also determine the greater resistance of this structure to hypoxia. After pressure chamber adaptation of highly tolerant animals for 1 month, correlation between the RNA–protein values strengthened, while the sign of the correlation was preserved. This can evidently be interpreted as maintenance of homeostasis, for the trend of metabolism initially present in each structure was preserved ($r = -1.0$ in the cortex and $r = +0.2$ in RF). Analysis of this parameter in animals with low tolerance reveals very high negative correlation ($r = -0.97$) for the cortex of the control rats, and that in RF correlation was almost absent ($r = -0.03$). After pressure chamber adaptation, while correlation in the cortex remained at a very high level, its sign was reversed ($r = +1.0$), and in the writers' view this indicates greater economy of energy-yielding material if RNA and protein synthesis follow similar trends. In RF of the animals of this group, negative correlation ($r = -0.68$) was found between RNA and protein concentrations, and this can probably be regarded as evidence of the inadequate development of compensatory changes in RF during long-term exposure to hypoxia.

Animals differing in their individual tolerance to hypoxia thus have a strictly individual level of structural metabolism in their brain tissue and realize their reserve capacity during adaptation to hypoxia differently. In the group of animals with high tolerance to hypoxia the principal changes in structural metabolism take place in subcortical structures (RF), whereas in animals with low tolerance, adaptive changes take place mainly in the cerebral cortex. RNA and total protein concentrations and, in particular, the RNA/protein ratio in the cytoplasm of the neurons are parameters adequately reflecting the functional state of the neurons in animals differing in their individual tolerance to hypoxia.

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CHARACTERISTICS OF THE CORONARY VASODILATOR RESERVE DURING PARTIAL RESTRICTION AND SUBSEQUENT RESTORATION OF THE CORONARY BLOOD FLOW

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The leading place among adaptive responses of the coronary vascular bed, activated during coronary insufficiency, is occupied by reactive hyperemia, which is manifested as the use of the coronary vasodilator reserve, and is aimed at restoring the disturbed dynamic equilibrium between the blood supply of the myocardium and its oxygen consumption [1, 5, 8]. It is this response which, even in the case of a subcritical narrowing of the coronary vessels, enables an adequate level of coronary blood flow to be maintained unchanged for a long time in a state of relative rest [10, 15], and during reperfusion it is a very important mechanism determining the effectiveness of reperfusion and reoxygenation measures as regards restoration of the contractile function of the heart [3, 6, 7].

The main aim of this investigation was to study the state of the coronary vasodilator reserve in experimental coronary insufficiency and in the early reperfusion period after its termination.

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EXPERIMENTAL METHODS

Experiments were carried out on anesthetized dogs (chloralose, urethane). To reproduce coronary insufficiency in animals with a closed chest a model of partial limitation of the lumen of a large coronary artery [4], graded in severity and duration, was used. Adequate coronary perfusion after catheterization of the circumflex branch of the left coronary artery was used as the initial background. The coronary circulation was investigated by means of an electromagnetic flowmeter. By catheterization of the chambers of the heart the state of its contractile function was monitored. The state of the coronary vasodilator reserve was assessed by determining the increase in the coronary blood flow in the response of reactive hyperemia to short-term (10-15 sec) total cessation of coronary perfusion.

RESULTS

The presence and extent of the coronary vasodilator reserve were analyzed consecutively in three stages: during adequate coronary perfusion, on limitation of the coronary blood flow by 70%, and during the hyperemic response after the end of partial occlusion for 30 min. Reactive hyperemia and its changes during limitation of the coronary blood flow and reperfusion were characterized by the following parameters ($n = 15$): with an adequate blood flow ($168.8 \pm 9.9\%$), with a limited blood flow ($92.2 \pm 4.7\%$; $P < 0.001$), during reperfusion for 1 min ($59.9 \pm 21.4\%$; $P < 0.02$), for 5 min ($52.4 \pm 27.3\%$; $0.1 > P > 0.05$), for 15 min ($3.8 \pm 29.6\%$; $P > 0.5$), and for 30 min ($19.3 \pm 26.9\%$; $P > 0.2$).

When the coronary blood supply was adequate, complete arrest of the coronary blood flow for a short time was thus accompanied by distinct reactive hyperemia: The maximal momentary value of the volume velocity of the blood flow increased on average to $168.8 \pm 9.9\%$, evidence of the presence of a marked coronary dilator reserve. During limitation of the coronary blood flow by 70%, significant inhibition of reactive hyperemia was observed. In each investigation the intensity of reactive hyperemia, reproduced against the background of an adequate coronary blood flow, was taken as 100%. All subsequent responses were compared with this value and their changes expressed in percent.

Data on the degree of blockade of the test reactive hyperemia during limitation of the coronary blood flow indicated considerable use of the coronary vasodilator reserve, and the response was reduced by $92.2 \pm 4.7\%$.

After the end of 70% limitation of the coronary blood flow for 30 min, a hyperemic response also occurred, and this must be regarded as reperfusion hyperemia. Immediately after restoration of the blood flow it was manifested as an increase on average to $173.3 \pm 12.5\%$. The increase in the blood flow decreased significantly during the first 5 min of reperfusion, and by the 15th minute became irregular. By the 30th minute of reperfusion the coronary blood flow remained increased over the pre-occlusion level in fewer than one-fifth of tests. Consequently, in most observations the duration of reperfusion hyperemia did not exceed 15 min. Values reflecting the contractile function of the heart under these circumstances remained moderately depressed (dp/dt_{max} for the left ventricle was $13.6 \pm 5.7\%$ lower than initially, $p < 0.05$). Characteristically, data in the literature on the effectiveness of restoration of the contractile function of the heart even after transient disturbances of its blood supply are contradictory [11-13].

After the first minutes of cessation of partial coronary occlusion, against the background of reperfusion hyperemia the coronary vessels began to restore their vasodilator reserve. This was shown by a decrease in the degree of inhibition of the test reactive hyperemia. By the 15th and 30th minutes of reperfusion the responses closely resembled those observed initially, during an adequate coronary blood flow. Such changes in the response that remained were not significant and irregular in character.

Assessment of reactive hyperemia under reperfusion conditions also enabled some possible mechanisms of the early termination of reperfusion hyperemia to be analyzed. It was considered that this condition may be based on an increase in the passive component of resistance of the coronary vessels as a result of an increase in extravascular compression influences on them [2], connected with the conditions under which the heart functions, and on weakening of active vasodilator responses due to altered reactivity with respect to local regulatory factors.

The response of reactive hyperemia produced against the background of reperfusion hyperemia, in our opinion, is a response to additional short-term ischemia. Incidentally, if

limitation of the duration of reperfusion hyperemia were due to an increase in the passive component of resistance of the coronary vessels in connection with an increase of the intramyocardial tension or profound andlasting disturbances of the "no reflow" phenomenon type [14], it would hardly be possible to abolish these factors temporarily during exposure to an additional ischemic stimulus. Thus according to our data, an increase in the passive component of resistance of the coronary vessels could not play a definite role in inhibition of reperfusion hyperemia and cessation of true realization of the coronary vasodilator reserve.

Quantitative analysis of the response of reactive hyperemia [9], against the background of reperfusion, enabled changes in reactivity of the coronary vessels to be assessed. During the first 15 min of reperfusion, in most cases their reactivity to additional ischemic stimulation was inhibited. Under these circumstances, in one-third of cases a definite decrease in reactive hyperemia ($-57.6 \pm 10.8\%$, $P < 0.02$) was combined with early cessation of reperfusion hyperemia. These data were evidence of the possible role of inhibition of coronary vascular reactivity in the limitation of reperfusion hyperemia. Meanwhile, in one-fourth of the experiments at the 15th minute of reperfusion, and in almost half of the experiments at the 30th minute, restoration or even potentiation of coronary vascular reactivity to ischemic stimulation was observed, even though at this time the response of reperfusion hyperemia had ended. Thus, inhibition of coronary vascular reactivity could not be the only mechanism determining changes in the reperfusion hyperemic response during the reperfusion period. Another possibility is that the absence of complete correlation between changes in reactive and reperfusion hyperemia was due to certain differences in the concrete mechanisms responsible for their occurrence. In conclusion, it must be emphasized that during the reperfusion period the coronary vessels regained their ability to dilate additionally, evidence that, in principle, it is possible to exert correcting influences on the true realization of the coronary vasodilator reserve under these conditions.

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