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Effects of Smoking Cessation on Airflow Obstruction and Quality of Life in Asthmatic Smokers

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Purpose: Smoking elicits airway inflammation and airflow obstruction in patients with asthma, even after smoking cessation. The aim of this study was to examine the effects of smoking cessation on lung function and quality of life (QOL) in asthmatic patients. **Methods:** Thirty-two patients with asthma who were active smokers were recruited. After education on the effects of smoking on asthma, 22 patients continued to smoke, and 10 quit smoking. All patients were treated with inhaled fluticasone propionate (1 mg/day) for 3 months. We compared forced expiratory volume in 1 s (FEV1), FEV1/forced vital capacity (FVC), forced expiratory flow between 25 and 75% FVC ($FEF_{25-75\%}$), and scores on a QOL questionnaire at baseline, 1, 2, and 3 months. **Results:** Quitters showed a greater percent change in FEV1 (19.1±6.3 vs. 7.9±2.4%, P=0.024) and FEV1/FVC (6.5±4.14 vs. 3.5±1.5%, P=0.05) than smokers. Both quitters and smokers showed improved QOL scores after 1, 2, and 3 months of fluticasone treatment. **Conclusions:** Patients with asthma who quit smoking showed less airway obstruction, suggesting that smoking cessation is crucial in the management of asthma.

Key Words: Smoking; asthma; lung function; quality of life

INTRODUCTION

Cigarette smoking is an important factor associated with poor symptom control and treatment resistance in patients with asthma.[1-3] In our previous study in Korea, 18.8% of patients with asthma were current smokers.[4] Asthmatic patients who smoke have more emergency department admissions with exacerbations,[5] worse symptom control,[6-8] accelerated decline in lung function,[9,10] and increased mortality rates[11] compared to non-smokers with asthma. Asthmatic smokers have a greater need for rescue medication,[12] poorer health-status indices,[13] reduced therapeutic response to corticosteroids,[2,3] and enhanced airway inflammation.[14-16] Thus, a need exists to develop novel therapies to target this subgroup of patients with asthma.

Although previous studies on the effects of smoking on asthma have improved our understanding of airway inflammation and therapeutic response, further research is needed to clarify the role of smoking in asthma. Few studies have examined the effects of smoking cessation on symptoms, lung function, therapeutic responsiveness, and quality of life (QOL). In the present study, we evaluated the effect of smoking cessation on lung function and QOL in patients with asthma during corticosteroid treatment.

MATERIALS AND METHODS

Subjects and study protocol

The subjects were recruited from the Asthma Genome Research Center, Soonchunhyang University Bucheon Hospital, Korea. A clinical history was obtained for each patient on the first day of the study using a physician-administered questionnaire. Chest posterior–anterior and Water's view radiography, allergy skin prick tests, and spirometry (including bronchodilator respons-

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es after the inhalation of two puffs of 100 μg aerosolized albuterol) were performed. On the second visit, airway hyperresponsiveness (AHR) was measured in cases with predicted values for forced expiratory volume in 1 s (FEV1) ≥70%. All patients showed airway reversibility, as indicated by inhalant bronchodilator-induced improvement of >15% in FEV1 and/or airway hyperreactivity under <10 mg/mL methacholine.[17] All asthmatics smoked during the first and second visit. Asthmatics (n=35) with moderate persistent severity had compatible clinical symptoms and physical characteristics according to the Global Initiative for Asthma guidelines.[18] All subjects provided informed consent, and the protocols were approved by the local ethics committees. The patients were educated visually in the use of inhaled glucocorticoid (GC) by a trained nurse until their accuracy scores reached 12 (out of a maximum score of 14). GC inhalation was maintained for 3 months. Inhaled GC was 1 mg/day fluticasone propionate, which was self-administered using a multi-dose dry-powder inhaler (two puffs b.i.d.; Diskhaler, GSK, Durham, NC, USA). The patients used short-acting bronchodilators as needed. We educated all patients with asthma regarding the effects of smoking on health. Patients were classified into quitters and continuing smokers. FEV1, FEV1/forced vital capacity (FVC), forced expiratory flow between 25 and 75% FVC ($FEF_{25-75\%}$), and score on the asthma-related QOL questionnaire (AQLQ) at baseline and at 1, 2, and 3 months were compared between groups.

Lung function tests

Baseline FVC and FEV1 measurements were obtained in the absence of recent bronchodilator use (within 8 h) and selected according to the American Thoracic Society criteria.[19] Basal and post-bronchodilator FEV1, FVC, and $FEF_{25-75\%}$ were measured. AHR was measured via methacholine challenge and was expressed as the provocation concentration that caused a fall in FEV1 of 20% (PC20) in non-cumulative units.[20]

IgE measurement and skin allergy tests

Total IgE was measured using the UniCAP system (Pharmacia Diagnostics, Uppsala, Sweden). Allergy skin prick tests were performed using commercially available inhalant allergens (Bencard, Devon, UK), which included dust mites (*Dermatophagoides farinae* and *D. pteronyssinus*) and histamine (1 mg/mL). No subject had received oral antihistamines in the 3 days preceding the study. All tests included positive (1 mg/mL histamine) and negative (diluent) controls. After 15 minutes, the mean diameter of the wheals formed by each allergen was compared with that formed by histamine. If the former was the same or larger than the latter (A/H ratio ≥1.0) or the mean diameter was >3 mm, the reaction was deemed positive. Atopy was determined by the presence of an immediate skin reaction to one or more aeroallergens, as described previously.[21]

QOL measurement

The AQLQ was evaluated at baseline and after 4 weeks of treatment, using a Korean translation of the Juniper AQLQ.[22] The answers to each question were scored on a five-point scale, with a score of 1 representing the greatest impairment, and a score of 5 representing no impairment (lower AQLQ scores reflected increased impairment). Items were weighted equally and reported as the mean score for each domain (activity limitation, emotions, symptoms, and exposure to environmental stimuli), along with the overall score.

Statistical analysis

Group differences were compared using two-sample t-tests, Wilcoxon rank-sum tests, and the Pearson χ^2 test for normally distributed, skewed, and categorical data, respectively. Data are expressed as the mean and standard error of the mean. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Thirty-five asthmatic patients who were active smokers were recruited for this prospective study (Fig. 1). Three patients withdrew; two patients had restarted smoking, and one patient was not able to complete the QOL. Thus, 32 patients with asthma were enrolled. After education about the effects of smoking on overall health and on asthma in particular, 22 patients continued to smoke, and 10 quit smoking. Descriptive statistics according to smoking status in patients with asthma are shown in Table. Current smokers had a higher number of pack-years compared with patients who quit smoking (23.5±13.6 versus 6.5±2.2, respectively; *P*=0.001). The level of IgE and atopy prevalence tended to be higher among current smokers than among quitters.

Both quitters and smokers showed an increase in predicted FEV1 following steroid treatment (baseline versus 1, 2, and 3 months: quitters, 73.6±5.6 versus 91.1±5.2, 92.5±4.3, and 101.1±10.1%; smokers, 68.2±2.4 versus 76.9±3.7, 75.5±4.1, and 78.4±5.9%; Fig. 2A). FEV1/FVC (baseline versus 1, 2, and 3 months: quitters, 68.8±3.3 versus 75.5±2.7, 77.0±4.4, and 87.6±6.3%; smokers, 67.1±1.9 versus 70.5±2.3, 68.5±2.5, and 69.5±3.9%; Fig. 2B) tended to be higher in quitters than in smokers. $FEF_{25-75\%}$ was higher in quitters than in smokers (baseline versus 1, 2, and 3 months: quitters, 49.2±6.1 versus 70.8±7.5, 77.0±4.4, and 100.6±

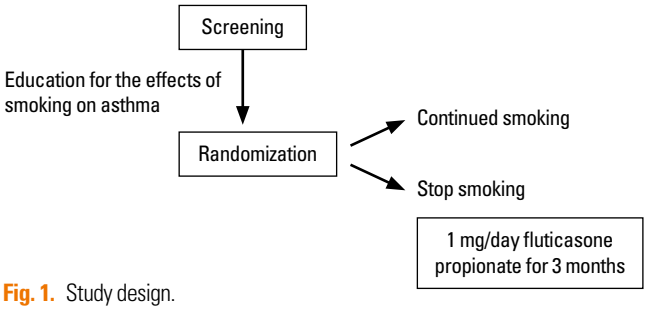

Fig. 1. Study design.

Table. Baseline clinical profiles of the subjects

	Quit group	Smoking group
No. of patients	10	22
Gender (male/female)	7/3	20/2
Age (yr)	53.3±4.3	45.6±2.5
FEV1, % predicted	73.6±5.6	68.2±2.4
FVC, % predicted	77.8±3.7	77.2±1.9
FEV1/FVC	68.8±3.3	67.1±1.9
$FEF_{25-75\%}$	49.2±6.1	44.5±4.0
Atopy (%)	33.3 (2/6)	75 (12/16)
Duration of asthma (yr)	16.6±10.3	10.2±2.2
Pack years smoked	6.5±2.2	23.5±13.6*
PC20 methacholine	5.3±7.9	5.4±6.4
Total IgE (Unit)	463.3±156.2	600.3±228.2

Plus–minus values are mean±SE.
FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% FVC; PC20 methacholine, the concentration of methacholine required to decrease the FEV1 by 20%.
*P=0.001 compared with quit group.

18.4%; smokers, 44.5±4.0 versus 60.8±5.9, 56.7±6.1, and 59.5±8.0%; Fig. 2C). Quitters showed a significantly greater increase in percent change in FEV1 and FEV1/FVC than did current smokers at 1 month (FEV1: 19.1±6.3 versus 7.9±2.4%, P=0.024; FEV1/FVC: 6.5±4.14 versus 3.5±1.5%, P=0.05; Fig. 3). Both quitters and smokers showed improved AQLQ scores (baseline versus 1, 2, and 3 months: quitters, 52.1±2.5 versus 62.5±3.1, 68.7±3.5, and 76.8±2.4; smokers, 53.2±1.7 versus 64.3±1.6, 68.9±2.5, and 67.7±3.3; Fig. 4). The percent change in QOL did not differ between quitters and smokers.

DISCUSSION

In this study, smoking cessation in patients with asthma improved lung function, indicating that smoking cessation is a very important factor in asthma management.

Both morbidity and mortality due to asthma increase in individuals who smoke compared with those who have never smoked.[1-4] Asthmatic smokers show more severe asthmatic symptoms,[6] a greater need for rescue medication,[12] and poorer health-status indices than never-smokers.[12,13] Smoking a ciga-

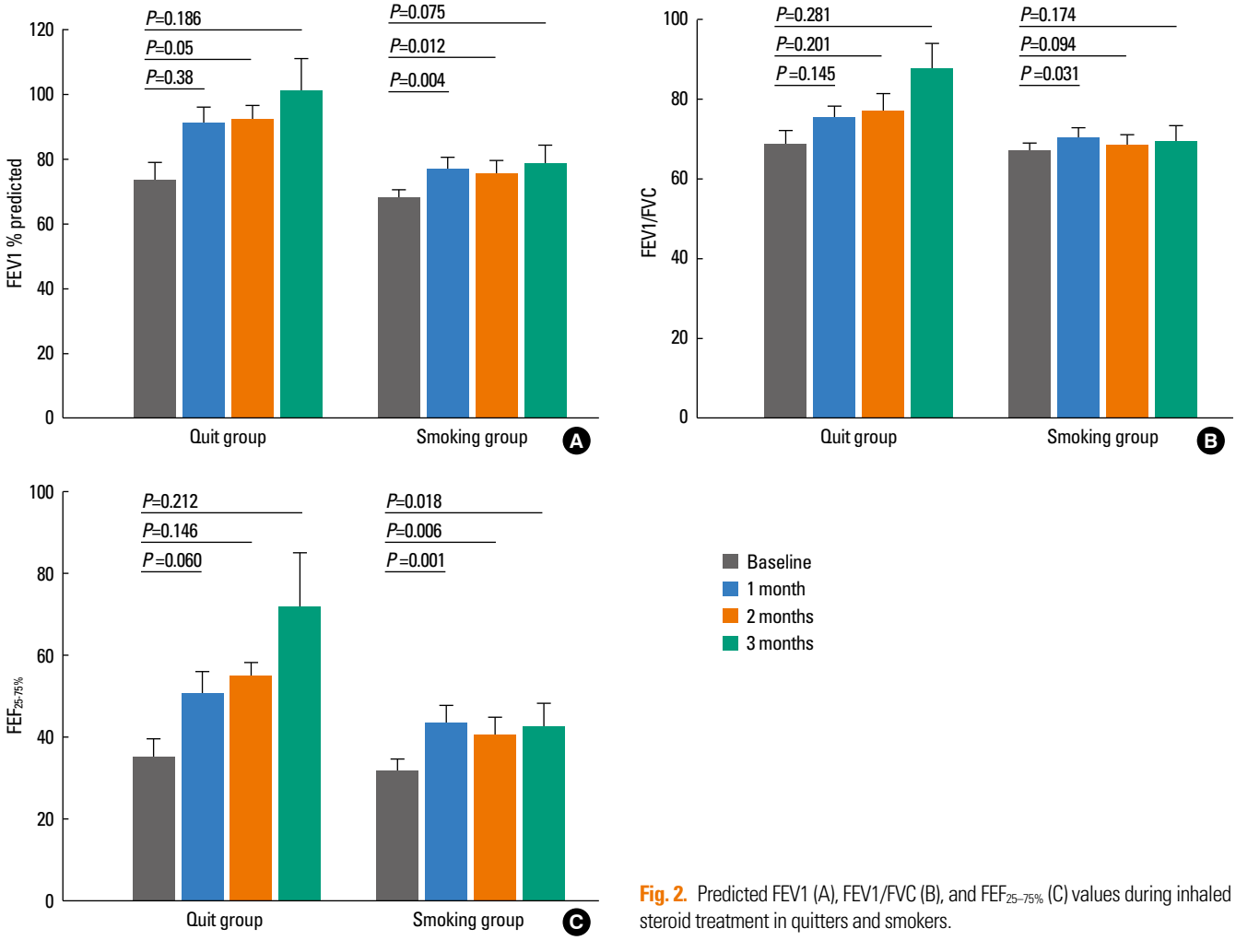

Fig. 2. Predicted FEV1 (A), FEV1/FVC (B), and $FEF_{25-75\%}$ (C) values during inhaled steroid treatment in quitters and smokers.

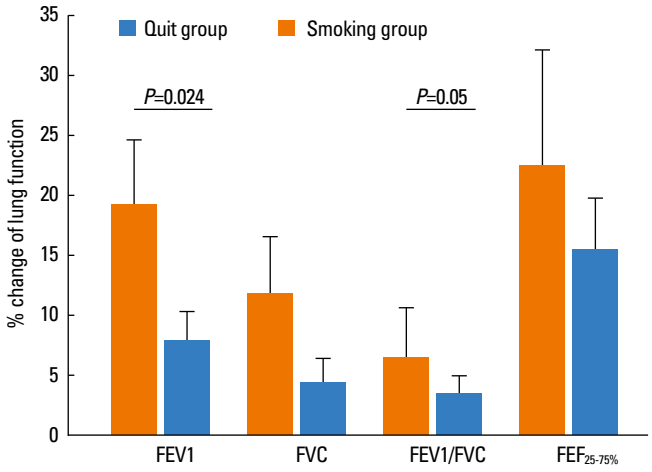

Fig. 3. Percent change in predicted forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC, and forced expiratory flow between 25 and 75% FVC ($FEF_{25-75\%}$) values in quitters and smokers at 1 month after initiating inhaled steroid treatment.

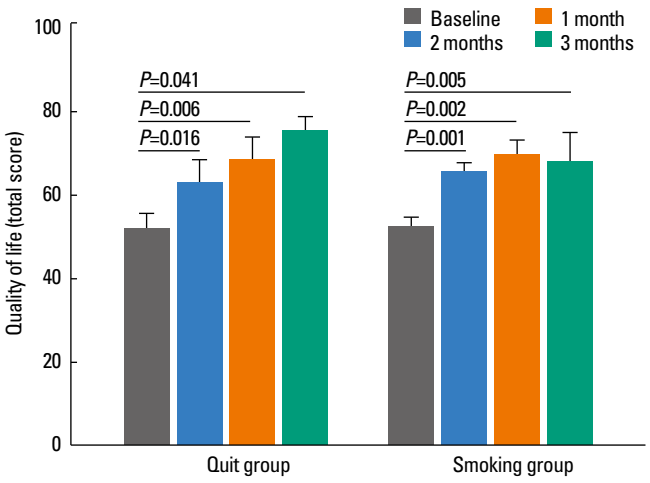

Fig. 4. Changes in quality of life in quitters and smokers at 1, 2, and 3 months after initiating inhaled steroid treatment.

rette can cause acute bronchoconstriction, although tobacco smoke does not act as an acute irritant in all patients.[23] Baseline FEV1 is directly related to the immediate response to inhaling cigarette smoke,[24] suggesting that asthmatic smokers with relatively poor lung function are particularly susceptible to the acute effects of tobacco smoke. Emergency department visits as a result of exacerbated asthma occur more frequently among heavy cigarette smokers after days with high levels of ambient ozone pollution,[25] and hospital admission rates for asthma and hospital-based care are higher in smokers.[13,18,26] There is conflicting evidence as to whether current smoking is a risk factor for near-fatal or fatal asthma.[27,28] In a previous prospective controlled study, subjects who quit smoking achieved considerable improvement in lung function and decreased sputum neutrophil count within 3 months compared with subjects who continued to smoke.[29] In our study, patients with asthma who were current smokers tended to have lower baseline FEV1 values than did quitters, suggesting that continued smoking results in a greater decrease in lung function in long-term asthmatic smokers. The differences between our results and those of Chaudhuri et al.[29] seem to be due to patient selection and study duration.

Combined cigarette smoking and asthma accelerate the decline in lung function to a greater degree than either factor alone.[9,10,30] In a previous study, the synergistic effect of combined asthma and smoking resulted in a 17.8% decline in FEV1 over 10 years.[9] In contrast, smoking cessation improved symptoms and bronchial hyper-responsiveness and decreased airway inflammation.[3] In our study, asthmatic smokers had a higher number of pack-years (23.5±13.6) than asthmatics who had quit (6.5±2.2, P=0.001), indicating that a long-term addiction is more difficult to break. Therefore, long-term smokers are likely to require more anti-smoking education.

International guidelines for asthma management recommend inhaled corticosteroids as the most effective anti-inflammatory therapy for chronic asthma.[18] The evidence for this recommendation is based on clinical studies that have been undertaken largely in patients with asthma who have never smoked or who were former smokers. Asthmatic smokers, however, may be resistant to the beneficial therapeutic effects of corticosteroids due to several clinical factors.[2,3] The mechanism underlying corticosteroid resistance in asthmatic smokers is largely unstudied, but may include one or more of the pathways implicated in asthmatic non-smokers and other inflammatory diseases. Alternative or additional treatment to inhaled corticosteroids may be required for asthmatics who are unable to stop smoking or who have persistent symptoms after quitting.[14] In our study, patients who quit smoking showed greater improvement in lung function than current smokers, indicating that quitting is an important factor in asthma treatment. Among atopic patients with asthma, smokers are less responsive to inhaled adenosine than non-smokers, which reflects differences in airway inflammation.[31] Cigarette smoking may modulate inflammation associated with asthma. In previous studies, cigarette smoking induced airway inflammation in non-asthmatic smokers without airflow obstruction compared to non-smokers.[32,33] Normal smokers show increased T-lymphocyte cell counts, particularly CD8 cells,[32] and macrophage cell counts within airway walls, higher neutrophil numbers within bronchial secretions, and infiltration of peripheral airways by mononuclear cells and macrophages.[16,32,33]. In our study, we did not identify the effects of smoking on airway inflammation. Further studies are needed to clarify the effects of smoking on airway inflammation using sputum cells in a larger population of patients with asthma.

Recent studies of outcomes in patients with asthma have focused on clinical and physiological measures.[34] Because such clinical measures do not provide a complete, accurate view of the impact of a disease on an individual's physical, social, or emotional well being, health-related QOL measures are increasingly

being integrated into clinical research on asthma.[22,34,35] AQLQ scores have been used as a tool to measure the outcome of drug treatment. AQLQ scores may reveal benefits of asthma treatment not apparent via objective monitoring and complement clinical and physiological assessments of treatment outcome.[36] In the present study, we found that overall AQLQ scores improved in quitters and continuing smokers after treatment with inhaled GCs, indicating that corticosteroids may be valuable in the control of asthma regardless of smoking status. The limitations of this study were that the number of subjects was small and that the smoking group had more pack years; therefore, we could not exclude a long-standing smoking effect on pulmonary function.

In conclusion, patients with asthma who quit smoking showed greater improvement in airway obstruction than patients who continued smoking, suggesting that smoking cessation is of therapeutic benefit in the management of asthma.

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