PROTEINS OF CARDIAC AND SKELETAL MUSCLES IN EXPERIMENTAL MYOCARDIAL INFARCTION

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In experimental myocardial infarction the total protein content in the intact and damaged regions of the heart and in the skeletal muscles of dogs is close to normal, but changes take place in their fractional composition. The level of soluble (sarcoplasmic and myofibrillary) proteins is lowered, especially that of actomyosin, while the content of stromal proteins, including collagen, increases. In the zone of the infarct these changes are severe and irreversible, while in the intact region of the heart and the skeletal muscles they disappear after 1-6 months.

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Existing information [1, 4, 5-7] concerning myocardial proteins in cases of infarction is inadequate. The proteins of intact tissues in myocardial infarction have remained almost completely unstudied, although the possibility of disturbances of their metabolism in this condition cannot be ruled out [3, 8]. The present investigation was therefore carried out to study this problem.

EXPERIMENTAL METHOD

After high ligation of the descending branch of the left coronary artery in 70 dogs, sacrificed in groups of 9-14 animals at intervals of 1, 3, 5, 10, and 30 days and 6 months after the operation, the region of the infarct, the left ventricle outside the area supplied by the ligated blood vessel (intact zone of myocardium) and the femoral muscles were investigated. Tissues from 25 apparently healthy animals were used as the control. Total protein was determined by the Kjeldahl's method, the protein content of the sarcoplasm, myofibrils, stroma, and actomyosin by Helander's method [10], collagen by the method of Spenser and coworkers [11], and ATPase activity by Zubenko's method [2]. The results of the analyses were calculated per moist weight of tissues, for no significant change occurred in their water content.

EXPERIMENTAL RESULTS

Throughout the investigation, including the acute stage of the process, the total content of myocardial proteins remained close to normal, amounting to 90-93% of the initial level in the region of the infarct and 95-97% in the intact zone of the myocardium. This was probably due to inhibition of proteases and, perhaps, to the later periods of activation of protein synthesis [9].

In the zone of necrosis considerable changes took place in the composition of the protein fractions, with an increase in the insoluble and decrease in the soluble fractions, i.e., myofibrillary and sarcoplasmic proteins (Table 1). The decrease in the latter by 30-40% compared with normal in the acute stage of the condition ($P < 0.05$) was evidently irreversible in character, for 6 months later the damaged tissue contained only about two-thirds of the initial content of sarcoplasmic proteins. Similar changes affected the content of myofibrillary proteins, the decrease in this fraction being determined mainly by loss of actomyosin (Table 1). It is interesting to note that the ATPase activity of the myocardium, normally almost entirely associated with actomyosin, fell during infarction by a lesser degree than the level of this protein, possibly on account of activation of water-soluble ATPase.

The decrease in content of soluble proteins in the region of the myocardial infarct was accompanied by an increase in the content of insoluble fractions, reaching a maximum after 5 days, when it amounted to 20-25% of normal ($P < 0.02$-0.05), from the 10th day until the end of the period of observation. Between 1

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TABLE 1. Proteins of Region of Myocardial Infarct (M ± m)

Duration of infarct (in days)	No. of experiments	Total protein content (in %)	Proteins (in %)			Collagen (in %)	Actomyosin (in %)	ATPase activity (mg P/g tissue)
			Sarcoplasmic	Myofibrillary	Stromal			
Control	25	16,36±0,36	4,68±0,14	4,40±0,19	7,28±0,37	2,18±0,11	3,23±0,14	9,55±0,43
1	14	14,81±0,26	3,31±0,28	3,92±0,31	7,49±0,51	3,12±0,21	2,30±0,33	8,53±0,97
3	11	15,20±0,36	2,89±0,09	2,94±0,35	9,37±0,84	3,12±0,28	1,45±0,22	6,73±0,86
5	9	14,80±0,62	2,79±0,28	1,96±0,23	10,05±0,61	3,07±0,27	0,98±0,15	7,42±1,53
10	14	14,69±0,37	3,02±0,19	2,74±0,38	8,93±0,47	3,21±0,15	1,47±0.13	8,48±1,16
30	13	14,82±0,57	2,84±0,24	3,29±0,36	8,69±0,60	4,12±0,33	1,40± 13	7,42±0,61
6 months	9	15,09±0,54	3,19±0,21	3,11±0,39	8,79±0,71	4,62±0,44	2,27±0,25	8,95±0,46

TABLE 2. Proteins of Intact Zone of Heart in Experimental Myocardial Infarction (M ± m)

Duration of infarct (in days)	No. of experiments	Total protein content (in %)	Proteins (in %)			Collagen (in %)	Actomyosin (in %)	ATPase activity (mg P/g tissue)
			Sarcoplasmic	Myofibrillary	Stromal			
Control	25	16,36±0,36	4,68±0,14	4,40±0,19	7,28±0,37	2,18±0,11	3,23±0,14	9,55±0,43
1	14	15,66±0,23	3,91±0,10	4,48±0,28	7,29±0,43	2,11±0,20	3,13±0,33	9,52±0,87
3	11	15,92±0,31	3,52±0,34	4,24±0,23	8,16±0,54	2,26±0,18	2,52±0,20	9,25±0,59
5	9	15,14±0,50	3,20±0,25	3,08±0,25	8,86±0,49	2,27±0,26	2,03±0,25	12,79±2,46
10	14	15,38±0,28	3,54±0,22	4,11±0,28	7,70±0,58	2,31±0,16	2,85±0,22	10,31±1,15
30	13	15,63±0,39	3,35±0,22	4,11±0,31	8,17±0,32	2,33±0,20	2,47±0,22	9,43±0,45
6 months	9	15,79±0,38	4,09±0,21	3,70±0,30	8,00±0,44	2,52±0,21	2,64±0,31	9,71±0,83

and 6 months after creation of the myocardial infarct, when gross scar changes had developed in the region supplied by the ligated artery, the increase in stromal proteins was due to accumulation of collagen, the content of which was twice normal in this region (Table 1). In the early periods, together with a moderate increase in collagen, a decrease in solubility of some proteins readily extractable under normal conditions probably occurred.

Biochemical changes similar in character to those in the region of the infarct, but less severe (Table 2), also took place in the intact region of the heart of the experimental animals. A moderate increase in the content of stromal proteins occurred, without significant changes in the collagen content, but accompanied by a decrease in the content of sarcoplasmic and myofibrillary proteins and of actomyosin. These changes mainly disappeared one month after the beginning of the experiment, and if they continued longer, they were of slight severity (± 10-15% of the initial values).

Changes in the composition of the protein fractions in myocardial infarction were also observed in the skeletal muscles of the experimental animals. From the 5th to the 30th days of the experiment, the content of stromal proteins was increased by 15-20%, this increase being due only partially to an increase in collagen, while the level of sarcoplasmic and myofibrillary proteins fell by 15-20%.

Of the soluble skeletal muscle proteins, actomyosin underwent the most prolonged change, for its level fell progressively after the first day to reach 69% of normal after one month ($P < 0.02$), and it had not completely recovered even 6 months after the onset of myocardial infarction.

Although the changes described are small, they could be responsible for the familiar functional impairment of the skeletal muscles in myocardial infarction. In addition, because of the considerable total mass of the skeletal muscles, even slight changes in their chemical properties are of considerable importance to the organism as a whole.

In experimental myocardial infarction the composition of the protein fractions thus undergoes similar changes in the damaged and intact regions of the heart and in the skeletal muscles. These changes consist of a decrease in the level of soluble, functionally active sarcoplasmic and myofibrillary proteins, especially actomyosin, and an equivalent increase in the content of insoluble proteins, including collagen. These changes are slight in extent in the zone of the infarct, and are evidently irreversible, while in the intact region of the heart and the skeletal muscles they are moderate in degree and gradually disappear.

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