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Safety and Feasibility of Bronchial Thermoplasty in Asthma Patients with Very Severe Fixed Airflow Obstruction: A Case Series

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Abstract

Objective—Bronchial thermoplasty (BT) can provide relief for patients with severe, uncontrolled asthma despite maximal medical therapy. However, it is unclear whether BT is safe in patients with very severe airflow obstruction.

Methods—We performed BT in eight patients with severe asthma as defined by Expert Panel Report 3 (EPR-3) guidelines who were poorly controlled despite step 5 therapy. Data were available on each subject for 1 year prior to and 15–72 weeks following BT.

Results—The mean (±SEM) pre-bronchodilator forced expiratory volume in one second (FEV_1) prior to BT was 51.8 ± 8.6% of predicted, and the mean (±SEM) number of hospitalizations for asthma in the year prior to BT was 2.9 ± 1.2. No subject had an unexpected severe adverse event due to BT. Among the eight patients with follow-up of at least 15 weeks, there was no significant decline in FEV_1 ($p = .4$).

Conclusion—We suggest that BT may be safe for asthma patients with severe airflow obstruction and higher hospitalization rates than previously reported.

Keywords

airway smooth muscle; persistent airflow obstruction; poorly controlled asthma; radiofrequency ablation; refractory asthma

Introduction

Bronchial thermoplasty (BT), approved by the US Food and Drug Administration (FDA) in 2010 (1), is a new therapeutic intervention for patients with uncontrolled, severe asthma refractory to standard medical treatment. In BT, all visible and reachable airways are treated with radiofrequency energy provided by the Alair catheter (Asthmatx, Inc., Mountain View, CA, USA) introduced via a flexible bronchoscope in order to reduce airway smooth muscle

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Declaration of Interest

Dr. Hogarth has given three industry-funded lectures on Bronchial Thermoplasty. The remaining authors report no conflicts of interest.

mass and decrease bronchial reactivity. The benefits of this therapy include reduced asthma symptoms, fewer exacerbations, and improved quality of life (2–8). Three randomized clinical trials in a total of 260 patients have demonstrated the safety and benefits of BT in adults with moderate to severe asthma (3–5,8,9). However, the larger part of these two studies included adults with only mild to moderate airflow obstruction as measured by forced expiratory volume in one second (FEV_1). We report eight patients with severe asthma symptoms and severe airflow obstruction who have successfully and safely undergone BT at our institution.

Patients and Methods

In this single-center case series, we identified eight patients with severe asthma from the University of Chicago who had previously underwent BT. All patients met criteria for a diagnosis of severe asthma as defined by the National Asthma Education and Prevention Program's Expert Panel Report 3 (NAEPP EPR-3) guidelines (10) and had poorly controlled asthma, despite maintenance medical therapy including high dose inhaled corticosteroid (ICS) (≥1000 mcg/day fluticasone or equivalent), and long-acting β_2-agonist (LABA) (≥100 mcg salmeterol or equivalent). Patients were consented prior to BT and completed the treatment in a series of three bronchoscopic procedures using the Alair Bronchial Thermoplasty System from October 2010 to February 2012. Patients received prednisone (50 mg daily) for 3 days, prior to the day of procedure, at the day of procedure, and 1 day after each BT procedure as per protocol. Adverse events in the BT treatment period (from the first procedure to 6 weeks following the last BT procedure) and the post-treatment period (follow-up beyond that period) were collected. Data were available on each subject for at least one year prior to the initial BT treatment, and follow-up was available from 15 to 72 weeks following the final BT procedure. All patients were provided written consent for use of their information (Institutional Review Board approval 15,543B). Data were collected through chart abstraction. Stata® 11.0 software was used for a paired *t*-test analysis comparing pre-bronchodilater FEV_1 before BT and 15 weeks after completion of BT (Stata Corporation, College Station, TX, USA).

The clinical characteristics of the eight patients at the time of the first BT procedure are presented in Table 1. All patients had severe asthma as defined by the NAEPP EPR-3 guidelines (10) and were poorly controlled on Step 5 or 6 asthma therapy prior to BT. Of the six patients with computed tomography scans of the chest available prior to undergoing BT, five patients had evidence of airway thickening.

Safety and Outcomes

Six of the eight patients in this series received conscious sedation with midazolam, fentanyl, and/or diphenhydramine. Two patients received general endotracheal anesthesia; these patients were previously identified to have a history of difficulty tolerating conscious sedation prior to their assessment for BT due to severe obstructive sleep apnea and anxiety, respectively.

No subject had an unexpected severe adverse event due to bronchoscopy or BT (Table 2). There were no deaths, and no patients required intubation or noninvasive positive pressure ventilation (NIPPV) following BT. Of the adverse events suffered, four patients required overnight observation following their initial BT procedure due to wheezing and/or increased frequency of rescue bronchodilator use. Two patients required overnight observation after their second BT procedure: one had left lower lobe atelectasis and one required increased frequency of bronchodilators. Three patients required overnight observation after the final BT procedure: two required admission for frequent bronchodilator use and one had a lower

respiratory tract infection. Finally, one patient developed mild hemoptysis and lower respiratory tract infection 6 days and 23 days following his third BT procedure, respectively. A bronchoscopic inspection following the episode of hemoptysis did not reveal a source of bleeding, and the patient did not require further intervention.

There was no change in percent predicted prebronchodilator FEV_1 noted at least 15 weeks after BT (pre-BT FEV_1 51.8 ± 8.6% vs. post-BT FEV_1 52.1 ± 9.2%, $p = .4$). In addition, no patient had an increase in his or her hospitalization rate following the post-treatment period after completion of BT (mean of 2.88 ± 1.20 hospitalizations for asthma in the year prior to BT compared to 0.50 ± 0.33 hospitalizations during the median follow-up of 31 weeks following BT).

Discussion

The majority of morbidity and health care cost related to asthma is attributable to patients with severe or poorly controlled asthma (11–13). These patients suffer from increased hospitalizations and reduced quality of life despite the use of maximum medical therapy recommended for asthma by many (14,15). BT is a promising treatment for severe asthma patients who are refractory to medical therapy. However, to date this procedure has been studied almost exclusively on patients with mild to moderate airflow obstruction. Therefore, it is difficult to discern its role in severe asthma patients from the existing literature. Our case series presents data on patients with severe asthma symptoms and significant airflow obstruction who have safely undergone BT in an experienced medical center with complete clinical support. Current literature does not report routine BT in patients with airflow obstruction more severe than what has been described in the largest studies, Asthma Intervention Research trials 1 and 2, which excluded asthma patients with a prebronchodilator FEV_1 of less than 60% of predicted (4–6). In the Research in Severe Asthma (RISA) trial, patients with more severe airflow obstruction were included (mean FEV_1 of 62.9% of predicted in the BT group). However, the RISA trial excluded patients with an FEV_1 less than 50% of predicted (3). In our case series, five of our eight patients had a prebronchodilator FEV_1 less than 50% of predicted with a mean FEV_1 of 37.4%. Our case series is the first to demonstrate that BT can be performed in patients with an FEV_1 below 50%. Further, patients were excluded from the AIR trials if they required oral corticosteroids (OCS) in excess of 10 mg/day (4,5). While the smaller RISA trial did include subjects on OCS doses of up to 30 mg/day, the mean OCS dose among the 8 of 15 subjects undergoing BT was only 14.4 mg/day (3). In contrast, in our series four patients required an average of 27.5 mg/d. Finally, patients in our series had an average of 2.9 asthma-related hospitalizations in the year prior to BT, whereas the BT group in the RISA trial had only 0.67 hospitalizations per patient (10 events for 15 subjects undergoing BT) (3).

No unexpected adverse events occurred. Similar to other BT trials (3,5), adverse events in the treatment period following BT in our series included wheezing, increased bronchodilator use, atelectasis, lower respiratory tract infection, and hemoptysis. Given that the patients in our series had been identified with a low baseline FEV_1, we elected a conservative approach in recommending overnight observation following BT when necessary. Patients in our series had more overnight observations compared to those included in the BT group of the RISA trial (11 events for 8 patients and 24 procedures vs. 7 events for 15 patients and 45 procedures) (3). However, no patient in the case series had an unexpected severe adverse event such as death or the requirement of ventilator support. Further, seven of the eight patients in our series did not have worsened airflow obstruction or an increase in hospitalization rates following BT.

We did not have sufficient data to show whether all the patients had significant improvements in quality of life or asthma control following BT in this study. Careful observation is required in larger series to determine whether BT in patients with severe airflow obstruction will lead to improvements in clinical course, improvement in asthma-free days, and reduction in hospitalizations similar to that seen in patients with milder degrees of airflow obstruction.

Conclusion

We present a case series of asthma patients with severe airflow obstruction and high hospitalization rates who have successfully completed BT without unexpected severe adverse events. With the proper expertise, BT may be a safe option for patients with severe, refractory asthma who have exhausted currently available medical therapy.

Acknowledgments

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Table 1

Patient characteristics prior to bronchial thermoplasty.

Characteristic	Mean ± SEM
Age (years)	47 ± 4.3
Female, *n*	4
Race, *n*	
White	5
African American	1
Other	2
BMI (kg/m^2)	30.0 ± 2.3
Pre-BD FEV_1 (% predicted)	51.8 ± 8.6
Pre-BD FEV_1 <50%, n	5
ICS dose[a] (mcg/day)	1000
Other medications, *n*	
LABA (≥100 mcg[b])	8
OCS	4
Leukotriene modifiers	6
Omalizumab	2
Methylxanthines	2
Anticholinergics	3
OCS dose (mg/day)	27.5 ± 4.8
SABA use (puffs/day)	6 ± 0.8
Avg. night wakings (nights/week)	4.5 ± 1.0
Hospitalizations last year (total no.)	23 ± 1.2
eNO (ppb)	55 ± 17.4
IgE (IU/mL)	155 ± 8.7
Comorbid conditions, *n*	
GERD	5
Allergic rhinitis	5
OSA	
HTN	1
Diabetes	2
PAF	2
MAI	1

Notes:

[a] Fluticasone or equivalent.

[b] Salmeterol or equivalent.

Abbreviations: BD bronchodilator; LABA Long-acting bronchodilator; SABA Shortacting bronchodilator; eNO Exhaled nitric oxide; IgE Immunoglobulin E; GERD Gastroesophageal reflux disease; OSA obstructive sleep apnea; HTN Hypertension; PAF Paroxysmal atrial fibrillation; MAI *Mycobacterium avium-intracellulare*.

Table 2

Complications from bronchial thermoplasty.

Overnight observations, *n*	
Total no. of events	11
Total no. of patients with an event	5
Cause, *n*	
Increased BD use	5
Wheezing	2
Lower respiratory tract infection	2
Atelectasis	1
Hemoptysis	1
Intubations, *n*	0
NIPPV, *n*	0
Deaths, *n*	0