EFFECT OF ANABOLIC STEROIDS ON THE DIAPHRAGM OF RABBITS WITH CHOLESTEROL ATHEROSCLEROSIS

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Anabolic steroids (AS) possess myotrophic activity, i.e., they promote an increase in mass and development of striated muscles. After castration, atrophic processes are observed in the striated muscles, but after administration of androgens and AS these are replaced by hypertrophy and repair processes [3]. Meanwhile, administration of testosterone to castrated rats has no effect on the weight of the diaphragm or incorporation of [^{14}C]-glycine [5, 6].

For the reasons given above it was decided to study the effect of AS on the diaphragm of intact rabbits and of animals with cholesterol atherosclerosis.

EXPERIMENTAL METHOD

Forty apparently healthy male chinchilla rabbits weighing 2.6 kg, kept under identical conditions, were used. The animals were under observation for 4 months. The control consisted of 20 rabbits, of which 10 received Retabolyl* in a dose of 25 mg at intervals of 10 days, six injections per course. Cholesterol atherosclerosis was induced in 20 rabbits by Anichkov's classical method; 10 of these animals were given Retabolyl injections after the development of atherosclerosis (at the same times and in the same doses as in the control). The rabbits were killed after the end of the observations. The native weight of the diaphragm was determined, the D/M ratio (the ratio of the weight of the diaphragm to the body weight) was calculated, and a histological and histochemical study made of the muscle tissue of the diaphragm.

EXPERIMENTAL RESULTS

In rabbits of the control group the weight of the diaphragm was 3.99 ± 0.22 g and the D/M ratio was $1.5 \times 10^{-3} \pm 0.7 \times 10^{-4}$. The tissue of the diaphragm consisted histologically of muscle fibers with a normal structure, rich in RNA, and with a well-marked fibrillary composition. Thin connective-tissue strands could be seen between the muscle fibers.

In the group of animals with cholesterol atherosclerosis the weight of the diaphragm was a little greater (4.97 ± 0.36 g; $P = 0.05$), but the D/M ratio was somewhat less than in the control group ($1.4 \times 10^{-3} \pm 9.2 \times 10^{-5}$; $P > 0.05$). Meanwhile, individual muscle fibers in the experimental animals were thinner and poorer in RNA; their sarcoplasm was homogeneous. Coarse strands of connective tissue, with large numbers of collagen fibers, could be seen among the muscle fibers and sometimes there were areas of adipose tissue. Consequently, the small increase in the absolute weight of the diaphragm was due to excessive development of connective tissue.

After administration of AS to healthy rabbits the weight of the diaphragm reached 5.29 ± 0.18 g and was significantly higher than in the control group ($P < 0.01$); the D/M ratio, which was $1.9 \times 10^{-3} \pm 6.1 \times 10^{-5}$, also was significantly greater ($P < 0.01$). Hypertrophy of the muscle fibers was observed everywhere: Their sarcoplasm had a high content of RNA and respiratory enzymes. Their nuclei were large, juicy, and rich in DNA.

*Soviet equivalent of Nandrolone (19-norandrostenolone) — Translator.

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TABLE 1. Body Weight and Weight of Diaphragm of Experimental Animals

Group of animals	Body weight, g	Weight of diaphragm, g	D/M
Control			
intact rabbits	2585,71±102,76	3,99±0,22	0,0015±0,0,0070
receiving AS	2785,71±52,0	5,29±0,18	0,0019±0,000061
Experimental (cholesterol atherosclerosis)			
intact rabbits	2125,71±127,57	4,97±0,36	0,0014±0,000092
receiving AS	2921,42±112,25	5,64±0,20	0,0019±0,000118

In the group of animals with cholesterol atherosclerosis and treated with AS the weight of the diaphragm was significantly greater than in rabbits of the control group, namely 5.64 ± 0.2 g ($P < 0.001$). The D/M ratio was $1.9 \times 10^{-3} \pm 1.18 \times 10^{-4}$, significantly higher than in the control ($P < 0.05$) in the intact rabbits or animals with experimental atherosclerosis ($P < 0.02$). Besides muscle fibers of the normal size, groups with well-marked hypertrophy were found; their fibrillary structure was ill-defined. The sarcoplasm of the myocytes was rich in RNA and enzymes of cell respiration. The changes described above are a feature of so-called intracellular regeneration [1]. The intermuscular connective tissue was coarser in structure.

Administration of AS to intact animals and to rabbits with experimental cholesterol-induced atherosclerosis thus causes an increase in weight of the diaphragm and an increase in the ratio of its weight to the body weight. This is evidence of the myotrophic action of AS on the diaphragm and, at the same time, that the diaphragm contains receptors for AS. It is a noteworthy fact that the increase in weight of the diaphragm in animals receiving AS was relatively greater than the increase in body weight. The discovery of the positive action of AS on the rabbit diaphragm may be a useful contribution to the study of the mechanism of the anabolic action of AS on skeletal muscles, which has not so far been explained [2, 4]. Fibrous changes and thinning of the muscle fibers develop in the diaphragm of rabbits with experimental cholesterol atherosclerosis, and this is bound to have an adverse effect ultimately on the function of this organ. These unfavorable changes are completely abolished by therapeutic administration of AS; hypertrophy of the muscle fibers arises in the experimental animals and manifestations of fibrosis are reduced, which must contribute to an increase in functional capacity of the diaphragm. The effect described above can serve as an additional indication for the use of AS in patients with ischemic heart disease, especially in those with postinfarct cardiosclerosis.

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