MUSCLE PROTEINS OF BLOOD VESSEL WALLS, AND CHANGES IN THEIR COMPOSITION DURING HYPERTENSIVE DISEASE

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When one analyzes the factors producing a rise in arterial pressure during hypertensive disease, most clinicians and pathologists start from the assumption that changes in the basic level of tension and in the strength of contraction of vessel musculature are chiefly or even exclusively determined by causes external to the vessel wall [10, 11].

In its most general and categorical form, this point of view has been expressed by A. L. Myasnikov [12]: "Rise in blood pressure during hypertensive disease depends upon various factors lying outside the sphere of the vessels."

However, a number of clinical investigators adhere to other views concerning the origin of vessel tension. Thus, V. A. Val'dman [1, 2], while accepting the important role of neuropsychic, hormonal, and other influences on vessel tonus, nevertheless views arterial hypertensive disease as a disease of the vascular system. In this formulation of the nature of the disease, great significance is attached to changes in the vessels themselves during the development of arterial hypertension.

One might suppose that since contraction of vessels is directly connected with the musculature of vessel walls, a comparative study of the fractional composition of vascular muscle proteins under normal conditions and during hypertensive disease could shed some light on this question.

As is well known, the more pronounced is a muscle's ability to contract tetanically and tonically, the higher is its percentage content of proteins of the actomyosin complex.

Unlike the contractile function, the holding function of smooth musculature (unfatiguing resistance to stretch), as shown by numerous investigations of I. I. Ivanov and co-workers [3-7], depends upon proteins of a type distinct from actomyosin. The view formulated by I. I. Ivanov in 1948 concerning the existence of two different substrates of muscular activity – contraction and tonus, and the distinctness of the substrate of unfatiguing tonus from actomyosin – has received further experimental support in recent years from the work of other authors [13-16].

Therefore, the aim of the present study was to investigate the fractional composition of vascular muscle proteins under normal conditions and during hypertensive disease.

EXPERIMENTAL METHODS

For this study we used the renal arteries and their branches, and also muscular arteries of other human viscera.

The vessels were removed from a corpse at the time of post-mortem on the day of death or on the following day, but usually no later than twenty-four hours after death.

From our results and also the results of B. S. Kasavina and Yu. M. Torchinskii [9], the fractional composition of muscle proteins undergoes no change of any significance for twenty-four hours and even for longer periods of time under conditions when the corpse is kept at low temperatures (0-4°). This assumption also receives indirect support from the evidence of V. A. Val'dman and A. A. Nechaev [1], obtained in the laboratory of N. P. Kravkov; these authors found no change in the vascular reactions of isolated organs for many hours after death.

Normal human vessels were obtained from the bodies of people who were not afflicted with diseases of the circulatory system and had died as the results of accidental causes or other reasons.

Corresponding vessels were taken from bodies of people who were afflicted with a severe chronic form of arterial hypertension.

Pieces of vessels were freed from external and internal membranes. Thoroughness of the dissection, as a result of which the middle, muscular strip was isolated, was checked by microscopic observation of the resulting material in a number of cases, especially in the first period of the work.

Tissue of the vascular muscle layer was cut up with sharp scissors and then ground with finely-divided quartz. The resulting homogenate was fractionated by the method described in the work of I. I. Ivanov and co-workers [4]. Total tissue nitrogen, nonprotein nitrogen, and protein nitrogen in all fractions were determined by a micro-Kjeldahl method. The results given below were typical of each experimental series.

EXPERIMENTAL RESULTS

In the first experimental series, we studied the fractional composition of the muscular layer from normal vessel walls.

Vessel musculature differs somewhat in its protein composition from other types of smooth muscle (for instance, stomach or uterus). However, it should be noted that the object of our study was not vascular muscle tissue but the muscular layer as a definite anatomical structure. As is well known, these concepts are not identical, since the middle layer of vessels, apart from the muscular elements, contains a certain and sometimes a very considerable quantity of elastic fibers.

The high content of stromal proteins which we found in vessel wall musculature is closely connected with these details of its histological structure. Nevertheless, this fact could not have significant influence on the quantitative ratios between different fractions of muscle proteins, and in particular, between fractions of myofibrillar proteins.

Results concerning the protein composition of vessel wall muscle are set out in the table.

Besides the high percentage content of stromal proteins, one should note details of the composition of myofibrillar proteins.

Myofibrillar proteins were extracted by Weber's solution from a homogenate of muscle tissue after preliminary exhaustive extraction of sarcoplasmic proteins, and after dialysis against distilled water or very dilute solutions, the myofibrillar proteins could be separated into two fractions: 1) proteins soluble in salt solutions with high ionic strength; under these conditions this fraction precipitated out (the AM fraction); 2) proteins soluble in salt solutions of low ionic strength and found in the supernatant fluid (fraction T, according to the nomenclature of I. I. Ivanov and co-workers [4]).

In detecting connections between protein composition of muscle and details of its function, the greatest interest attaches to results concerning the fractional composition of myofibrillar proteins.

The AM/T ratio in muscle of different types varies noticeably. Skeletal muscle, which is suited to rapid phasic contraction, has a relatively high content of proteins of the AM fraction. On the other hand, tonic smooth muscle has a relatively higher content of myofibrillar proteins soluble at low ionic strength [4].

However, it should be observed that the composition of myofibrillar proteins (fractions AM and T) in different types of muscle is not the same. Thus, if fraction AM in skeletal muscles is almost exclusively actomyosin, fraction AM extracted under analogous conditions from smooth muscle contains, in addition to actomyosin, significant quantities of nucleoproteins and possibly other proteins. The composition of fraction T is also not the same in muscles of different types.

Fractional Composition of Proteins of Vessel Wall Muscle (in percentages of total nitrogen due to nitrogen in the fraction)

Residual nitrogen	Sarcoplasmic proteins soluble in salt solutions with low ionic strength	Myofibrillar proteins				Stromal proteins
		total	soluble in salt solutions with high ionic strength (AM)	soluble in salt solutions with low ionic strength (T)	AM/T	
Vessels of a healthy man						
1,95	10,81	9,94	1,9	7,87	1:4	75,7
Vessels of cattle						
1,49	18,45	9,17	1,35	7,41	1:5	71,42
Vessels of a man suffering from hypertension						
2,79	13,05	9,13	5,18	3,52	1,5:1	73,88

Vessel muscle tissue has a very high relative content of proteins of fraction T. The AM/T ratio in such muscle is approximately 1 :4, with small variations in individual cases.

We may recall that this quantity is 1 :1.5 for stomach muscle of the rabbit and 1 :3 for myometrium [4].

This property of the composition of myofibrillar proteins is evidently closely connected with the ability of vascular muscle to maintain prolonged, unfatigued tonic tension.

It is interesting to observe that the protein composition and, in particular, composition of myofibrillar proteins of the muscular wall of homologous vessels in man and animals (cattle) are rather similar (see the table).

Vessels of animals have a significantly higher relative content of sarcoplasmic proteins.

The following series of experiments was devoted to studying the fractional composition of proteins of vessel wall muscle during hypertensive disease (see the table).

When one compares the results in the table, it is evident that the percentage content of myofibrillar proteins in vessels of patients with hypertension is approximately the same as in normal vessels, but the AM/T ratio in these vessels is completely different. Whereas in normal vessels the predominant part of the myofibrillar proteins consists of proteins of fraction T, while fraction AM, containing the contractile proteins of muscle, represents about 25%, in patients with hypertension the vessel proteins soluble in salt solutions with high ionic strength (fraction AM) represent the greater part of the total myofibrillar proteins.

Patients with hypertension have somewhat higher relative content of residual nitrogen and sarcoplasmic proteins in their vessels. The quantity of stromal proteins under normal and pathological conditions is approximately the same. The absolute content of total nitrogen and the nitrogen of the fractions, calculated per unit weight of dry tissue, shows some scatter in different experiments, since tissue dried out during the dissection to separate the muscular layer of vessels.

From the point of view of greatest interest to us, the results concerning differences in fractional composition of myofibrillar proteins are of the highest significance.

In a study of changes in the composition of proteins of skeletal muscle during paralysis arising from poliomyelitis, I. I. Ivanov, V. A. Yur'ev, and others [8] showed that biochemical changes in contractile proteins provide an objective and highly sensitive index, which permits one to estimate the functional state of the muscles. The observed changes in fractional composition of vessel myofibrillar proteins during hypertensive disease are exactly the reverse of those observed during impairment of motor activity of skeletal muscles due to the paralytic form of poliomyelitis, denervation of muscles, cutting of the tendons, etc.

In evaluating these results, one should, of course, bear in mind that the nature of the contractile reaction in muscles may be influenced not only by the composition of myofibrillar proteins but also by various other factors; but one, nevertheless, gains the impression that hypertensive disease involves not only hypertrophy of cardiac muscle but also an increased contractile ability of vessel wall musculature, and conditions are created for independent hyperfunction of contractile elements.

This impression is confirmed by the results of other authors.

In particular, the ATP-ase activity of myofibrillar proteins extracted from diseased vessels is much higher than in normal vessels, and this also provides evidence for a higher content of the primary proteins of the actomyosin complex.

At present we are carrying out a more detailed study of the fractional composition and enzymatic properties of myofibrillar proteins from normal and pathological vessels.

These changes in the protein composition of vessel musculature can doubtless play an important role in the origin of peculiar vessel reactions, not only to pathological but also to the usual physiological stimulants.

It is quite probable that changes in fractional composition of vessel muscle proteins can take place in other forms of persistent vessel dysfunction as well.

SUMMARY

Fractional composition of protein in the muscular layer of arterial wall was studied in persons without any cardiovascular affection, and in the patients suffering from a severe form of arterial hypertension. There was a relative increase in the content of myofibrillar proteins soluble in salt media of high ionic concentration in the patients with prolonged and severe arterial hypertension. The relationship existing between the shifts in the protein composition of the vascular musculature and the changes in the contractile function of the vessels is discussed.

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