

Abstract

Background of study:

Parkinson's disease (PD) is a debilitating neurodegenerative movement disorder that is manifested by the gradual emergence of a broad spectrum of motor and non-motor symptoms caused by its underlying neuropathology. The two pathological hallmarks of PD include the progressive deterioration of dopaminergic neurons in the substantia nigra (SN) and the widespread distribution of Lewy bodies. Thus, a great number of dopaminergic neurons are needed to replace the depleted cells and revert the symptoms demonstrated by PD patients. One suggestion has been the utilization of dental pulp stem cells (DPSCs), which have recently shown high neuronal differentiation capacity, enhanced migratory activity rate and regenerative potential.

Objectives:

Graft survival and sufficient enrichment of therapeutic cells in the brain are greatly influenced by stem cell delivery methods. In the present study, transplantation efficiency and therapeutic efficacy of intranasally delivered DPSCs were investigated in a 1-Methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) induced PD mice model to determine the feasibility of intranasal DPSC treatment as a potential therapeutic strategy for PD.

Methodology:

Adult male Swiss albino mice were subjected to intraperitoneal MPTP treatment (20 mg/kg in saline, 4 times a day at 2-hr intervals), for the establishment of a PD mice model. Isolated DPSCs were cultured, identified, labelled with PKH26 and delivered intranasally into MPTP lesioned mice. A series of behavioural assessments were performed to evaluate the olfactory and sensorimotor function. Tyrosine hydroxylase (TH) immunofluorescence was used to evaluate MPTP neurotoxicity in the neurons of SN.

Results:

The ex vivo-expanded DPSCs acquired neuronal morphology and expressed neuronal specific markers at gene and protein levels. Following exposure to neuronal inductive media, culture expanded DPSCs displayed the capacity to secrete dopamine and intracellular calcium with functional dopaminergic like cells. More importantly, MPTP-induced motor dysfunctions and olfactory impairments were significantly improved by the intranasal delivery of PKH26 labelled DPSCs. The severe reduction of TH positive

neurons in the SN of PD brain tissues were also gradually attenuated following intranasal delivery of DPSCs.

Conclusion:

Cumulatively, the results suggest that intranasal delivery of stem cell based therapeutics is a viable and highly efficacious treatment modality that enhanced the delivery of PKH26 labelled DPSCs to the brain, subsequently optimizing the therapeutic efficacy of DPSCs by protecting against dopaminergic neuron degeneration and improving neurological functions of the PD mouse model.