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EVALUATION OF HUMAN MONONUCLEAR UMBILICAL CORD BLOOD CELLS SYSTEMIC ADMINISTRATION EFFICIENCY IN THE ACUTE PERIOD OF EXPERIMENTAL SEVERE SPINAL CORD INJURY

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Aim. To evaluate the efficiency of systemic (intravenous) application of cryopreserved human umbilical cord blood mononuclear cells (HUCBCs) in animal models of acute contusion spinal cord injury for the restoration of hind limb motor function and formation of posttraumatic cysts using clinically significant examination methods.
Materials and methods. Adult female Sprague–Dowley rats were used for the study. Severe acute contusion spinal cord injury model was performed using standard "weight-drop" method. All samples of cryopreserved HUCBCs concentrate were prestored prior to infusion for 3 to 4 years at –196 °C. Hind limbs motor function was evaluated using open-field technique and standard BBB testing system. Magnetic resonance scanning was performed using high-field magnetic resonance CleanScan 7.0 T tomography (Bruker BioSpin, Germany).
Results. Intravenous infusions of HUCBCs were performed on Day 1 following acute severe spinal cord injury. Motor function assessment demonstrated significant (p <0.05) improvement of hind limbs motor function (up to 40–50 %) comparing to self-healing outcomes. Moreover, by the Days 4 and 5 after severe spinal cord injury, the volume of post-traumatic cystic cavity decreases significantly (up to 40 %) (p <0.05).
Conclusion. The obtained results demonstrated that cryopreserved HUCBCs can be used as an effective source for cell therapy of acute contusion spinal cord injury.

Keywords: spinal cord injury, cell therapy, human umbilical cord blood mononuclear cells

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INTRODUCTION

Spinal cord injury (SCI) is severe structural damage of the central nervous system, resulting not only in the loss or profound impairment of the sensory, motor, and vegetative functions of the body, but possibly in the death or profound disablement of the injured person, most often for the lifetime. The estimated incidence of SCI is 10.4–83 cases per 1 million people annually, varying widely among regions and countries. SCI most often occurs in young people aged 20–35 years, the most able-bodied and active population group. Since the favorable outcome rate is 9–53 cases per 1 million people, the loss of effective years of life has huge economic and social implications [1, 2].

As the condition of the injured persons is severe and there are virtually no effective pathogenetic treatment methods, the level of disablement is extremely high, with up to 80–85 % of those who experienced SCI becoming group I–II disabled, which then requires lifetime inpatient treatment in neurological hospitals and rehabilitation centers [3, 4].

There is an ongoing search for new treatments for SCI that would improve the spinal cord functions and restore its structure after its traumatic damage or lower the grade of this damage. of particular interest is cell therapy, which may be promising as a treatment for spinal cord damage [5, 6].

As one of the most accessible and effective sources of cell material, human umbilical cord blood cells have been numerously and successfully used in a number of clinical studies for various–cardiological, vascular, hepatic, muscular, neurological, and mental – pathologies, including stroke, spinal cord injury, brain injury, cerebral palsy, Alzheimer's disease, Parkinson's disease, cardiac and hepatic insufficiency, depression, schizophrenia, and autism [7].

The problem with conducting clinical studies of SCI is that they are dependent on standardized indicators of the neurological function to enroll the patients (which does not really take into account the heterogeneous development of the traumatic process, its localization, severity, and the patient's genetics), and to evaluate the efficacy of the treatment. Overall, it is extremely unlikely to encounter two identical cases of SCI, which makes standardization impossible and thus substantially hinders the evaluation of the efficacy of any treatment conducted.

In turn, animal models are standardized a lot better, well controlled, and allow for research into SCI treatment options *in vivo*, a major step towards the clinical use of any therapy. One experimental model is contusion (impact) spinal cord injury, imitating the most common spinal cord damage in humans [8–10].

A complicated fracture or dislocation of the spine results in damage to the nervous system structures, which in turn gives rise to an impact focus (contusion focus) and hemorrhage into the spinal cord tissue. In regard to impairment of the motor activity in the limbs and morphological changes in the spinal cord, similar damage to the spinal cord in rats is the closest to that in humans. Hence this model can be used to evaluate the efficacy of the treatment and may be of interest to applied medicine [11].

Numerous preclinical studies showed that cell therapy, in particular umbilical cord blood cells, helps restore the motor function of the limbs. We also noted in our work that systemic use of umbilical cord blood cells significantly and substantially reduces the volume of the posttraumatic spinal cord cyst, which is inevitably present in every case of spinal cord contusion. This suggests that human umbilical cord blood mononuclear cells (HUCBCs) have a neuroprotective action. However, there has been no work whose authors would assess the correlation between functional outcomes of cell therapy and the trend of the posttraumatic cyst volume.

The aim of the study is to evaluate the efficiency of intravenous application of cryopreserved HUCBCs in the early acute period of severe contusion SCI in regard to hind limb motor function and the structure of posttraumatic spinal cord cysts using clinically significant examination methods: magnetic resonance imaging (MRI) and assessment of the neurological status.

MATERIALS AND METHODS

Adult female Sprague–Dowley rats, weighing 230–250 grams, were used in this study. These were kept in individual cages under standard conditions of an experimental biological laboratory with a 12/12 light schedule and unrestricted access to water and food. The animals were obtained from the Pushchino Livestock Breeding Complex, a branch of the Federal State Budgetary Institution of Science, Shemyakin–Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences (Pushchino town, Moskovskaya Region, Russia). All the experimental protocols were approved in accordance with the ethical and scientific recommendations of the Ministry of Health of the Russian Federation (Order No. 267 of 19/06/2003), the National Standard of the Russian Federation GOST R 53434–2009, and the rules for the maintenance and care of experimental animals, in accordance with the directives of the Council of the European Community 86/609/EEC on the use of animals for experimental research.

Surgical technique and modeling of injury. Severe contusion SCI model was performed using standard "weight-drop" method [12]. A rat with an injury of this kind is unable to achieve full self-recovery of the motor activity of the limbs. After narcotizing the animal by intraperitoneal injection of 5 % ketamine solution (100 mg/kg) and 2 % xylazine solution (20 mg/kg), laminectomy was performed at the T_9 level and the spine was fixated with clips at the spinous processes of T_8 and T_{10}. In the event of hemorrhage, a SURGIFLO hemostatic matrix with thrombin was used to ensure quality hemostasis and reduce the impact on the dural sac. The contusion injury model was performed using a metal rod of 2 mm in diameter and 10 g in weight, falling vertically from a height of 25 mm. After contusion, the muscles and skin were sutured permanently (Fig. 1). After the surgery, the animals received antibacterial therapy of gentamicin sulfate 1 mg/kg of body mass intramuscularly for 7 days. No cytostatics were administered. In the first 2–5 days after the injury, manual massage of the anterior abdominal wall was performed to empty the urinary bladder until regression of urinary retention [13].

HUCBC samples. The cryopreserved HUCBC concentrate was provided by a specialized cryobank (Krio Tsentr LLC, Moscow) free of charge and stored for 3–4 years at –196°C (quarantine and storage of specimens in liquid nitrogen). Before administration, the cells were defrosted, washed clear of the cryoprotector, and resuspended in physiological solution [14]. The number of living cells in the sample was assessed with trypan blue staining before administration. Evaluation of viability showed the number of living cells amounting to 93–95 % in every case.

Experimental groups. After inducing the injury, the rats were randomized into 3 groups: 1) control group (self-recovery) (n = 7): administration of 1 ml of physiological solution in the caudal vein 24 hours after the injury; 2) 1st-day cell therapy group (n = 6): administration of 10×10^6 HUCBC in 1 ml physiological solution in the caudal vein on Day 1 after inducing the SCI; 3) 5th-day cell therapy group (n = 5): administration of 10×10^6 HUCBC in 1 ml physiological solution in the caudal vein on Day 5 after inducing the SCI.

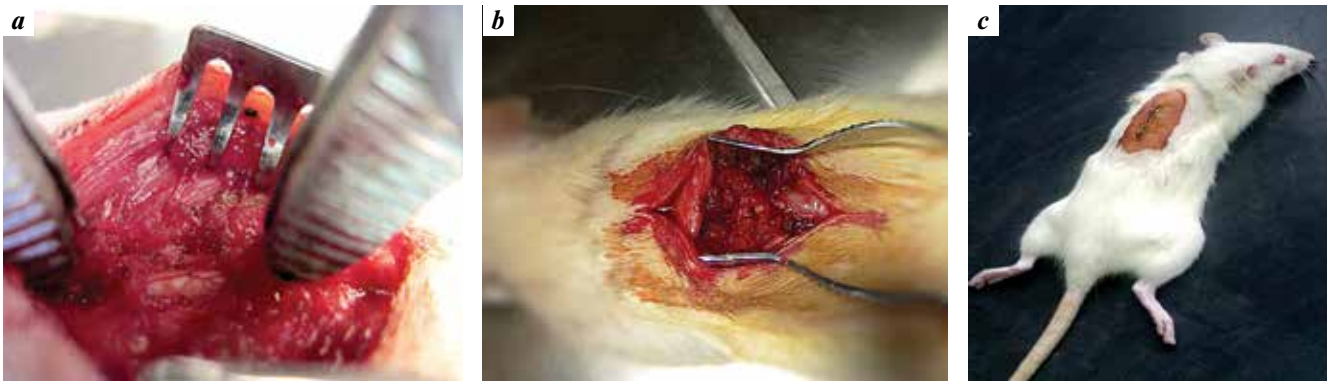

Fig. 1. *Stages of spinal cord contusion (SCC) modeling in a lab rat: a – surgical wound prior to SCC application: laminectomy of the Th_9 vertebra is performed, the dorsal surface of the spinal cord is visualized; b – surgical wound after SCC application: parenchymatous hematoma in the spinal cord structure is visualized; c – rat after wound closure: anterior paraplegia after SCC is observed*

The efficacy of cell therapy was evaluated using clinically significant examination methods.

Assessment of the neurological status. The motor function of the limbs was evaluated by the standard method in the open field using Basso, Beattie Bresnahan (BBB) scale, the standard scale for evaluation of the locomotor system in rats [15]. The movements of the animals, which had been priorly accustomed to testing, were captured visually and by video recording in the open field of 75 × 125 cm in size for 4 minutes with subsequent evaluation using a 21-point scale, where 0 points meant completely immobile hind limbs and 21 points meant a consistent and coordinated gait of a healthy animal with parallel position of the hind limb paws and consistent stability of the trunk.

The blind evaluation was performed by two independent experts, without marking the animal number or group. The tests were performed weekly for 5 weeks, starting from Day 7 after the SCI. Coordination of the limb movement was also tested using the narrow beam walking test [16].

Diagnosis and evaluation of spinal cord damage using MRI. MRI is the gold standard to study the soft tissue structure and diagnose damage to the structures of the central nervous system, including SCI. Besides computed tomography to assess the spinal osseous structures, all admitted inpatients with a suspected complicated spinal fracture undergo an obligatory MRI to assess the spinal cord structure, to diagnose for possible damage to the spinal cord and its roots and for traumatic damage of intervertebral discs, or to identify intracanal hemorrhages [17]. The MRI devices to diagnose spinal cord damage in humans are mostly 0.3–0.5 to 3 T. However, this intensity of magnetic field and, in particular, the large diameter of the gantry is not suitable for small lab animals. The similar diagnostic process in animal models may employ ultra-high-field MRI devices with a small gantry.

In this study, MRI was conducted using an ultra-high-field ClinScan 7.0 T (Bruker BioSpin, Germany), designed specifically for small lab animals. The analysis was performed on 2D images in axial, sagittal, and frontal planes obtained with the following scanning parameters: TR = 40 ms, TE = 29 ms, base resolution 320 × 230, FOV 45 × 32 mm, turning angle 15°, slice thickness 0.5 mm. Reference MRI myelography was also used in certain cases.

The MRI images were analyzed and the volume of posttraumatic cystic cavities was calculated for 6 weeks after the SCI in axial, sagittal, and frontal planes using the specialized viewing software for DICOM images, RadiAnt DICOM Viewer (by Medixant, Poland) and MicroDicom 3.9.5.666 (by MicroDicom Ltd., Bulgaria), which are widely used in clinical practice. Selected images were used to assess the structure of the spinal cord contusion focus cavities and their dimensions, calculating the three transverse radii. In the vast majority of cases, posttraumatic spinal cord cysts are close to ellipsoid in their shape, which makes it possible to calculate the cavity volume using the standard formula for the ellipsoid volume:

$$V = \frac{4}{3} \times \pi \times a \times b \times c\,.$$

The *a* radius was half the cavity length in sagittal or frontal plane cutting through the cavity epicenter; the *b* radius, half the anteroposterior cavity dimension in sagittal projection cutting through the cavity epicenter; the *c* radius, half the cavity width in frontal or axial projection cutting through the cavity epicenter (Fig. 3).

Statistical analysis of the obtained data was performed using Microsoft SPSS Statistics 25.0. The data were processed and results in each group were compared using

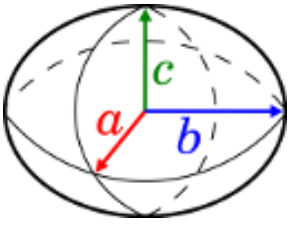

Fig. 2. *Ellipsoid radii (semi-axes) for calculation of cavity volume*

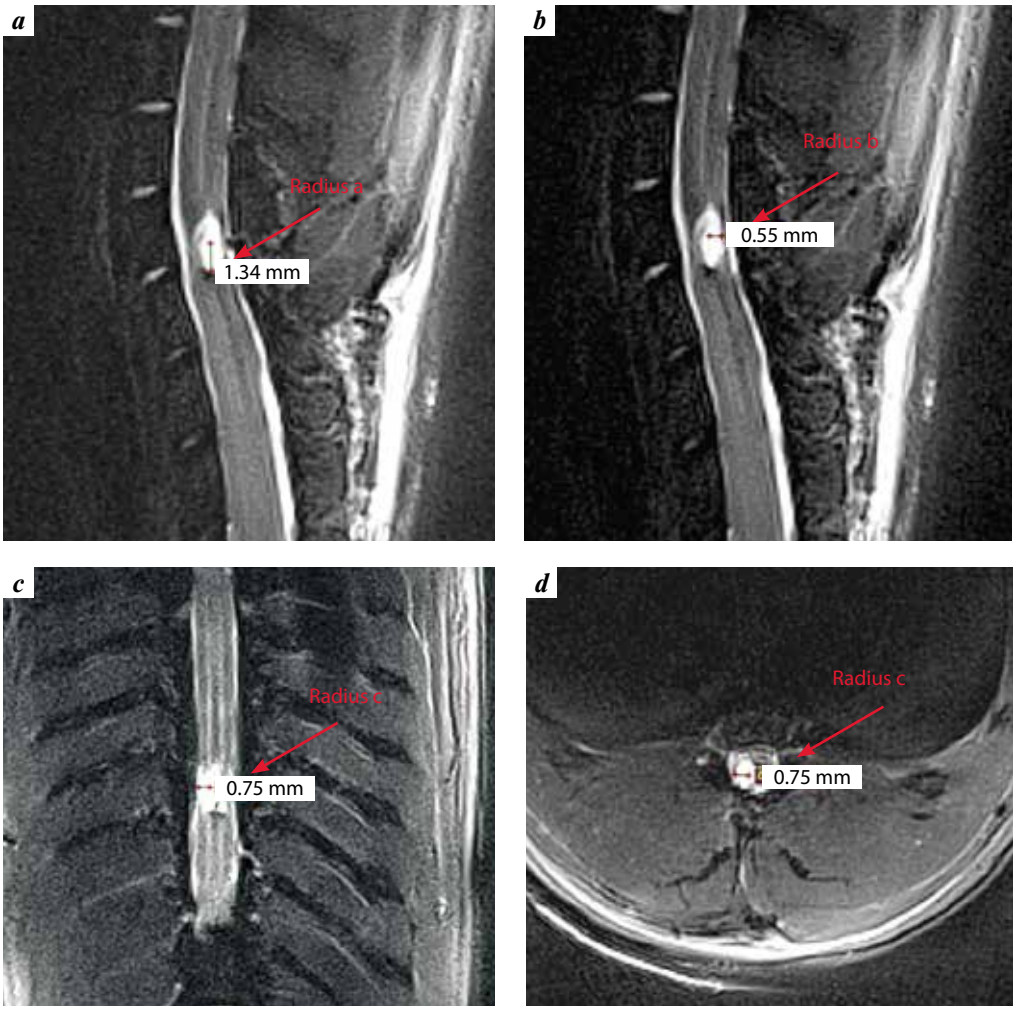

Fig. 3. *Calculation of posttraumatic cystic cavity volume based on its size determined using magnetic resonance images (ClinScan tomograph, Brucker BioSpin, Germany). T2-weighted images: sagittal (a, b), frontal (c) and axial (d) projections centered on the posttraumatic cavity. Arrows show radii measured on every image*

single-factor analysis of variance and the Newman – Kales criterion. Significant differences were considered those with $p < 0.05$. This criterion was chosen to compare several samples of parametric data and is also often used to analyze the efficacy of administration of medications in various patient groups. The results are presented as mean values and standard errors of mean (M ± SEM).

RESULTS

Assessment of the trend in motor functions. Posterior paraplegia was observed in both animal groups within Day 1 from the SCI. Impaired function of the pelvic organs was also observed, mainly as urinary retention, which regressed 3–5 days after the SCI.

It was shown that the animals receiving cell therapy after SCI were characterized by faster and substantially better recovery of the motor activity of the hind limbs than those in the control group, with indicators being significantly different as early as week 2 after the injury (Fig. 4). As of weeks 4 and 5 after the injury, the mean BBB scores in the self-recovery group were 4.7 ± 0.9 and 5.3 ± 0.7 respectively, indicating minor movements in three joints: hip, stifle, and ankle joint. The animal groups receiving HUCBC featured a recovery of movements scoring 7.3 ± 0.6 and 7.5 ± 0.6 points over the same time period, which indicates more extensive movements in the hind limb joints. Thus, administering HUCBC significantly ($p < 0.05$) improves the recovery of motor function in hind limbs, up to 40–50 % as compared to the control group. Apart from that, there were no significant differences found between the 1st- and 5th-day cell therapy group (see Fig. 4).

It should be noted that the narrow beam walking test, which requires that weight maintenance and movement coordination of the front and hind limbs, did not show any positive effect from the HUCBC cell therapy. Considering the low sensitivity of this test, where the animal is required to exert a fairly high level of physical activity, the gross motor deficit does not allow for significant detection of any differences. We refrained from using this test any further because of its inefficacy.

Diagnosis and assessment of spinal cord damage with MRI. MRI done on Day 2 after inducing the injury showed

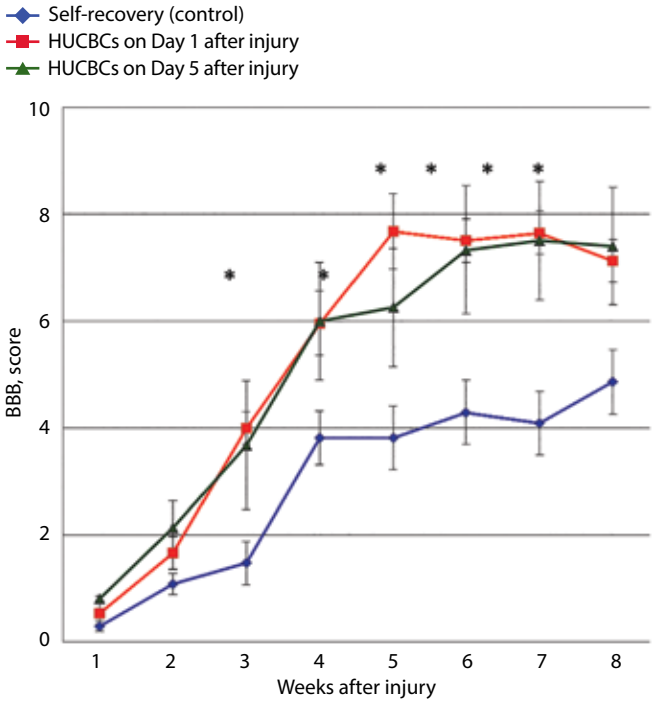

Fig. 4. *Dynamics of recovery of motor activity of the hind limbs in rats after injury (bruisng) of the spinal cord: during self-recovery and after cell therapy using human umbilical cord blood mononuclear cells (HUCBCs) on days 1 and 5. BBB scoring system in the open field. *p <0.05*

an intramedullary hematoma forming into the spinal cord tissue. Further examinations done at weekly intervals showed an ongoing formation of the contusion focus and formation of posttraumatic cystic cavities (Fig. 5). In weeks 4 and 5 after the injury, MRI shows typical pathological changes in the spinal cord tissue, namely posttraumatic cystic cavities of high intensity in T2-weighted images. These traumatic cysts are surrounded with a scar tissue area, which according to the histology consists of a thinner layer of astrocytes, directly adjacent to the cyst (astroglial scar), and a much thicker layer of fibrocytes, located further outwards (fibrous scar). Thus, by week 4–5 after the injury, the animals form a complete cystic-glial-fibrous transformation of the damaged areas of the spinal cord. The areas transformed in this way substantially prevent the nerve tissue from further repair and lock out the damaged area, thus blocking many biologically active factors from entering it.

The volume of the posttraumatic cystic cavity was determined by manual calculation based on T2-weighted MRI images over 6 weeks after the SCI, which showed that the mean volume in the self-recovery group in week 4 after the SCI amounted to 9.2 ± 0.9 mm^3; in the 1st-day HUCBC-receiving group, 3.7 ± 0.4 mm^3; in the 5th-day HUCBC-receiving group, 4.2 ± 0.8 mm^3. The same indicator in the control group in week 5 amounted to 8.5 ± 0.7 mm^3; in the 1st-day cell therapy group, 3.08 ± 0.3 mm^3; in the 5th-day cell therapy group, 3.94 ± 0.7 mm^3 respectively (see table). Further, the maximum volumes of the contusion focus were substantially different: in the control group, 23.9 mm^3 in week 2 after the SCI; in the 1st-day cell therapy group, 8.1 mm^3 in week 3; in the 5th-day cell therapy group, 6.5 mm^3 (see table).

This study of 15 animals divided into 3 groups showed that administering HUCBC on Day 1 or 5 after inducing the SCI significantly reduces the volume of the contusion focus formed in the spinal cord by a factor of 2.6–3.3, a substantial amount for the small spinal cord in rats. Comparison of the experimental groups receiving HUCBC on Days 1 and 5 after inducing the trauma demonstrated a significant unidirectional trend showing a higher efficacy of cell therapy when administered on Day 1, but the difference between the mean indicators was minor (Fig. 6).

The most illustrative period is the late acute period of the traumatic process, corresponding to weeks 4–5 after the injury for the SCI model in rats. An analysis of the indicators obtained shows that cell therapy with HUCBC reduces the volume of the posttraumatic cystic cavity in animal models of severe contusion SCI in the acute period substantially (up to 40 % as compared to the control group) and significantly (p <0.05) (Fig. 7).

DISCUSSION

The treatment of traumatic spinal cord damage remains a clinically and socially significant medical problem unresolved as yet. All treatment methods available today are basically palliative and are aimed at ensuring conditions for the spinal cord to recover itself. However, the recovery of the damaged spinal cord tissues and its functions is extremely low, with favorable outcomes of treatments only in cases of relatively mild damage. The vast majority of the most severe cases of damage, featuring ASIA A and B neurological deficits, do not achieve any substantial recovery.

Considering the above, we consider that it is of utmost importance to develop new methods that would be more effective and primarily target the factors of secondary damage to the spinal cord. Regenerative therapy technologies, in particular cell therapy, have proven to be successful in many preclinical and some clinical study. However, most of the published works show that authors focus on evaluating the efficacy of the regenerative cell action, while the neuroprotective action is often overlooked.

This is because it is fairly easy to evaluate the efficacy of cell therapy on the recovery of the function or structure of the spinal cord, since there are numerous, both objective and more subjective, tests to assess the trend of the spinal cord functions, while it is a lot more difficult to assess the neuroprotective action.

When focusing on studying the neuroprotection in SCI, one of the parameters to be assessed is the dimensions of the area of posttraumatic changes in the spinal cord. Contusion damage inevitably leads to the formation of a posttraumatic cyst in the spinal cord structure in the long-term trauma period. This cyst is not some "extra" mass like a tumor, but basically arises right upon the trauma, though filled with hematoma or detritus in the early period. The detritus subsequently disappears, rendering the cyst more manifest.

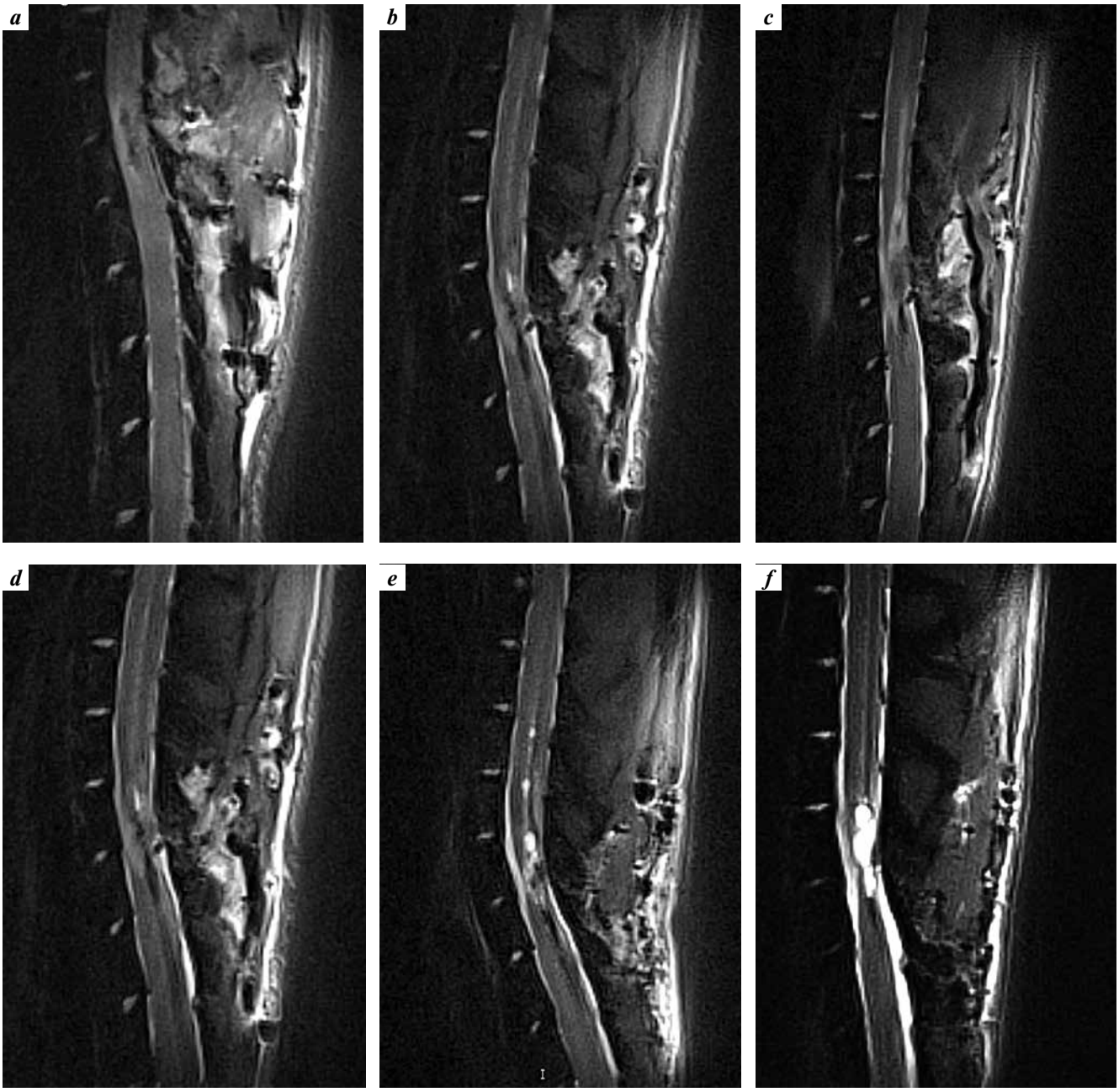

Fig. 5. *Dynamics of changes in the spinal cord after spinal cord contusion in rats per magnetic resonance imaging (sagittal sections, T2-weighted images): a – day 2 after injury; b – 1 week after injury; c – 2 weeks after injury; d – 3 weeks after injury; e – 4 weeks after injury; f – 5 weeks after injury. In the early period after spinal cord injury, hypointense signal is visualized on the T2-weighted images corresponding to parenchymatous hematoma in the spinal cord tissue (a–c), and blood is observed in the extended central canal of the spinal cord (a). Weak hyperintense signal in the injured area and around it corresponds to perifocal edema (a–d). With time, hypointense signal regresses (retraction of blood clots and dendrite elimination) (d, e), weak hyperintense signal of the perifocal edema also regresses (e). Hyperintense signal with a clear boundary appears corresponding to posttraumatic cystic cavity filled with cerebrospinal fluid (e, f). Additionally, significant decrease in spinal cord thickness is observed which is a consequence of tissue retraction during cystic gliotic fibrous transformation of the injured areas of the spinal cord (e, f)*

Importantly, however, there is a complex changed structure forming around the cyst. Considering the complicated interactions between the layers of the scar being formed, it would make sense here to refer to a complex cystic-glial-fibrous transformation of the damaged spinal cord. This structure substantially prevents the recovery of normal nerve tissue structure. Thus, the very important factor is the potential capacity of cell therapy to prevent this transformation or at least reduce it.

It is well-known that the actual spinal cord trauma is the primary factor of damage to the spinal cord. The injury immediately triggers an entire set of factors of secondary damage to the spinal cord, including edema, infiltration of the nerve tissue by immune cells (neutrophils and

Results of manual evaluation of contusion lesion volume in animals of the 3 groups based on magnetic resonance imaging (MRI) data

MRI No.	Contusion lesion volume in animals, mm³																
	Cell therapy group on day 5 after injury					Cell therapy group on day 1 after injury					Control group (self-recovery)*						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14**	15**	16	18
I	1.6	2.1	2.8	3	2.9	2.7	2.2	2.5	2.1	2.4	3.1	2.4	2.9	1.2	–	2.9	2.2
II	4.5	4	3.2	4.7	4.6	4	3.8	4.1	4.5	5	9.6	6.9	12.3	1.19	–	23.9	14.7
III	5	4.8	6.3	6.5	6.5	8.1	4	4.9	5.4	6.7	18.5	13	19.3	1.9	4.6	19	15.9
IV	4.2	4.5	4	4.4	5.5	4	3.6	3.8	5.2	4.5	12.4	6.1	11.7	1.9	–	14.9	12
V	4	4.1	3.8	4.2	5.3	3.7	2.5	3.3	4.8	4.3	9	6	9.3	1.9	–	11.4	10.4
VI	3.4	3.8	3.8	4.1	4.6	3.3	2.1	2.6	3.3	4.1	8	6.1	7.8	2	–	10.9	9.6
VII	3.8	4	4.7	6.4	–	5.2	4.2	3.2	–	–	12.8	–	12.1	–	–	–	18.6

**Injection of physiological solution on day 1 after injury. **Excluded animals.*

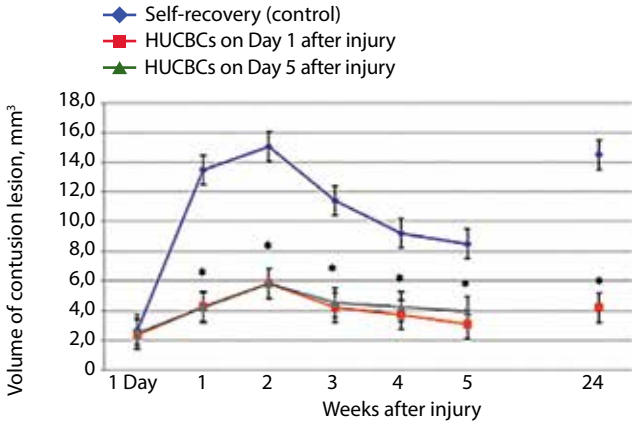

Fig. 6. *Dynamics of contusion lesion volume in severe spinal cord contusion injury in rats: in the control group and 2 treatment groups – cell therapy on day 1 and day 5. Significant decrease of the lesion volume in the treatment groups compared to the control group is observed. Between the treatment groups, no significant differences were observed. *Significant differences, p <0.05*

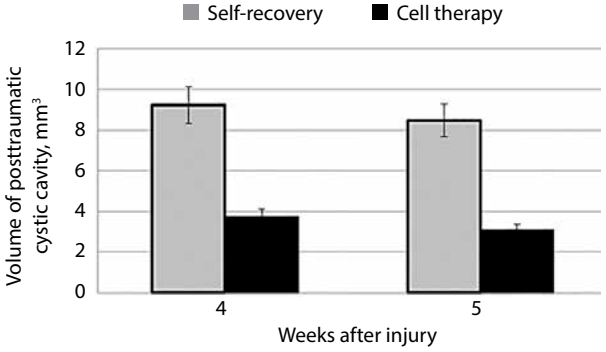

Fig. 7. *Volume of the posttraumatic cystic cavity at weeks 4 and 5 after injury during self-recovery and after cell therapy using mononuclear cells from human umbilical-placental blood (mean value in 2 treatment groups). *p <0.05*

macrophages), macrophages involving fibroblasts that form the fibrous part of the scar, aseptic inflammatory response, increase in the concentration of biologically active factors by several times, etc. The factors of secondary damage remain in effect long after the actual trauma and substantially worsen the spinal cord damage. It should be noted that the nerve tissue in the contusion epicenter dies within the first hours and days after the SCI, while the surrounding tissue in the area of perifocal edema preserves viability for some time. This pattern is basically analogous to the penumbra zone in the development of ischemic stroke of the brain. It is important to keep in mind that the neurons and their axons located in this area surrounding the contusion epicenter may survive under certain conditions and are the targets of the neuroprotective action of cell therapy. The indirect sign of such neuroprotection is the dimensions of the posttraumatic spinal cord cyst, a parameter that is convenient for analysis, since it can be assessed very reliably by precision methods of visualization, such as high-field MRI.

Thus, our main aim in this work has been to compare the dimensions of the area of posttraumatic changes in the spinal cord with and without cell therapy is used, which suggests neuroprotective action of HUCBC. We used manual calculation of the dimensions of the spinal cord cysts to compare the animals from the experimental and control groups.

The results of the study show that HUCBC, administered intravenously either 1 or 5 days after the SCI, help recover the motor function of the hind limbs in animals, even restoring extensive movements in three joints: hip, stifle, and ankle joint. Some of the animals were able to maintain the body mass at rest but not when moving, while most were able to move around on a surface with certain limitations. The movement recovery trend improves as early as week 2 after the trauma. However, in the same 2 weeks after the SCI, MRI showed no substantial differences between the two groups of animals in the spinal cord structure that would be related to the subsequent formation of posttraumatic cystic cavities. In week 4, the movement recovery rate begins to stabilize and

the MRI images show signs of incipient formation of typical posttraumatic spinal cord cysts.

Thus, administering HUCBC on Day 1 or 5 after inducing the SCI significantly reduces the volume of the contusion focus formed in the spinal cord by a factor of 2.6–3.3, a substantial amount for the small spinal cord in rats. Comparison of the experimental groups receiving umbilical cord blood cells on Days 1 and 5 after inducing the trauma demonstrated a significant unidirectional trend showing a higher efficacy of cell therapy when administered on Day 1, but the difference between the mean indicators was minor. The first three examinations showed no difference in the volume of the contusion focus between the two groups, while the fourth showed a difference of 0.3 mm^3. Subsequently, the difference in the focus volume increased to 0.56 and 0.86 mm^3 respectively. The data obtained confirm the suggestion that the neuroprotective cell action does help preserve the spinal cord fibers and prevents secondary damage to the neurons and axons. In early stages of the traumatic process, when the primary damage arises from the blood accumulating in the tissue (hematomyelic focus) and the contusion focus itself is still being formed, the cells administered on Day 1 or 5 only begin to take effect. However, considering the significant difference between the experimental groups, it may be suggested that the cell therapy administered on Day 1 after the trauma is more effective.

Yet it should be noted that, notwithstanding the obvious correlation of the trend of the dimensions of the posttraumatic spinal cord cyst and the trend of recovery of the lost spinal cord functions, the localization and structure of the cyst itself may also play a role. Also, one cannot be completely certain that the cyst dimensions do comprehensively reflect the functional neurological status. On the other hand, the correlation between the graphs showing the recovery degree of the neurological functions and the reduction in the volume of the posttraumatic spinal cord cysts is highly suggestive of a connection here. However, further research into the structures of posttraumatic spinal cord changes is needed using high-technology methods, such as MRI 7.0 T. This is also the occasion to benefit from the method involving computer analysis of the structure of posttraumatic spinal cord changes, developed by us and scheduled for use in the following stages of the study, its results to be published as a separate article.

CONCLUSION

The results obtained in the study demonstrate that cryopreserved HUCBCs administered systemically once to animal models of severe SCI help effective recovery of the spinal cord functions and have a neuroprotective action, ensuring the survival of the neurons and their axons that were damaged but did not die upon the trauma. A single-time administration of 40–43 million HUCBC per 1 kg of body mass helps increase the preservation of the nerve tissue of the spinal cord and ensures a better recovery of the lost functions of the spinal cord.

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V.A. Smirnov: research design development, animal surgery, collection and analysis of material, article writing, approval of the final text of the article;
S.I. Ryabov: research design development, analysis of the data obtained, article writing;
M.A. Zvyagintseva: functional testing of animals, collection of material, analysis of the data obtained;
S.A. Bazanovich: analysis of the data obtained, statistical processing of the data obtained;
Ya.V. Morozova: collection and analysis of material;
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Compliance with patient rights and principles of bioethics
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