Extended Abstract Journal of Biological and Medical Sciences 2019
Vol.3 No.5

Human Bone Marrow-Derived Mesenchymal Stromal Cells Injected Intrathecally in NOD/SCID Mice Preclinical Study of Biosafety and Biodistribution

Mari Paz Quesada[1]*, David García-Bernal[1,2], Diego Pastor[3], Alicia Estirado[4], Miguel Blanquer[1,2], Ana M García-Hernández[1], José M Moraleda[1,2] and Salvador Martínez[4,5,6]

1. Cellular Therapy and Hematopoietic Transplant Unit, Hematology Department, Virgen de la Arrixaca Clinical University Hospital, Biomedical Research Institute of Murcia, IMIB-Arrixaca, Campus of International Excellence "Campus Mare Nostrum" University of Murcia, Murcia, Spain

2. Internal Medicine Departments, Medicine School, University of Murcia, Murcia, Spain

3. Sport Research Center, University Miguel Hernández of Elche, Alicante, Spain

4. Neuroscience Institute UMH-CSIC, University Miguel Hernández of Elche, Alicante, Spain

5. CIBERSAM-ISCIII, Spain

6. Human Anatomy Department, Medicine School, University Miguel Hernández of Elche, Alicante, Spain

Introduction

Objective: Mesenchymal stromal cells (MSCs) have powerful immunomodulatory and neuroprotective properties, and have been tested in neurodegenerative diseases leading to significant clinical improvements. The regulatory guidelines specify the need for preclinical studies before any clinical trial, including bio-distribution tests and the exclusion of tumorigenesis. We conducted a preclinical study of human bone marrow MSCs (hBM-MSC) injected intrathecally into immunosuppressed NOD / SCID mice, to explore cellular biodistribution and toxicity as the preferred method of administration for cell therapy in Friedreich's ataxia (FRDA). Methods: To this end, hBM-MSCs were characterized according to ISCT standards and 3 × 105 cells were injected intrathecally into 12 animals (experimental group) and the same volume of culture medium in 6 animals (control group) . Blood samples were taken 24 hours (n = 9) or 4 months (n = 9) to assess toxicity, and eight organs were taken for histological studies. Genomic DNA was isolated from all tissues, and the mouse GAPDH and β2M and human β-actin genes were amplified by qPCR to analyze the biodistribution of hBMMSC. Results: There were no deaths or acute or chronic toxicity. Hematology, biochemistry and body weight were within the range of normal values in all groups. At 24 hours, hBM-MSC were detected in 4/6 vertebral cords and 1/6 hearts, and at 4 months in 3/6 hearts and 1/6 brains of transplanted mice. No tumors were found. Conclusion: This study demonstrated that the intrathecal injection of hBM-MSC is safe, non-toxic and does not produce tumors. These results provide additional evidence that hBM-MSC could be used in a clinical trial in patients with FRDA.

Methods: For this purpose, 3 × 105 cells were injected intrathecally into 12 animals (experimental group) and the same volume of culture medium in 6 animals (control group). Blood samples were taken at 24 h (n = 9) or 4 months (n = 9) to assess toxicity, and nine organs were taken for histology and safety studies. Genomic DNA was isolated from all tissues, and mouse GAPDH genes and human β2M and β-actin genes were amplified by qPCR to analyze the biodistribution of hBM-MSC.

Results: There were no deaths nor acute or chronic toxicity. Hematology, biochemistry and body weight were in the range of normal values in all groups. At 24 h hBM-MSCs were detected in 4/6 spinal cords and 1/6 hearts, and at 4 months in 3/6 hearts and 1/6 brains of transplanted mice. No tumours were found.

Conclusion: This study demonstrated that intrathecal injection of hBM-MSCs is safe, non toxic and do not produce tumors. These results provide further evidence that hBM-MSCs might be used in a clinical trial in patients with FRDA.

This work is partly presented at 2nd International Conference on Antimicrobial and Antibacterial Agents on November 11-12, 2019 at Istanbul, Turkey