GENERAL PATHOLOGY AND PATHOPHYSIOLOGY

Changes in Myocardial Blood Supply during Experimental Hypertension Treated with Verapamil in Rabbits

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Rabbit hearts were studied at different periods of experimental arterial hypertension and its treatment with verapamil. Morphological study revealed a progressive decrease in the number of capillaries per unit mass during the development of myocardial hypertrophy in hypertensive hearts. In hypertensive animals treated with verapamil the density of capillaries in both ventricles did not decrease, but verapamil injected to intact animals sharply decreased this parameter.

Key words: *myocardium*; *arterial hypertension*; *hypertrophy*; *coronary vessels*

Calcium antagonists reducing vascular tone [2,8-10] and blood pressure [3,6,11,12] are widely used in medical practice as antihypertensive drugs. However, their effects are systemic. Evaluation of the effects of these drugs on coronary circulation is of great practical and theoretical importance, because coronary circulation in hypertension considerably affects the state of the heart.

MATERIALS AND METHODS

Experiments were performed on 30 male Chinchilla rabbits weighing 3.0-3.5 kg. Three rabbits were intact. Other three rabbits were injected with verapamil (1.5 mg/kg, intramuscularly) for 2 weeks. In 24 rats Goldblatt hypertension was reproduced by clumping of the abdominal aorta (by 1/3 of the initial diameter) above the point of renal artery branching. One week after surgery, both systolic and diastolic blood pressures increased significantly [3]. One half of the test group was treated with verapamil for 2 weeks.

One, 2, 4, and 6 weeks after surgery, rabbits from the experimental (3 animals per point) and 3 untreated rabbits were anesthetized, the chests were opened, the hearts were perfused with 2.5% glutaraldehyde via the ascending aorta. Papillary muscles of both ventricles were excised, routinely postfixed for preparing semithin sections, and embedded in araldite. Ultrathin sections were cut with a Reicher-Jung-Ultracut ultramicrotome, stained [7], and examined under an immersion microscope.

In each experimental series, morphometric analysis in 30 vision fields was performed using an Avtandilov grid and the volume percentages of muscle fibers and capillaries was determined. Basing on these data, the relative number of capillaries per myocardium unit mass was calculated, since during progression of myocardial hypertrophy this index rather than total area of capillaries provides an adequate assessment of myocardial circulation [5].

The data were statistically processed using Student's t test. The differences between the means were significant at $p \leq 0.05$.

RESULTS

As hypertrophy developed, a progressive decrease in the number of capillaries per unit mass was observed

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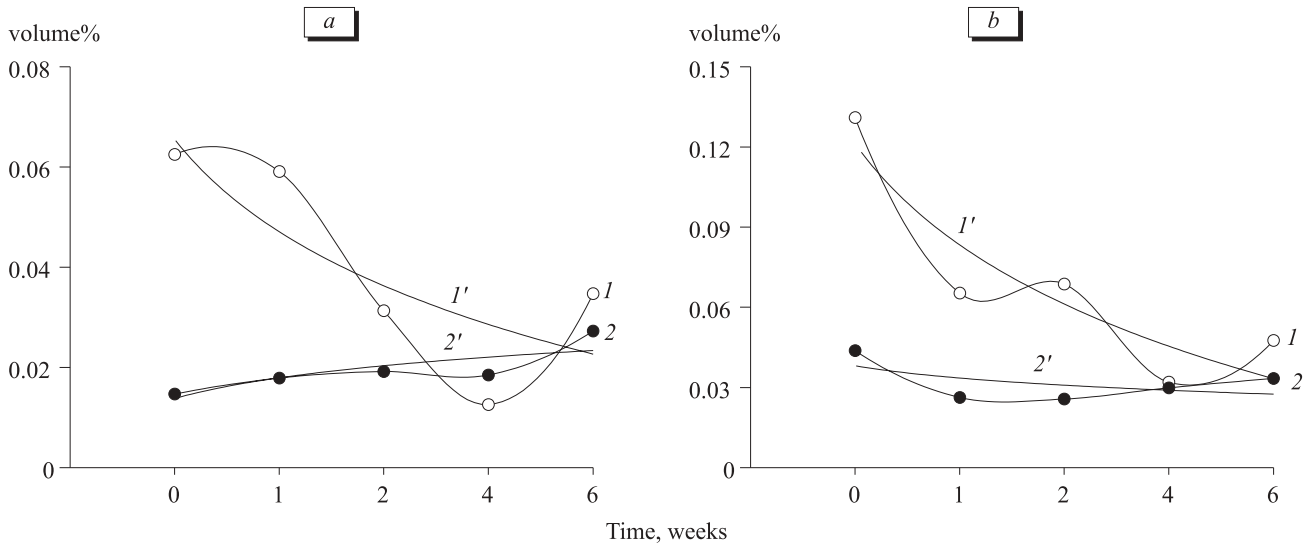

Fig. 1. Changes in the number of capillaries per unit mass of the myacardium in the left (*a*) and right (*b*) ventricules during the development of arterial hypertension without treatment (*1*) and with verapamil treatment (*2*). *1'* and *2'* are the corresponding trend lines.

in the myocardium of both ventricles (Fig. 1). Our results agree with previous findings [1] that capillary proliferation during myocardial hypertrophy lags behind myofibril proliferation, which finally leads to insufficient oxygen supply to myocytes and development of so-called "hypertrophic heart wearing-out complex".

In rabbits treated with verapamil the density of capillaries in the myocardium remained practically unchanged throughout the experiment (variations in this index were insignificant). Thus, we can conclude that verapamil prevents blood supply insufficiency and deficit of oxygenation in the myocardium. However, verapamil substantially decreased this index when administered to intact rabbits. Thus, hypertension in verapamil-treated animals developed under conditions of initially low levels of blood supply to myofibrils. Under conditions of increased afterload (due to increased vascular resistance) and hyperfunction of contractile elements, these relationships can considerably decrease myocardial contractility and promote progression of 'hypertrophic heart wearing-out complex'.

Thus, effects of Ca^{2+}-antagonist verapamil on myocardial circulation during AH can not be considered as undoubtedly positive.

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