Секция «Экспериментальные исследования»

Therapeutic Evaluation of Autologous Genetically Enriched Leukoconcentrate in a Mini Pig Model of Ischemic Stroke

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Background and aims. Ischemic stroke is on the first place from the point of view of morbidity and prevalence to compare with other diseases, and causing more than 50% disability. In the same time there is no complete and effective treatment. Earlier we developed an ischemic stroke model on mini pigs, that shown its efficiency and was proven experimentally. The result of middle brain artery occlusion revealed locomotor disabilities, and after pathomorphological brain examination neurodegenerative areas consists of cavities in brain cortex was shown [1]. The present study shows the results of efficiency of an autologous genetically-enriched leucoconcentrate (GEL) in therapy for ischemic stroke therapy.

Methods. Autologous leucoconcentrate was prepared from venous blood of each animal. Leucocytes were separated and transduced by adenovirus carrying therapeutic genes of vascular endothelial growth factor (VEGF), glial derived neurotrophic factor (GDNF), neuronal cell adhesion molecule (NCAM) [2]. Mini-pigs 4 hours after occlusion of left middle cerebral artery accompanied with ligation of the opposite carotid artery, were infused intravenously (IV) by autologous leucoconcentrate enriched with therapeutic genes (n=3) or saline (n=3). The therapeutic efficiency was estimated on 21st day after surgery. In the open field test, animals were placed in the arena (3×3 m) divided into 6 squares by lines, and the assessment of the horizontal activity was accomplished by counting the number of lines crossed in 10 min. The absolute infarct volume (AIV) was calculated using digital images of the cerebral hemispheres, which were cut into 3-mm-thick slices, and each slice was photographed from both sides. Relative infarct volume (RIV) was calculated as AIV/(AIV+V of brain).

Results. Behavioral test revealed better performance in the therapeutic group (20 [12.5;20.0]) in comparison with control group (10.5 [4.2;13.8]). The RIV in the control group (0.7% [0.7;0.7]) was higher than in therapeutic group (0.6% [0.5;0.7]). Significant vasodilation was observed in the right hemisphere in both groups. Neurodegeneration cavity of the brain surface affects cortex and underlying structures.

Conclusions. Even there is no significant difference between two groups, experimental group activity was higher and more vigorous according our observation. IV infusion of an autologous GEL carrying *vegf, gdnf, ncam* genes has a positive effect on behavioral performance and reduces the infarct volume in mini-pigs with a model of ischemic stroke.

References

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