



Effect of Regenerative Medicine Interventions on Chronic Lung Disease in 2782 Patients



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Introduction

We studied 2782 patients treated with regenerative medicine-based treatment for chronic lung disease. These diseases consisted of chronic adult asthma (13 patients), chronic obstructive pulmonary disease (COPD) (2316 patients) and Interstitial lung disease (ILD) (453 patients). Most patients in the cohort suffer from COPD, which is a life-limiting, debilitating and costly chronic disease. COPD is complex, and its symptoms heterogeneous. Characterized by chronic airflow obstruction, impaired gas exchange and destruction of alveoli, COPD is a progressive and often fatal disease¹. Worldwide, more than 210 million people suffer from COPD. By the year 2020, population estimates predict that COPD will be third leading cause of death globally². According to 2010 economic analyses, indirect and direct costs related to COPD treatment, missed work and disability totaled over 35 billion dollars³. COPD is an often-overlooked disease and many patients have been told that there is nothing more that can be done. Many COPD patients are marginalized once conventional treatment options have failed.

Current management of COPD is aimed at alleviating symptoms, although no conventional treatment can modify the progressive course of the disease except for lung transplant surgery. Although this has been considered curative, the 5-year mortality rate for this surgery has been reported to be 50%. Inhalers, steroids and lung reduction surgery may temporarily reduce symptoms, yet COPD continues to have a significant negative impact on quality of life, especially in the late stages of disease⁴⁻⁷. ILD, like COPD, is a disease of chronic inflammation as the primary cause of damage to the tissue but unlike COPD, ILD has resultant fibrosis which makes control of this disease much more difficult and progression from diagnosis to death more rapid⁸.

Objectives

Recent advances in the field of regenerative medicine have found that autologous cell therapy along with activated platelets may safely affect chronic airflow obstruction by reducing inflammation and aid in promoting maintenance and/or repair of damaged lung tissue⁹⁻¹². The long-term mechanism of action is not yet completely known and remains under investigation.



Methods

This was a descriptive, observational study. All participants signed informed consent that indicated that response to treatment is not guaranteed. Due to additional regulations required in the state of Texas, at our Dallas clinic consent and protocols are reviewed and approved by a third-party independent Institutional Review Board (IRB), that is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). Our procedures and protocols are consistent across all clinics.

Patients underwent cellular therapy with their own cells harvested from peripheral blood or bone marrow with mesenchymal stem cells. Patients underwent pre-treatment spirometry to obtain a baseline FEV1% (percentage of predicted Forced Expiratory Volume at 1 second). FEV1 is a direct reflection of the severity of obstruction and is the standard of care for determining a patient's COPD GOLD stage (stages I-IV with 1 being mild and IV being very severe obstruction). As COPD worsens, FEV1 decreases. After 3 months, patients having the **venous** harvest underwent post-treatment spirometry to detect any change after treatment.

The Clinical COPD Questionnaire (CCQ) was administered to all patients at pre-treatment and again at 3 months, 6 months and 12 months post-treatment by phone. The CCQ is a 10-item Likert-type scale that measures quality of life based on symptom, functional status and mental status domains on a 0-6 scale with higher scores representing lower quality of life.

Figure 1: FEV1% Change from Baseline

OVERALL SAMPLE SUMMARY				
	Frequency	Percent	Valid Percent	Cumulative Percent
Valid IMPROVED AT 3 MONTHS	224	34.5	56.0	56.0
DECLINED AT 3 MONTHS	140	35.0	35.0	91.0
NO CHANGE AT 3 MONTHS	36	9.0	9.0	100.0
Total	400	100.0	100.0	

Figure 2: FEV1% Change from Baseline to 3 Months Post-Cell Therapy

STATUS OF IMPROVEMENT, NO CHANGE OR DECLINE				
	Frequency	Percent	Valid Percent	Cumulative Percent
Valid IMPROVED 1-5%	138	34.5	34.5	34.5
IMPROVED 6-10%	46	11.5	11.5	46.0
IMPROVED 11-15%	25	6.3	6.3	52.3
IMPROVED 16-20%	8	2.0	2.0	54.3
IMPROVED >20%	7	1.8	1.8	56.0
NO CHANGE	36	9.0	9.0	65.0
DECLINED 1-5%	102	25.5	25.5	90.5
DECLINED 6-10%	30	7.5	7.5	98.0
DECLINED 11-15%	5	1.3	1.3	99.3
DECLINED 16-20%	1	.3	.3	99.5
DECLINED >20%	2	.5	.5	100.0
Total	400	100.0	100.0	

Results

The mean age of the sample was 71 years. 59.8% were men, 40.2% women. Because patients often came to our facilities from a considerable distance there was significant attrition of the sample size during the follow-up period with 2782 subjects at the start, 2066 at 3 months, 1618 at 6 months and 702 at 12 months. 87% of the sample were former smokers. No patients were smoking at the time of treatment.

Just 3 months post-cellular therapy, 56% (N=224) of patients had improvement in their FEV1. The mean improvement was 6.2%. 35% of the sample had a decline in FEV1 with an average decline of 3%, and 9% of the total sample had no change from baseline.

The CCQ was measured on all patients at baseline, 3, 6 and 12 months. The minimum clinically important difference (MCID) per Alma, et. al. is a score change of +/- 0.4 or more. For those undergoing the venous protocol, at 3 months post-treatment 73.4% (N=1357) had a clinically meaningful improvement, 8.9% (N=165) declined and 17.6% (N=326) had no change. At 6 months, 71.2% (N=1076) improved, 10.8% (N=165) declined and 18% (N=272) had no change. At 12 months, 62.8% (N=412) improved, 14.6% (N=96) declined and 22.6% (N=148) had no change.

For those undergoing the bone marrow protocol, at 3 month post-treatment 71.9% (N=87) had a clinically meaningful improvement, 6.6% (N=8) declined and 21.5% (N=26) had no change. At 6 months, 58.9% (N=63) improved, 14% (N=15) declined and 27.1% (N=29) had no change. At 12 months, 47.4% (N=18) improved, 23.7% (N=9) declined and 26.3% (N=11) had no change.

T-tests comparing CCQ scores from baseline to 3, 6 and 12 months post-treatment are statistically significant at all intervals.

At 12 months post-treatment, 57% of the entire sample (n=702) continued to report an improvement in perceived quality of life per their CCQ scores with a mean clinically significant change of 0.8. We feel this supports that the "placebo effect" is not a factor at 12 months post-treatment. 15% of the sample had a decline in quality of life and 28% of the sample had no appreciable change.

Conclusions

We feel that the results of our study show promise for the application of regenerative medicine modalities in patients suffering from chronic lung disease. As these are complex, heterogeneous diseases, a comprehensive approach to their management is needed including innovative and novel therapies. Autologous, cellular therapy may directly affect chronic airflow obstruction by reducing inflammation and promoting the repair of diseased tissue. Future management should focus on a wide-ranging approach including regenerative therapies both cellular and non-cellular, pulmonary rehabilitation and supportive coping strategies for these patients.

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