

Short communication

Role of symptoms and lung function in determining asthma control in smokers with asthma

Background: Cigarette smoking in asthma increases the severity and accelerates the decline in lung function. The relative role of symptoms and lung function in determining asthma control in smokers with asthma is not known.

Aim of the study: The aim of this study was to compare asthma control in smokers *vs* never-smokers with asthma, using the validated Juniper asthma control questionnaire (ACQ), and assess if any difference was because of a particular symptom or the forced expiratory volume in one second (FEV₁) value.

Methods: This was a cross-sectional study of 134 asthmatics (74 never-smokers and 60 smokers) with $\geq 15\%$ reversibility in FEV₁ after salbutamol. All subjects completed the ACQ, recording FEV₁ and asthma symptoms (night awakening, morning symptoms, dyspnoea, wheeze, activity limitation and use of reliever inhaler).

Results: Compared with the never-smokers, smokers with asthma had significantly worse median (IQR) total asthma control score [1.6 (1.1–2.3) *vs* 2.8 (1.7–3.4); ($P < 0.0001$)] and in each of the six individual symptom question scores ($P < 0.001$), but no difference in FEV₁ levels ($P = 0.908$).

Conclusion: Asthma control is significantly worse in asthmatics who smoke compared with never-smokers, with all symptoms related to asthma control uniformly worse in smokers, independent of FEV₁.

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Current smoking is common in adults with asthma with rates ranging from 17% to 35% (1). Particularly high rates of smoking have been reported among individuals presenting to hospital emergency departments with acute asthma. Smokers with asthma are known to have more severe disease (1), accelerated decline in lung function (2) and impaired therapeutic response to corticosteroids (3–5) compared with never-smokers. A recent large survey of patient characteristics noted that smoking was one of the factors related to poor asthma control. However, in this study, lung function was not recorded and the diagnosis of asthma was not confirmed objectively (6).

The goal of asthma management is to achieve and maintain control of the disease with minimal adverse effects of medication used. The Juniper asthma control questionnaire (ACQ) is a validated scoring system including questions on daytime symptoms for asthma, night awakening, reliever inhaler use and forced expiratory volume in one second (FEV₁) (7). Asthma

control assessed by the ACQ has been reported to be worse in smokers compared with non-smokers with asthma in some studies (4, 8), but no different in others (3, 9). This variability could be as a result of small numbers of patients studied. The combination of asthma and heavy smoking has a synergistic effect on the decline in FEV₁ (2). If asthma control is worse in smokers with asthma, it is not known whether this is caused by a difference in any particular symptom related with control or whether it is because of reduced lung function.

Our aim was to compare each of the questions and the spirometry value used to measure asthma control in smokers *vs* never-smokers with asthma using the ACQ, and assess if a lower total score in the smokers with asthma group was because of a particular symptom or a lower FEV₁ value.

Methods

Subjects

Sixty asthmatic smokers and 74 never-smokers aged between 18 and 65 years were recruited. Asthma was diagnosed using the American Thoracic Society (ATS) criteria. All asthmatics had an improvement in FEV₁ after nebulized salbutamol of $\geq 15\%$ and > 200 ml. Smokers

Abbreviations: CO, carbon monoxide; FEV₁, forced expiratory volume in one second; FEV₁, forced expiratory volume in one second; ICS, inhaled corticosteroids.

Table 1. Baseline demography of asthmatic smokers and never-smokers

	Asthmatic	
	Smokers (<i>n</i> = 60)	Never-smokers (<i>n</i> = 74)
Age (years)	53.7 (45.0–61.0)	42.0 (52.0–61.0)
Males, <i>n</i> (%)	27 (45%)	50 (68%)*
Years smoked	27 (21–35)	–
Cigarettes/day	20.0 (20.0–30.0)	–
Pack years	31.0 (22.0–40.5)	–
Asthma duration (years)	12 (8–25)	22 (10–40)*
On treatment with ICS, <i>n</i> (%)	45 (75%)	61 (82%)
Equivalent dose of beclometasone (mcg)	800 (50–1600)	400 (400–1000)
FEV ₁ % predicted, presalbutamol	70.5 (58.5–79.0)	71.0 (58.7–79.5)
FVC% predicted, presalbutamol	86.5 (78.0–99.0)	87.5 (76.2–96.7)
FEV ₁ /FVC ratio	66.0 (54.2–76.5)	67.5 (60.0–74.7)
Salbutamol reversibility (%)	17 (16–22)	20 (16–30)
Carbon monoxide (ppm)	19.44 (14.67–27.01)	4.09 (3.40–4.65)**
Serum cotinine (ng/ml)	276 (122–378)	3.0 (2–3)**

Data depicted as median (IQR).

ICS, inhaled corticosteroids; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity.

Number of subjects: carbon monoxide, *n* = 89; serum cotinine, *n* = 65.

P* < 0.05; *P* < 0.001.

had ≥10 pack-year smoking history. This was a cross-sectional study. Some subjects from previous studies were included (3, 8). All subjects were stable on therapy for at least 4 weeks with no upper or lower respiratory tract infection for the previous 3 weeks. Informed consent from subjects and ethical approval from the West Ethics Research Committee was obtained for study procedures.

Study design and measurements

A validated ACQ was completed, recording FEV₁ and six questions about asthma in the past week on a 7-point scale (ranged: 0–6 for increasing severity) (7). The items are equally weighted and the total score is a mean of the individual scores (7). The first six questions were completed by the subject in a quiet room prior to performing other study procedures. The last question relating to FEV₁ was completed by the research clinic staff after the spirometry test.

Spirometry, before and after 2.5 mg nebulized salbutamol, was performed with a dry spirometer (Vitalograph Ltd, Buckingham, UK). Carbon monoxide (CO) was measured in a sub-group (depending on availability), using a chemiluminescence analyser (Logan Research Ltd, Rochester, UK). Smokers were asked to abstain for an hour prior to their visit. Serum cotinine was measured in a sub-group using an enzyme immunoassay (Cozart Bioscience Ltd, Abingdon, UK). Serum IgE tests to house dust mite, grass pollen and cat dander were performed in the majority of subjects and atopy was defined as a positive test to any one of the three common antigens.

Statistical methods

Continuous variables were compared in smoking, gender or treatment categories by Mann–Whitney *U*-tests. The interactions between smoking, gender, steroid treatment and the asthma control scores were tested by ANOVA. Correlation between the continuous variables (age, asthma duration, pack-year smoked and steroid dose) was tested after log transformation to normality if necessary and calculating Spearman's rho. Significance was accepted at a level

of *P* < 0.05. Data was analysed using MINITAB 14 software (Minitab Inc., State College, PA, USA).

Results

There were no significant differences between the groups for age, spirometry and inhaled corticosteroid dose (Table 1). Males exceeded females in the never-smoker group (*P* = 0.011). Never-smokers had a longer duration and an earlier age of onset of asthma compared with smokers. Serum cotinine and exhaled CO were higher in smokers.

There was a significant difference (*P* < 0.001) in total asthma control score for each of the five individual symptom questions and reliever inhaler use with smokers displaying a uniform worsening of all symptoms with no difference in FEV₁ levels (Fig. 1, Table 2). The first six questions of the ACQ correlated with each other (*P* < 0.001) in all subjects taken together as well as for individual groups of smokers and never-smokers. The FEV₁% predicted score did not correlate with any of the other six questions in never-smokers, and in the smokers only correlated with the question related with limitation of activities because of asthma (*r* = 0.381, *P* = 0.003) and morning symptoms of asthma (*r* = 0.266, *P* = 0.041).

In the asthmatic smokers, the total asthma control score correlated with the smoking history as measured by pack years (*r* = 0.27, *P* = 0.039). In the whole group (*n* = 134), the total asthma control score did not significantly correlate with age or duration of asthma, but correlated with the dose of inhaled corticosteroids (ICS) (*r* = 0.362, *P* < 0.001). This suggested that the dose of inhaled corticosteroid was higher in those with worse asthma control. The number of subjects not taking ICS was small (*n* = 27); however, ANOVA showed no significant effect on ACQ in this group of smokers (*P* = 0.225) or gender (*P* = 0.881).

Serum cotinine and exhaled CO levels correlated positively with total ACQ score (*r* = 0.34, *P* = 0.006; *r* = 0.40, *P* < 0.001 respectively). Thirty-one of 49 smokers (63%) were atopic and 58/63 never-smokers (92%) were atopic, *P* < 0.001. There was no influence of atopy on the total asthma control score in all subjects considered together (*P* = 0.061), in the smoker group (*P* = 0.208) or in the never-smoker group (*P* = 0.350). The median ACQ was 1.71 in males and 2.29 in females with a trend towards the total score being worse in females (*P* = 0.055). Gender did not affect the difference in the asthma control score in smokers and never-smokers (ANOVA, *P* = 0.155).

Discussion

In this study, we compared the symptoms, reliever inhaler use and FEV₁ in asthmatics who smoke vs never-smokers,

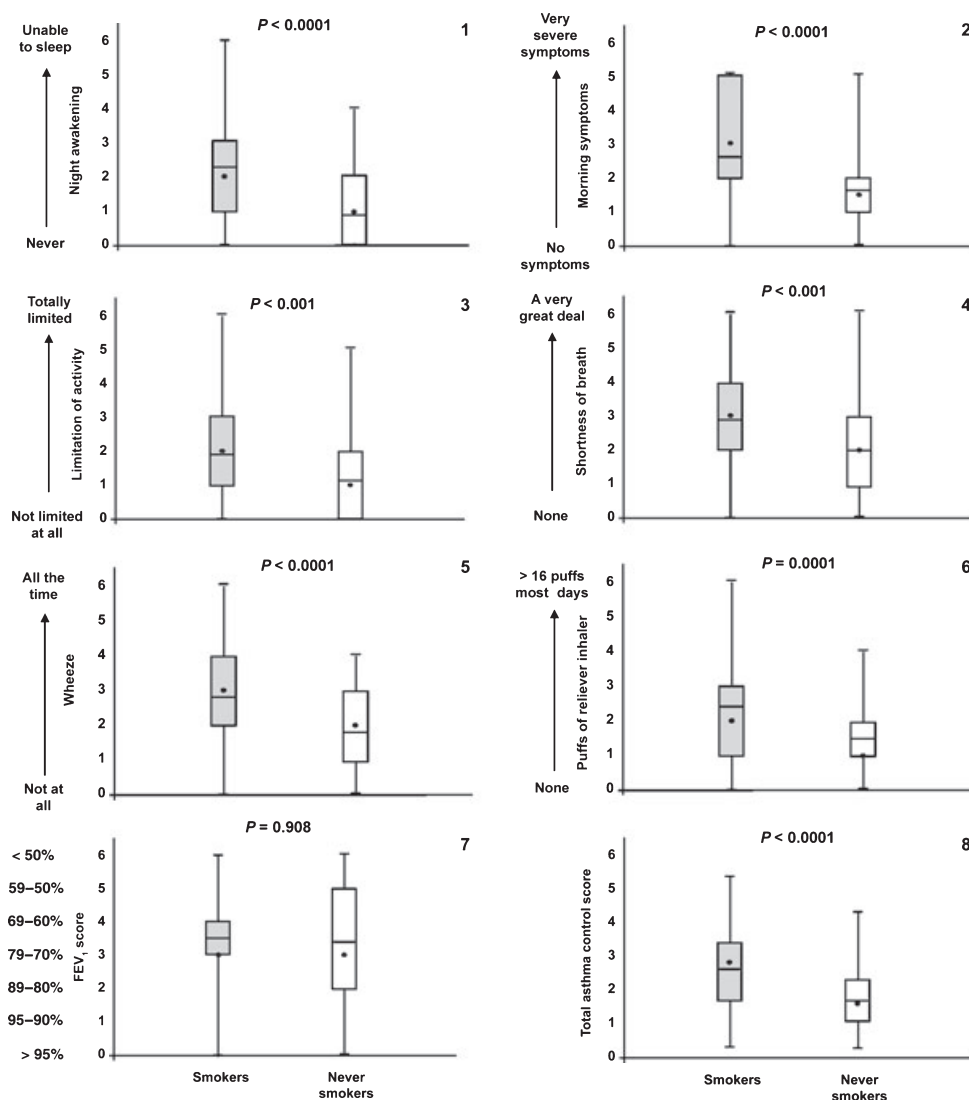


Figure 1. All aspects of asthma control using the Juniper asthma control questionnaire are worse in smokers with asthma (■) compared to never-smokers (□), except FEV₁ (parts 1–7). Part (8) depicts the total asthma control score. The box represents the inter-quartile range, median (–), mean (●) and the whiskers represent the maximum and minimum values.

Table 2. ACQ in asthmatic smokers and never-smokers

	Asthmatic		P-value
	Smokers (n = 60)	Never-smokers (n = 74)	
1. How often were you woken by your asthma?	2 (1–3)	1 (0–2)	<0.0001
2. How bad were your asthma symptoms when you woke up in the morning?	3 (2–4)	1.5 (1–2)	<0.0001
3. How limited were you in your activities because of your asthma?	2 (1–3)	1 (0–2)	<0.001
4. How much shortness of breath did you experience because of your asthma?	3 (2–4)	2 (1–3)	<0.001
5. How much of the time did you wheeze?	3 (2–4)	2 (1–3)	<0.0001
6. How many puffs of short-acting broncho-dilator have you used each day?	2 (1–3)	1 (1–2)	0.0001
7. FEV ₁ score	3 (3–4)	3 (2–5)	0.908
Total asthma control score	2.8 (1.7–3.4)	1.6 (1.1–2.3)	<0.0001

Data depicted as median (IQR).

ACQ, asthma control questionnaire; FEV₁, forced expiratory volume in one second.

using a validated asthma control questionnaire (ACQ), and showed that all symptoms related with asthma control were worse in smokers despite similar mean baseline FEV₁ levels between the groups. This finding emphasizes the important contribution that the increased symptoms of asthma make to poor asthma control in smokers with asthma.

These results confirm and extend the findings of Tomlinson et al. (4), wherein the asthma control scores were worse in smokers with asthma, using the shortened version of the ACQ without FEV₁ values and of Laforest et al. (6), who in a large survey of asthmatics, but in whom lung function was not measured, found that smoking along with age, female gender and body mass index predicted poor asthma control. Boulet et al. (9) found no difference in the asthma control score between smokers and non-smokers with asthma. The differences could be as a result of a smaller sample size, shorter inclusion criteria on duration of pack-years smoked and the inclusion a few mild ex-smokers in the non-smoker group. In addition, their subjects had milder asthma. Asthmatic smokers with poorer lung function may be particularly susceptible to the acute effect of tobacco smoke (10).

The reasons for poor asthma control in smokers are not clear. Smokers with asthma could have worse control, as they are less likely to attend asthma education programmes and to use appropriate methods to manage acute and chronic asthma (11). Inhaled and oral corti-

costeroids are less effective in smokers than non-smokers (3–5) and this could account for some of the worsening of asthma symptoms in smokers. The pattern of inflammation is different in asthmatics who smoke (1, 9, 12) with non-eosinophilic inflammatory cell phenotype commonly noted. This could reduce the efficacy of corticosteroid treatment in these patients, although other mechanisms may account for corticosteroid insensitivity (1).

A clear difference in the asthma control score between smokers and never-smokers is demonstrated in this study. A study of smokers with asthma noted that after smoking cessation, the ACQ score improved by 6 weeks (13). The effect of a longer duration of smoking cessation on asthma control is not known nor whether the levels return to those of never-smokers.

In this study, subjects had a baseline FEV₁% predicted median (IQR) of 70 (58–80%). The relationship between control and lung function may vary according to baseline obstruction and severity. To generalize the findings, we would need a larger population of asthmatics with different severity grades.

In conclusion, asthma control is significantly worse in asthmatics who smoke compared with never-smokers. Each individual symptom of asthma control is worse in smokers, independent of FEV₁ values, emphasizing the important contribution that increased symptoms of asthma make to poor asthma control in smokers with asthma.

References

1. Thomson NC, Chaudhuri R, Livingston E. Asthma and cigarette smoking. *Eur Respir J* 2004;**24**:822–833.
2. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15 year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998;**339**:1194–1200.
3. Chaudhuri R, Livingston E, McMahon AD, Thomson L, Borland W, Thomson NC. Cigarette smoking impairs the therapeutic response to oral corticosteroids in chronic asthma. *Am J Respir Crit Care Med* 2003;**168**:1308–1311.
4. Tomlinson JEM, McMahon AD, Chaudhuri R, Thompson JM, Wood SF, Thomson NC. Efficacy of low and high dose inhaled corticosteroid in smokers versus non-smokers with mild asthma. *Thorax* 2005;**60**:282–287.
5. Chalmers GW, Macleod KJ, Little SA, Thomson LJ, McSharry CP, Thomson NC. Influence of cigarette smoking on inhaled corticosteroid treatment in mild asthma. *Thorax* 2002;**57**:226–230.
6. Laforest L, Van Ganse E, Devouassoux G, Chretien S, Osman L, Baugil G et al. Influence of patients' characteristics and disease management on asthma control. *J Allergy Clin Immunology* 2006;**117**:1404–1410.
7. Juniper E, O'Byrne P, Guyatt G, Ferrie P, King D. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;**14**:902–907.
8. Livingston E, Chaudhuri R, McMahon AD, Fraser I, McSharry CP, Thomson NC. Cutaneous vasoconstrictor response to corticosteroids is reduced in smokers with asthma. *Eur Respir J* 2007;**29**:64–70.
9. Boulet L-P, Lemiere C, Archambault F, Carrier G, Descary MC, Deschesnes F. Smoking and asthma: clinical and radiologic features, lung function, and airway inflammation. *Chest* 2006;**129**:661–668.
10. Jensen E, Dahl R, Steffensen F. Bronchial reactivity to cigarette smoke; relation to lung function, respiratory symptoms, serum- immunoglobulin E and blood eosinophil and leukocyte counts. *Resp Med* 2000;**94**:119–127.
11. Janson C, de Marco R, Accordini S, Almar E, Bugiani M, Carolei A et al. Changes in the use of anti-asthmatic medication in an international cohort. *Eur Respir J* 2005;**26**:1047–1055.
12. Chalmers G, MacLeod K, Thomson L, Little S, McSharry C, Thomson N. Smoking and airway inflammation in patients with mild asthma. *Chest* 2001;**120**:1917–1922.
13. Chaudhuri R, Livingston E, McMahon AD, Lafferty J, Fraser I, Spears M et al. Effects of smoking cessation on lung function and airway inflammation in smokers with asthma. *Am J Respir Crit Care Med* 2006;**174**:127–133.