

PULMONARY FUNCTION CHANGES AFTER BRONCHOSCOPIC BIOLOGICAL LUNG VOLUME REDUCTION THERAPY USING AUTOLOGOUS BLOOD

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ABSTRACT

Background: Bronchoscopic lung volume reduction (BLVR) using biological agents is one of the new alternatives to lung volume reduction surgery.

Objectives: To evaluate the potential efficacy of bronchoscopic biological lung volume reduction using autologous blood injection in pulmonary emphysema patients.

Methods: 7 male patients were enrolled in the study. After determining the targeted emphysematous segment by high resolution computerized tomography (HRCT), 30 ml autologous blood was injected via balloon catheter over 10 to 15 seconds into the targeted segment and left in position for 3-6 minutes allowing time for blood to coagulate. The bronchoscope was then repositioned at the following targeted segment. Changes in residual volume (RV), residual volume to total lung capacity ratio (RV/TLC), forced expiratory volume in one second (FEV1) and forced expiratory volume to forced vital capacity ratio (FEV1/FVC) were evaluated at 12-week post procedure as well as for complications.

Results: At 12-week post procedure there was statistically significant reduction in RV/TLC ($p = 0.038$). FEV1 significantly increased ($p = 0.018$). In addition, there was significant improvement in FEV1/FVC % ($p = 0.003$). All cases tolerated the procedure with no mortality. There was one case that developed pneumonia at the same side of intervention, and two cases developed mild haemoptysis (blood streaked sputum). There was no life threatening complications e.g (pneumothorax, pulmonary embolism, cardiac ischaemia or myocardial infarction) occurred throughout the study.

Conclusion: Bronchoscopic lung volume reduction using autologous blood injection could be an effective, cheap and relatively safe method to treat advanced emphysema in comparison to other agents used in the clinical trials.

Keywords: Emphysema; Bronchoscopy; Lung volume reduction.

INTRODUCTION

Emphysema is a chronic and progressive disease, characterized by abnormal permanent enlargement of air spaces distal to the terminal bronchioles.¹

The clinical usefulness of bronchoscopic techniques for achieving lung volume reduction has been studied in patients with advanced emphysema as these procedures are considered to be safer than surgical volume reduction.²

Biological lung volume reduction is a new bronchoscopic approach that uses biological agents aiming to reduce lung volume by blocking off the most emphysematous areas with a rapidly polymerizing sealant. The mechanism of action involves resorption atelectasis from airway occlusion, subsequent airspace inflammation, and then remodeling. This remodeling will lead to scarring that induces contraction of lung parenchyma and

functional volume reduction can be expected within 6-8 weeks.³ Biological lung volume reduction occurs independent of the presence or absence of collateral ventilation.²

AIM OF THE WORK

The aim of this study is to evaluate the potential efficacy of bronchoscopic biological lung volume reduction using autologous blood injection in pulmonary emphysema patients.

PATIENTS AND METHODS

This study was carried out in Chest Medicine Department in collaboration with Clinical Pathology Department, Mansoura University Hospital. Seven patients with heterogeneous emphysema were enrolled, and all patients provided written informed consent prior to participation.

➤ **Study population:**

Inclusion criteria:

1. Heterogenous emphysema determined by HRCT of the chest plus:

(a) FEV1 /FVC < 70% and FEV1 20- 50%

(b) Hyperinflation: total lung capacity (TLC) \geq 110% pred and residual volume/ total lung capacity (RV/TLC) \geq 120% pred.

2. Patients not candidate for or had refused LVRS.

3. Age > 40 yrs.

Exclusion criteria:

1. Airflow limitation with FEV1 < 20%.

2. DLCO < 20%.

3. Current smoker.

4. Patients not candidate for FOB.

➤ **Study design:**

All selected patients were subjected to the following:

□ Thorough history taking and clinical examination.

□ Routine investigations including: Chest X ray, Complete blood picture, prothrombin time, INR, liver and kidney function tests, electrocardiogram and arterial blood gases analysis.

Pulmonary function tests were done on admission as a basic value, then at 12 week post procedure including:

- RV, RV/TLC ratio, using single breath helium dilution method.

- Spirometry (FEV1, FEV1/FVC ratio).

Post procedure evaluation:

All patients were monitored for 24 hour post procedure for the development of any early complications e.g. (COPD exacerbations, pneumothorax, pulmonary

embolism, cardiac ischaemia or myocardial infarction) and also monitored during the follow up period for the development of late complications e.g. (pulmonary abscess and empyema).

➤ **Outcomes evaluation:**

(A) The primary end-point:

Reduction in the volume of the targeted emphysematous part, at 12 weeks post procedure, detected by reduction in RV/TLC ratio from baseline.

(B) The secondary end-points:

(1) Changes from baseline at 12 weeks in FEV1 and FEV1/FVC ratio.

(2) Safety: presence or absence of complications.

➤ **Procedure:**

The procedure was done in the bronchoscopy unit, Chest Medicine Department, Mansoura University Hospital using fiberoptic bronchoscope under conscious sedation. The bronchoscope was introduced to just below the targeted segmental bronchus that was previously determined by high resolution CT chest. A balloon catheter was introduced into the targeted segmental bronchus with the tip positioned 3 to 4 cm further than the end of the bronchoscope.

After inflation of the balloon, the biological agent (30 ml autologous blood) was injected via the catheter over 10 to 15 seconds and left in position for 3-6 minutes allowing time for blood to coagulate. The bronchoscope was then repositioned at the following targeted segment.

RESULTS

This study included seven male patients with severe to very severe COPD.

Table (1): Age and COPD grouping according to GOLD (2013)

Age(Years) (mean \pm SD)		55.71 \pm 4.03
COPD group [N (%)]		
	GOLD III	1 (14.3%)
	GOLD IV	6 (85.7%)

Patients had severe to very severe airflow obstruction based on GOLD classification.

Table (2): Baseline assessment of spirometric measures, residual volume, residual volume/total lung capacity ratio (RV/TLC).

RV/TLC% (mean±SD)	154 ±23
FEV1 (% Predicted) (mean±SD)	26 ± 4
FEV1/FVC% (mean±SD)	50 ± 8
RV (% Predicted) (mean±SD)	122 ±12

Efficacy Results:**A) Primary outcome:** **RV/TLC:**

Table (3): Changes in RV/TLC after 12 weeks.

Baseline	12 weeks	P* value
154 ± 23	125 ± 20	0.038

There was statistically significant reduction in RV/TLC ($p = 0.038$)

B) Secondary outcomes: **Spirometric measures:**

Table (4): Changes in post-bronchodilator FEV1 and FEV1/FVC after 12 weeks:

	Baseline	12 weeks	P* value
FEV1(% Predicted)	26 ± 4	34 ± 5	0.018
FEV1/FVC %	50 ± 8	66 ± 10	0.003

FEV1 significantly increased after 12 weeks post procedure ($p = 0.018$). There was significant improvement in FEV1/FVC % ($p = 0.003$).

Safety results (presence or absence of complications).

All cases tolerated the procedure with no mortality. There was one case developed pneumonia at the same side of intervention 10 days post procedure (incidence: 14.3%) that was improved by 10 days course of antibiotic and two cases developed mild haemoptysis (blood streaked sputum) (incidence: 28.5%). No life threatening complications e.g (pneumothorax, pulmonary embolism, cardiac ischaemia or myocardial infarction) occurred.

DISCUSSION**A) Primary outcome:** **RV/TLC:**

In our study there was statistically significant reduction in RV/TLC at 12 weeks post procedure compared to baseline values. These results were in agreement with the first study related to biological lung volume reduction performed by *Reilly et al.*³ who used fibrin hydrogel. Efficacy data

demonstrated significant decrease in RV/TLC.

*Herth et al.*⁴ were the first who assessed the safety and efficacy of polymeric lung volume reduction (PLVR) using AeriSeal in treatment of advanced heterogeneous emphysema. Regarding the outcome measure RV/TLC, there were more favorable results in heterogeneous than in homogenous emphysema.

B) Secondary outcomes:

As regard spirometric measures outcomes, in our study, FEV1% significantly increased after 12 weeks post procedure ($p = 0.018$). In addition, we found significant improvement in FEV1/FVC % at 12 weeks post procedure compared to baseline values ($p = 0.003$). These results were in parallel to those found by *Refaely et al.*⁵ and *Criner et al.*² (2009) where there was significant improvement in the same parameters.

C) Posttreatment Complications

In our study, no deaths were encountered. Pneumonia occurred in one case at the same side of intervention 10 days post procedure (incidence: 14.3%) that was improved after 10 days of inpatient treatment. This ratio appear to be much higher than that found by *Criner et al.*⁶ who reported one case of pneumonia (evaluated in emergency room) out of 28 (incidence: 3.5%) There were no other serious complications observed during the study.

CONCLUSION

Bronchoscopic lung volume reduction using autologous blood injection could be an effective and cheap method to treat advanced emphysema in comparison to other agents used in the clinical trials with a relatively safe profile.

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