PHENOTYPIC DIFFERENCE BETWEEN SMOKER AND NON- SMOKER CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

BACKGROUND

Smoking is one of the major risk factor associated with COPD. Other risk factors could be exposure to biomass fuel (in females), air pollution, occupational factors, etc. There are few studies that really characterise smoker & non-smoker COPD phenotype so that treatment can be individualised.

Aim- The study was designed to assess phenotypic differences between smoker & non-smoker COPD.

MATERIALS & METHODS

All consecutive patients with confirmed diagnosis of COPD in Department of Pulmonary Medicine in the month of July 2016 were included in the study. We compared smoker and non-smoker COPD with set parameters such as COPD grade, frequency of exacerbation, associated comorbidities like diabetes, hypertension, BMI, clinical symptom, lung function parameters. Non-smokers were defined as having <1-pack year of tobacco exposure; otherwise, the patients were classified as smokers.

RESULTS

A total of 78 stable COPD patients who were not in exacerbation included in study. The average age was 59.4 & 61.4 years in non-smoker & smoker COPD cases respectively. FEV1 and FVC were significantly lower in non-smokers (0.74 L, 1.44 L) with COPD than in smokers (0.83 L, 1.74 L) with COPD. Cough (76.3% vs. 65%) & sputum production (60.5% vs. 36.5%) was more prevalent in smoker COPD. History of more than one exacerbation was detected more in smoker COPD (36.8% vs. 30%). Severe & very severe COPD was more prevalent in non-smokers when compared to smokers, but moderate COPD was more frequent in smokers.

CONCLUSION

COPD patients who are smokers have more symptoms of chronic bronchitis like cough with expectoration and have more frequent exacerbations when compared to non-smokers. Hypertension and cor pulmonale was detected more in COPD patients who are non-smokers.

KEYWORDS

COPD, Smoker, Non-smoker, Pulmonary Function, Exacerbation.

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BACKGROUND

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality worldwide, and represents a huge and growing economic and social burden.¹ Chronic obstructive pulmonary disease (COPD) is characterised by progressive airflow obstruction and destruction of lung parenchyma, and is caused by chronic exposure of genetically susceptible individuals to environmental factors. The association between tobacco smoking with risk of COPD has been known since 1950s.²⁻³ Smoking was established as a causative risk factor by the

findings of Fletcher and Peto's⁴ 8-year prospective study of 792 men, and the larger and longer Framingham cohort offspring study confirmed these results.⁵ As little as 50% of cases worldwide are related to smoking³ and an estimated 10% – 12% of individuals with COPD have never smoked.⁶ Analysis of data from the international, population-based Burden of Obstructive Lung Disease (BOLD) study showed that 23.3% of subjects with Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade 2–4 COPD were never smokers.⁷

Very few studies investigated the non-smoking phenotype of COPD or compared with the smoking phenotype. Ramírez-Venegas and colleagues⁸ reported that Mexican women who had COPD and had been exposed to smoke from biomass fuel had similar clinical characteristics, quality of life, and mortality of those with COPD due to tobacco smoking. However, Shavelle and co-workers⁹ showed that in US patients with COPD the reduction in life expectancy was less for those who had never smoked than for those with COPD due to smoking.

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The purpose of the study is to compare smoker & non-smoker COPD in clinical presentation, lung function and frequency of exacerbation.

Objectives

1. To measure differences in clinical presentation between smoker & non-smoker COPD.
2. To assess difference in pulmonary function between smoker & non-smoker COPD.
3. To assess differences in comorbidities between smoker & non-smoker COPD.

MATERIALS AND METHODS

The study was carried by Department of Pulmonary Medicine, All India Institute of Medical Sciences, Patna.

Study Design

Hospital based cross-sectional study.

Inclusion Criteria

All patients who were diagnosed as COPD with age > 40 years in Department of Pulmonary Medicine, All India Institute of Medical sciences, Patna in July 2016 were included in study.

Exclusion Criteria

1. Subjects with other lung diseases such as pulmonary tuberculosis, bronchiectasis, pneumonia, interstitial lung disease, or pleural effusion, were also excluded, as were patients who had airflow limitation due to abnormalities in the large airways.
2. Subjects who were diagnosed COPD outside of AIIMS.
3. Patients with exacerbation in last one month are excluded.

Data Collection

The data were collected with pre-design Proforma (Given below).

The following information was collected: Patient's age, sex, smoking status (Never smoker, ever smoker, current smoker), quantity of tobacco smoking exposure (Pack-years), respiratory symptoms (Chronic cough, chronic sputum, a history of/or concurrent wheezing), modified Medical Research Council Dyspnoea Score, exacerbation in last one year and comorbidity (Hypertension, coronary heart disease, Osteoporosis, diabetes, etc.).

Definitions

The lung function tests had been performed according to ATS guidelines using calibrated PFT equipment (Jaeger Co, Würzburg, Germany). The diagnosis of COPD was according to the GOLD definition. Briefly, COPD was considered to be present if post-bronchodilator forced expiratory volume in the first second of expiration (FEV₁)/forced vital capacity (FVC) ratio was less than 0.70. Significant bronchodilator reversibility was defined as an increase in FEV₁ or FVC of at least 12% and 200 mL, respectively, from baseline values.

The grade of COPD based on pulmonary function & dyspnoea was classified as shown below in Table 6. The severity of airflow obstruction was assessed by post-bronchodilator FEV₁ (>80% mild, 50-80% moderate, 30-50% severe, <30% very severe).

Non-smokers were defined as having <1 pack-years of tobacco exposure; otherwise, the patients were classified as smokers.

Outcome (Variable)

We compared smokers and non-smokers with set parameters.

1. COPD grade.
2. Frequency of exacerbation.
3. Associated comorbidities (Diabetes, Hypertension).
4. BMI.
5. Dyspnoea (mMRC scale >1).
6. Lung function parameters.

Statistical Analysis

The continuous data expressed as the mean and bivariate analysis were performed using unpaired t-tests and Pearson correlation. For discrete data Chi-squared value has been used. All Data were entered and analysed using SPSS software (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.).

RESULTS

A total of 78 stable COPD patients who were not in exacerbation were included in study. The average age was 59.4 & 61.4 years in non-smoker & smoker COPD cases respectively. 84.2% (32/38) patients in smoker group and 42.5% (17/40) patients in non-smoker group were male. Baseline characteristics of COPD patients are given below in Table 1.

FEV₁ and FVC were significantly lower in non-smokers (0.74 L, 1.44 L) with COPD than in smokers (0.83 L, 1.74 L) with COPD. But these differences could be due to gender difference between non-smokers and smokers & to avoid this percentage predicted was used to analyse differences in lung function parameters. FEV₁ percentage (38.2 vs. 36.9) and FVC percentage (63.1 vs. 58.2) predicted was higher in non-smokers with COPD than in smokers with COPD. The FEV₁/FVC percentage predicted was higher in non-smokers when compared to smokers (55.7 vs. 55.1) as shown in Table 2.

Cough (76.3% vs. 65%) & sputum production (60.5% vs. 36.5%) was more prevalent in smoker COPD when compared to non-smoker COPD. Dyspnoea with severity of more than 1 mMRC was found in similar number of patients. Cor pulmonale was detected in 10% patients of non-smoker COPD. History of more than one exacerbation was detected more in smoker COPD cases (36.8% vs. 30%) (Table 3, Figure 2).

Overall, among all the patients with COPD, 20.5%, 41%, and 38.4% respectively, had moderate (grade 2), severe (grade 3), and very severe disease (grade 4). There was no patient with grade 1 (GOLD) COPD. Severe & very severe COPD was more prevalent in non-smokers compared to smokers but moderate COPD was more frequent in smokers. Most of the patients of COPD (64.1%) belong to class C according to GOLD classification. Class A & C COPD more frequent in non-smokers whereas Class B & Class D were more frequent in smoker COPD. If we look on comorbidities, hypertension was detected more in non-smoker COPD compared to smoker COPD (30% vs. 13.5%) (Table 4).

Characteristics	Non-smoker COPD (n = 40)	Smoker COPD (n = 38)	P value
Age (Years)	59.4	61.4	0.473
Sex (Male %)	17/40 (42.5%)	32/40 (84.2%)	Chi-square = 14.51; p = 0.0001
BMI	22.2	20.1	0.854
Smoking duration (Yrs.)		6.82	N/A

Table 1. Baseline Characteristic of Study Patients

Spirometric Variable	Non-smoker COPD (n = 40)	Smoker with COPD (n = 38)	P value
FEV1 (L)	0.74	0.83	0.123
FEV1% predicted	38.2	36.9	0.056
FVC (L)	1.44	1.74	0.008
FVC % predicted	63.1	58.2	0.415
FEV1/FVC %	55.7	51.1	0.245

Table 2. Comparisons of Spirometric Variables between Non-smokers and Smokers with COPD

	Non-smoker COPD (n = 40)	Smoker COPD (n = 38)	Total (n = 78)	Chi-square; P-value
Chronic Cough	26 (65%)	29 (76.3%)	55 (70.51%)	0.72; 0.396
Sputum Production	15 (37.5%)	23 (60.5%)	38 (48.71%)	3.265; 0.070
SOB (mMRC) >1	38 (95%)	37 (97.3%)	75 (96.15%)	0.0021; 0.963
h/o Cor pulmonale	4 (10)	0 (0%)	4 (5%)	2.213; 0.136
>One exacerbation in previous year	12 (30%)	14 (36.8%)	26 (33.3%)	0.41; 0.632

Table 3. Differences in Clinical Symptoms between Smoker & Non-smoker COPD

Severity	Non-smoker COPD (n = 40)	Smoker COPD (n = 38)	Total (n = 78)
Grade 1 (Mild) COPD	0	0	0
Grade 2 (moderate) COPD	5 (12.5%)	11 (28.9%)	16 (20.5%)
Grade 3 (Severe) COPD	18 (45%)	14 (36.8%)	32 (41%)
Grade 4 COPD (Very severe)	17 (42.5%)	13 (34.2%)	30 (38.4)
COPD Class			
A	2 (5%)	1 (2.6%)	3 (3.8%)
B	4 (10%)	8 (21.0%)	12 (15.3%)
C	29 (72.5%)	21 (55.26%)	50 (64.1%)
D	5 (12.5%)	8 (21.0%)	13 (16.6%)

Table 4. Comparison between Severity of COPD and COPD Class between Smoker & Non-smoker COPD

Comorbidities	Non-smoker COPD (n = 40)	Smoker COPD (n = 38)	Total (n = 78)	Chi-square; P-value
Hypertension	12 (30%)	5 (13.15%)	17 (21.7%)	3.083; 0.096
Diabetes	1 (2.5%)	1 (2.6%)	2 (2.5%)	0.004; 1.00

Table 5. Differences in Comorbidities between Smoker & Non-smoker COPD

Gold COPD Classes A, B, C, D			
FEV1 < 50%	C	D	≥ 1
> 50%	A	B	0
	mMRC 0-1	mMRC ≥ 2	Exacerbation

Table 6. GOLD COPD Classes

Figure 1. Clinical Difference between Smoker & Non-smoker COPD

Figure 2. Severity & Classes of COPD in Smoker & Non-smoker COPD

DISCUSSION

A total of 78 consecutive patients in which 40 patients of smoker COPD & 38 patients of non-smoker COPD were included in the study. Airflow obstruction (Percentage predicted FEV1) was found lower in smokers with COPD when compared to non-smoker COPD. This is because tobacco smoking leads to thickening and narrowing of the small conducting airways, along with destruction of the parenchyma and reduced alveolar-bronchiolar attachments.¹⁰ Cough with expectoration, one of the classic features of COPD, is associated with exacerbations and both conditions are related to progressive loss of airflow.¹¹ In this study, smokers with COPD reported significantly more chronic cough and sputum production than non-smokers. When we look for

number of patients having more than one exacerbation in previous years, studies show that exacerbation was found more in smoker group than non-smoker which is similar to other studies.¹² None of the patients in our study had malnutrition (BMI<20), but it was found lower for smoker COPD than non-smoker COPD which is in line with other studies.¹³ Our studies shows that severe & very severe COPD was more prevalent in non-smoker when compared to smoker but moderate COPD was more frequent in smoker group. There are studies which show that smoking history does not appear relevant to determine severity of COPD which agree with our finding that higher number of cases with severe disease found in non-smoker group.¹⁴ Most of the patients of COPD belong to class C according to GOLD classification. Class A & Class C COPD were more frequent in non-smokers, whereas Class B & Class D were more frequent in smoker COPD. This reflects that patients who are smokers will be more symptomatic and more prone to exacerbation. If we look on comorbidities, hypertension was detected more in non-smoker COPD when compared to smoker COPD which is different from many studies, this could be due to a small sample size & smoking duration.

CONCLUSION

COPD patients who are smokers have more symptoms of chronic bronchitis like cough with expectoration and have more frequent exacerbations when compared to non-smokers. Hypertension and cor pulmonale was detected more in COPD patients who are non-smokers.

Limitation of Studies

The biggest limitation of this study could be the small sample size. We couldn't quantify smoking because most of the patients used bidi & hukka and there was no method to quantify them similar to cigarette smoking. P value is also not significant for most of the variables. COPD disease is associated with many comorbidities, but we assessed only diabetes & hypertension.

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