

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

1- PRELIMINARIES

A. Background:

COPD is projected to become the 3rd cause of disease mortality worldwide by 2020, creating a substantial increase in medical, economic, and social burden [1,2]. COPD is caused by a combination of small airways disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). The pathophysiology of COPD is mediated primarily by a pathogenic triad: inflammation, oxidative stress, and protease-antiprotease imbalance. The inflammatory process in the lungs of COPD patients involves concentration of macrophages, neutrophils, CD8+ cytotoxic lymphocytes in the small airways and the subsequent release of humoral factors cytokines, chemokines, and elastolytic enzymes [5]

B. Causes of COPD:

Lung Irritants: extended exposure to lung irritants that impair the lungs

- Firsthand smoke (cigarette, pipe, cigar, etc)
- Air pollution, chemical fumes, or dust from environment
- *Alpha-1 Antitrypsin Deficiency*: A rare genetic condition characterized by low levels of alpha-1 antitrypsin (AAT). This rare condition induces COPD to progress more aggressively.
- *Asthma*: is a chronic lung disease that inflames and narrows the breathing airways

C. Treatment Options:

Avoid Lung Irritants

Lifestyle Changes: These include: quitting smoking, maintain a healthy weight, increase of physical activity, and any other initiative to improve overall wellness.

- Bronchodilators
- Combination Bronchodilators Plus Inhaled Glucocorticoids
- Oxygen Therapy.
- Bullectomy: the removal of over enlarged bullae(s) from the lungs
- Lung Volume Reduction Surgery: the removal of damaged tissue from the lungs
- Lung Transplant: removal of damaged lung and replacement with a healthy lung from a deceased donor

MONONUCLEAR LAYER CORD BLOOD PRODUCT TREATMENT OPTION :

Concentrated human stem cell product comprised of donated cord blood, that has been processed to remove excess plasma, red blood cells, vascular material and tissue solids leaving stem cells and other cellular components, which are then concentrated and banked through a validated process.

- a. Objective:
To provide the patient with a treatment that regenerate lung structure and induce lung functional recovery through reduction of inflammation, and induction of immunomodulation.
- b. Patient management:
 - Initial patient evaluation: Reviews the medical information, lab work, and diagnostic imaging provided by the patient in order to determine the stage of the medical condition and any other secondary conditions. Application of the COPD evaluation questionnaire.
 - Patient consultation. Informed consent is obtained from all patients and medical records are updated, including patient's most recent physical exam, medication history, most up-to-date lab results and imaging studies to include:
 - Complete Blood Count /Metabolic Panel
 - CT scan/ MRI of lungs
 - Alpha 1 Antitripsin
 - C Reactive Protein.
 - Pulmonary Function tests.
 - Complete a 6 min walking distance test.
 - Treatment day:
 - Premedication infusion protocol is started one hour before product application.
 - Benadryl 25mg IM, Zantac 200mg IV, Solumedrol 125mg IV. Single Dose.
 - Attach certificate of analysis to patient's chart.
 - Place the bottle in the palm of your hand until product is in a complete liquid form which can take about 3-5 min.
 - Swab the outside of the vial with alcohol, then remove the sterile cover and draw the contents into a syringe using aseptic technique.

- Sample should be injected within 2 hours of thawing.
- Product should not be mixed with any other biologic compound.
- Respiratory conditions require a dose of 1 million cells per kg of body weight injected via IV push in two doses 1 month apart.
- Intrabronchial instillation has also been documented as and adjuvant therapy to be considered.
- Pulmonary rehabilitation program.

c. Risks:

There are possibilities for unwanted effects related to the injection of stem cells. Even with the most established protocol, adequate technique, and careful administration; a medical team may encounter uncontrollable events. Although there is no guarantee of perfect results, excellent results can be attained. The risks of complications with the administration of cord blood products are very low. Possible risks include but are not limited to:

- Pain at site of injections
- Malaise
- Fever
- Allergic reaction

d. Outcomes : Clinical response evaluated by use of COPD evaluation questionnaire, improvement in the 6 min walking distance, radiology and PFT improvement.

e. Follow Up Plan:

- Pre-injection:
 - Patient follow-up with his pulmonologist for a baseline.
 - Clinical evaluation of symptoms
 - Use of COPD evaluation questionnaire. Baseline testing.
- 3 months after injection:
 - Patient follow-up.
 - Clinical evaluation of symptoms
 - Use of COPD evaluation questionnaire
- 6 months after injection:
 - Patient follow-up.
- Clinical evaluation of symptoms. Use of COPD evaluation questionnaire. Repeat testing ordered before infusion.

REFERENCES

- 1- Janczewski, A., Wojtkiewicz, J., Malinowska, E., & Doboszyńska, A. (2017). Can youthful mesenchymal stem cells from Wharton's jelly bring a breath of fresh air for COPD? *International Journal of Molecular Sciences*, 18(11), 2449. doi:10.3390/ijms18112449
- 2- Chapman KR, Mannino DM, Soriano JB, et al. Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J* 2006;27:188-207. 10.1183/09031936.06.00024505 [PubMed]
- 3- Chung, E.; Son, Y. Crosstalk between mesenchymal stem cells and macrophages in tissue repair. *Tissue Eng. Regen. Med.* 2014, 11, 431–438.
- 4- English, K. Mechanisms of mesenchymal stromal cell immunomodulation. *Immunol. Cell Biol.* 2013, 91, 19–26.
- 5- Weiss, D.J. Current status of stem cells and regenerative medicine in lung biology and diseases. *Stem Cells* 2014, 32, 16–25.

