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TRANSPLANTATION OF MESENCHYMAL STROMAL CELLS IN EXPERIMENTAL ACUTE REVERSIBLE CEREBRAL ISCHEMIA (COMPARATIVE ANALYSIS)

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The issue of treating cerebrovascular disorders is very important due to their wide occurrence in the human population, especially in the elderly. The resulting ischemia of brain tissues leads to mortality, violent behaviour, biochemical and morphological changes in the brain. Correlation analysis allows evaluating the statistical relationship between two random variables or two-dimensional data. In recent years, the neuroprotective properties of mesenchymal stromal cells (MSCs) have been actively studied. Stem cell transplantation for ischemic stroke is one of the ways of the modern regenerative strategy in the treatment of this pathology.

Aim. The study was to analyse the correlations between biochemical indicators determined in the somatosensory cortex and hippocampus, morphological manifestations of neuroapoptosis, and parameters of CNS functioning in acute cerebral ischemia in rats after MSCs transplantation.

Methods. A 20-minute bilateral cerebral ischemia-reperfusion in rats. Experimental animals were intravenously injected with mesenchymal stromal cells from human umbilical cord Wharton jelly (hWJ-MSCs) or adult adipose-derived stem cells (hAD-MSCs). Rats were evaluated for mortality dynamics, neurological deficits, and biochemical parameters 7 and 14 days after surgery.

Results. Mortality after transplantation of hWJ-MSCs was 10% versus 65% in the control group and 32% in the group of rats that received hAD-MSCs. On day 7, the mean McGraw scores were 7.1 ± 0.19/ 8.9 ± 0.23 /11.8 ± 0.48 points in rats injected with hWJ-MSCs/ hAD-MSCs/saline; on day 14, these were 4.9 ± 0.15/ 5.7 ± 0.23/ 9.1 ± 0.30 points, respectively. Transplantation of mesenchymal stromal cells eliminated energy deficiency in ischemic rat brain tissue, reduced metabolic acidosis and oxidative damage to neurons, and had a positive effect on nitric oxide metabolism, but hAD-MSCs were less effective.

Conclusions. Transplantation of hWJ-MSCs had a better therapeutic effect than transplantation of hAD-MSCs.

Key words: somatosensory cortex, ischemia-reperfusion, mesenchymal stromal cells, Wharton jelly, adipose stem cells, biochemical parameters.

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Ischemic stroke is one of the dangerous vascular diseases with a high level of disability and mortality among people having acute cerebrovascular accidents [1]. Within the framework of the regenerative strategy, a new impetus has been given to stem cell transplantation in ischemic stroke. It is posible to use embryonic and fetal stem cells (SCs), cells of Wharton's jelly (substantia gelatinea funiculi umbilicalis) and umbilical cord (UC) blood, as well as SCs from an adult organism for cell therapy [2]. Encouraging results regarding endogenous mechanisms of neuroregeneration in response to ischemic damage of brain structures have been demonstrated by cell therapy using mesenchymal stromal cells (MSCs) [3]. MSCs are pluripotent cells obtained from adult tissues, which makes them ethically preferable for both preclinical and clinical research [4]. Mechanisms underlying favourable outcomes in stromal cell transplantation include "bystander" effects, paracrine mechanisms, or restorative effects mediated by extracellular vesicles [5]. Among all MSC types, MSCs derived from umbilical cord (frequently called Wharton's jelly mesenchymal stem cells — WJ-MSCs) are of interest. MSCs derived from bone marrow or adipose tissue, unlike perinatal organs MSCs, have some limits, such as an invasive procedure to get them, a higher risk of transmitting infectious diseases, the donor's age, and the limited proliferative potential [6].

In contrast to the available published results of experimental studies, our work will analyse and compare the therapeutic effects of MSCs transplantation (isolated from human umbilical cord Wharton jelly, i.e., hWJ-MSCs and adult adipose-derived SCs (hAD-MSCs)) in conditions of cerebral ischemia-reperfusion with the aim to identify the most active culture with cerebroprotective effect.

Materials and Methods

The research was done on 99 Wistar male rats weighing 160–190 g. Eighty-five animals underwent transient bilateral cerebral ischemia-reperfusion (IR) by ligation of the internal carotid arteries (ICA) for 20 min with subsequent blood supply restoration. Fourteen animals (the group of sham-operated rats) were subjected to the following interventions (anaesthesia, skin incision, vascular dissection) except for ICA ligation. The Bioethics Committee in the National Pirogov Memorial Medical University (protocol No. 2, dated 01.31.2024) approved all animals taken for the research. Surgical interventions, traumatic manipulations were performed under propofol anaesthesia ("Propofol-novo", Novopharm-Biosyntez production, Ukraine, 60 mg/kg intraperitoneally). After modelling the pathology, 20 animals were injected with hWJ-MSCs (1 million cells/animal suspended in 0.2 ml of saline) into the femoral vein. Another group of experimental rats ($n = 25$) was transplanted with hAD-MSCs (1 million cells/animal suspended in 0,2 ml of saline) intravenously. Animals of the control group ($n = 40$) were intravenously injected with 0.2 ml of saline. The method for obtaining MSCs to transplant them into rats is described in our previous publications [8].

For biochemical studies, the brain was removed from rats (by decapitation), washed with a cold 1.15% KCl solution. The tissue of the somatosensory region was homogenized in a medium of 1.15% KCl (ratio 1:3) at 3000 rpm (Teflon-glass). Succinate dehydrogenase (SDH) content was determined by the rate of potassium hexacyanoferrate (III) reduction in order to assess the parameters of energy and carbohydrate metabolism in the tissue of the somatosensory region of a rat brain. For the same purpose, the content of glucose (by glucose oxidase method using standard kits from Filisit-Diagnostics, Ukraine), lactate, and pyruvate (by colorimetric method) was determined [9].

Oxidative stress was assessed by determining the content of malondialdehyde (MDA), which is its final product (by reaction with thiobarbituric acid) [10]. In addition, the activity of superoxide dismutase (SOD) was measured (by the percentage of inhibition in quercetin oxidation) [11] to analyse the state of antioxidant protection and total NO synthase activity (by the amount of formed nitrite anion (NO_2^-) after incubation of the postnuclear supernatant in NADPH Sigma medium, USA (1 ml of which contains 50 mM KH_2PO_4-NaOH buffer (pH 7.0), 1 mM $MgCl_2$, 2 mM $CaCl_2$, 1 mM NADPH, 2.2 mM L-arginine) for 60 min [12].

We determined the dynamics of mortality, neurological deficit (according to the C.P. McGraw stroke-index scale), biochemical indicators such as glucose, lactate, succinate dehydrogenase (SDH), malondialdehyde (MDA), superoxide dismutase (SOD), total NO synthase (NOS) activity in the somatosensory cortex of rats with cerebral IR in the subacute period of ischemia (day 7) and the recovery period (day 14 after pathology modelling).

Statistical processing of the results was carried out using the computer program Statistica 7.0 (StatSoft Inc., USA) using non-parametric (Mann-Whitney U-test) statistical methods.

Results

In the group of sham-operated rats, in which ICA preparation was performed under propofol anaesthesia. Ligatures were applied without further arterial ligation, no case of mortality was recorded during the entire observation period (96 hours) (Fig. 1). An injection of 0.9% NaCl solution into the femoral vein of the rats from the control group (in 20 minutes after bilateral ICA ligation followed by subsequent reperfusion) was accompanied with a progressive increase in the animal mortality rate. Most animals (45%) died 12 hours after cerebral ischemia modelling, which can be considered a critical period in the development of this pathology. In 24 hours, mortality in this group reached 65% and didn't change further during the entire observation period (see Fig. 1).

Experimental therapy of acute cerebral ischemia using intravenous hWJ-MSC transplantation in rats contributed to a reduction in mortality, when mortality was recorded at 10% level, in contrast to the control group having 65% level ($P < 0.05$) (Fig. 1). Intravenous transplantation of hAD-MSCs to rats with cerebral IR also contributed to their survival, in which the mortality rate was at the 32% level and was significantly lower than in the control group of rats ($P < 0.05$) (Fig. 1). Therefore, intravenous transplantation of hWJ-MSCs significantly improved the survival of experimental animals after IR brain damage compared to intravenous transplantation of hAD-MSCs.

An integral indicator that allows us to assess the magnitude of the protective effect on the ischemic brain for a cerebroprotector, along with a decrease in the mortality rate, is the positive dynamics of changes in the neurological status of experimental animals. Thus, intravenous transplantation of hWJ-MSCs and hAD-MSCs led to a significant regression in neurological deficit. On the day 7 after IR, the average score on the McGraw Stroke-index scale was 7.1 ± 0.19 points in the rats administered with hWJ-MSCs and 8.9 ± 0.23 points in the rats having hAD-MSCs treatment versus 11.8 ± 0.48 points in the control group. On the day 14: 4.9 ± 0.15 points and 5.7 ± 0.23 points versus 9.1 ± 0.30 points respectively ($P < 0.05$).

Transplantation of hWJ-MSC tended to have a better modulating effect on the neurological deficit dynamics in rats with IR brain damage than hAD-MSCs transplantation (Fig. 2).

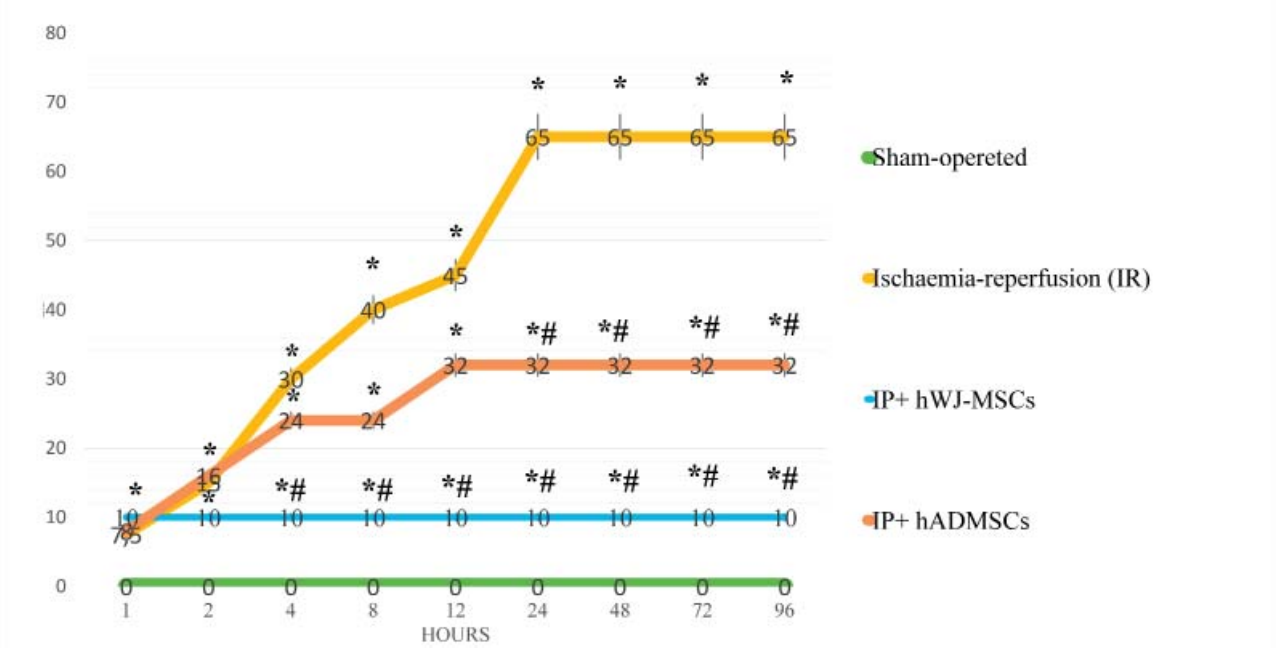

Fig. 1. **Rat mortality rates in the studied groups (%)**
* — $P < 0.05$ relative to the corresponding group of sham-operated animals;
\# — $P < 0.05$ relative to the control group of animals.

Taking into account the powerful cerebroprotective properties in MSCs, it is advisable to investigate the possible biochemical mechanisms in their influence on glucose metabolism, indicators of oxidative and nitrosative stress. The cerebroprotective effect of the studied MSCs is closely related to their sham-operated brain metabolism [13-15].

During our study (on days 7 and 14 after IR brain injury), a significant increase in glucose levels was observed in the somatosensory cortex of rats compared to sham-operated animals (Fig. 3), which averaged 3.2 ± 0.10 μmol/g of dry tissue and 2.9 ± 0.07 μmol/g of dry tissue, versus 2.1 ± 0.10 μmol/g of dry tissue and 2.2 ± 0.08 μmol/g of dry tissue ($P < 0.05$). hWJ-MSCs transplantation had a modeling effect on the increase in glucose levels in the somatosensory cortex of rats having IR lesion, which was manifested by a significant decrease in glucose content compared to the control group and was found to be on average 2.6 ± 0.07 μmol/g of dry tissue and 2.4 ± 0.05 μmol/g of dry tissue ($P < 0.05$). Simultaneously, intravenous transplantation of hAD-MSCs showed a tendency to normalize glucose levels in the somatosensory cortex in rats with IR (Fig. 3).

At the phase of energy shifts, it compensatory activates the anaerobic pathway in glucose metabolism. It improves the formation of lactate and hydrogen ions. causing metabolic acidosis development (Fig. 3). Thus, on days 7 and 14 after cerebral IR, a significant increase in lactate levels was observed in the somatosensory cortex of rats. Its level averaged 6.5 ± 0.14 μmol/g of dry tissue and 5.9 ± 0.13 μmol/g of dry tissue, respectively, compared to sham-operated animals — 1.6 ± 0.03 μmol/g of dry tissue and 1.5 ± 0.05 μmol/g of dry tissue ($P < 0.05$).

We found that hWJ-MSCs in conditions of brain IR significantly reduced metabolic acidosis development in the somatosensory cortex during the studied periods — the lactate level was 4.6 ± 0.08 μmol/g of dry tissue and 3.6 ± 0.12 μmol/g of dry tissue on days 7 and 14, respectively ($P < 0.05$). HAD-MSCs transplantation had no positive effect on lactate levels in the somatosensory cortex of rats with IR; hence, the average lactate concentration was 6.2 ± 0.11 μmol/g of dry tissue on day 7 after IR and 5.6 ± 0.14 μmol/g of dry tissue on day 14.

The leading cause of brain damage due to stroke is energy deficiency caused by changes in mitochondrial metabolism. Therefore, the next stage of our study was to assess the effect of MSC therapy on mitochondrial dysfunction through the investigation of a key enzyme of the Krebs cycle — SDH activity (Fig. 4). Thus, after cerebral IR in rats a sharp decrease in SDH activity was observed in the somatosensory cortex, both on day 7 (SDH activity was on average 3.1 ± 0.17 μmol/min • mg protein) and day 14 (4.0 ± 0.22 μmol/min • mg protein) in comparison with the sham-operated animals

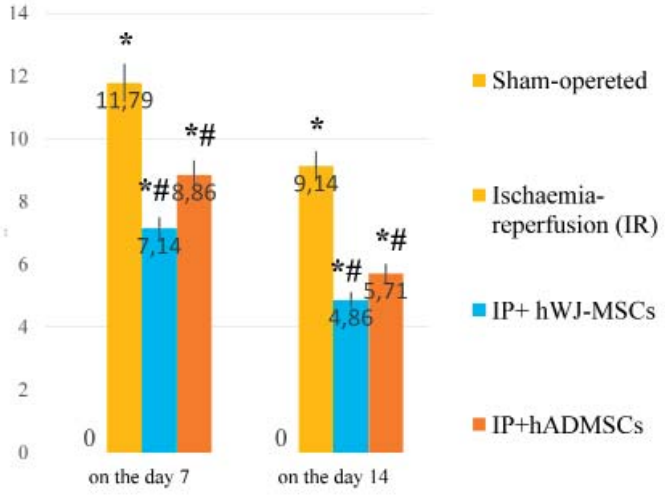

Fig. 2. **Dynamics of neurological deficit in rats of the observed groups in keeping with the McGraw Stroke-index scale**

* — $P < 0.05$ relative to the corresponding group of sham-operated animals;
# — $P < 0.05$ relative to the control group of animals.

in which SDH activity was on average 8.2 ± 0.21 μmol/min • mg protein and 8.4 ± 0.17 μmol/min • mg protein, respectively, (P <0.05) (see Fig. 4). A positive effect of hWJ-MSCs transplantation on SDH activity was noted in the studied periods, which significantly increased the level of SDH activity in comparison with the control animals (on average to 6.1 ± 0.36 μmol/min • mg protein and 7.7 ± 0.14 μmol/min • mg protein (P <0.05). Also, therapy with hWJ-MSCs transplantation was significantly better than hAD-MSCs transplantation, in which SDH activity averaged 3.5 ± 0.25 μmol/min • mg protein on day 7 and 4.3 ± 0.24 μmol/min • mg protein on day 14 (P < 0.05) (Fig. 4).

The implementation of oxidative stress processes occurred against the background of a significant lowering in the antioxidant enzymes activity, such as SOD (Fig. 5), and intensification of free radical oxidation, which induces lipid peroxidation processes. Thus, SOD activity in the somatosensory cortex of rats after IR during the subacute and recovery periods decreased in comparison to the indicators of the sham-operated

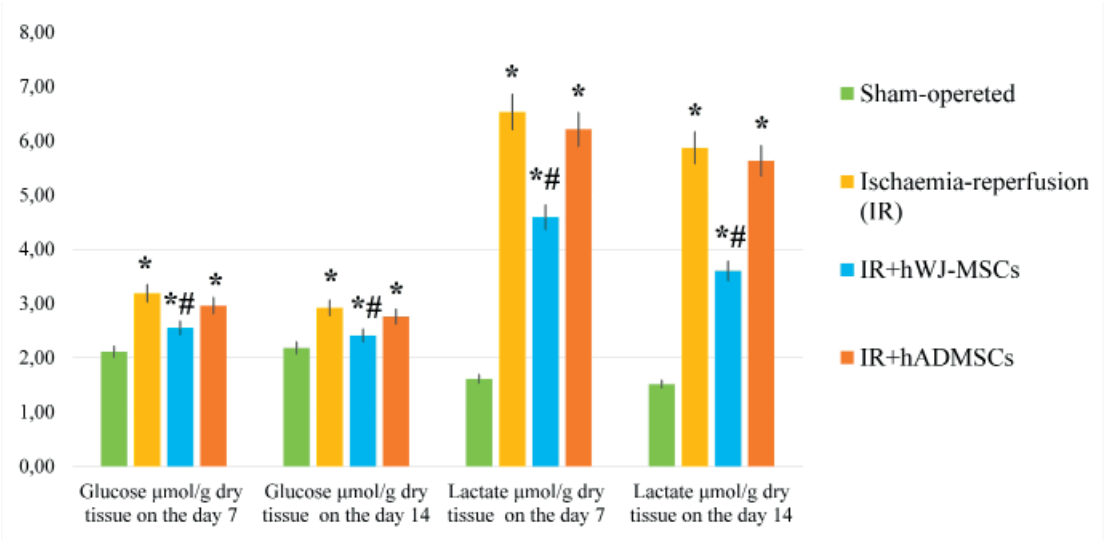

Fig. 3. **Glucose and lactate levels in the somatosensory cortex of the observed rat groups on days 7 and 14 after IR**
* — P < 0.05 relative to the corresponding group of sham-operated animals;
# — P < 0.05 relative to the control group of animals.

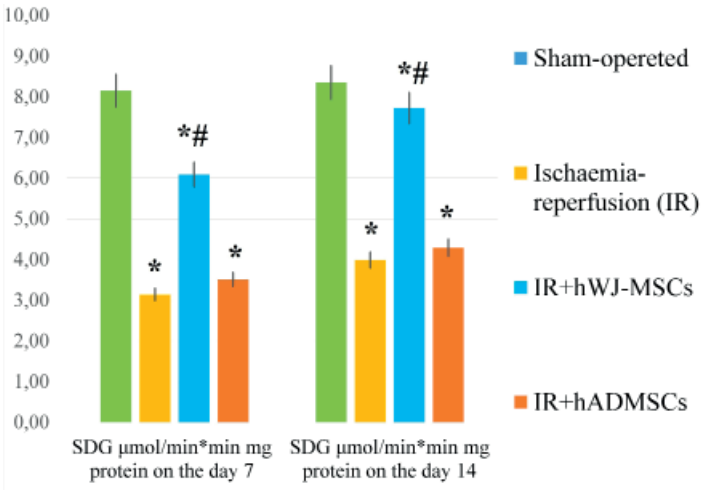

Fig. 4. **SDH activity in the somatosensory cortex of the observed rat groups on days 7 and 14 after IR**
* — P < 0.05 relative to the corresponding group of sham-operated animals;
# — P < 0.05 relative to the control group of animals.

animals and averaged 1.3 ± 0.26 standard units/mg protein on day 7 and 1.7 ± 0.15 standard units/mg protein on day 14, versus 2.7 ± 0.17 standard units/mg protein and 2.8 ± 0.10 standard units/mg protein respectively (P <0.05) (Fig. 5). Cure with hWJ-MSCs transplantation had an assertive effect on the antioxidant enzymes — SOD activity significantly exceeded the corresponding indicators in animals of the control group and amounted to an average of 2.2 ± 0.16 standard units/mg protein on the day 7 and 2.3 ± 0.16 standard units/mg protein on the day 14 (P <0.05). Additionally, hWJ-MSCs transplantation was credibly preferable than hAD-MSCs transplantation, after which SOD activity in the somatosensory cortex was on average 1.2 ± 0.20 standard units/mg protein (day 7) and 1.6 ± 0.08 standard units/mg protein (day 14) (P <0.05) (Fig. 5).

Therapeutic intravenous transplantation of MSCs to rats with cerebral IR reduced lipid peroxidation processes in the somatosensory cortex. Thus, MDA (Fig. 6) levels in rats having IR followed by intravenous hWJ-MSCs transplantation were on average 17.2 ± 1.02 μmol/g of dry tissue on the day 7 and 10.5 ± 0.58 μmol/g of dry tissue on the day 14, that was significantly lower than in the animals with IR receiving 0.9% NaCl solution intravenously — 31.1 ± 0.87 μmol/g of dry tissue and 24.9 ± 0.65 μmol/g of dry tissue respectively (p<0.05). Transplantation of hAD-MSCs was worse than hWJ-MSCs regarding lipid peroxidation reduction in the somatosensory cortex of rats with cerebral IR (Fig. 6).

One of the foremost mechanisms in the protective action of a modern cerebroprotective agent is its corrective effect on nitric oxide metabolism, in particular on the development of nitrosative stress in brain tissues. In the course of our studies it was found that IR in rats leads to growing in the total NOS (Fig. 7) activity in the somatosensory cortex on days 7 and 14 after IR which averages 223.6 ± 9.18 pmol/min · mg protein and 208.6 ± 8.70 pmol/min · mg protein, when in sham-operated animals the total NOS activity averaged 122.6 ± 4.66 pmol/min · mg protein and 121.3 ± 3.90 pmol/min · mg protein respectively, which may indicate hyperproduction of nitric oxide (P < 0.05) (Fig. 7). Treatment of rats using hWJ-MSCs in the subacute and recovery periods of cerebral ischemia had a positive modulating effect on the nitric oxide cycle and was superior to treatment with hAD-MSCs. Thus, during the indicated experimental days (7th and 14th), total NOS activity in the somatosensory cortex of rats transplanted with hWJ-MSCs decreased relative to the control group. It averaged 149.6 ± 5.11 pmol/min · mg protein and 145.0 ± 3.21 pmol/min · mg protein (P < 0.05) (Fig. 7). hWJ-MSCs were better than hAD-MSCs at restoring normal functioning of the nitric oxide system in acute cerebral ischemia in rats (both in the subacute and recovery periods of stroke), which may be one of the foremost mechanisms of its cerebroprotective action in post-reperfusion brain damage.

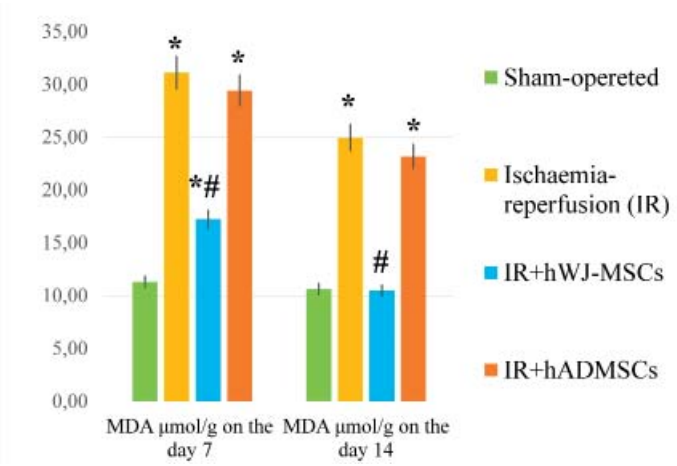

Fig. 5. **SOD activity in the somatosensory cortex of the observed rat groups on days 7 and 14 after IR**
* — P < 0.05 relative to the corresponding group of sham-operated animals;
# — P < 0.05 relative to the control group of animals.

Discussion

The pronounced cerebroprotective activity of hWJ-MSCs was demonstrated during their therapeutic application in conditions of IR modelling in rats. Thus, in the capability to reduce the mortality rate in the critical period of the research, hWJ-MSCs were superior to hAD-MSCs of rats with IR. An integrative indicator that allows for assessing the quality of the protective effect in cerebral ischemia is, along with a decline in mortality, the rapid disappearance of neurological deficit.

K.J. Wu et al. showed that intracerebral transplantation of hWJ-MSCs significantly reduced neurological deficit manifestations in rats on days 3 and 5 baft middle cerebral artery occlusion [16]. In another study made by H. Cao et al., it was found that intracerebral transplantation of human umbilical cord MSCs 24 hours after middle cerebral artery occlusion at a dose of 1×10^6 cells/animal credibly reduced the indexes of neurological deficit in rats [17].

This is consistent with the outcomes of our study in rats with acute cerebral IR, which, along with significant mortality, developed severe neurological deficits within the first 2 days. Experimental cell therapy in rats with the IR model contributed not only to a reduction in mortality, but also in

Fig. 6. **MDA levels in the somatosensory cortex of the observed rat groups on days 7 and 14 after IR**
* — $P < 0.05$ relative to the corresponding group of sham-operated animals;
\# — $P < 0.05$ relative to the control group of animals.

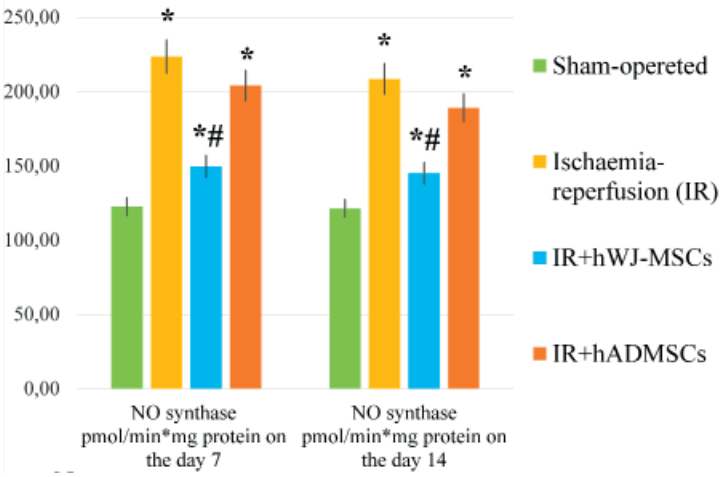

Fig. 7. **NOS activity in the somatosensory cortex of the observed rat groups on days 7 and 14 after IR**
* — $P < 0.05$ relative to the corresponding group of sham-operated animals;
\# — $P < 0.05$ relative to the control group of animals.

the manifestations of neurological disorders. HWJ-MSCs exerted the best modelling effect on neurological deficit.

Variations in paracrine factors of different MSC populations contribute to varying levels of regenerative activity. hWJ-MSCs or hAD-MSCs have different effects on CNS cell populations; thus, hWJ-MSCs have a better influence on the metabolic viability of somatosensory cortex neurons in rats. Therefore, during our study, an increment in the levels of glucose, lactate, MDA, total NOS activity, and a decrease in the activity of SDH and SOD were found in the somatosensory cortex of rats on days 7 and 14 after brain IR. A burst of free radicals and reactive oxygen species accompanies reperfusion. Free radicals' appearance next to blood vessels is one of the agents in reperfusion-induced damage by increasing blood-brain barrier permeability [18, 19]. At the same time, the liver, as the central metabolic organ, contributes not only to immunosuppression after stroke, but also to stress-induced hyperglycemia [20]. Systemic hyperglycemia associated with infarction may promote glucose entry into ischemic brain tissue due to injury to the blood-brain barrier [21].

It is known from literature that lipid peroxidation processes occur mainly in the membrane structures of neurons, which, with a sharp decrease in the function of the antioxidant defence system and appearance of uncompensated acidosis, inevitably leads to disruption of cytoarchitectonics, interneuronal connections, and death of a neuron as a structural unit of the CNS [22]. Therefore, intensive therapy of IR damage by hWJ-MSCs transplantation exhibited the most potent antioxidant effect, as evidenced by the ability to eliminate imbalance in the enzyme pro- and antioxidant systems and by slowing down of lipoperoxidation processes.

Conclusions

Twenty minutes of transient cerebral ischemia-reperfusion in rats, induced by ligation of the internal carotid arteries, was accompanied by substantive metabolic disorders in the somatosensory cortex in the mode of energy imbalance and appearance of lactic acidosis, nitrosative and oxidative stress, leading to severe neurological deficits and death of the experimental animals.

The complex mechanism of hWJ-MSCs' cerebroprotective action in acute cerebrovascular accident is associated with abolition of energy deficiency, metabolic acidosis, oxidative damage to neurons, affirmative effect on nitric oxide metabolism, which had a normalizing impact on the neurological status and increased survival of rats.

Intravenous transplantation of hWJ-MSCs to rats with cerebral ischemia-reperfusion contributed to better stabilization of neurological changes than hAD-MSCs, as well as increased survival of experimental animals, restored disturbed energy processes, and had a modulating effect on nitrosative and oxidative stress in the somatosensory cortex.

Prospects for further research

Results of the study substantiate the feasibility of creating a new medication for the therapy of ischemic stroke. The data obtained can be used to seek new ways to treat ischemic-reperfusion injury of the brain.

Compliance with ethical requirements

When executing the study, the authors adhered to the principles of the basic bioethical norms of the Helsinki Declaration adopted by the General Assembly of the World Medical Association, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant provisions of the WHO, the International Council of Medical Societies, the International Code of Medical Ethics (1983), the Council of Europe Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes of 18.03.1986.

Conflict of interest

The authors declare no conflict of interest.

Authors' contribution to the writing of the article

Konovalov S. V. — planning and conducting the research, analyzing the results, and writing the article; Moroz V. M. — development of the research concept; Yoltukhivskyi M. V. — conducting the research, writing certain sections of the article; Gusakova I. V. — final editing of the article; Stelmashchuk A. O. — design of graphic materials; Deryabina O. G. — writing certain sections of the manuscript; Kordium V. A. — contributed to the development of the research concept

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REFERENCES

1. Feske, S. K. (2021). Ischemic Stroke. *The American journal of medicine*, 134(12), 1457–1464. https://doi.org/10.1016/j.amjmed.2021.07.027
2. Derakhshankhah, H., Sajadimajd, S., Jafari, S., Izadi, Z., Sarvari, S., Sharifi, M., Falahati, M., …, Presley, J., F. (2020). Novel therapeutic strategies for Alzheimer's disease: Implications from cell-based therapy and nanotherapy. *Nanomedicine : nanotechnology, biology, and medicine*, 24, 102149. https://doi.org/10.1016/j.nano.2020.102149
3. Chung, J. W., Chang, W. H., Bang, O. Y., Moon, G. J., Kim, S. J., Kim, S. K., Lee, J. S., …, STARTING-2 Collaborators (2021). Efficacy and Safety of Intravenous Mesenchymal Stem Cells for Ischemic Stroke. *Neurology*, 96(7), e1012-e1023. https://doi.org/10.1212/WNL.0000000000011440
4. Guo, Y., Peng, Y., Zeng, H., Chen, G. (2021). Progress in Mesenchymal Stem Cell Therapy for Ischemic Stroke. *Stem cells international*, 2021, 9923566. https://doi.org/10.1155/2021/9923566
5. Brooks, B., Ebedes, D., Usmani, A., Gonzales-Portillo, J. V., Gonzales-Portillo, D., Borlongan, C. V. (2022). Mesenchymal Stromal Cells in Ischemic Brain Injury. *Cells*, 11(6), 1013. https://doi.org/10.3390/cells11061013
6. Semenova, E., Grudniak, M. P., Machaj, E. K., Bocian, K., Chroscinska-Krawczyk, M., Trochonowicz, M., Stepaniec, I. M., …, Rozwadowska, N. (2021). Mesenchymal Stromal Cells from Different Parts of Umbilical Cord: Approach to Comparison & Characteristics. *Stem cell reviews and reports*, 17(5), 1780–1795. https://doi.org/10.1007/s12015-021-10157-3
7. Patel, A. A., Mohamed, A. H., Rizaev, J., Mallick, A. K., Qasim, M. T., Abdulmonem, W. A., Jamal, A., …, Ahmad, F. (2024). Application of mesenchymal stem cells derived from the umbilical cord or Wharton's jelly and their extracellular vesicles in the treatment of various diseases. *Tissue & cell*, 89, 102415. https://doi.org/10.1016/j.tice.2024.102415
8. Konovalov, S., Moroz, V., Konovalova, N., Deryabina, O., Shuvalova, N., Toporova, O., Tochylovsky, A., Kordium, V. (2021). The effect of mesenchymal stromal cells of various origins on mortality and neurologic deficit in acute cerebral ischemia-reperfusion in rats. *Cell Organ Transpl.*, 9(2), 104–108. https://doi.org/10.22494/cot.v9i2.132
9. Chekman, I. S., Byelenichev, I. F., Nahorna, O. O., Horchakova, N.O., Luk'yanchuk, V. D., Bukhtiyarova, N. V., Horbachova, S. V., Syrova, H.O. (2016). Preclinical study of the specific activity of potential drugs of primary and secondary neuroprotection. Methodological recommendations. Kyiv.
10. Mihara, M., Uchiyama, M. (1978). Determination of malonaldehyde precursor in tissues by thiobarbituric acid test. *Analytical biochemistry*, 86(1), 271–278. https://doi.org/10.1016/0003-2697(78)90342-1
11. Baylyak, M. M., Semchyshyn, H. M., Lushchak, V. I. (2006). The participation of catalase and superoxide dismutase in the response of Saccharomyces cerevisiae to the action of hydrogen peroxide in the exponential growth phase. *Ukr. biochem. journal*, 78(2), 79–85.
12. Gula, N. M., Kosyakova, G. V., Berdyshev, A. G. (2007). The effect of N-stearoylethanolamine on the NO-synthase pathway of nitric oxide generation in the aorta and heart of rats with streptozotocin-induced. *Ukr. biochem. journal*, 79(5), 153–158.
13. Han, M., Cao, Y., Xue, H., Chu, X., Li, T., Xin, D., Yuan, L., Ke, H., Li, G., Wang, Z. (2020). Neuroprotective Effect of Mesenchymal Stromal Cell-Derived Extracellular Vesicles Against Cerebral Ischemia-Reperfusion-Induced Neural Functional Injury: A Pivotal Role for AMPK and JAK2/STAT3/NF-κB Signaling Pathway Modulation. *Drug design, development and therapy*, 14, 2865-2876. https://doi.org/10.2147/DDDT.S248892
14. Tang, W., Lv, X., Huang, J., Wang, B., Lin, L., Shen, Y., Yao, Y. (2022). Neuroprotective Effect of Stroke Pretreated Mesenchymal Stem Cells Against Cerebral Ischemia/Reperfusion Injury in Rats. *World neurosurgery*, 165, e1-e11. https://doi.org/10.1016/j.wneu.2021.04.114
15. Pan, K., Peng, Q., Huang, Z., Dong, Z., Lin, W., Wang, Y. (2023). Temporal patterns and distribution of pyroptosis-related molecules and effects of human mesenchymal stem cells on pyroptosis following cerebral ischemia/reperfusion in rats. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*, 32(8), 107199. https://doi.org/10.1016/j.jstrokecerebrovasdis.2023.107199
16. Wu, K. J., Yu, S. J., Chiang, C. W., Lee, Y. W., Yen, B. L., Tseng, P. C., Hsu, C. S., Kuo, L. W., Wang, Y. (2018). Neuroprotective Action of Human Wharton's Jelly-Derived Mesenchymal Stromal Cell Transplants in a Rodent Model of Stroke. *Cell transplantation*, 27(11), 1603–1612. https://doi.org/10.1177/0963689718802754
17. Cao, H., Cheng, Y., Zhang, J., Xu, M., Ge, L. (2020). The Effect of Umbilical Cord Mesenchymal Stem Cells Combined with Tetramethylpyrazine Therapy on Ischemic Brain Injury: A Histological Study. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*, 29(12), 105298. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105298

18. Ju, F., Ran, Y., Zhu, L., Cheng, X., Gao, H., Xi, X., Yang, Z., Zhang, S. (2018). Increased BBB Permeability Enhances Activation of Microglia and Exacerbates Loss of Dendritic Spines After Transient Global Cerebral Ischemia. *Frontiers in cellular neuroscience*, 12, 236. https://doi.org/10.3389/fncel.2018.00236
19. Liu, Q., Sorooshyari, S. K. (2021). Quantitative and Correlational Analysis of Brain and Spleen Immune Cellular Responses Following Cerebral Ischemia. *Frontiers in immunology*, 12, 617032. https://doi.org/10.3389/fimmu.2021.617032
20. Inderhees, J., Schwaninger, M. (2024). Liver Metabolism in Ischemic Stroke. *Neuroscience*, 550, 62–68. https://doi.org/10.1016/j.neuroscience.2023.12.013
21. Song, K., Li, Y., Zhang, H., An, N., Wei, Y., Wang, L., Tian, C., Yuan, M., Sun, Y., Xing, Y., Gao, Y. (2020). Oxidative stress-mediated blood-brain barrier (BBB) disruption in neurological diseases. *Oxidative Medicine and Cellular Longevity*, ID 4356386, 1–27. https://doi.org/10.1155/2020/4356386
22. Chavda, V., Lu, B. (2023). Reverse Electron Transport at Mitochondrial Complex I in Ischemic Stroke, Aging, and Age-Related Diseases. *Antioxidants (Basel, Switzerland)*, 12(4), 895. https://doi.org/10.3390/antiox120408

ТРАНСПЛАНТАЦІЯ МЕЗЕНХІМАЛЬНИХ СТРОМАЛЬНИХ КЛІТИН ПРИ ЕКСПЕРИМЕНТАЛЬНІЙ ГОСТРІЙ ОБОРОТНІЙ ЦЕРЕБРАЛЬНІЙ ІШЕМІЇ (ПОРІВНЯЛЬНИЙ АНАЛІЗ)

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Питання лікування цереброваскулярних порушень є дуже важливим через їх широку поширеність у людській популяції, особливо у людей похилого віку. Ішемія тканин мозку призводить до смертності, агресивної поведінки, біохімічних та морфологічних змін у мозку. Кореляційний аналіз дозволяє оцінити статистичний зв'язок між двома випадковими величинами або двовимірними даними. За останні роки набуло особливого значення дослідженнч нейропротекторних властивостей мезенхімальних стромальних клітин (МСК). Трансплантація стовбурових клітин при ішемічному інсульті є одним із шляхів сучасної регенеративної стратегії в лікуванні цієї патології.

Мета. Проаналізувати кореляцію між біохімічними показниками, визначеними в соматосенсорній корі та гіпокампі, морфологічними проявами нейроапоптозу та параметрами функціонування ЦНС при гострій ішемії головного мозку у щурів після трансплантації МСК.

Методи. 20-хвилинна двостороння церебральна ішемія-реперфузія у щурів. Експериментальним тваринам внутрішньовенно вводили мезенхімальні стромальні клітини з Вартонових драглів пуповини людини (hWJ-MSCs) або мезенхімальні стовбурові клітини жирової тканини дорослих людей (hAD-MSCs). Стан щурів оцінювали за динамікою смертності, неврологічним дефіцитом та біохімічними показниками через 7 та 14 днів після операції.

Результати. Смертність після трансплантації hWJ-MSCs становила 10% проти 65% у контрольній групі та 32% у групі щурів, які отримували hAD-MSCs. На 7-й день значення за шкалою McGraw становили 7,1 ± 0,19/8,9 ± 0,23/11,8 ± 0,48 балів у щурів, яким вводили hWJ-MSCs/hAD-MSCs/фізіологічний розчин; на 14-й день ці показники були 4,9 ± 0,15/ 5,7 ± 0,23/ 9,1 ± 0,30 балів, відповідно. Трансплантація мезенхімальних стромальних клітин усунула енергетичний дефіцит в ішемізованій тканині мозку щурів, зменшила метаболічний ацидоз та оксидативне пошкодження нейронів, а також позитивно вплинула на метаболізм оксиду азоту, але hAD-MSC були менш ефективними.

Висновки. Трансплантація hWJ-MSC мала кращий терапевтичний ефект, ніж трансплантація hAD-MSC.

Ключові слова: соматосенсорна кора, ішемія-реперфузія, мезенхімальні стромальні клітини, вартонівське желе, жирові стовбурові клітини, біохімічні параметри.