



BRONCHIAL HYPER-REACTIVITY IN TOBACCO SMOKERS

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ABSTRACT

Bronchial hyper-responsiveness (BHR) is defined as excessive narrowing of the airways to various inhaled stimuli. It is commonly but not exclusively, seen in asthmatics. There is evidence which shows that the prevalence of BHR is higher in smokers, compared to the normal population. This may be an indicator of airway inflammation in the subjects. Relationship between smoking and development of chronic airflow limitation has been established. But all smokers do not develop chronic airflow limitation. The reason behind this observation remains unknown. The smokers with BHR may be at a higher risk of progression to COPD. We enrolled 50 asymptomatic smokers in the study. These patients were subjected to Bronchial challenge using graded dilutions of histamine. We found that as the Pack Years smoked increased, there was a statistically significant increase in the frequency of patients with positive Bronchial Challenge Test. Also, the number of smokers with a positive test at a given concentration of Histamine, increased as the Pack Years smoked increased, though not found to be statistically significant. Smoking and BHR were dose-dependently associated.

KEYWORDS: Bronchial Hyper-reactivity, Bronchial Challenge Test, Smoking, COPD.

INTRODUCTION

Tobacco smoke leads to airway inflammation, which over time becomes chronic, associated with airway remodeling, leading to persistent breathlessness, cough and sputum production. Smoking causes airway damage via multiple mechanisms, such as direct epithelial cell injury, DNA damage via free radical species, carcinogens, impairing mucociliary clearance, goblet cell hyperplasia leading to mucus hyper secretion etc.^[1] Some of these patients eventually land up with chronic airway obstruction, as evidenced by abnormally declining FEV1 as the years go by.^[2]

Large-scale international studies have shown that smoking is a risk factor for BHR, but whether the quantity of smoking exposure is associated with the severity of BHR is still in question.^{[3],[4]} A dose-dependent association of smoking and BHR severity as possible independent trigger factors for small airway obstruction has not been explored in detail. Doing so, may help us find out patients, who are at higher risk of developing COPD and plan for aggressive smoking cessation measures as well as get better insight into the pathogenesis of COPD.

MATERIALS AND METHODS

The study was a prospective study, conducted over a period of two years. The study group included 50

patients of either gender, aged 20-50 years, visiting the outpatient department (OPD) of Pulmonary Medicine of our hospital, who were asymptomatic active smokers, with normal Spirometry, Chest X ray and Serum IgE levels. The patients were then subjected to Histamine based Bronchial challenge tests, after obtaining consent.

All the tests were carried out in the our PFT laboratory, between 9am & 12 noon. The Pulmonary function tests were performed as per the ATS guidelines, on the machine manufactured by Medgraphics and the bronchial challenge tests were performed on machine manufactured by Bioptronics (model Pro-1). Spirometry was performed 30sec & 90sec after each histamine dose & drop in FEV₁ was observed. The dose of Histamine at which there is a 20% fall in FEV1 compared to baseline is denoted as PD₂₀. If the drop was >20%, then the test was stopped there & the patient was given a short acting 400microgram of salbutamol & reversibility was performed. Numbers and percentages were calculated. If 25% or more expected numbers in cells were <5, Fisher's Exact Test (Two Tailed Test) was used as test of significance. If less than 25% of expected numbers in cells were <5, Pearson's Chi Square Test was used as test of significance. P< 0.05 indicates statistical significance. Stata 13.1 was used for analysis of data.

RESULTS

Of the 50 patients, 9(18%) patients were females and 41(82%), males (Fig. 1). 12 Patients (24%) belonged to the 20-29 years age group, 21(42%) belonged to the 30-39 years group, 17 (34%) belonged to 40-49 years group (Fig. 2). The oldest patient in the study group was 48 years old and the youngest, 22 years. 17 Patients smoked less than 5 pack years, 15 smoked between 5-15 pack years and 18 smoked more than 15 pack years (Fig. 3). 33(66%) had a positive Bronchial Challenge Test and 17(34%), had negative Bronchial Challenge Test (Fig. 4). This was higher than the rates observed among the general population reported in literature.



Fig. 1

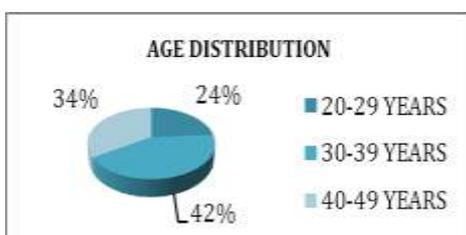


Fig. 2

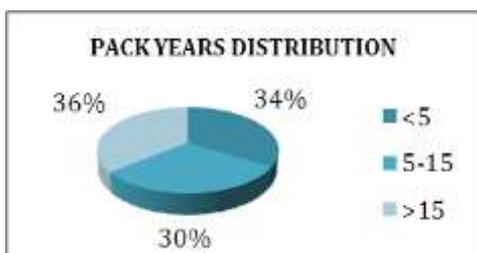


Fig. 3

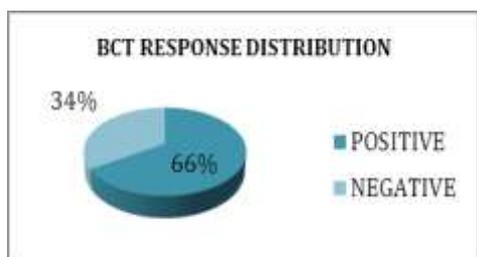


Fig. 4

27 (out of 41) males and 6 (out of 9) females had a positive BCT (Fig. 5). In the study population, 7 (out of 17) patients with <5 Pack Years, 11 (out of 15) patients with 5-15 Pack Years and 15 (out of 18) patients with >15 Pack Years had a positive BCT (Fig. 6). Using the Fisher's Exact test, this was found to be significant, p value: 0.0287, that is, as the smoking index (Pack Years

smoked) increases, the prevalence of bronchial hyper-responsiveness also increases.

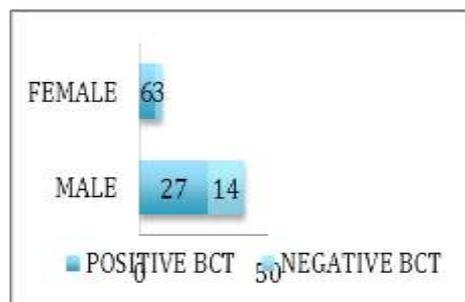


Fig. 5

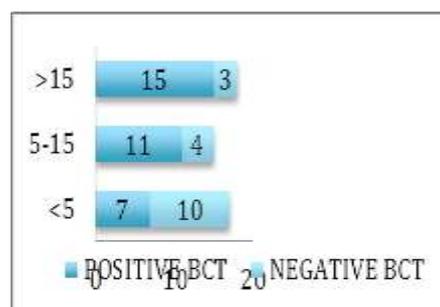


Fig. 6

Of the patients, 17(34%) had no response to Histamine challenge, 22(44%) showed a positive response at PD₂₀ of 4-16mg/mL, 10(20%) showed a positive response at PD₂₀ of 1-4 mg/mL and 1(2%), showed a positive response at <1mg/mL of histamine concentration (Fig. 7).

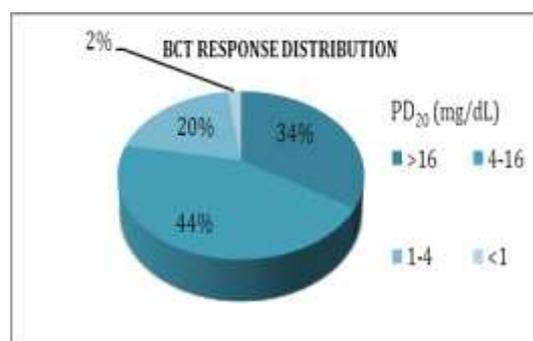


Fig. 7

In the study, in patients with <5 Pack Years, 0,1 and 6 patients showed strongly positive, mildly positive and borderline responses to BCT respectively. In patients with 5-15 Pack Years, 0,4 and 7 patients showed strongly positive, mildly positive and borderline responses to BCT respectively. In patients with >15 Pack Years, 1,5 and 9 patients were found to have Strongly positive, mildly positive and Borderline responses to the BCT respectively (Fig. 8). Using the Fischer's exact test, p = 0.112, hence not significant.

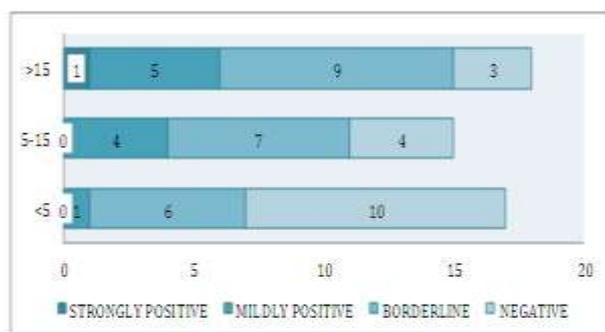


Fig. 8

DISCUSSION

In the general population, BHR to histamine or methacholine is observed in 16-30% of children and 10-16% of adults.^[5] Prevalence rates of Bronchial Hyper-responsiveness are higher in Asthma and COPD patients.^{[6],[7]} Even though BHR is generally accompanied by respiratory symptoms (such as wheezing, cough and shortness of breath), population studies have shown that a significant proportion of individuals with BHR do not have any respiratory symptoms. The prevalence of individuals with asymptomatic or “silent” BHR varies in different studies from 2.2 to 14.3%.^[8]

Relationship between smoking and development of chronic airflow limitation has been established. But all smokers do not develop chronic airflow limitation. The reason behind this observation remains unknown. The patients with chronic airflow obstruction have increased BHR, and this is not solely owing to increased airflow limitations.^[9] Studies have shown association between smoking, airway hyper-reactivity and chronic airflow obstruction.

Smoking per se seems to influence the responsiveness of airways because prevalence rates of 30-40% in current smokers and 18-25% in ex-smokers without airflow limitation have been documented.

In our study, we found that as the Pack Years smoked increased, there was a statistically significant increase in the frequency of patients with positive Bronchial Challenge Test ($p = 0.03$). These findings were comparable to those obtained from other studies^[10] which found that there was a significant association between smoking index in Pack Years and Bronchial Hyper-responsiveness. Also, the number of smokers with a positive test at a given concentration of Histamine, increased as the Pack Years smoked increased, though not found to be statistically significant.

CONCLUSIONS

- There is a co-relation between smoking and bronchial hyper-reactivity.

- Also, it was seen, that as the Pack Years smoked increased, there was a statistically significant increase in the prevalence of BCT positivity.

- The grade of BCT positivity too showed a similar increase as the Pack Years smoked increased.

Hence, it is important to subject smokers to Bronchial Challenge Tests and intervene with a multipronged approach to help them quit smoking and adopt a healthy lifestyle, as Bronchial Hyper-reactivity may be a harbinger of / preliminary step in, more sinister airway disorders.

REFERENCES

1. Beasley MB. Smoking-related Small airway disease--a review and update. *Adv Anat Pathol.*, 2010 Jul; 17(4): 270-6. doi: 10.1097/PAP.0b013e3181e3bf97. Review. PubMed PMID: 20574172.
2. Lams BE, Sousa AR, Rees PJ, Lee TH. Immunopathology of the small-airway submucosa in smokers with and without chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.*, 1998 Nov; 158(5 Pt 1): 1518-23. PubMed PMID: 9817702.
3. Chinn S, Jarvis D, Luczynska CM, et al. An increase in bronchial responsiveness is associated with continuing or restarting smoking. *Am J Respir Crit Care Med*, 2005; 172: 956-961.
4. Janson C, Chinn S, Jarvis D, et al. Effects of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health Survey: a cross-sectional study. *Lancet*, 2001; 358: 2103-2109.
5. Ramakant Dixit et al, Bronchial Hyperresponsiveness among active smokers, passive smokers and non smokers: a comparative analysis : *Indian J Allergy Asthma Immunol*, 2007; 21(1): 25-30
6. Gerrard JW, Cockcroft DW, Munk JT, Cotton DJ, Poonawalla RP, Dosman JA, Increased nonspecific bronchial reactivity in male smokers with normal lung functions. *Am Rev Resp Dis*, 1980; 122: 577-81.
7. T K Lim, R G Taylor, A Watson, H Joyce and N B Pride. (Changes in bronchial responsiveness to inhaled histamine over four years in middle aged male smokers and ex-smokers.) *Thorax.*, Aug 1988; 43(8): 599-604. PMID: PMC461394.
8. Jansen DF, Timens W, Kraan J, Rijcken B, Postma DS. Asymptomatic bronchial hyper-responsiveness and asthma. *Respir Med.*, 1997; 91(3): 121-34.
9. Taylor RG, Joyce H, Gross E, Holland F, Pride NB. Bronchial Hyper-reactivity to inhaled Histamine and annual rate of decline in FEV₁ in male smokers and ex-smokers. *Thorax*, 1985; 40: 9-16.
10. Juusela, M., Pallasaho, P., Rönmark, E., Sarna, S., Sovijärvi, A. & Lundbäck, B. Dose-dependent association of smoking and bronchial hyperresponsiveness In: *European Respiratory Journal.*, 2013; 42(60): 1503-1512.