LETTERS TO EDITOR

Mesenchymal stem cells: can it be used for the treatment of trauma hemorrhagic shock?

Dear Editor,

Hemorrhagic shock (HS) is a major leading cause of death after trauma [1], condition with no therapeutic options until now. Fluid, blood and its component and stopping of bleeders have been the cornerstone of management since many decades. The previous study has shown that resuscitation fluids (blood and its components) induce ischemia-reperfusion, promotes the production of reactive oxygen species, and activation of immune cells [2]. The excessive release of inflammatory cytokines contribute to tissue damage and is associated with the suppression of bone marrow stromal cells (BMSCs), hematopoietic progenitor cells (HPCs) leading to multi-organ failure and death [3,4]. No study has addressed on the dysfunction of BMSCs and HPCs may be reactivated by bone marrow mesenchymal stem cells (BM-MSCs) in T/HS patients. Authors feel BM dysfunction may be corrected by the MSCs in T/HS patients.

MSCs are the precursor cells for stromal tissue that supports hematopoiesis. Hematopoiesis including extracellular matrix (ECM) proteins are maintained and regulated by BM-MSCs. ECM-derived peptides promote cell adhesion, express on HPCs and are important in erythropoiesis, and controls immature HPCs within BM compartment [4,5].

MSCs are found in almost all tissues. MSCs have the capacity of self-renewal and differentiate into chondrocytes, osteocytes, and adipocytes as well as myocytes and neurons. Differentiation of MSCs leads to development of skeleton and bone formation and this development os regulated by bone morphogenetic proteins (BMPs). BMPs belong to the members of transforming group factor-beta superfamily. BMPs are grouped of homologous signaling proteins has diverse functions and plays an important role in embryogenesis, organogenesis, cell proliferation, and stem cell differentiation [6]. BM-MSCs have the ability to adhere plastic surface when grown in culture, its appear fibroblast-like morphology. MSCs are expressed CD73, CD90, and CD105 surface markers. They are used for the characterization of MSCs and are not expressed in hematopoietic lineage markers. MSCs can be isolated from the BM, adipose tissue, umbilical cord, fetal liver, muscle, and lung and have the potential expanded *in vitro* [6]. MSCs also have immunomodulatory properties; they act as an immunomodulator, controls peripheral tolerance, transplantation tolerance, autoimmunity, tumor evasion, as well as fetal-maternal tolerance. The previous study reported that pro-inflammatory cytokines viz. interferon gamma (IFNγ), tumor necrosis factor (TNFα), and interleukin-1beta (IL-1β) are secreted by MSCs. Sometimes, these pro-inflammatory cytokines may induce the secretion of anti-inflammatory immunosuppressive factors under local microenvironment condition [7]. Previous studies demonstrated that human MSCs maintained immunosuppressive microenvironment by secreting the cytokines, avoid allorecognition, and interfere with dendritic cells and T-cells function [8].

Administration of a single dose of MSCs impaired wound healing via regulatory treg cells after trauma in a rat model [9]. The recent studies demonstrated that treatment with MSCs after polytrauma (PT) to reduce inflammation and tissue regeneration [10,11]. MSCs have therapeutic promise in numerous preclinical and clinical models of diseases such as graft-versus-host disease, sepsis, hepatic failure, and acute renal failure. Previously published reports have shown preclinical and clinical use of BM-MSCs for tissue regeneration [11].

Recently, more than 283 clinical trials were registered with MSCs (www.clinicaltrials.gov) and 45 studies for MSCs in December 2012, of which two were related to lung injury [12]. The role of MSCs in T/HS has been poorly understood. Previous studies indicated that the allogeneic BM-MSCs transplantation improved rats rehabilitation scores after experimental PT [13]. Intravenously administered MSCs reduced pulmonary endothelial cell permeability, inflammation, and impaired wound healing in a rat model of HS and trauma [14].

The authors feel that MSCs may have the therapeutic option not only for the reactivation of BM dysfunction, but also for acute lung injury, acute respiratory distress syndrome caused by T/HS in humans. Differentiation capacity of MSCs may be applied for the treatment of T/HS. Further research on this subject needs to be done.

References

1. Bouglé A, Harrois A, Duranteau J. Resuscitative strategies in traumatic hemorrhagic shock. *Ann Intensive Care* 2013;3(1):1.
2. Kumar M, Rao DN, Mohanty S, Selvi A, Bhoi S. Interleukin (IL)-8 is an early predictor of mortality following trauma hemorrhagic shock. *Int J Adv Res Biol Sci* 2015;2(7):12-20.
3. Finfer S, Liu B, Taylor C, et. al. Resuscitation fluid use in critically ill adults: an international cross-sectional study in 391 intensive care units. *Crit Care* 2010;14(5):R185.
4. Livingston DH, Anjaria D, Wu J, et. al. Bone marrow failure following severe injury in humans. *Ann Surg* 2003;238(5):748-53.
5. Beederman M, Lamplot DJ, Nan G, et. al. BMP signaling in mesenchymal stem cell differentiation and bone formation. *J Biomed Sci Eng* 2013;6:32-52.
6. Wei X, Yang X, Han ZP, Qu FF, Shao L, Shi YF. Mesenchymal stem cells: a new trend for cell therapy. *Acta Pharmacol Sin* 2013;34(6):747-54.

7. Kyurkchiev D, Bochev I, Ivanova-Todorova E, et. al. Secretion of immunoregulatory cytokines by mesenchymal stem cells. *World J Stem Cells* 2014;6(5):552-70.
8. Ryan JM, Barry FP, Murphy JM, Mahon BP. Mesenchymal stem cells avoid allogeneic rejection. *J Inflamm (Lond)* 2005;2:8.
9. Gore AV, Bible LE, Song K, Livingston DH, Mohr AM, Sifri ZC. Mesenchymal stem cells increase T-regulatory cells and improve healing following trauma and hemorrhagic shock. *J Trauma Acute Care Surg* 2015;79(1):48-52.
10. Lee S, Choi E, Cha MJ, Hwang KC. Cell adhesion and long-term survival of transplanted mesenchymal stem cells: a prerequisite for cell therapy. *Oxid Med Cell Longev* 2015;2015:632902.
11. Hengartner NE, Fiedler J, Schrezenmeier H, Huber-Lang M, Brenner RE. Crucial role of IL1beta and C3a in the *in vitro*-response of multipotent mesenchymal stromal cells to inflammatory mediators of polytrauma. *PLoS One* 2015;10(1):e0116772.
12. Xu F, Hu Y, Zhou J, Wang X. Mesenchymal stem cells in acute lung injury: are they ready for translational medicine? *J Cell Mol Med* 2013;17(8):927-35.
13. Krumina G, Babarykin D, Krumina Z, et. al. Effects of systemically transplanted allogeneic bone marrow multipotent mesenchymal stromal cells on rats' recovery after experimental polytrauma. *J Trauma Acute Care Surg* 2013;74(3):785-91.
14. Pati S, Gerber MH, Menge TD, et. al. Bone marrow derived mesenchymal stem cells inhibit inflammation and preserve vascular endothelial integrity in the lungs after hemorrhagic shock. *PLoS One* 2011;6(9):e25171.

Author's Contributions

MK, SB drafted the manuscript. All the authors read and approved the final manuscript.

Competing Interest

The authors declare that they have no competing interests.

Funding

Sources of funding: None.

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Please cite this paper as: Kumar M, Bhoi S. Mesenchymal stem cells: can it be used for the treatment of trauma hemorrhagic shock?. *Int J Stud Res* 2015;5(1):15-6.

Received: 31 Jul 2015, Accepted: 05 Aug 2015

Access this article online	
Quick Response Code:	Website: www.ijsronline.com
	DOI: 10.4103/2230-7095.180089