Stem cells for COPD

Overview by JA Shehadi MD 10-21-2021

I. **Overview/background:**

a. COPD, including chronic bronchitis and emphysema, is the third-leading cause of death in the United States, resulting in > 126,000 deaths (one in every 20 deaths) in 2005. Further, mortality due to COPD is increasing, and actuarial projections suggest that COPD will be the third-leading cause of death worldwide by the year 2020. COPD also has significant economic impact in health-care expenditure and in illness-related decreased productivity. New therapeutic approaches are, thus, desperately needed for COPD.

b. See below for several paper abstracts

II. Paper #1: Bratisl Lek Listy 2020;121(3):188-191. Improving effects of mesenchymal stem cells on symptoms of chronic obstructive pulmonary disease

Abstract

Aim: We aimed to identify the improving effects of umbilical cord tissue-derived (UCTD) MSCs on the symptoms of COPD in our phase 1.2 clinical study.

Methods: Our study consisted of **five patients** with COPD. Respiratory function tests, SGRQ symptom, activity and impact scores and 6-minute walk test (6MWT) were examined before UCTD MSC treatment. All the patients were administered a total of 4 doses of UCTD MSCs by intravenous infusion at two-week intervals. All the tests were repeated three months after the treatment for evaluation of the response to MSCs treatment.

Results: The mean age of five male patients was 56. The mean pretreatment FEV1/FVC ratios were 66.9 %. Pretreatment mean SGRQ symptom, activity and impact scores of the patients were 78.2, 83.8 and 58.02 respectively. The mean walking distance of the patients was 307 meters before MSCs treatment. The mean FEV1/FVC value of raised to 69.58 % after the treatment. The mean SGRQ symptom, activity and impact scores were noted as 39.8, 60.98 and 45.18 respectively. The mean walking distance of the patients raised to 362 meters after the treatment.

Conclusions: Our results showed that four doses of MSC treatment considerably alleviated the severity of symptoms of COPD.

III. Paper #2:

Xiangde Liu et al.: Review PLoS One 2016 Jun 9;11(6): Preclinical Studies of Mesenchymal Stem Cell (MSC) Administration in Chronic Obstructive Pulmonary Disease (COPD): A Systematic Review and Meta-Analysis,

Abstract

Background: In the last two decades, mesenchymal stem cells (MSCs) have been pre-clinically utilized in the treatment of a variety of kinds of diseases including chronic obstructive pulmonary disease (COPD). The aim of the current study was to systematically review and conduct a meta-analysis on the published pre-clinical studies of MSC administration in the treatment of COPD in animal models.

Methods and results: A systematic search of electronic databases was performed. Statistical analysis was performed using the Comprehensive Meta-Analysis software (Version 3). The pooled Hedges's g with 95% confidence intervals (95% CIs) was adopted to assess the effect size. Random effect model was used due to the heterogeneity between the studies. A **total of 20 eligible studies** were included in the current systematic review. The overall meta-analysis showed that MSC administration was significantly in favor of attenuating acute lung injury ($P < 0.001$, stimulating lung tissue repair ($P < 0.001$) and improving lung function ($P< 0.001$). The mechanism of MSC therapy in COPD is through ameliorating airway inflammation ($P< 0.001$) and stimulating cytokine synthesis that involves lung tissue repair ($P< 0.001$).

Conclusion: This systematic review and meta-analysis suggest a promising role for MSCs in COPD treatment. Although the COPD models may not truly mimic COPD patients, these pre-clinical studies demonstrate that MSC hold promise in the treatment of chronic lung diseases including COPD. The mechanisms of MSCs role in preclinical COPD treatment may be associated with attenuating airway inflammation as well as stimulating lung tissue repair.

IV. Paper #3: Weiss, DJ, et al: A Placebo-Controlled, Randomized Trial of Mesenchymal Stem Cells in COPD, Chest. 2013 Jun; 143(6): 1590–1598.

V. Abstract

VI. Background:

Previous studies have demonstrated efficacy of both systemic and direct airway MSC administration in rodent models of lung diseases, including COPD. We hypothesized that MSCs would reduce chronic pulmonary and systemic inflammation in patients

with COPD with corresponding improvement in pulmonary function and in quality-of-life (QOL) indicators.

Methods:

Sixty-two patients at six sites were randomized to double-blinded IV infusions of either allogeneic MSCs (Prochymal; Osiris Therapeutics Inc) or vehicle control. Patients received four monthly infusions (100 × 106 cells/infusion) and were subsequently followed for 2 years after the first infusion. End points included comprehensive safety evaluation, pulmonary function testing (PFT), and quality-of-life indicators including questionnaires, 6MWT, and assessments of systemic inflammation.

Results:

All study patients completed the full infusion protocol, and 74% completed the 2-year follow-up. There were no infusional toxicities and no deaths or serious adverse events deemed related to MSC administration. There were no significant differences in the overall number of adverse events, frequency of COPD exacerbations, or worsening of disease in patients treated with MSCs. There were no significant differences in PFTs or quality-of-life indicators; however, an early, significant decrease in levels of circulating C-reactive protein (CRP) was observed in patients treated with MSCs who had elevated CRP levels at study entry.

Conclusions:

Systemic MSC administration appears to be safe in patients with moderate to severe COPD and provides a basis for subsequent cell therapy investigations ClinicalTrials.gov; No.: NCT00683722; URL: www.clinicaltrials.gov