Immediate and short term effects of smoking on nasal mucociliary clearance in smokers

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Received 9 November 2010; accepted 22 December 2010

Abstract

Background and objectives: The efficiency of mucociliary transport may vary in different conditions, such as in exposure to harmful particles of the cigarette smoke. The present study evaluated the acute and short term effects of smoking on nasal mucociliary clearance in current smokers by the quantification of the Saccharin Transit Time (STT), and to investigate its correlation with the history of tobacco consumption.

Methods: Nineteen current smokers (11 men, 51 ± 16 years; BMI 23 ± 9 kg/m², 27 ± 11 cigarettes per day, 44 ± 25 pack-years), entering a smoking cessation intervention program, responded to a questionnaire concerning smoking history and were submitted to lung function assessment (spirometry) and the STT test. STT was assessed immediately after smoking and 8 hours after smoking. The STT test was also performed in nineteen matched healthy non-smokers’ who served as control group.

Results: When compared to STT in non-smokers’ (10 ± 4 min; mean ± standard deviation), smokers presented similar STT immediately after smoking (11 ± 6 min; p = 0.87) and slower STT 8 hours after smoking (16 ± 6 min; p = 0.005 versus non-smokers and p = 0.003 versus immediately after smoking). STT 8 hours after smoking correlated positively with age (r = 0.59; p = 0.007), cigarettes per day (r = 0.53; p = 0.02) and pack-years index (r = 0.74; p = 0.0003).

Conclusions: In smokers, although the mucociliary clearance immediately after smoking is similar to non-smokers’, eight hours after smoking it is reduced, and this reduction is closely related to the smoking habits.
Introduction

Mucociliary transport is the main defense mechanism of the respiratory tract against pathogens and toxins, both in the upper and lower airways. However, it should be noted that the efficiency of transport may vary in different conditions, such as exposure to harmful particles of cigarette smoke.

In vitro and in vivo studies have shown that exposure of the ciliated epithelium to particles of cigarette smoke results in a significant decrease in ciliary beat frequency. Cohen et al. showed that ciliary beats were diminished as a result of exposure to tobacco smoke, thus impairing mucociliary clearance. These results are in contrast to the findings of Stanley et al., who did not find any difference in ciliary beat frequency between smokers and nonsmokers and reported a normal ciliary beat frequency. Nevertheless, they described that mucociliary transport was slower in regular smokers, and suggested that the exposure of nasal mucosa to cigarette smoke varies considerably depending on the type of cigarette and whether the smoke is exhaled by the nose or mouth. Others observed, moreover, that the mucus velocity in nonsmokers is faster than in ex-smokers.

Therefore, generally speaking, differences in mucociliary transport between smokers and nonsmokers are common. However, despite these preliminary data, mucociliary transport has not been yet studied with the necessary depth. For example, neither the differences between acute and chronic responses of the mucociliary system to tobacco smoke exposure nor the association between mucociliary transport impairment and the individual’s tobacco use history have been deeply investigated. Thus, the aim of this study was to evaluate the effects of smoking on mucociliary clearance in smokers, immediately and eight hours after smoking, by quantifying the saccharin transit time (STT) and to investigate its correlation with the subject’s history of tobacco consumption.

Methods

Participants

Two groups of subjects were evaluated: 19 current smokers, classified in their majority as heavy smokers (smoking 20 or more cigarettes/day) who were entering an Anti-Tobacco Awareness Program, and 19 healthy matched nonsmokers (Table 1). Individuals with cystic fibrosis, bronchiectasis,
known to be reproducible.14

slightly extended. Granulated sodium saccharin (5

breathe deeply, talk, cough, sneeze or sniff. They were also

with a T track Pro chronometer. Individuals were instructed

tion of a sweet taste in the mouth was recorded in minutes

placed, under visual control, 2 cm inside the right nostril. 

STT,12 as described by Rutland and Cole,13 a test

technique was in accordance with the American Thoracic 

spirometry testing. After this, they were requested to smoke 1 

was immediately followed by STT quantification. All STT 

took place between 5:00pm and 7:00pm. On the following day, 

the same subjects were asked to start the day by maintaining their regular smoking habit 

and nozzle for the STT,12 were inserted, under visual control, 2 cm inside the right nostril. 

The time from particle placement until the first perception 

of a sweet taste in the mouth was recorded in minutes 

with a TrackPro chronometer. Individuals were instructed 

to maintain their initial position and were not allowed to 

breathe deeply, talk, cough, sneeze or sniff. They were also 

instructed to swallow only a few times per minute until sensing a sweet taste in the mouth. If the sensation did not occur 

within 60 minutes, the test was stopped and the subject’s 

ability to perceive the taste of saccharin was verified by placing it on the tongue. If the subject was able to taste 

the saccharin directly, the test procedures were repeated on 

another occasion. Each subject was clearly instructed not 

to use pharmacological agents such as anaesthetics, anal-

gesics, barbiturates, tranquilizers or antidepressants for at 

least 12 hours before the test, as well as alcohol or caffeine-

based substances.

Statistical Analysis

Statistical analysis was performed with GraphPad Prism 3.0 

(GraphPad Software, Inc., San Diego, USA). Normality of 
data distribution was verified with the Shapiro-Wilk test. 

Parametric statistics were used since variables were nor-

mally distributed. Results were expressed as mean ± SD. 

Comparison between the two moments in the smoking group 

was performed by the paired t test. For the comparison 

between smokers and nonsmokers, the unpaired t test was 

used. Correlations were evaluated using the Pearson coeffi-

cient. The level of statistical significance was set at p < 0.05 

for all analysis.

Results

Thirty-eight individuals were included, nineteen smokers 

and nineteen nonsmokers (Table 1). No exclusions were nec-

essary according to the exclusion criteria adopted.

Compared to STT in nonsmokers (10±4 min; 

mean±standard deviation), smokers presented similar 

values immediately after smoking (11±6 min; p = 0.87) and 

lower values 8 hours after smoking (16±6 min; p = 0.005 

versus non-smokers, and p = 0.003 versus immediately after 

smoking) (Fig. 1).

There was no significant correlation between STT imme-

diately after smoking with any of the analysed variables. 

There was significant positive correlation of STT 8 hours 

after smoking with age (r = 0.59; p = 0.007), consumption 

of cigarettes/day (r = 0.53; p = 0.02), duration of smoking 

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have been due to an increase in ciliary beat frequency against an aggressor agent such as cigarette smoke. It may represent an acute epithelial response, could represent a defense mechanism for such a finding is that this apparent "increase" were similar to those of nonsmokers (Fig. 1). One hypothesis for these results immediately after smoking may be related to the activation effect triggered by the sympathetic nervous system, which could include a possible acceleration of cilia beating. However, the circulating nicotine is metabolized in two hours, indicating that after this period the stimulatory effect ceases, and the smoker's cilia beat rate (or the efficiency of transport and defense mechanism) returns to its "normal" (i.e., Impaired), such as was observed in this study after the abstinence period.

Discussion

The present study showed the acute and chronic response of nasal mucociliary clearance to tobacco smoke exposure in smokers. Immediately after exposure, mucociliary transport in smokers with relatively heavy consumption habits has values similar to those presented by non-smokers. However, the evaluation of these same smokers eight hours after smoking showed that the efficiency of the mucociliary system had decreased. This study also demonstrated that the slower the mucociliary transport eight hours after smoking, the longer the duration and intensity of the smoking habit had been.

Tobacco exposure has profound effects on mucociliary function, but the basic mechanisms have not yet been elucidated. The difficulty in explaining these mechanisms is linked to several factors: the complexity of mucociliary system components, the complexity of the various substances in cigarette smoke and the fact that the techniques for measuring time of particle removal depend not only on mucociliary velocity, but also the particle distribution and patterns of deposition. Additionally, the lack of standardization in the control of temperature, humidity and the moment of analysis can lead to incongruity between the results, making the comparison with studies of a similar nature rather difficult.

The STT results of smokers immediately after smoking were similar to those of nonsmokers (Fig. 1). One hypothesis for such a finding is that this apparent "increase" in nasal mucociliary transport immediately after smoking, an acute epithelial response, could represent a defense against an aggressor agent such as cigarette smoke. It may have been due to an increase in ciliary beat frequency because of stimulation to the inflammatory mediators, or it could have been the result of stimulation to the nerve receptors found around the luminal cells. In a study by Lindberg & Dolata, the acute exposure of rabbits to cigarette smoke was associated with an increase in mucociliary activity. This effect was primarily mediated by a reflex from stimulation of NK1 receptors, followed by the irritant effects of smoking on sensory afferent nerves of the upper airway.

The difference between the STT immediately and 8 hours after smoking may also be an effect of nicotine on the autonomic nervous system (ANS). It should be emphasized that this substance causes neural sympathetic stimulation, which leads to activation of the body's general metabolism. Moreover its effect on the parasympathetic nervous system is related to nicotinic acetylcholine receptors, which increase in situations of chronic smoking. Such conditions could alter mucociliary transport, since the nose has motor, sensory and autonomous innervation. The stimulated ANS generates nasal effects such as glandular hypersecretion and vasodilatation, which could justify increased mucociliary transport. Thus, the normal STT values found in smokers immediately after smoking may be related to the activation effect triggered by the sympathetic nervous system, which could include a possible acceleration of cilia beating. However, the circulating nicotine is metabolized in two hours, indicating that after this period the stimulatory effect ceases, and the smoker's cilia beat rate (or the efficiency of transport and defense mechanism) returns to its "normal" (i.e., Impaired), such as was observed in this study after the abstinence period.

The present study suggests that, in a sample composed of individuals without immediate exposure to pollutants, there was slow mucociliary clearance in chronic smokers eight hours after smoking compared to healthy nonsmokers (Fig. 1). Stanley et al. compared the time of mucociliary transport in smokers and nonsmokers, and also concluded that the smokers' time (21 ± 9 min) was greater than that of nonsmokers (11 ± 4 min). However, no differences were detected in mean ciliary beat frequency. If such slowness of mucociliary activity is not associated with changes in cilia beat, it may be a consequence of structural changes, such as a reduced number of cilia and/or changes in mucus viscoelasticity. Using clinical data and radiographic and respiratory function tests, Verra et al. observed that the percentage of structural abnormalities in the bronchial epithelium was higher in smokers and former smokers than in the control group. The authors suggested that chronic smoking can induce an increase in the number of abnormal cilia, which could play a role in the impairment of tracheobronchial clearance. Moreover, the fact that the group of ex-smokers also exhibited structural abnormalities shows that tobacco abstinence was insufficient to restore the already damaged structures.

The exposure of the nasal mucosa to cigarette toxins depends on the number and type of cigarettes smoked and smoking habits. This study observed a significant correlation between STT values after 8 hours without smoking and the subjects' consumption of cigarettes per day, duration of smoking and pack-year index. Possibly, the effect of chronic exposure to tobacco caused more intense damage in the population included in this study, since cigarette consumption was high and long-lasting. The fact that STT results immediately after smoking were not related to pack-year index reminds us that the action of nicotine on the ANS remains unchanged, even with the possible anatomical and physiological changes resulting from chronic exposure to cigarette smoke.
Finally, it should be pointed out that the findings of this study add new information to the scarce literature on mucociliary transport in smokers, particularly the acute response of this respiratory defense mechanism to tobacco smoke and the relationship of mucociliary transport with smoking habits. However, studies that include longer periods of abstinence and smokers with a wider range of smoking habits should be carried out using different protocols in order to verify the extent of damage to mucociliary transport in smokers.

Conclusions

In conclusion, although the mucociliary clearance immediately after smoking is similar to nonsmokers, eight hours after smoking it is reduced. This reduction is related to the intensity of tobacco consumption, characterizing a deficiency of this pulmonary defense mechanism in this population.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgements

This work was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

References