# COMPARISON OF ARTERIAL AND VENOUS RESPONSES OF SKELETAL MUSCLE TO COMBINED ADRENERGIC STIMULATION

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Humoral regulation of visceral hemodynamics depends on concentrations of circulating vasoactive substances, including catecholamines [4], which act on the effector formations of the blood vessels, and it reflects the conditions of maintenance of the blood supply to the organs by the cardiovascular system as they really exist. In this connection the study of the combined effect of humoral stimuli on the visceral hemodynamics is an urgent task in circulatory physiology. However, data on the combined action of adrenergic humoral stimuli on visceral vessels are very limited. References in the literature deal mainly with the study of the combined action of vasoactive substances on vascular strips [1] or on the parameters of the systemic hemodynamics, more especially the blood pressure [7]. Because of the specificity of the techniques and objects used in these investigations, their results cannot provide a basis on which to evaluate the cooperative action of adrenergic stimuli on visceral vessels.

The aim of this investigation was to compare responses of the arteries and veins supplying the gastrocnemius muscle to separate presentation of increasing doses of adrenalin and noradrenalin (giving rise to vascular effects of similar magnitude) with the analogous responses to the combined action of these same substances.

## EXPERIMENTAL METHOD

Experiments were carried out on cats (12 animals of both sexes weighing 3-5 kg), anesthetized with urethane (1.1 g/kg), and receiving heparin (2000 U/kg). The vascular bed of the hemodynamically and neuronally isolated gastrocnemius muscle (leg preparation [2]) was perfused through the popliteal artery with the animal's own blood by means of a constant delivery pump (made at the Experimental Production Workshop, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR).

Adrenalin hydrochloride and noradrenalin hydrotartrate solutions were injected into the afferent artery of the leg preparation separately and in combinations of increasing doses: 2:2, 4:4, 8:8, and 12:12 $\mu$g (in 0.1 ml of 6% dextran solution). Changes in resistance of the arteries of the muscle in response to vasoactive stimuli were determined by recording shifts of perfusion pressure (the resistography method [6]) and corresponding changes in the veins were determined by a specially developed method [3], enabling changes in the venous perfusion pressure to be recorded, and changes in resistance in the deep veins of the muscle could be estimated from them.

Measurements of perfusion pressure in the arterial and venous portions of the vascular bed of the muscle were made by electromanomebers with mechanotron tranducers (made by the Experimental Production Workshop, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR), and the temperature of blood entering the muscle preparation was maintained at 37 $\pm$ 0.5°C by means of a thermostat (U-1, East Germany) and recorded by the tranducer of a TPÉM-1 electrothermometer; the parameters were recorded on an N-327-5 automatic writer.

The numerical results were subjected to statistical analysis by Student's $t$ test.

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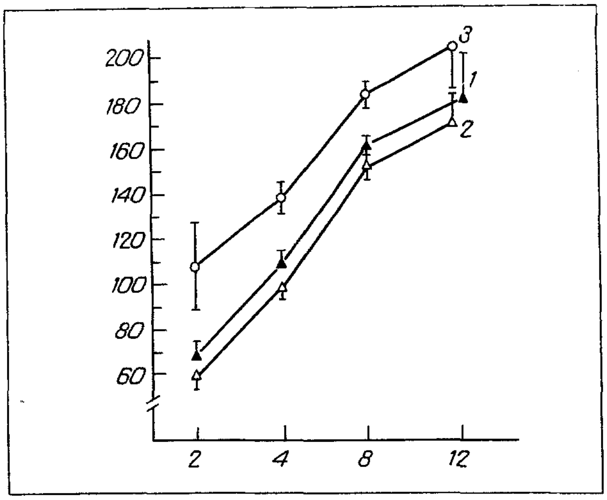


Fig. 1. Mean values of increase in arterial perfusion pressure in response to separate and combined action of adrenalin and noradrenalin. Abscissa, doses of adrenalin and noradrenalin (in $\mu$g); ordinate, changes in resistance (in mm Hg). 1) Magnitude of vascular responses to adrenalin, 2) increase in perfusion pressure in response to noradrenalin, 3) values of constrictor vascular responses to combined action of catecholamines in doses of 2, 4, 8, and 12 $\mu$g of each. Vertical lines indicate mean error of the means ($\pm m_{\bar{x}}$).

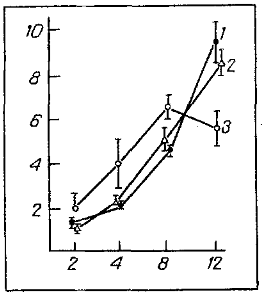


Fig. 2. Increase in venous perfusion pressure in response to separate and combined action of adrenalin and noradrenalin. Legend as to Fig. 1.

## EXPERIMENTAL RESULTS

The experiments showed that adrenalin and noradrenalin, in the doses used, caused the resistance of the arteries and veins of the skeletal muscle to increase, and this was reflected in a dose-dependent increase in arterial and venous perfusion pressure (Fig. 1, 2). The magnitude of the constrictor responses of the arteries to separate injection of equal doses of these drugs into the main artery of the muscle preparation did not differ statistically significantly ($p > 0.05$; Fig. 1). The data in Fig. 1 show that the constrictor responses of the arteries of the muscle to the separate action of catecholamines were less in absolute terms than the analogous responses obtained to the combined use' of the same humoral stimuli. This difference was seen most clearly in response to the combined action of the two vasoactive drugs in doses of 4:4 and 8:8 $\mu$g ($p < 0.05$; Fig. 1). The increase in arterial perfusion pressure under these circumstances did not exceed 160-165 mm Hg. In cases when the increase in arterial perfusion pressure in response to the separate action of these humoral agents (in doses of 12 $\mu$g each) was significantly above 160 mm Hg, whereas the combined administration of the drugs led to an increase of perfusion pressure by an amount virtually equal ($p > 0.05$) to the increase in the parameter of the resistive function of the arteries in response to the separate action of the drugs on the vessel (Fig. 1). Consequently, there was an increase in the degree of constriction of the arteries to the combined action of the adrenergic stimuli compared with the separate action of the catecholamines, inducing equal constrictor effects, if the latter did not exceed a certain value. In this investigation, in which perfusion of the visceral vascular bed was used under constant blood volume codditions, this increase of perfusion pressure amounted to 160-165 mm Hg. Incidentally, in this investigation complete summation (arithmetic sum) of the values of the separate adrenergic effect was not found in response to the combined use of the catecholamines (whatever the doses of the substances used separately or whatever the intensity of the responses to single stimuli respectively).

The resistance of the veins of the muscle to the blood flow also was increased in response to the separate action of the same doses of catecholamines, as shown by an increase in the venous perfusion pressure (Fig. 2). Equal doses of the two catecholamines, acting separately on the vessel (regardless of their magnitude), caused virtually equal constrictor responses of the deep veins of the gastrocnemius muscle (Fig. 2). The combined action of these humoral stimuli in doses of 2:2, 4:4, and 8:8 μg, led to an increase in venous resistance (as judged by absolute values of changes in venous perfusion pressure) compared with their separate administration in the same doses. However, differences between the values compared were not statistically significant ($p > 0.05$; Fig. 2).

It can be concluded from the data described above that investigation of the combined action of catecholamines on the veins of a muscle (just as also on its arteries) did not reveal summation of the vascular effect observed in response to the separate action of adrenalin and noradrenalin. Moreover, the responses of the veins to the separate and combined action of the drugs used were virtually equal in magnitude to those obtained with the use of doses of 2:2, 4:4, and 8:8 μg. This fact distinguishes the response of the veins to the combined action of adrenergic stimuli, for in the analogous situation, i.e., when doses of 4:4 and 8:8 μg (adrenalin: noradrenalin) were used the responses of the arteries to separate and combined action of catecholamines differed significantly.

The main distinguishing feature of the veins was that in response to supramaximal stimuli (12:12 μg of adrenalin:noradrenalin respectively) the combined adrenergic responses were statistically significantly ($p < 0.05$) less than responses of the veins of the muscle obtained to the separate action of adrenalin and noradrenalin in the same doses (Fig. 2). The sharp decrease in the intensity of the responses of the veins of the muscle to a combination of adrenergic stimuli compared with the magnitudes of the vascular responses of the intramuscular veins to the separate action of the catecholamines (Fig. 2) suggests that their adrenergic regulation differs significantly from that of the arteries of the skeletal muscles. The arterial section of the vascular bed of the skeletal muscle proved to be more resistant in response to the double adrenergic stimulus when a combination of supramaximal doses of catecholamines was used. The results are evidence of distinguishing features of responses of the veins by comparison with the arteries to the combined action of adrenalin and noradrenalin. This conclusion is confirmed by data in the literature [5], indicating relatively greater lability of the veins in the presence of different types of stimuli (neurogenic and humoral), and even the possibility of development of qualitatively different adrenergic responses of the visceral veins compared with changes in the combined lumen of the arterial bed. In this context the investigation constitutes yet another fact confirming the views expressed in the literature [5] on features distinguishing adrenergic regulation of the visceral veins compared with arteries.

The facts presented in this paper on the combined action of catecholamines on arteries and veins of skeletal muscle thus demonstrate the specific sensitivity of functionally different portions of. the visceral vascular bed to the combined action of maximal humoral stimuli of adrenergic nature on the myocytes of blood vessels. It can accordingly be concluded that veins of the skeletal musculature are more resistant to combined application of adrenergic stimuli than arteries.

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