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ORIGINAL RESEARCH

Short-Term Benefits of Smoking Cessation Improve Respiratory Function and Metabolism in Smokers

Aldo Pezzuto[1], Alberto Ricci[1], Michela D'Ascanio[1], Alba Moretta[1], Giuseppe Tonini[2], Noemi Calabrò[1], Valeria Minoia[1], Alessia Pacini[1], Giuliana De Paolis[1], Eleonora Chichi[1], Elisabetta Carico[3], Antonella Tammaro[4]

[1]Department of Cardiovascular and Respiratory Sciences, S Andrea Hospital, Sapienza University, Rome, Italy; [2]Oncology Department, Campus Bio-Medico University, Rome, Italy; [3]Clinical and Molecular Medicine Department, S Andrea Hospital, Sapienza University, Rome, Italy; [4]Department of Neuroscience- NESMOS, S.Andrea Hospital, Sapienza University, Rome, Italy

Correspondence: Aldo Pezzuto, Email aldo.pezzuto@uniroma1.it

Background: Cigarette smoke exposure is the main preventable cause of chronic obstructive pulmonary disease (COPD). Airflow limitation is closely associated with smoking exposure. Smoking could also interfere with lipid metabolism.

Aim: To determine the respiratory functional and metabolic changes after smoking cessation in smokers in the short term.

Methods: All patients were current smokers. They were assessed by spirometry and questionnaires such as COPD assessment test(CAT), modified Medical Research Council (mMRC) test for dyspnea, Fagestrom's test for nicotine dependence. Exhaled CO was detected in order to evaluate smoking exposure and smoking cessation (normal value<7 ppm). A blood sampling was eventually taken for vitamin D and cholesterol assay. All patients underwent therapy with counselling and varenicline as first-line treatment according to its schedule. Detection time: at baseline and one month after smoking cessation.

Results: All patients quit smoking during treatment. The mean age was 62 with a prevalence of males. The analysis revealed the following mean values at baseline: CAT mean score was 15, pack-years 35.5, Fagestrom's Test mean score 5.0. The West's value was 8.5, whereas Body mass index (BMI) was 25.5.Cigarette daily consumption mean value was 22.5. The comparison before and at follow up one month after smoking cessation about functional and metabolic parameters, show us the following results: FEV 1 was increased by 200 mL ($p<0.02$), FEF 25/75 was improved as well as mMRC test. The eCO was dropped to as low as 8 ppM. Interestingly the vitamin D level was increased from 25 to 28 ng/mL without any support therapy. The cholesterol total level was reduced and CAT value and DLCO were also significantly improved.

Conclusion: Quit smoking is useful to improve symptoms, respiratory function and metabolic parameters in the short term.

Keywords: airflow limitation, smoking cessation, lipid metabolism

Introduction

Refrain from smoking is the main therapeutic intervention effective in curbing and reducing the patient's respiratory functional decline. It is reported in the COPD guidelines.[1–3] The main consequence of a long-time cigarette exposure is airflow limitation involving both large and small airways.[4] A major component of bronchial obstruction is represented by small airways which is characterized by inflammation of bronchioles and airway wall narrowing.

The evolution of the disease can be influenced by the presence of exacerbations that correlate with the degree of obstruction, influencing mortality.[5,6]

The purpose of the present study is to point out the benefit of quit smoking on respiratory functional and metabolic parameters.

Methods

From April to December 2021, 120 patients who referred to a smoking cessation outpatients service were recruited and retrospectively analyzed. The setting was a university hospital, at the outpatient anti-smoking center of the pulmonology operating unit.

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Exclusion criteria were: patients who were taking oral steroid therapy or bronchodilators were ruled out as well as patients with severe comorbidities.

Inclusion criteria were the following: patients smokers for at least 20 pack-years who were not taking neither therapy for lipid metabolism nor bronchodilators. The expected duration of the smoking cessation program was six months The assessment was done at baseline and at one month after smoking cessation. Data management was by the physicians attached to the smoke-free center and an expert statistician.

Smoking cessation program was accomplished through motivational counselling along with a drug that reduces addiction. It was varenicline that acts as a partial agonist on α4β2 nicotinic-acetylcholine receptor. Counselling was also applied consisting of a psycho-behavioural analysis by identifying the stage of change according to the transtheoretical approach. Smoking abstinence was achieved as the eCO value was less than 7 ppm.

Several tests and questionnaires were being administered: the test for nicotine dependence (FTND) (range 0–2 no dependence, 3–4 low, 5–7 moderate, 8–10 high dependence), the questionnaire COPD assessment test, CAT (range 0–40),[7] the questionnaire for detection of dyspnea, mMRC (range 0–4).[8] The West's test for the assessment of motivation to quit was also performed. The spirometry (Jaeger system masterscreen, Germany) was performed according to the ERS-ATS guidelines.

Post-bronchodilation values were obtained by inhaling 400 μg of salbutamol.[9] A smokerlyzer device was used for eCO detection (Bedfont, USA).[10] Each patient underwent a 6 min walking test (WT) with walking distance detection (NoninMed Inc., Plymouth,MN, USA).[11] Finally, a venous blood sample was taken for detection of cholesterol, HDL and vitamin D total level. The time of detection was at baseline and at one month after smoking cessation.

The study was approved by Sapienza Ethic Committee. Each patient provided the consent to the study. The patients were informed about the purpose of the study. Our study complies with the Declaration of Helsinki.

Statistical Analysis

Data are represented as mean ±SD or median ± interquartile range as appropriate.

Data comparison before and after smoking cessation was performed by the Wilcoxon signed rank test.

The statistical significance value was set at $p<0.05$. SPSS 24.0 for windows was the statistical program used for the analysis of data (Chicago, Il).

Results

The baseline values are shown in Table 1: the mean age is 62 years.

Males were prevalent: 65 versus 55. Hypertension was the main comorbidity.

At baseline smoking exposure was major than 20 pack-years which represent the cutoff about the risk of developing COPD. The mean daily consumption of cigarettes exceeded the packet. The Fagestrom's test indicates a moderate level of nicotine dependence.

By contrast, the West's test revealed a high motivation and therefore a good probability to achieve smoking cessation. The mean value of body mass index was in the normal range. Finally the average of CAT value (15±2.5) indicates a moderate increase of the risk of exacerbation.

In Table 2 we can find the variation of the parameters one month after smoking cessation from baseline. No significant differences between different genders were detected.

A significant increase of the main obstruction parameters was observed. Notably FEV 1 absolute value in litres was significantly increased ($p<0.02$), as well as indices of capacity and volume such as FVC were increased.

An index of peripheral airway obstruction such as the FEF 25/75% of predicted was also increased in a short time ($p<0.05$) as an expression of reduced inflammation. The six minute walking test results show that a significant increase of the walking distance was obtained along with a reduction of heart rate ($p<0.05$). This goes hand in hand with improved respiratory symptoms and exercise tolerance. In fact the other parameter of respiratory symptoms,CAT, decreased ($p<0.01$) whereas mMRC test which refers to the extent of dyspnea improved by 0.5 ($p<0.0.05$).

The main index of smoking exposure, as a tobacco combustion product, such as exhaled CO was reduced ($p<0.02$).

Table 1 Demographic Baseline Data

Gender:	Males	Females
	65	55
	Mean	SD
Age	62.0	8.5
Pack-Years	35.5	9.2
Cigarette consumption	22.5	4.5
Fagestrom's test	5.0	1.6
West's test	8.5	2.5
CAT	15.0	2.5
BMI	25.5	3.5

Notes: Fagestrom's test score: 0–2 mild dependence, 3–4 moderate, 5–7 high dependence, 8–10 very high dependence. West's test: 0–5 low motivation, 6–10 high motivation. CAT >10 high exacerbation rate, mMRC 0–4 (0: no breathless, 4: breathless for daily activity).

Table 2 Differences Among Baseline and at the Follow-Up One Month After Quit. Gender: 55 Females, 65 Males

	Baseline	**One Month After Quit**	**P**
FEV1 l	2.4(1.3–2.9)	2.6(1.2–3.0)	<0.02
FVC% predicted	94(89–108)	98(92–110)	<0.08
FEF 25/75% predicted	45(24–58)	50(38–59)	<0.05
mMRC	1.5 (0.5–2)	1.0(0–1)	<0.05
HR	85(65–95)	75(60–85)	<0.01
eCO ppm	17(12–22)	9 (7–19)	<0.02
Vit D3 ng/mL	25(18–29)	28(21–33)	<0.01
CAT	14 (10–16)	8 (6–12)	<0.01
DLCO%predicted	70(58–83)	75(61–82)	<0.05
WT distance	350 (300–400)	400 (350–450)	<0.05
Total Cholesterol mg/dl	184 (156–227)	150 (150–200)	<0.001
HDL cholesterol mg/dl	52.0 (48–60)	58 (45–66)	<0.02

Note: Data as median and interquartile range, test Wilcoxon.
Abbreviations: FVC, forced vital capacity l; WT, walking test in meters; eCO, exhaled CO ppm; FEF 25/75, forced expiratory flow 25/75% of predicted; FEV1, forced expiratory volume; mMRC, modified medical research council; HR, heart rate; DLCO, diffusion test for CO % of predicted.

Regarding metabolic parameters and molecules examined on peripheral venous blood, the data show an improvement. In particular, an important decrease of total cholesterol had been achieved without the use of specific drugs, as well as vitamin D levels had been raised (Respectively $p<0.02$, $p<0.01$).

Discussion

The purpose of this study was to highlight the effects of smoking cessation in the short term, not only on clinical and respiratory function indices but also on metabolic indices and in particular on the level of macromolecules important for many of our functions, such as cholesterol and vitamin D. To our knowledge it is the first study that highlights the rapid benefits of smoking cessation therapy on symptoms and metabolism-expressing molecules. Our findings suggest that smoking cessation confirms its efficacy on respiratory obstruction parameters. Its effectiveness is also extended to the effect of reducing the level of a cholesterol, which when in excess, increases the risk of heart and vascular disease. Similar studies highlighted that cigarette smoke increases the level of fatty acids and glycerol.[12]

In previous studies a higher concentration of high-density lipoprotein cholesterol (HDL-C) in ex-smokers than smokers has consistently been observed.[13] Our findings suggest that there is a recovery of HDL and total cholesterol levels by quitting smoking.

We know that smoke exposure is the main cause of COPD that is the third cause of mortality and it is closely smoke-related. Under the continuous stimulus of tobacco smoke, large and small airways are affected by inflammation and structural remodeling.[14,15]

In the present study, the effects of smoking cessation on respiratory function in the short time are shown and an improvement of all considered parameters was achieved in both large and small airways.

We know that long-term smoking patients experience a respiratory function decline, furthermore there is an association of bronchial obstruction with nicotine metabolism rate.[16]

Chronic inflammation of the airways causes COPD, which in turn is characterized by flow limitation that occurs in the small and large bronchial branches.[15]

Lung function decline is closely related to age and smoking habit leading to symptoms worsening, conversely smoking cessation allow an improvement of functional and clinical parameters.[17,18]

Our findings provide novel insights in the clinical approach and evolution of bronchial obstruction highlighting a benefit in lipid metabolism, too.

As we know small airways are involved in smoke-induced inflammation by an alteration of the basal cells differentiation.[19–21]

With regard to smoking cessation therapy, the first-line treatment of smoking cessation, aside from replacement therapy, is represented by varenicline which increases the percentage of quit smoking.[22] The latter showed its efficacy both as a brief treatment and as a maintenance treatment.[23]

Smoking can affect the lung's local immune defenses by reducing them, and at the same time it can alter the local bacterial flora by increasing the pathogenic power of microorganisms. This ultimately promotes exacerbations in COPD patients.[24]

Regarding the effects of smoking on metabolism, it is associated with an increase of triglycerides and cholesterol lipoproteins, due to the interference of cigarette smoking with cytochrome enzyme system involved in lipid, cholesterol metabolism and its transport.[25]

Cigarette smoking promotes an altered level of cholesterol and lipoproteins[26,27] and we demonstrated that after smoking cessation the levels improve without any therapeutic supplement. Finally, the increased level of vitamin D after smoking cessation suggests that smoking reduces bowel absorption of the vitamin and conversely smoking cessation leads to a fast improvement of its level.[28]

The study has some limitations mainly due to the small sample of patients, however it lends itself as a basis for further clinical and biological studies.

Conclusions

Smoking cessation confirms its efficacy leading to an improvement of all respiratory functional parameters including symptoms and obstruction parameters in the short time. It also affects lipid metabolism leading to a decrease of total cholesterol and at the same time it brings about an increase of HDL cholesterol level. Patients who quit benefit about their quality of life, by reducing dyspnea, and other respiratory symptoms, eventually preventing bronchitis exacerbations.

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Disclosure

Professor Giuseppe Tonini reports on advisory board for Molteni, MSD, Novartis, Roche, and Pharmamar, outside the submitted work. The authors report no other conflicts of interest in this work.

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