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Update on the Clinical Applications of Mesenchymal Stem Cells

Mesenchymal stem cells are heterogenous adult multipotent stromal cells that can be isolated from various sources including bone marrow, peripheral blood, umbilical cord blood, dental pulp, and adipose tissue. They have certain regenerative, anti-inflammatory, immunomodulatory, immunosuppressive, antimicrobial, and other properties that enable them to have several therapeutic and clinical applications including treatment of various autoimmune disorders; role in hematopoietic stem cell transplantation and regenerative medicine; treatment of skin, pulmonary and cardiovascular disorders; treatment of neurological and eye diseases; as well as treatment of various infections and their complications.
Different factors including donor age, biological source, route of administration, and signaling pathways have an impact on the functions and consequently the clinical applications of mesenchymal stromal cells. The products of mesenchymal stem cells such as extracellular vesicles and exosomes reproduce the biological effects and most of the therapeutic actions of the parent stem cells. Genetic engineering and the use of specific mesenchymal stromal cell products have improved their clinical efficacy and decreased their adverse effects. However, despite the recent progress in the use of mesenchymal stem cells, the clinical application of these cells in the treatment of several diseases still faces real challenges that need to be resolved. The current status of mesenchymal stem cells and the controversies related to their clinical utilization in various disease conditions will be thoroughly discussed in this review.

Review Article **Published Date:-2023-12-05 14:50:06**

Update on the Use of Mesenchymal Stem Cells in the Treatment of Various Infectious Diseases Including COVID-19 Infection

Mesenchymal Stem Cells (MSCs) have antimicrobial, anti-inflammatory, immunomodulatory, and regenerative potentials. Additionally, utilization of MSCs in the clinical arena has been shown to be safe and well tolerated. Hence, this form of cellular therapy has gained particular attention in the treatment of several infectious disorders and their complications.
MSCs have been successfully used in the treatment of the following infections and their complications: bacterial infections including complicated sepsis; viral infections including Human Immunodeficiency Virus (HIV), hepatitis B and C viruses, and Coronavirus disease (COVID-19) complicated by acute respiratory distress syndrome; parasitic infections including schistosomiasis, malaria, and Chagas disease; and mycobacterial infections including tuberculosis. The use of MSCs derived from certain sources and Extracellular Vesicles (ECVs) derived from MSCs has improved their efficacy and reduced their side effects. However, the clinical application of MSCs in the treatment of several infectious diseases still faces real challenges that need to be resolved. The current status of MSCs and the controversies related to their utilization in various infections will be thoroughly discussed in this review.

Review Article **Published Date:-2023-11-29 14:45:34**

Update on the Use of Mesenchymal Stem Cells and their Products in Hematopoietic Stem Cell Transplantation

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Graft Versus Host Disease (GVHD) is a major limitation to the success of allogeneic Hematopoietic Stem Cell Transplantation (HSCT) as Steroid-Refractory (SR) acute GVHD carries poor prognosis due to the absence of an efficacious second-line therapy. Mesenchymal Stem Cells (MSCs) which have immunosuppressive, immunomodulatory, and regenerative properties may become a highly effective therapeutic modality for SR-GVHD in the near future.
MSCs have already been approved to treat childhood SR-GVHD in Japan, and they have been conditionally licensed in New Zealand and Canada. It is expected that MSCs will be approved for the treatment of SR-GVHD in adults in Europe, North America, and other parts of the world within a few years. Utilization of the recently introduced techniques including the use of MSC products such as exosomes and Extracellular Vesicles (ECVs) instead of the parent MSCs, robotic manufacturing technology, and genetic engineering of MSCs will ultimately overcome the remaining obstacles facing the widespread utilization of MSCs and their products as therapeutics not only in HSCT but also in other medical fields. The aim of this review is to provide an update on the remarkable progress achieved in the use of MSCs and their products in the field of HSCT.

Retrospective Study **Published Date:-2023-04-14 09:54:48**

Role of measurable residual disease quantified by 4 to 6 color flow cytometry before allogeneic hematopoietic stem cell transplantation for high-risk Philadelphia-negative acute lymphoblastic leukemia

Background: Measurable residual disease (MRD) status before allogeneic hematopoietic stem cell transplantation (AHSCT) is commonly associated with a high risk of relapse. It is still uncertain whether AHSCT could overcome the negative impact of MRD positivity (MRD+), especially in patients with high-risk Philadelphia negative acute lymphoblastic leukemia (Ph-negative ALL).

Materials and methods: An observational retrospective study was conducted on patients with high-risk Ph-negative ALL who underwent AHSCT between January 2005 and June 2022. The patients selected were in complete remission (CR): with 80% in CR1 (n = 69) and 20% in CR2 (n = 17). Graft sources were bone marrow (BM) in 71% of patients and peripheral blood stem cells in 29% of patients. The conditioning regimen was TBI or chemotherapy-based (CT). Bone marrow MRD level was quantified using 4-6 color multiparametric flow cytometry (MFC). The threshold for MRD positivity was ? 0.1%.

Results: The study included 86 patients (45 B-ALL and 41 T-ALL) with a median age of 18 years (range, 4–55 years). The median level of MRD pre-AHSCT (pre-MRD) was 0.4×10-3 (range, 0.01-75.6×10-3). After a median follow-up of 25 months (range 1-205 months), the cumulative incidence of relapse (CIR) was significantly higher in the MRD+ group (39% vs. 20%, p = 0.04). The median time of relapse post-AHSCT was 14 months (range, 1-203 months) in the MRD+ group and 32 months (range, 4-209 months) in the MRD- group (p = 0.28). Non-relapse mortality (NRM) was 15% in both groups (p = 0.97). The 2-year estimated overall survival (OS) and event-free survival (EFS) were 61% vs. 74% (p = 0.07) and 58% vs. 70% (p = 0.10) in the MRD+ and MRD- groups, respectively. A subgroup analysis in MRD+ patients showed that a TBI-based conditioning regimen was distinctly associated with lower CIR (22% vs. 60% respectively, p = 0.04), improved OS (82% vs. 36% respectively, p = 0.007) and better EFS (73% vs. 38%, p = 0.04) compared to CT-based. In a multivariate analysis, pre-AHSCT MRD+ status and non-TBI-based conditioning were significantly associated with inferior OS (OR, 2.30; 95% CI, [1.027-5.168], p = 0.04 and OR, 3.91; 95% CI, [1.624-9.418], p = 0.002, respectively). The only predicting factor of lower EFS was the non-TBI-based regimen (OR, 2.82; 95% CI, [1.308-6.097], p = 0.008). Non-TBI-based and CR2 were significantly associated with higher CIR (OR, 6.25; 95% CI, [1.947-20.055], p = 0.002 and OR, 4.74; 95% CI, [1.197-18.791], p = 0.03, respectively). Peripheral stem cell source was significantly associated with higher NRM (OR, 6.55; 95% CI, [1.488-28.820], p = 0.01).

Conclusion: High-risk Ph-negative ALL patients with MRD ? 10-3 prior AHSCT had lower OS compared to MRD- patients and may benefit from TBI as a conditioning regimen before AHSCT.

Retrospective Study **Published Date:-2023-03-08 15:01:54**

Outcome of Outpatient Autologous Hematopoietic Stem Cell Transplantation in Patients with Multiple Myeloma and Relapsed and Refractory Hodgkin Lymphoma. The Experience of King Fahad Specialist Hospital in Dammam, Saudi Arabia

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Background: Autologous hematopoietic stem cell transplants (HSCT) is the standard of care for transplant-eligible patients with newly diagnosed multiple myeloma (MM) and patients with relapsed and refractory Hodgkin lymphoma (R/R-HL) who achieve chemosensitivity after salvage therapy. Although autologous HSCT is routinely performed in an inpatient setting, the procedure can safely be performed in an outpatient setting.
Methods and materials: A retrospective study of patients with MM and R/R- HL who received outpatient autologous HSCT at King Fahad Specialist Hospital (KFSH) in Dammam, Saudi Arabia between the first of April 2017 and the 31st of January 2022 was performed.
Results: Over the study period of 4 years and 10 months, a total of 90 outpatient autologous HSCTs were performed for 79 patients (54 patients with MM; 4 of them received planned tandem autografts and 7 other myeloma patients received second autologous HSCTs for relapsed or progressive disease; and 25 patients with R/R-HL) at our institution. The median ages of patients with MM and those with R/R-HL at HSCT were 50.4 years and 27.8 years respectively.
At the presentation of their MM, the following high-risk (HR) features were encountered: stage II and III diseases according to the revised international scoring system (RISS) in 53.7%; adverse cytogenetics in 42.6% and extensive bone involvement in 53.7% of patients. In patients with HL at presentation, 48% of patients had stage IV disease according to Ann Arbor staging classification and 84% of patients had B symptoms.
Survival for 100 days post-HSCT for all patients with MM and HL who received outpatient autologous transplants was 100%. For patients with MM, the overall survival (OS) rates at 3 years and 4 years post-HSCT were 80% and 67%, while the progression-free survival (PFS) rates over 3 years and 4 years were 58% and 38% respectively. For patients with HL, the OS at 6 years post-HSCT was 95% while the PFS rates at 3 years and 6 years post-HSCT were 84% and 62% respectively.
Conclusion: Outpatient autologous HSCT for patients with MM and HL is safe, and feasible and can lead to short-term as well as long-term outcomes that are comparable to autologous transplantation performed in an inpatient setting. Additional benefits of outpatient autologous include saving beds and reducing hospital costs.

Opinion **Published Date:-2023-02-14 17:07:12**

The complement cascade as a target against SARS-CoV-2-induced pneumonia

Fox, et al. [1] reported on the relevant cardiopulmonary findings in a series of autopsies of patients deceased from SARS-CoV-2 infection. In particular, regarding the histologic examination of the lungs, they observed bilateral diffuse alveolar damage with a lymphocytic infiltrate, thickened alveolar capillaries, fibrin thrombi within the capillaries and small vessels, and entrapment of neutrophils, without any significant neutrophilic, infiltrate within airways or the interstitium.