of interacting and countervailing influences"(7). Ongoing work with other adrenergic agonists and urea in pathological concentrations will contribute for a further elucidation of the problem studied.



F1. F2.

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