

Traumatic Brain Injury and Stem Cell Therapy

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ABSTRACT

Traumatic brain injury is a major health issue globally. Recently, there is no effective treatment, which can improve functional recovery of the TBI patients. Recent studies conclude that stem cell therapy has got tremendous regenerative potential, which can cure CNS injuries. Experimental Success in stem cell therapy also raise a hope in researchers to investigate more. The therapeutic aspects of stem cell therapy are based on the potential to differentiate in to tissue specific cells and integrate in to host tissue to regenerate the lost cells or injured cells. This commentary reflects the role of variety of stem cells in treating TBI.

Key words: Traumatic brain injury, Mesenchymal stem cells, Stem cell therapy, Neural stem cells, Endothelial progenitor cells

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SHORT COMMENTARY

Traumatic brain injury (TBI) is the reason for 50% of all trauma related mortalities. Blunt and penetrating injuries to brain contributes to an enormous public health issue. There are strong chances of a lifetime physical, mental or cognitive impairment, following a moderate or severe brain injury. With Helmets, we can effectively avoid disability or lost life from traumatic brain injury [1].

TBI is a major health issue in modern world. Currently, there is no definitive treatment to improve outcomes after TBI. According to WHO, TBI will be the main cause of human mortality and morbidity after2020.It will make huge financial burdens to patients and their families [2].

TBI causes the destruction of normal brain function. Pathophysiology of TBI mainly manifests as Neurodegenerative lesion, extensive neuroinflammation, diffuse axonal injury, and breakdown of the blood brain barrier [3]. Study revealed that a variety of stem cells like mesenchymal stem cell (MSCs), Neural stem cells, Endothelial progenitor cells (EPCs) and Multipotent adult progenitor cells (MAPCs) can treat neurological impairments after TBI [4].

Another study suggested that Multipotent neural stem cells/progenitor cells (NSCs/NPCs) persist in selected regions of the brain throughout the life span of an animal, making the brain capable of generating new neurons and glia [5].

Numerous clinical and experimental studies expanded the knowledge and understanding of TBI, which may open new horizon for the treatment. In recent times Traumatic brain injury is the main cause of mortality and morbidity in most of the trauma cases. The principal mechanisms of TBI are classified as:

Focal brain injury due to contusion, laceration, and intracranial haemorrhage.

Diffuse brain injury due to acceleration/deceleration injury types resulting in diffuse axonal injury or brain Edema [6-8].

TBI is a multidimensional cascade of injury, which combines mechanical stress to brain tissue with an

imbalance between metabolism and cerebral blood flow (CBF), brain Edema, excitotoxicity, inflammatory, and apoptotic phenomenon. A better understanding about TBI may offer wide spectrum of therapeutic strategies, such as, management of CPP (cerebral perfusion pressure), mechanical hyperventilation, kinetic therapy for improving oxygenation, to reduce excitotoxicity, and Intracranial Pressure (ICP). Even after adopting all the appropriate strategies, the individual's recovery often remains unpredictable. It requires meticulous planning and monitoring of individuals injured brain function in order to giving a multidimensional therapeutic approach according to specific condition of the patient [9].

Clinical trials indicated that MSC transplantation has potential to become an effective treatment for TBI Patients. Additionally, umbilical cord mesenchymal stem cells transplantation improved the neurological outcomes safely and effectively in the patient with TBI consequences [10].

Contrarily, MSCs cannot act as agent of cell replacement as they do not differentiate in to neural cells or tissues, which can be grafted. This is the reason, because of which, therapeutic role of MSC in TBI lesion and its relevance to human remains unknown [11].

Endothelial progenitor cells (EPCs) play a key and active role in revascularization, repair of tissues damaged by traumatic injury, ischemic, and inflammatory injuries. EPCs may also serve as prognostic marker for TBI. This study also demonstrated that increase in circulating EPCs is closely associated with improved clinical outcome in TBI patients. Factors that limit or prevent EPC mobilization remain unidentified. Furthermore, the level of circulating EPCs don't show any relation with type of injury or Type of treatments given [12].

Interestingly ,circulating EPCs have been found to rapidly accumulate in the ischemic area in order to improve local blood flow , as there is enough evidences to suggest that peripheral EPCs actively participate in tissue repair ,angiogenesis ,and vascular repair to restore normal blood flow in traumatised area [13]. And number of circulating EPCs is reversely associated with the size of ischemic area [14]. Investigation of Neural Stem Cells (NSC)seeding on to polymer scaffolds and their implantation into infarcted brain cavities of mouse brain has shown an increase in neuronal tissue differentiation and regeneration of cortical tissue [15].

Another finding reveals that transplantation of intracerebral rat neural stem cell 7 days after a moderate TBI can improve motor functions but does not show improvement in cognitive function recovery [16].

Previous study has shown that acute NSC transplantation may be helpful in the recovery after TBI. Fetal rodent cortical tissues were isolated and transplanted in to injured cortical tissue of adult rats 24 h after a fluid percussion injury. Significant Improvements in motor and cognitive function, along with remarkable transplant survival and interaction between injured brain and transplanted cells were reported [17].

CONCLUSION

Stem cell therapy may be an important breakthrough in the handling TBI, as It has made a tremendous progress in recent years. We need to enhance our knowledge , understanding, and factors, which can improve the outcome of stem cell therapy in the treatment of TBI patient . Moreover, large number of issues like safety and efficacy of stem cell therapy, are also remains to be solved. Therefore, large sized clinical trials warranted before giving any premature consensus.

REFERENCES

- 1. Kraus JF, Fife D, Conroy C. Paediatric brain injuries: The nature, clinical course, and early outcomes in a defined United States population. Pediatr 1987; 79:501-507.
- 2. Maas AIR, Menom DK, Adelson PD, et al. Traumatic brain injury: Integrated approaches to improve prevention, clinical care, and research. Lancet Neurol 2017; 16:987-1048.
- 3. Xiong Y. Mahmood A, Lu D, et al. Histological and functional outcomes after traumatic brain injury in mice null for the erythropoietin receptor in the central nervous system. Brain Res 2008; 1230:247-257.
- 4. Cox CS. Cellular therapy for traumatic neurological injury. Pediatr Res 2018; 83:325-332.
- 5. Lois C, Alvarez-Buvlla A. Proliferating subventricular zone cells in the adult mammalian forebrain can differentiate into neurons and glia. Proc Natl Acad Sci 1993; 90:2074-2077.
- 6. Baethmann A, Eriskat J, Stoffel M, et al. Special aspects of severe head injury: Recent developments. Curr Opin Anaesthesiol 1998; 11:193-200.
- McIntosh TK, Smith DH, Meany DF, et al. Neuropathological sequele of traumatic brain injury :relationship to neurochemical and biochemical mechanisms. Lab Invest 1996; 74:315-42.
- 8. Nortje J, Menon DK. Traumatic brain injury: Physiology,mechanisms, and outcome. Curr Opin Neurol 2004; 17:711-718.
- 9. Steiner LA, Andrew PJ. Monitoring the injured brain: ICP and CBF. Br J Anaesth 2006; 97:26-38.
- 10. Wang S, Cheng H, Dai G, et al. Umbilical cord mesenchymal stem cell transplantation significantly improve neurological function in patients with sequelae of traumatic brain injury. Brain Res 2013; 1532:76-84.
- 11. Clervius H, Baig M, Mahavadi A, et al. Human neural stem cell transplants to address multiple pathologies associated with traumatic brain injury. Neural Regen Res 2019; 14:1699-700.
- 12. Liu L, Wei H, Chen F, et al. Endothelial progenitor cells correlate with clinical outcome of traumatic brain injury. Critical Care Med 2011; 39:1760-1765.
- 13. Rouhl RPW, van Oostenbrugge RJ, Damoiseaux J, et al. Endothelial progenitor cell research in strike: A

potential shift in Pathophysiological and therapeutical concepts. Stroke 2008; 39:2158-2165.

- 14. Gill M, Dias S, Hattori K, et al. Vascular trauma induces rapid but transient mobilisation of VEGFR2 (+) AC133(+) endothelial precursor cells. Circ Res 2001; 88:167-174.
- 15. Park KI, TengYD, Snyder EY. Injured brain interacts reciprocally with neural stem cells supported by scaffolds to reconstitute lost tissue. Nat Biotechnol 2002; 20:1111-1118.
- 16. Matthew TH, Sloan LE, Jimenez F, et al. Subacute neural stem cell therapy for traumatic brain injury. J Surg Res 2009; 153:188-194.
- 17. Sinson G, Voddi M, McIntosh TK. Combined fetal neural transplantation and nerve growth factor infusion: Effect on neurological outcome following fluid percussion brain injury in the rat. J Neurosurg 1996; 84:655.