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Parkinson's Disease

1. Parkinson's disease and mesenchymal stem cells: potential for cell-based therapy.
Kitada M, Dezawa M.
Parkinson's Disease 2012
Cell transplantation is a strategy with great potential for the treatment of Parkinson's disease, and many types of stem cells, including neural stem cells and embryonic stem cells, are considered candidates for transplantation therapy. Mesenchymal stem cells are a great therapeutic cell source because they are easy accessible and can be expanded from patients or donor mesenchymal tissues without posing serious ethical and technical problems. They have trophic effects for protecting damaged tissues as well as differentiation ability to generate a broad spectrum of cells, including dopamine neurons, which contribute to the replenishment of lost cells in Parkinson's disease. This paper focuses mainly on the potential of mesenchymal stem cells as a therapeutic cell source and discusses their potential clinical application in Parkinson's disease.

2. Open-labeled study of unilateral autologous bone-marrow-derived mesenchymal stem cell transplantation in Parkinson's disease.
Venkataramana NK, Kumar SK, Balaraju S, Radhakrishnan RC, Bansal A, Dixit A, Rao DK, Das M, Jan M, Gupta PK, Totey SM.
Translational Research 2010

Parkinson's disease (PD) is a progressive neurodegenerative disease for which stem cell research has created hope in the last few years. Seven PD patients aged 22 to 62 years with a mean duration of disease 14.7+/-7.56 years were enrolled to participate in the prospective, uncontrolled, pilot study of single-dose, unilateral transplantation of autologous bone-marrow-derived mesenchymal stem cells (BM-MSCs). The BM-MSCs were transplanted into the sublateral ventricular zone by stereotaxic surgery. Patients were followed up for a period that ranged from 10 to 36 months. The mean baseline "off" score was 65+/-22.06, and the mean baseline "on" score was 50.6+/-15.85. Three of 7 patients have shown a steady improvement in their "off"/"on" Unified Parkinson's Disease Rating Scale (UPDRS). The mean "off" score at their last follow-up was 43.3 with an improvement of 22.9% from the baseline. The mean "on" score at their last follow-up was 31.7, with an improvement of 38%. Hoehn and Yahr (H&Y) and Schwab and England (S&E) scores showed similar improvements from 2.7 and 2.5 in H&Y and 14% improvement in S&E scores, respectively. A subjective improvement was found in symptoms like facial expression, gait, and freezing episodes; 2 patients have significantly reduced the dosages of PD medicine. These results indicate that our protocol seems to be safe, and no serious adverse events occurred after stem-cell transplantation in PD patients. The number of patients recruited and the uncontrolled nature of the trial did not permit demonstration of effectiveness of the treatment involved. However, the results encourage future trials with more patients to demonstrate efficacy.

3. Clinical application of stem cell therapy in Parkinson's disease.

Politis M, Lindvall O.
Biomed Central Medicine 2012

Cell replacement therapies in Parkinson's disease (PD) aim to provide long-lasting relief of patients' symptoms. Previous clinical trials using transplantation of human fetal ventral mesencephalic (hfVM) tissue in the striata of PD patients have provided proof-of-principle that such grafts can restore striatal dopaminergic (DA-ergic) function. The transplants survive, reinnervate the striatum, and generate adequate symptomatic relief in some patients for more than a decade following operation. However, the initial clinical trials lacked homogeneity of outcomes and were hindered by the development of troublesome graft-induced dyskinesias in a subgroup of patients. Although recent knowledge has provided insights for overcoming these obstacles, it is unlikely that transplantation of hfVM tissue will become routine treatment for PD owing to problems with tissue availability and standardization of the grafts. The main focus now is on producing DA-ergic neuroblasts for transplantation from stem cells (SCs). There is a range of emerging sources of SCs for generating a DA-ergic fate in vitro. However, the translation of these efforts in vivo currently lacks efficacy and sustainability. A successful, clinically competitive SC therapy in PD needs to produce long-lasting symptomatic relief without side effects while counteracting PD progression.

4. Transplantation of mesenchymal stem cells: a future therapy for Parkinson's disease?
Sergey V Anisimov & Gesine Paul
Future Neurology 2014

Parkinson's disease (PD) is a common, progressive neurodegenerative disorder associated with a loss of dopaminergic cells in the substantia nigra pars compacta and a lack of dopamine in the striatum. To halt or reverse this disease, neurorestorative approaches or neuroprotective treatments are urgently needed. Recently, the first clinical trials transplanting mesenchymal stem cells (MSCs) have been performed in PD. MSCs are adult stem cells abundant in several tissues, such as the umbilical cord, the bone marrow, the adipose tissue and other tissues. These cells are multipotent, and able to synthesize and secrete a wide spectrum of biologically active factors. MSCs of various origins have been explored as possible substrates for cell therapy in PD animal models. In this review, we summarize MSC-based experimental transplantation studies in PD, and discuss biological mechanisms that may explain the effects of MSC seen in PD models. Furthermore, we critically evaluate the recent clinical transplantation trials using MSCs in patients with PD.

5. Mesenchymal stem cells and neuroregeneration in Parkinson's disease.
Glavaski-Joksimovic A, Bohn MC.
Experimental Neurology 2013

Parkinson's disease (PD) is a prevalent neurodegenerative disorder characterized by a progressive and extensive loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc) and their terminals in the striatum, which results in debilitating movement disorders. This devastating disease affects over 1 million individuals in the United States and is increasing in incidence worldwide. Currently available pharmacological and surgical therapies ameliorate clinical symptoms in the early stages of disease, but they cannot stop or reverse

degeneration of DA neurons. Stem cell therapies have come to the forefront of the PD research field as promising regenerative therapies. The majority of preclinical stem cell studies in experimental models of PD are focused on the idea that stem cell-derived DA neurons could be developed for replacement of diseased neurons. Alternatively, our studies and the studies from other groups suggest that stem cells also have the potential to protect and stimulate regeneration of compromised DA neurons. This review is focused on strategies based on the therapeutic potential for PD of the neurotrophic and neuroregenerative properties of a subclass of stem cells, mesenchymal stem cells (MSCs).

6. A Meta-Analysis of Mesenchymal Stem Cells in Animal Models of Parkinson's Disease.
Riecke J, Johns KM, Cai C, Vahidy FS, Parsha K, Furr-Stimming E, Schiess M, Savitz SI.
Stem Cells and Development 2015

Multiple studies have been performed to evaluate the effects of mesenchymal stem cells (MSCs) in animal models of Parkinson's disease (PD). We performed a meta-analysis to estimate the treatment effect of unmodified MSCs on behavioral outcomes in preclinical studies of PD. We performed a systematic literature search to identify studies that used behavioral testing to evaluate the treatment effect of unmodified MSCs in PD models. Meta-analysis was used to determine pooled effect size for rotational behavior and limb function, and meta-regression was performed to explore sources of heterogeneity. Twenty-five studies, including three delivery routes, a wide range of doses, and multiple PD models, were examined. Significant improvement was seen in the pooled standardized mean difference (SMD) for both rotational behavior [SMD: 1.24, 95% confidence interval (95% CI): 0.84, 1.64] and limb function (SMD: 0.84, 95% CI: 0.01, 1.66). Using meta-regression, intravenous administration and higher dose had a larger effect on limb function. Treatment with MSCs improves behavioral outcomes in PD models. Our analyses suggest that MSCs could be considered for early-stage clinical trials in the treatment of PD.