

Caring for the smoking asthmatic patient

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The asthmatic patient who smokes can represent a distinct disease entity in which a combination of asthma and chronic obstructive pulmonary disease–like phenotypes are blended to a variable degree. Appreciation of a smoking asthma phenotype might have important clinical, prognostic, and therapeutic implications. The goal of this article is to discuss clinical pearls that will assist physicians in managing these challenging patients.

Smoking is associated with a higher incidence of asthma and is strongly predictive of the development of new-onset asthma in allergic adults.¹

Compared with nonsmoking asthmatic patients, smoking asthmatic patients are at risk of more severe symptoms and worse asthma-specific quality of life, with a huge effect on health care resources because of unscheduled doctor's office visits and frequent hospital admissions.² Moreover, cigarette smoking in asthmatic patients is associated with higher frequencies of exacerbations, increased numbers of life-threatening asthma attacks, and greater asthma mortality. Asthma severity is higher and asthma control is worse in asthmatic patients who smoke, with the strongest association with more severe disease being observed in those who smoked more than 20 pack years.³ Exposure of adults and children to passive smoking also increases their asthma risk and worsens their respiratory symptoms.⁴

In most studies smoking accelerates the decrease in lung function and increases the severity of airflow obstruction in asthmatic patients.⁵ It is worth noting that lung function changes can be reversed with smoking cessation.⁶

Smoking asthmatic patients appear to be less sensitive to the beneficial effects of inhaled corticosteroids (ICSs) compared with nonsmoking asthmatic patients. Although ICS dosage might relieve unresponsiveness, loss of responsiveness to ICSs continues to be present in spite of the length of treatment, steroid molecule used, and type of formulation (inhaled vs oral).⁷ Few clinical trials have

Abbreviations used

AHR: Airway hyperreactivity

ICS: Inhaled corticosteroid

studied the reversibility of corticosteroid unresponsiveness in smoking asthmatic patients. A noncontrolled study demonstrated that low-dose theophylline in addition to inhaled beclomethasone improved both lung function and asthma symptoms in 68 smoking asthmatic patients.⁸ A randomized clinical trial suggested that leukotriene antagonists might have a beneficial effect in smokers with mild asthma,⁹ but this study has not yet been replicated. To the best of our knowledge, only 1 study has examined the role of smoking cessation on corticosteroid responsiveness. Progressive improvement in FEV₁ and restored corticosteroid responsiveness have been reported after 6 weeks of smoking cessation in 21 patients compared with 11 smoking control subjects.⁶ The mean improvement in FEV₁ in the quitting group was 356 mL at 1 week, 390 mL at 3 weeks, and 450 mL at 6 weeks of abstinence versus no difference in FEV₁ in the smoking group. Moreover, asthma control improved, corticosteroid responsiveness in smoking asthmatic patients was restored, and there was a decrease in sputum neutrophil counts after 6 weeks of abstinence.

ASTHMA AND SMOKING CESSATION

Abstinence from smoking might be beneficial for several specific aspects of asthma. Despite the reported deleterious effects of smoking on asthma symptoms, lung function, and corticosteroid responsiveness, few studies have examined the role of smoking cessation on asthma outcomes. Overall, these studies show significant improvements in symptoms and lung function in those asthmatic patients who quit smoking.

A prospective study of 3 groups of asthmatic patients (smoking cessation, reduction in smoking, and continuation of smoking) was performed by Tonnesen et al.¹⁰ Smoking asthmatic patients who quit had significant improvement in specific asthma-related quality-of-life scores and reduction in nocturnal and daytime rescue β_2 -agonist use, ICS use, daytime asthma symptoms, and airway hyperreactivity (AHR). Smoking reducers had smaller improvements in nocturnal rescue β_2 -agonist use, doses of ICSs, and AHR, suggesting an apparent dose-response effect. These findings agree with our large longitudinal study demonstrating substantial improvement in AHR 1 year after smoking cessation in those smokers for whom an objective proof of cessation was obtained.¹¹

MANAGEMENT PEARLS FOR THE SMOKING ASTHMATIC PATIENT

The above findings highlight the importance of smoking cessation in improving many clinical and functional outcomes

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of asthma. Physicians have the responsibility both to alert their patients with asthma about the additional risks of smoking and also to engage in smoking cessation interventions. Unfortunately, the powerful addictive qualities of tobacco smoking create a huge hurdle, even for those with a strong desire to quit, and multiple attempts and long-term treatment might be needed to achieve enduring abstinence. However, only modest cessation rates are reported in adults with asthma,¹² and some studies have reported that smoking asthmatic patients do not believe that smoking could be a serious problem for their asthma.¹³

Current evidence-based recommendations indicate that systematic identification of all tobacco users at every visit is important.¹⁴ All smokers with asthma should be advised to quit. This advice should be clearly stated and personalized: "By quitting, you will not only improve your general health status but also your asthma symptoms. Did you know that?" Physicians should then be ready to assist patients who want to quit. This entails working together with the patient to set a sensible plan with a commitment to a quit date and frequent follow-up visits. Physicians should also determine whether the patient is likely to benefit from medications for the treatment of nicotine addiction, particularly in anticipation of specific abnormal physical responses, psychological responses, or both generated on abrupt discontinuation of nicotine, which are known as withdrawal symptoms. Key withdrawal symptoms include the following: central nervous system (dysphoric or depressed mood, irritability, frustration or anger, anxiety, and restlessness); cardiorespiratory (decreased heart rate and increased cough); and miscellaneous (craving, increased appetite and/or weight gain, malaise or weakness, and constipation) symptoms. Smoking cessation programs should combine counseling (mainly problem-solving/skills training and social support) and medications for nicotine addiction for best results.¹⁴ Presently, first-line medications for smoking cessation therapy include nicotine replacement therapy, bupropion, and varenicline.¹⁵ With the exception of varenicline, which has been shown to offer notable improvement in abstinence rates over bupropion,¹⁶ all first-line medications appear to achieve similar effectiveness by doubling success rates.^{14,15} In general, these medications have no specific contraindications in asthmatic patients, but some safety concerns bear mention.

US Food and Drug Administration pregnancy categories for nicotine replacement therapy include the following: category C for gum and lozenges and category D for nasal sprays, inhalers, and patches. Bupropion and varenicline are category C. Bronchospasm has been observed in patients using nicotine nasal sprays and inhalers.

Nicotine replacement therapy can be associated with increased heart rate and should not be used in the setting of acute cardiovascular events. Bupropion might lower the seizure threshold. It has been associated with increased suicidality, as with other antidepressants. Varenicline has been associated with erratic or aggressive behavior, suicidal ideation, and depression and carries a warning for appropriate monitoring for the above and agitation. Referral to specialized centers should be considered if a more intense intervention is required.

Unpleasant "surprises" can undermine an attempt to quit smoking. Patients need to be equipped with knowledge of what to expect. List potential withdrawal symptoms, but point out that some people do not experience any of these problems and a few might experience all of them. Also explain that the duration of

these problems varies from person to person. For most persons, any withdrawal symptoms peak in the first few days and subside after 2 to 4 weeks. Be aware that symptoms of asthma (primarily cough) can develop or worsen after smoking cessation.¹⁷ Thus the patient should be advised that his or her symptoms of asthma might increase within the first couple of weeks after smoking cessation. Smokers in this category will benefit from a temporary increase in antiasthma drugs. Urge the patient to seek help if any problems arise that might cause relapse and be prepared to provide prompt advice and medical assistance in dealing with these symptoms.

Recognizing risk factors that predict relapse might direct selection of more intensive treatment. Predictors of failure include the following: early age of smoking onset, short duration of prior quit attempts, depression, high degree of nicotine dependence, alcohol problems, and lack of sustained motivation.¹⁸ These have not been specifically studied in the smoking asthmatic patient population, however.

Patients who are unwilling to try quitting should receive a brief intervention designed to increase future quit attempts.¹⁴ For these smokers, it is better to wait until they feel ready and confident enough to quit. Smoking reduction might be a viable treatment approach to promote future smoking abstinence among smokers who are not ready to repeat a quit attempt. An additional option is to encourage them to switch to a less harmful source of nicotine, such as smokeless tobacco products or electronic cigarettes.^{19,20} Fig 1¹⁴ shows a decisional algorithm for assisting smokers with asthma.

Beyond smoking cessation, management of asthmatic patients who smoke might not be that much different from those who do not smoke. However, this simplistic view could be challenged given that most of the recommendations on drug treatment made in asthma guidelines are based on clinical studies in which patients are carefully selected to exclude smokers. The lack of information on the best approach to manage smokers is of significant concern, and clinical trials are urgently required that will provide evidence on which drugs and treatment strategies are most appropriate for this specific group.

In a recent study the addition of a long-acting β_2 -agonist has been shown to benefit smokers with mild-to-moderate asthma, and this was preferable to increasing the dose of ICS.²¹ In this study of smokers with mild-to-moderate asthma, the combination of inhaled fluticasone and salmeterol taken in a dose of 250/50 μg twice daily produced significant improvements in AHR, as well as in airway caliber, compared with doubling the dose of inhaled fluticasone. Moreover, a *post hoc* analysis of the Gaining Optimal Asthma Control trial found that smokers with asthma had reduced exacerbation rates with combination therapy with inhaled fluticasone and salmeterol (0.20 per patient per year) compared with those seen with inhaled fluticasone alone (0.35 per patient per year).²² Despite some methodological limitations in both studies, their results suggest that the use of combination therapy with an ICS and a long-acting β_2 -agonist should be preferred to the use of high-dose ICSs alone in smokers with asthma.

Reversal of corticosteroid unresponsiveness in smokers with asthma has been shown in a few studies discussed above by either increasing ICS dosage or adding low-dose theophylline to an ICS or using leukotriene antagonists, but this evidence requires confirmation in larger studies.

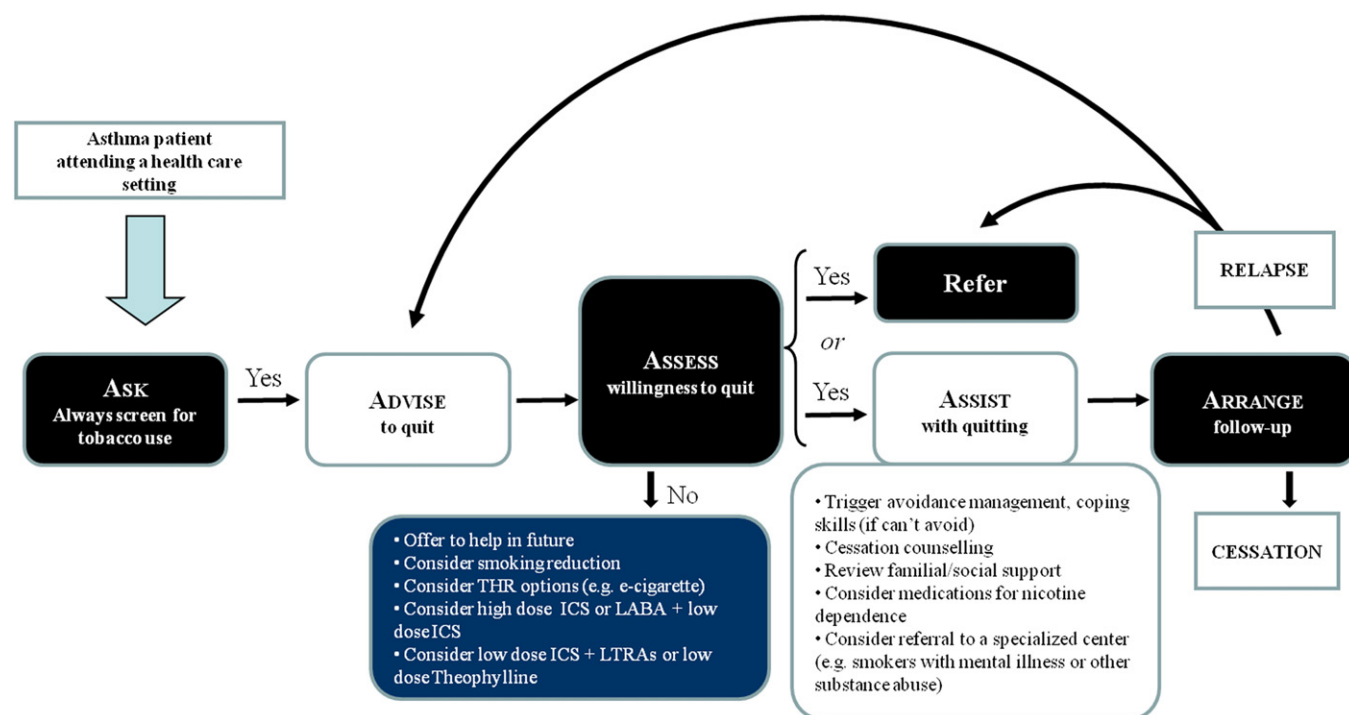


FIG 1. An algorithm for assisting the asthmatic smoker. The first step in treating tobacco use and dependence is to identify tobacco users. Asking systematically whether your asthmatic patients smoke at every visit is imperative (*ASK*). All smokers with asthma should be advised to quit. This advice should be clearly stated and specifically adapted in relation to the patient's asthma problems: "Did you know that by quitting you will not only improve your general health status but also your asthma symptoms?" (*ADVISE*). The willingness of smokers with asthma to make a quit attempt at this time should be assessed (*ASSESS*). If the patient is ready to quit, health care providers should be prepared to offer assistance. This entails working together with the patient to set a sensible plan with a commitment to a quit date and to frequent follow-up visits. Alternatively, referring the patient to a tobacco intervention resource (eg, a smoking cessation quit line or health educator) that would deliver additional treatment to the patient might be contemplated (*ASSIST*). All patients who receive a tobacco dependence intervention should be regularly assessed for abstinence, beginning within the first week after the quit date. Abstinent patients should have their quitting success acknowledged. Patients who have relapsed should be assessed to determine whether they are ready to repeat another quit attempt (*ARRANGE*). Modified from Fiore et al.¹⁴ LABA, Long-acting β_2 -agonist; LTRA, leukotriene receptor antagonist.

SUMMARY

- Smoking is associated with a higher incidence of asthma, and the asthmatic patient who smokes might represent a distinct phenotype.
- Smokers with asthma are at risk of a more severe form of the disease.
- Smoking accelerates the decrease in lung function and increases the severity of airflow obstruction in asthmatic patients.
- Smokers with asthma are less sensitive to the beneficial effects of steroids.
- Use of combination therapy with an ICS and a long-acting β_2 -agonist should be preferred to the use of high-dose ICSs alone in smokers with asthma.
- Smoking cessation improves asthma symptoms, lung function, and restores steroid responsiveness.
- All smokers with asthma should be advised to quit.
- Physicians have the responsibility both to alert their patients with asthma about the additional risks of smoking and also to engage in smoking cessation interventions.

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