

Correspondence

Adrenal reserve in acute exacerbation of non-cystic fibrosis bronchiectasis

Sir,

Bronchiectasis (BXSIS) is characterized by non-reversible airway dilatation due to a variety of respiratory insults, and a few evidence-based medical therapies exist for the treatment of non-cystic fibrosis bronchiectasis¹. Acute exacerbations of bronchiectasis (AE-BXSIS) result in episodic worsening of lung function and symptoms^{2,3}. Frequent exacerbations may accelerate decline in lung function and increase in mortality⁴. Goals of therapy in stable bronchiectasis include reduction in exacerbations and improvement in quality of life (QOL)³.

Patients with AE-BXSIS often experience increasing fatigue and expectoration, which significantly impair QOL and work capacity⁵. Increasing evidence suggests frequent adrenal insufficiency in stable bronchiectasis and correlates with symptoms and QOL as measured by the St. George's Respiratory Questionnaire (SGRQ)⁶. In a previous study, we found a similar prevalence of suppressed adrenal responses in patients from south India with stable bronchiectasis⁷. Little is known about adrenal responses during AE-BXSIS and relationship of these to longitudinal responses in stable state; also, the correlation of these responses with fatigue and QOL is unknown. We, therefore, conducted a pilot observational study at the St. John's Medical College Hospital, Bengaluru, India, between April 2009 and February 2012 to evaluate adrenal responses to 1 µg cosyntropin during AE-BXSIS and six weeks after resolution of AE-BXSIS. The study was approved by the Institutional Ethics committee. The inclusion and exclusion criteria for bronchiectasis, study setting and methodology, reason for choice of 1 µg test and cut offs (≤ 17.5 µg/dl post-stimulation) have been described previously⁷. The aetiology of bronchiectasis was made based on clinical history and appropriate use of testing as per guidelines^{1,8}. AE-BXSIS was defined

as subjective and persistent (≥ 24 h) deterioration in at least four of the following nine parameters: fever (temperature greater than 37.5°C), cough, dyspnoea, haemoptysis, sputum purulence or volume, chest pain, respiratory signs on examination, radiographic signs and systemic symptoms^{3,9}. The details of the enrolled patients are provided in Table I. Five patients (25%) failed to mount a positive response and fulfilled the criteria for adrenal insufficiency (post-stimulation cortisol ≤ 17.5 µg/dl). Basal cortisol values were not significantly different between patients with and without impaired adrenal reserve (IAR); 30-min post-stimulation values were significantly lower in patients with adrenal insufficiency ($P=0.001$). Tuberculosis as a cause of bronchiectasis was significantly associated with IAR [$P<0.01$ (Fisher's Exact test) Table II].

Data on repeat testing of 1 µg synacthen was available in 11 of 20 patients (Figure). While there was a clear trend towards an increase in both basal (mean difference=2.59, $P=0.14$) and 30-minute cortisol values (mean difference=1.94, $P=0.32$), these values did not reach statistical significance. Using a cut-off of 17.5 µg/dl for IAR, 8 of 11 (72.7%) patients were classified the same way on repeat 1 µg synacthen testing. Two (18%) patients who were classified as normal during exacerbation had value suggestive of impaired adrenal reserve when re-tested during stable state and one had normal testing during stable state but failed to show incremental response during an exacerbation.

The lack of association of basal values and AE-BXSIS is possibly because of heightened stress responses due to an exacerbation; however, a clear separation existed in 30-min stimulation values and this persisted after resolution of an exacerbation. A low 30-min cortisol response with active tuberculosis has been well documented^{11,12}. Our previous study on stable bronchiectasis showed a correlation between SGRQ

Table I. Characteristics of patients with acute exacerbation of bronchiectasis (N=20)

Parameter	Mean ± standard deviation or number (percentage)
Gender	Male 15 (75); female 5 (25)
Age (yr)	43.25 ± 16.75
Symptom duration (yr)	14.76 ± 9.93
Sputum amount per day (ml/day)	42.4 ± 9.93
Number of days with purulent sputum (N=12)*	12 ± 7.8 days per month
Smoking history	18 (90) never smokers; 2 (10) former smokers
Body mass index (kg/m ²)	20.11 ± 3.91
Nausea and/or vomiting	3 (15)
Fatigue	5 (25)
Weight loss	2 (10)
Postural drop in blood pressure (mm Hg)	1 (5)
Bronchiectasis aetiology	Idiopathic 8 (40); Post-tuberculosis 6 (30); Post-necrotizing pulmonary infections 2 (10); Others 4 (20)
Bronchiectasis extent	
Severe bronchiectasis (≥ grade 3)	11 (55)
Bronchiectasis severity score#	103.25 ± 41.07
Pulmonary artery hypertension	5 (25)
FEV ₁ (N=19)	1.37±0.48 l; 45.27 ± 12.80 per cent predicted
FVC (l) (N=19)	1.85±0.63 l; 51.22 ± 15.17 per cent predicted
Inhaled corticosteroids use	12 (60)
Six-minute walk distance (meters)	443.54±161.31
SGRQ	
Symptoms domain	66.10±19.12
Activity domain	68.88±28.06
Impact domain	62.05±25.33
Total	64.80±22.23
Adrenal responses	
Basal cortisol (µg/dl)	13.36 ± 2.94
30 min stimulated cortisol (µg/dl)	19.5 ± 3.38
1 µg synacthen test failures [§]	5 (25)
[§] Defined as 30-min post-1 µg synacthen stimulation cortisol value of ≤ 17.5 µg/dl SGRQ, St. George's Respiratory Questionnaire; FEV ₁ forced expiratory vital capacity in 1 sec; FVC, forced vital capacity *Data available only for 12 of the 20 patients #Ref. 10	

Table II. Comparison of characteristics between patients with and without relative adrenal insufficiency

Characteristic	Patients with adrenal insufficiency (N=5)	Without adrenal insufficiency (N=15)
Gender: Male/female	3/2	12/3
Age (yr)	52 ± 13.75	40.3 ± 17.05
Symptom duration (yr)	14.8 ± 9.42	14.74 ± 10.43
Sputum amount per day (ml/day)	28.0 ± 12.55	47.2 ± 40.0
Days with purulent sputum per month	11.67 ± 7.64	12.11 ± 8.31
Sputum purulence score % ≥ 3	2/5	9/15
Body mass index (kg/m ²)	23.16 ± 3.14*	18.94 ± 3.61
Nausea and/or vomiting	0/5	3/12
Fatigue	1/4	4/11
Bilateral (Unilateral/bilateral)	3/1	12/2
Severity of bronchiectasis (grade 4/total)	3/4	8/9
Bronchiectasis severity score [#]	94.4 ± 32.24	106.2 ± 44.2
Aetiology (Tuberculosis/other causes)	4/1**	2/13
Pulmonary artery hypertension (Y/N)	0/5	5/10
FEV ₁ /FVC %	81.25 ± 6.65	71.50 ± 12.49
FEV ₁ (l)	1.29 ± 0.34	1.40 ± 0.54
FVC (l)	1.67 ± 0.42	1.92 ± 0.69
Six minute walk distance (meters)	411.8 ± 150.03	463.38 ± 174.86
SGRQ		
Symptoms domain	59.28 ± 22.13	68.37 ± 19.12
Activity domain	81.83 ± 20.21	64.51 ± 29.52
Impact domain	61.52 ± 26.49	62.23 ± 25.88
Total	67.38 ± 22.14	63.94 ± 22.96
Number receiving ICS	4/5	8/15
Basal cortisol (µg/dl)	11.16 ± 2.83	14.09 ± 2.67
Stimulated cortisol response (µg/dl)	14.54 ± 1.37***	21.16 ± 1.81
SGRQ, St. George's Respiratory Questionnaire; ICS, inhaled corticosteroid; FEV ₁ , forced expiratory vital capacity in 1 sec; FVC, forced vital capacity		
P* < 0.05 ** < 0.01 *** < 0.001 compared with patients without adrenal insufficiency		
#Ref. 10		

scores and IAR, but we did not find a correlation with post-tuberculosis aetiology and IAR in that study⁷. Repeat testing was performed in only 11 patients. Most of the patients remained in the same class, suggesting that the IAR might be a persistent abnormality rather than being specific for the acute phase. It is well known that there is significant variability on repeat testing in adrenal stimulation tests¹³. Two patients who were classified as normal during exacerbation were diagnosed to have IAR on repeat examination.

Hypothalamo-pituitary-adrenal (HPA)-axis dysfunction could be a part of acute and/or chronic inflammatory disease because of its obvious therapeutic implications. Larger longitudinal studies with repeated examination of adrenal function in bronchiectasis both during acute exacerbation and in the stable phase are required for a better understanding of the contribution of HPA-axis to symptomatology, quality of life and mortality in bronchiectasis.

Conflicts of Interest: None.

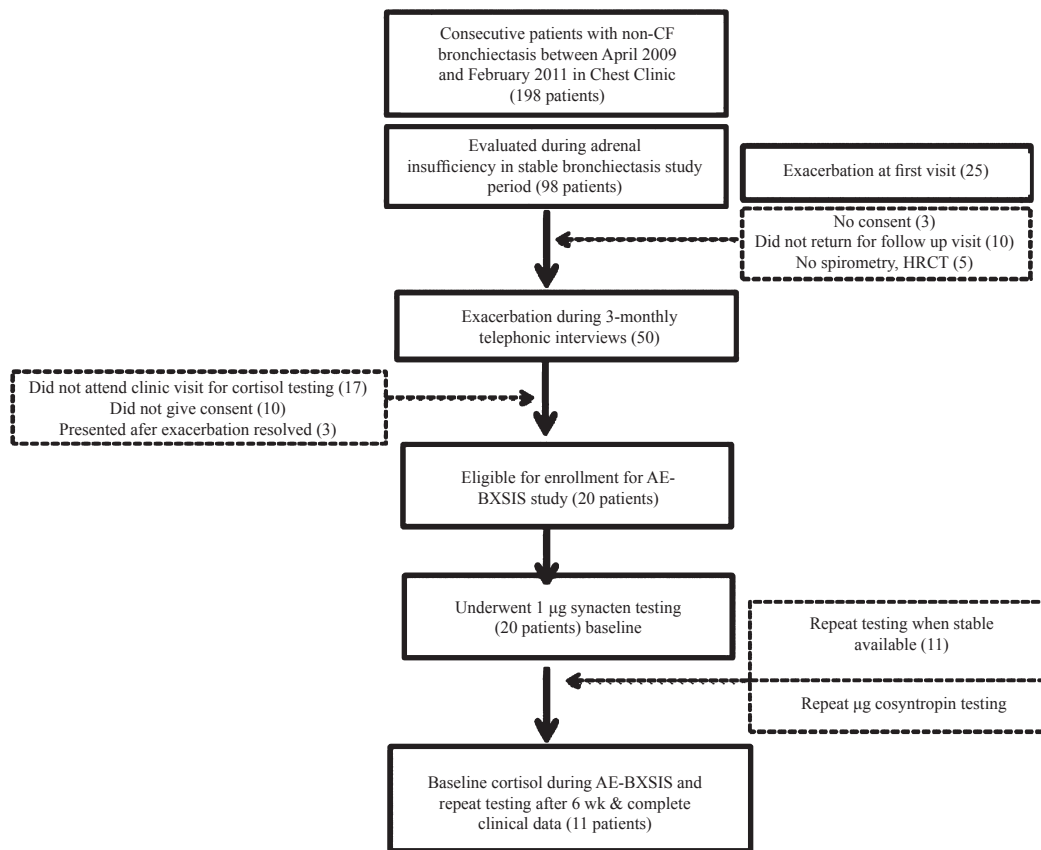


Figure. Flowchart of the patients enrolled in the study of adrenal insufficiency in acute exacerbation of non-cystic fibrosis bronchiectasis.

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