ELECTROCARDIOGRAPHIC CHANGEG IN RABBITS WITH EXPERIMENTAL ATHEROSCLEROSIS TREATED WITH PROTEIN HYDROLYSATE "HYDROPROT"

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The problem of atherosclerosis is still unclarified both in terms of etiological and pathogenetical aspects (Vihert, 1974; Chazov, 1964; Haut, More, 1972).

The functional state of the cardiovascular system in a complex of investigations is comparatively less studied insofar as experimental research in atherosclerosis and its pathogenesis is concerned, although literature data are available outlining important details of the blood circulation system (Gorev et al, 1972).

Object of the present investigation is to establish ECG changes in rabbits fed cholesterol and treated with protein hydrolysate "Hydroprot".

Materials and methods

Eighty male rabbits of the Chinchilla line with average weight 2.5 kg were used in the experiment. The animals were given cholesterol 0.2 g/kg weight together with the food. They were divided up in two groups. The rabbits from the first group (controls) were treated daily with 5 ml/kg weight physiological solution subcutaneously, while those of the second group — with the same amount protein hydrolysate.

ECG recordings were accomplished by using the method of Kemileva et al (1965) intended for rats, as modified by us for rabbits. The animals were fixed in pronation, and no narcosis was applied. ECG recording was done during a relaxing period without a preliminary physical loading. Some of the rabbits in either group were fed cholesterol for 45 days, while the rest were treated over a 90-day period. ECG recordings were done before the beginning of cholesterol feeding, and after the end of the experiment.

The average results of 15—20 complexes were taken to be the base for data processing. The width of the intervals was determined by the shortest relevant interval of the three standard ECG limb leads, recorded in a three-channel physioscript "Schwarzer" at band speed 50 and 100 mm/sec, and amplification 1 cm/1 mV. The mean Q- and S-wave was determined by the number of waves registered in the relevant lead only. Statistical elaboration of data was done using the method of non-parametric analysis (sign criterion and T-criterion).

Results and discussion

Rabbits fed cholesterol and subjected to treatment with physiological solution for 45 days (12 animals) show definite changes in the electrocardiogram compared to ECG data before the experiment. The P-waves show a de-

crease, with the difference being statistically reliable for the third lead only ($p<0.01$). The PQ-interval is elongated (from 0.063 sec before feeding to 0.068 sec after that; $p=0.05$). The QRS complex extends from 0.031 sec to 0.034 sec ($p=0.05$). The R-wave height decreases for the three standard leads, but only R_3 decreases reliably ($p=0.05$). These R-changes are recorded in 91.7 per cent of the animals. The S-wave depth also decreases for all three leads, but only lead II is reliable ($p=0.05$). The QT-interval is elongated ($p=0.05$). The T-wave height decreases unreliably for the first and third lead, and increases for the second lead. The heart rate is slightly delayed.

The P-wave decreases for the first ($p<0.05$) and second lead, and slightly increases for the third lead whenever the animals (22 rabbits) are subjected to treatment with protein hydrolysate simultaneously with cholesterol feeding over a period of 45 days. The PQ-interval slightly elongates from 0.062 sec to 0.064 sec ($p>0.05$). The QRS-complex extends, but not as much as that of the animals treated with physiological saline (from 0.030 sec to 0.032 sec; $p<0.01$). The R-wave height decreases for the second and third lead ($p<0.01$) in 81.8 per cent and 77.3 per cent of rabbits respectively, and increases for the first lead in 51.1 per cent. The S-wave depth decreases. The QT-interval elongates although not to the extent of the rabbits treated with physiological solution. The T-wave height increases reliably for the second ($p<0.01$) and third ($p<0.01$) lead. No changes in heart rate are registered. Splitting of the QRS-complex is noted in one animal (Table 1).

Animals fed choloesterol and treated with physiological solution for a longer period (90 days) display rather significant ECG changes compared to those in the group treated for 45 days. In 21 animals a decrease in P-wave is established in all three standard leads (reliably for the second and third lead; $p=0.01$).

Elongation of the PQ-interval is rather substantial (from 0.060 sec before feeding to 0.069 sec after that; $p<0.05$) in 71.4 per cent of the animals, whereas this percentage in the other group (45 days) is only 58.3 per cent. The QRS-complex similarly shows a more substantial extending (from 0.031 sec to 0.036 sec; $p<0.05$), and once again in a greater mumber of animals (61.9 per cent relative to 41.6 per cent). R-wave height decreases reliably for the second and third lead only ($p=0.01$ and $p<0.05$). S-wave depth decreases reliably for the first and second lead ($p<0.05$). QT-interval slightly elongates. The T-wave height decreases for the three leads, with most significant difference being established for T_3: from 0.362 mV prior to feeding to 0.162 mV after that ($p=0.05$). The heart rate shows a slight acceleration. In one animal very low complexes are established, and in another one — a QS-wave tendency for leads I and II.

Rabbits treated with protein hydrolysate and cholesterol for 90 days (25 animals) display less pronounced ECG changes, as compared to those treated with physiological solution and cholesterol for the same period of time. A P-wave decrease is noted for the first lead only ($p=0.05$). The third lead shows a tendency for the P-wave to increase. PQ-interval elongates rather slightly: from 0.062 sec to 0.068 sec ($p<0.01$) in 76 per cent of the animals. The QRS-complex is insignificantly extended, and in a smaller number of rabbits (56 per cent) by comparison with those treated with physiological solution and cholesterol. R-wave height considerably decreases for the second and third lead ($p=0.05$ and $p<0.01$ resp.), whereas for the first lead

Table 1

ECG Changes — Second Standard Limb Lead in Rabbits Fed Cholesterol for 45 Days: A — Injected with Physiological Solution, and B — Injected with Protein Hydrolysate

Height of P wave		p	PQ interval		p	Width of QRS complex		p	Depth of Q wave		p	Height of R wave		p
Before	After		Before	After		Before	After		Before	After		Before	After	
0.1883	0.1825 > 0.95		0.063	0.063 = 0.05		0.031	0.034 = 9.05		—	0.025/2 —		0.5717	0.4892 > 0.05	
Depth of S wave		p	QT interval		p	Height of S wave		p	Heart rate		p			
Before	After	p	Before	After		Before	After		Before	After				
0.6258	0.3983 = 0.05		0.133	0.140 = 0.05		0.1483	0.1817 > 0.05		291	285 > 0.05				

Height of P wave		p	PQ interval		p	Width of QRS complex		p	Depth of Q wave		p	Height of R wave		p
Before	After		Before	After		Before	After		Before	After		Before	After	
0.1636	0.1482 > 0.05		0.062	0.064 > 0.05		0.030	0.032 < 0.01		0.02/1	0.04/1 —		0.5445	0.3550 < 0.01	
Depth of S wave		p	QT interval		p	Height of T wave		p	Heart rate		p			
Before	After		Before	After		Before	After		Before	After				
0.4800	0.3277 > 0.05		0.133	0.136 > 0.05		0.1064	0.1695 < 0.01		293	292 > 0.05				

NOTE: (1) The heights and depths of waves are submitted in millivolts, (2) the intervals and widths of waves are submitted in seconds.

Table 2

ECG Changes — Second Standard Limb Lead in Rabbits Fed Cholesterol for 90 Days: A — Injected Physiological Solution, and B — Injected with Protein Hydrolysate

Height of P wave		p	PQ interval		p	Width of QRS complex		p	Depth of Q wave		p	Height of R wave		p
Before	After		Before	After		Before	After		Before	After		Before	After	
0·1486	0·1338=0.01		0.060	0.069<0.05		0.031	0.036<0.05		0.023/3/	0.028/6/—		0.4986	0.3557=0.01	
Depth of S wave		p	QT interval		p	Height of T wave		p	Heart rate		p			
Before	After		Before	After		Before	After		Before	After				
0.3129	0.2510<0.05		0.136	0.138>0.05		0.1090	0.1076>0.05		286	289>0.05				

Height of P wave		p	PQ interval		p	Width of QRS complex		q	Depth of Q wave		p	Height of R wave		p
Before	After		Before	After		Before	After		Before	After		Before	After	
0.1508	0.1544>0.05		0.062	0.068<0.01		0.032	0.035>0.05		—	0.02/3/ —		0.4896	0.3712=0.05	
Depth of S wave		p	QT interval		p	Height of T wave		p	Heart rate		p			
Before	After		Before	After		Before	After		Before	After				
0.3404	0.3192>0.05		0.137	0.136>0.05		0.0928	0.1264>0.05		292	294>0.05				

NOTE: (1) The heights and depths of waves are submitted in millivolts, (2) the intervals and widths of waves are submitted in seconds.

it increases ($p=0.01$). S-wave depth increases for the first, and decreases for the second and third lead. The QT-interval shows no variations worthy of notice. T-wave height tends to an increase for the second and third lead, and to a decrease for the first lead. The heart rate is slightly accelerated. The QRS-complex extends rather considerably in one of the animals, where an elevation of ST is also observed (Table 2).

Data submitted by various authors attest to non-uniform changes in the ECG elements of rabbits and other laboratory animals with experimentally induced atherosclerosis. Most of the opinions set forth point to slight or unclearly outlined changes. According to Schwatzabaya, Bostnov (1964) the ECG changes in rabbits are not significant, being connected mainly to changes in the P-wave without noteworthy variations of the configuration of the complexes. Tyavokin (1966) established rather manifested ECG changes after combining cholesterol feeding with immobilization of the rabbits. Gorev et al (1972) are absolutely right in emphasizing that detailed investigation of the changes in the functional state of the heart could be done in conditions of different effects on the animal organism (physical loading, hypoxia, stimulation of the central nervous system etc).

In the experimental setup described, the ECG changes in most of the rabbits fed cholesterol and injected with physiological solution might be linked to dystrophic changes in the myocardium. The histomorphological investigation of the myocardium in experimental atherosclerosis in guinea pigs reveals subendocardial small-area focal necrosis of the myofibrils (Maleva, Demireva, 1975). Cholesterol feeding and the development of experimental atherosclerosis lead to microcirculation disorders (Shomamoto, 1968; Balta, Mandache, 1974). The above opinion is corroborated also by the results of Demireva and Popdimitrov (1975[a]), obtained in the study of animals with experimental atherosclerosis using Rh^{86}.

Our data concerning changes in the interval and width of the QRS complex are somewhat different from those reported by Gorev et al (1972). In young rabbits aged 8—14 months, the cited authors observed changes in the wave heights only, with no changes whatsoever in the intervals. The only certain fact is that parallel to increasing the term of cholesterol feeding, the ECG changes become more clear cut.

It is obvious that our results point to slighter changes in rabbits fed cholesterol, and treated with protein hydrolysate. The assumption is warranted that hydrolysate improves myocardial trophism against the background of microcirculation enhancement (Demireva, Popdimitrov, 1975[b]). The latter, concept is supported by the experimental data of Praskjavitchus et al (1969) who were successful in demonstrating an increase in adenine-nucleotides (AMP, ADP and ATP) within the myocardium, following protein hydrolysate treatment of rabbits. Simkina (cited by Filatov and Tchapligina, 1975) also established a rise of ATP values upon protein hydrolysate administration. The elevation of these macroergic compounds within the myocardium involves meeting of its energy demands, and build-up of a sufficient quantity of adenosine, which has an essential bearing on blood flow in the coronary vessels (Kaverina, 1973).

In conclusion, we feel justified to recommend the application of protein hydrolysate in the complex treatment of atherosclerosis, especially when marked changes in the myocardium are present.

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ЭЛЕКТРОКАРДИОГРАФИЧЕСКИЕ ИЗМЕНЕНИЯ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ АТЕРОСКЛЕРОЗЕ У КРОЛИКОВ, ТРЕТИРОВАННЫХ БЕЛКОВЫМ ГИДРОЛИЗАТОМ «ХИДРОПРОТ»

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РЕЗЮМЕ

Изучены электрокардиографические изменения у кроликов с экспериментальным атеросклерозом. Животные получали обычную вивариумную пищу и в течение 45 или 90 дней к ней добавлялся холестерол — по 0,2 г/кг. Кролики разделены на две группы. Первой группе (контрольные животные) в течение всего срока питания вводили ежедневно подкожно по 5 мл/кг физиологического раствора, а второй (опытные животные) то-же самое количество белкового гидролизата «Хидропрот».

ЭКГ-записи осуществлялись в состоянии покоя, без предварительной физической нагрузки животных. Они проведены перед началом скармливания холестерола и на 45-ый или 90-ый день после начала опыта.

Обнаружено снижение зубцов P, R и S и нарушения проведения (удлинение интервала PQ и расширение комплекса QRS). Эти изменения лучше выражены у кроликов с большим сроком питания холестеролом. Наблюдаемые изменения выявлены слабее у животных, третированных белковым гидролизатом.