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Positive and negative aspects of cell technologies in cerebral diseases

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Abbreviations: DWI, diffusion weighted imaging; FITC, fluorescein isothiocyanate; MRI, magnetic resonance imaging; MSC, mesenchymal stem cells; PET, positron emission tomography; SC, stem cells; SPECT, single photon emission computed tomography; TBI, traumatic brain injury; WHO, world health organization

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Introduction

Discouraging statistics characterizes low efficiency of diagnostics and treatment of acute and chronic cerebrospinal diseases and initiates search of new, more effective technologies to resolve that socially important issue.[1,2] About 6 million people die due to stroke each year according to WHO.[1] Traumatic Brain Injuries (TBI) claim about 10 million lives annually.[3] Surgical intervention still remains the key method of treatment of such fatal cerebral diseases as stroke, TBI, cerebral aneurysms and neoplasms. Efficiency of surgery increases with the use of robotic devices (da Vinci Robotic System, SpineAssist, Renaissance Robotic Systems), assimilation of high-tech operations (microsurgical, endovascular, stereotaxic interventions etc.), implementation of combined therapy and new rehabilitation techniques.[4–6] Opportunities of diagnostic procedures in cerebral diseases are also increased through modern diagnostic equipment (MRI Scan, PET scan, SPECT scan, DWI MRI etc.), that is able to enhance early-stage diagnostics, but still has no effect on treatment outcomes.[7–9] Current situation remains the basis for constant search of new methods of treatment of cerebral diseases. And these methods have been developed lately in the field of cell biology and neurophysiology.

In particular, cell technologies have been adapted to treatment of socially important diseases in recent years.[10] There were both followers and opponents of cell technologies' implementation into clinical practice at the early stage, by the way that is usual for any novelty. We will pay attention in terms of observed problem to methods based on stem cells (SC) use in combined treatment of cerebral diseases. SC has been found in various organs and systems of living organism and their role is still not investigated in detail. Three main pools of SC were detected in brain: in the area of olfactory bulbs, in hippocampus and walls of brain ventricles.[11] Potential of endogenous brain stem cells in health and disease is constantly studied, but oppressive statistics of chronic brain diseases and high mortality due to TBI, stroke, inflammatory and neurodestructive processes speaks for their low effectiveness. There were experimental attempts performed to increase potential of endogenous SC by additional injection of exogenous SC by different ways into the area of pathological focus. The amount of preliminarily *in vitro* cultivated exogenous stem cells reached thousands and even millions per 1 ml. Three ways of administration of SC suspension or mesenchymal SC (MSC) are used in order to implement new method in cerebral diseases: into bloodstream of arterial and venous vessels, into cerebrospinal fluid via lumbar or suboccipital puncture and finally directly into the area of pathological focus in brain after additional craniotomy.[12,13] Several lacks have been stated at the experimental stage of all these ways of SC administration. Administration of SC into bloodstream – besides distribution in the whole volume of circulating blood – causes problems at the stage of SC penetration through blood-brain barrier. Necessity of additional surgical procedure – craniotomy – also becomes a negative approach for seriously ill patient after stroke or TBI. Administration of SC into cerebrospinal fluid requires measures in order to overcome craniospinal liquor flow and reach destructive area in brain (change of body position, lumbar or suboccipital punctures). First experience of cell technologies use also revealed one more negative effect coming from the risk of SC transformation into tumor cells.[14–16] Information about malignancy processes usually appears after surgical procedures in cosmetology rooms. However negative response in mass media forms awareness in future patients.

Despite of pronounced side effects, cell technologies demonstrated high effectiveness of reparative potential in cerebral diseases along with minimum of side effects after application of autologous MSC on the area of cranial nerves endings.[17,18] Olfactory and trigeminal nerves are the most common targets for application in the modelling of brain diseases.[17–19] For example, intranasal injection of FITC-labeled MSC into the area of olfactory nerve endings resulted in appearance of fluorescent MSC already in 30 minutes in olfactory bulbs and in several hours – in trauma region, mainly in anterior cranial fossa.[18,19] Somatotropic distribution of stem cells in brain was substantiated by the fact of predominant migration of MSC to destructed brain areas located in posterior cranial fossa after preliminary administration into the area of trigeminal nerve endings. Therefore, the technique of MSC administration based on perineural migration of MSC to neurodestructive region was experimentally developed for clinical application.[17–19]

The next self-evident conclusion should be mentioned: it was experimentally and clinically proved, that autologous stem cells are the safest biomaterial for recovery of violated brain functions. The use

of autologous SC minimizes risk of tumor development associated with administration of exogenous stem cells into living organism. Experimenter and clinician should follow unbreakable principle "first, do no harm" in order to constantly achieve positive effects of clinical technologies use and level negative effects.

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Conflicts of interest

All listed authors concur with the submission of the manuscript; all authors have approved the final version. The authors have no financial or personal conflicts of interest.

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