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A study to detect early lung function deterioration using forced oscillation technique in smokers

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ABSTRACT

Background: Scientists unequivocally evidenced that tobacco consumers suffer from three Ds: disease, disability, and death. The forced oscillation technique (FOT) is a non-invasive method with which to measure respiratory mechanics. **Aims and Objectives:** This study was done to evaluate the ability of FOT to detect early smoking-induced respiratory function deterioration and to compare the performance of FOT with spirometry in healthy smokers. **Materials and Methods:** A cross-sectional study was conducted at a medical college between January 1st, 2021, and June 31st, 2022, with a sample size of 30. Study participants included healthy smokers and non-smokers. Spirometry and FOT were taken into consideration as a diagnostic modality. Data analysis was done through statistical software with a confidence interval of 95% and $P<0.5$. **Results:** In a total of 30 sample size (15 cases and 15 control), smokers presented with an average age of 26.13 ± 5.55 years, with smoking index (SI) ranging from 5 to 80, none of the spirometry parameters were statistically significant between smokers and non-smokers, however, the FOT parameter, resistance at 6-hertz frequency R6, in smokers is 5.36 ± 3.36 and is statistically different from non-smokers ($P=0.02$). Similarly, the percent predicted value of R6 also was statistically different in smokers ($P=0.01$). The R6 parameter correlated with forced expiratory flow 25–75 parameter of spirometry ($r=0.567$, $P=0.027$) in smokers. **Conclusion:** FOT is a good diagnostic modality in detecting early airway changes in smokers. The FOT along with spirometry increases the chances of diagnosing early airway changes in even initial smokers having a low SI.

Key words: Forced oscillometric technique; Spirometry; Smoking index; Obstructive diseases

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INTRODUCTION

Smoking in India has been known since at least 2000 BC, when cannabis was smoked and is first mentioned in the Atharvaveda (compiled c. 1200BC–c. 1000 BC). Fumigation (dhupa) and fire offerings (homa) are prescribed in the Ayurveda for medical purposes and have been practiced for at least 3000 years while smoking (literally "Dhoomrapan" means "drinking smoke") has been practiced for at least 2000 years. Tobacco was introduced to India in the 17th century, which later merged with the existing practices of smoking (mostly of cannabis). By the start of the 20th century, tobacco smoking, especially among the youth, had become so common that the more health-conscious sections of the intelligentsia began to take note of public smoking and marketing of tobacco products as a growing social menace. Scientists unequivocally evidenced that tobacco consumers suffer from three Ds: death, disease, and disability. In the developed countries, smoking has been associated with over 85% deaths of all cancer deaths in men.[1,2] It is estimated that 40–45% of all cancers and 90–95% of all lung cancers have an association with smoking. Smoking increases the risk of developing respiratory, obstructive, and cardiovascular diseases and

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is responsible for causing many types of cancer, even in non-smokers exposed to second-hand tobacco smoke. Measuring lung function is an important component in decision-making process of obstructive diseases. This helps not only to establish diagnosis but also to assess the severity of disease. Spirometry is most utilized for this purpose which, however, fails to give definite results in some cases.[3]

The forced oscillation technique (FOT) is a non-invasive method with which to measure respiratory mechanics. This technique employs small-amplitude pressure oscillations superimposed on the normal breathing and therefore has the advantage over conventional lung function techniques that it does not require the performance of respiratory maneuvers and it can identify early small airway involvement in smoker. The FOT data, especially those measured at the lower frequencies, are sensitive to airway obstruction but do not discriminate between obstructive and restrictive lung disorders. There is no consensus regarding the sensitivity of FOT for bronchodilation testing in adults. Values of respiratory resistance have proved sensitive to bronchodilation in children, although the reported cut-off levels remain to be confirmed in future studies.[3]

Aims and objectives

To study the ability of FOT to detect early deterioration of lung function in smokers, and to compare the FOT with Spirometry in healthy smokers.

MATERIALS AND METHODS

This was a hospital-based cross-sectional case–control study conducted between study duration of January 2021–June 2022 at the respiratory medicine department of a Netaji Subhash Chandra Bose Medical College in Central India. The study was approved by Institutional Ethics Committee as per their letter no IEC/2020/148 dated March 04, 2021.

The study was planned with a sample size of 50 (25 cases and 25 controls) and the sample size estimation was done using formula n=z2pq/d2, where - n=sample size, z=1.96 (considering 0.05 alpha, 95% confidence limits, and 80% beta), P=assumed probability of occurrence or concordance of results, q=1–p, and d=marginal error (precision), but in view of COVID pandemic resulting in pre-occupation of facilities toward the pandemic management, the sample size had to be reduced to 30 subjects (15 smokers and 15 non-smokers).

For the purpose of study, the following definitions were used:

- Active smoker - One who has a history of smoking at least 1 cigarette or bidi a day and has smoked last for >6 months
- Non-smoker - Someone who has not smoked >100 cigarettes in their lifetime and does not currently smoke
- Pack year - A way to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked
- Smoking index (SI) - The SI is a unit for measuring cigarette consumption over a long period and was calculated using the following formula: SI=CPD×years of tobacco use. SI categories were non-smoker, <400, 400–799, and ≥800.

Methodology

All consenting adult subjects who met with the definition of active smoker and non-smokers were included after obtaining an informed written consent, whereas those subjects with any cardiorespiratory illnesses, chest wall/thoracic cage abnormalities such as scoliosis, kyphosis, orthopedic disabilities of one and joint diseases, and subject's whose clinical examination was suggestive of pallor were not enrolled in the study. These study participants were identified from the healthy attendants accompanying the patients coming to either OPDs or healthy visitors of inpatients. The smokers who attended the smoking cessation clinic of the department and other healthy volunteers from the society who were volunteered to participate in study after understanding the study details were enrolled.

Detailed history and physical examination were done and findings were recorded in data collection form. The subjects then underwent chest X-ray and ECG to rule out the presence of significant cardiorespiratory ailments. The subjects then performed the FOT and spirometry as per standard practices for lung function testing.

The following parameters of spirometery were recorded:

- Forced expiratory volume in the first s (FEV1)
- FEV1 % predicted
- Forced vital capacity (FVC)
- FVC % predicted
- Ratio of FEV1/FVC
- Forced expiratory flow (FEF25-75)
- Peak expiratory flow rate

In FOT the following parameters were recorded:

- R_6 (total resistance)
- R_{20} (central resistance)
- X_6 (respiratory reactance)
- F_{RES} (resonant frequency)
- $R_6 – R_{20}$ (peripheral resistance).

Statistical analysis

All the data collected during the study were recorded in data collection form. This data generated was assessed for statistical analysis by applying statistical tests as per the nature of data through a statistical software. The descriptive analysis for frequency and mean was obtained. Quantitative variables of spirometry and FOT were expressed in mean and standard deviation. Student's *t*-test was used to test the significant difference between the variables and P<0.05 was considered as statistically significant for the study purpose.

RESULTS

Total subjects enrolled in the study were 30 and their age ranged from 19 to 37 years where the average age is 26.13±5.55 years. The other demographic characteristics such as age, height, weight, and SI among the smoker subjects are shown in Table 1.

The mean FEV1 in smokers was 3.84±0.65 L. The mean value of FVC in smokers was 4.31±0.84 L. In the spirometry test of study subjects, none of the parameters of spirometry yielded significant results between smokers and non-smokers (i.e., P<0.05) as can be seen in Table 2. Peak expiratory flow mean value in smokers was less as compared to non-smokers, but it was not statistically significant.

In FOT parameters like R6 (i.e., resistance of airways when subjected to 6 Hz frequency this helps to determine the function of airways till the terminal airways), % Pre-R6 and R6 – R20 (i.e., it denotes the function of distal airways which means that it is the difference of resistance of airways at 6 Hz subtracted by that on 20 Hz) yielded significant results with P<0.05, i.e., FOT is able to detect early physiological airway changes in smokers due to initial smoking effects mainly in the peripheral and distal airways. The R6 parameter correlated with FEF25-75 parameter of PFT (r=0.567, P=0.027) in smokers. The difference of FOT parameters between the smokers and on smokers can be seen in Table 3.

The AUC or ROC curve and values represented the ability of these two diagnostic modalities spirometry and FOT to detect the early airway limitation in smokers with confidence and the confidence of detecting airway limitation increased with increase in SI as shown in Tables 4 and 5.

Table 1: Depicting age, smoking index, height, weight range, and mean of smokers (n=15) and non-smokers (n=15)

Variables	Minimum	Maximum	Mean	Standard deviation
Smokers				
Age	19.00	37.00	26.13	5.55
Smoking Index	5.00	80.00	27.00	20.68
Height	149.00	180.00	169.73	8.76
Weight	37.00	85.00	60.20	16.13
Non-smokers				
Age	20.00	48.00	27.47	7.83
Height	161.00	183.00	170.67	5.56
Weight	50.00	88.00	66.27	12.42

Table 2: Depicting spirometry values with *t*-test applied for both smokers and non-smokers along with mean, standard deviation, and P-value

Variables (Spirometry)	n	Mean	SD	t-value	P-value
FVC (in liters)					
Smoker	15	4.31	0.84	0.371	0.093
Non-smoker	15	4.21	0.63		
% Pre-FVC					
Smoker	15	104.27	15.54	0.615	0.772
Non-smoker	15	100.73	15.92		
FEV1 (in liters)					
Smoker	15	3.84	0.65	1.161	0.311
Non-smoker	15	3.59	0.53		
% Pre-FEV1					
Smoker	15	110.33	13.39	1.581	0.486
Non-smoker	15	101.93	15.62		
FEV1/FVC					
Smoker	15	89.67	5.34	1.187	0.890
Non-smoker	15	85.49	6.77		
FEF25–75% (in L/s)					
Smoker	15	4.87	0.87	1.249	0.276
Non-smoker	15	4.38	1.24		
FEF25–75% Pre					
Smoker	15	135.40	20.80	1.500	0.207
Non-smoker	15	121.67	28.72		
PEF (in L/s)					
Smoker	15	9.55	1.80	0.417	0.540
Non-smoker	15	9.80	1.47		
PEF % Pre					
Smoker	15	115.20	25.21	0.336	0.351
Non-smoker	15	117.93	18.84		

FEF25-75: forced expiratory flow, fvc: Forced vital capacity, FEV1: Forced expiratory volume in 1st s

DISCUSSION

Smoking is a widespread addiction in the Indian population, especially in the young individuals, and smoking has a variety of health issues out of which one is its effect over the lungs and pulmonary functions where it affects the airways which lead to obstructive changes in a long-term effect, and this may ultimately end up in chronic obstructive lung disease in case of long-term smokers having SI usually more than 200. It has been documented that smoking also results in exercise limitation in individuals thereby, it decreases exercise tolerance of individuals.[4,5]

As per the WHO tobacco report 2021,[6] the prevalence of smoking in India in adults aged >15 years is 42.6%

Table 3: Depicting FOT values with *t*-test applied for both smokers and non-smokers along with mean, SD, and P-value

Variables (FOT)	n	Mean	SD	t-value	P-value
R6					
Smoker	15	5.69	3.68	1.351	0.002
Non-smoker	15	8.29	6.48		
% Pre-R6					
Smoker	15	213.73	136.09	1.325	0.001
Non-smoker	15	307.07	236.38		
R20					
Smoker	15	3.99	2.68	0.442	0.609
Non-smoker	15	4.43	2.76		
% Pre-R20					
Smoker	15	139.13	92.21	0.451	0.558
Non-smoker	15	154.60	95.77		
R6–R20					
Smoker	15	1.69	2.25	1.738	0.011
Non-smoker	15	3.85	4.27		
X6					
Smoker	15	−5.60	7.21	0.146	0.970
Non-smoker	15	−5.96	6.48		
F_{RES}					
Smoker	15	24.19	13.47	0.016	0.290
Non-smoker	15	24.26	9.59		

FOT: Forced oscillation technique

Table 4: AUC for spirometry and FOT variables for all the smokers (n=15)

Variable (s)	Area
FEV1	0.622
FVC	0.536
FEV1/FVC	0.664
FEF25–75	0.620
PEF	0.467
R6	0.400
R20	0.436
R6 - R20	0.356
X6	0.498
FRES	0.498

FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1st s, FEF: forced expiratory flow, FOT: Forced oscillation technique

Table 5: AUC for spirometry and FOT variables in relation to the smoking index

Variable (s)	SI <10 (n=2)	SI 10–20 (n=6)	SI 20–30 (n=4)	SI >30 (n=3)
	Area	Area	Area	Area
FEV1	0.654	0.722	0.341	0.250
FVC	0.692	0.704	0.273	0.333
FEV1/FVC	0.423	0.444	0.818	0.250
FEF25-75	0.596	0.565	0.727	0.056
PEF	0.385	0.648	0.432	0.444
R6	0.423	0.444	0.636	0.472
R20	0.538	0.593	0.364	0.500
R6–R20	0.385	0.389	0.795	0.389
X6	0.769	0.556	0.455	0.278
FRES	0.769	0.444	0.636	0.222

FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1st s, FEF: forced expiratory flow, FOT: Forced oscillation technique

in males, 13.9% in females, and combined prevalence in both sexes is 28.3%. It suggests that around one-fourth of Indian population, i.e., around 3 billion Indian residents are at risk of smoking-induced side effects. Around 24% of population practices daily smoking out of which 6% of Indian population and around 13% of males resort to the cigarette or beedi smoking as the form of consumption of tobacco. The tobacco smoking prevalence in Madhya Pradesh is around 11% among men. The global youth tobacco survey[7] 2019 was conducted for the age 13–15 years of age. It showed a prevalence of around 39% of individuals practice current daily smoking. Moreover, this is the population which are the early and young smokers. If this target population is studied for detecting physiological changes and early effects of smoking, it can be a time-changing intervention in these individuals and will be helpful in further diagnostic and therapeutic modalities. Tobacco use is a major risk factor for many chronic diseases, including various cancers, lung diseases, cardiovascular disease, and stroke. It is one of the major causes of death and disease in India and accounts for nearly 1.35 million deaths every year.[6] India is also the second largest consumer and producer of tobacco. A variety of tobacco products are available at very affordable prices in the country.

As it is documented in the literature, the adolescent age is the most vulnerable age to adopt smoking as a habit in initial days.[7] Here, in this study, the focus was on detecting early airway changes and impaired lung function parameters in early and young smokers using a lesser-utilized technnique of FOT. Through this study, it is attempted to determine early effects of smoking in healthy smokers and comparing the physiological determinants with healthy non-smokers of comparative age group so as to assess the effect of smoking on early airway changes and exercise limitation in the individuals by the use of different diagnostic test modalities such as spirometry and FOT.

A comparitively younger age subjects with an average age of 26.5 years were studied compared to the similar other studies undertaken in the past such as by Amaral et al.,[8] in which he used FOT as the method of early diagnosis of smoking-induced respiratory changes. In a study by Su et al.,[9] they studied the early small airway obstruction by using both spirometry and FOT. Kobayashi et al.,[10] studied the effects of habitual smoking on cardiorespiratory fitness. However, all these studies had a higher age of participants and a higher SI in comparison to our study, so in comparison to all these literatures, we want to discuss that the initial effects of smoking are prevalent that too at an early age and a lower SI also. Further, in this study, the mean SI was 27.00±20.68 which was comparatively way lower than all the previous studies mentioned above, and hence, all the smoker group participants in the present study were early smokers and just adopted smoking as a habit during the recent past.

In spirometry test in the present study, none of the spirometry parameters yielded any significant results in comparison with control group, i.e., non-smokers. This infers that spirometry alone was not be able to detect any airway changes in these recent, young healthy smokers. We could not detect any literature that studied spirometry parameters between smokers and non-smokers at the early phase of smoking or conducted on young healthy individuals, along with the forced oscillometric technique. The present study is most likely the first attempt to use spirometry and FOT as a tool for the detection of early ill effects of smoking on lung functions. There are some studies done in smokers for detecting obstructive airway changes as compared to non-smokers such as those conducted by singh et al.[11] and Mistry et al.,[12] but their work was on subjects who were already symptomatic. In another study by Su et al.,[9] the subjects had a relatively higher age and an increased SI as compared to this study. Similarly, in a study by Berger et al.,[13] the study population had a mean age of 61 years, and that was the reason they were successful in finding significant results in their study using spirometry test.

In the present study, FOT yielded significant results in parameters R6 which denotes the resistance of airways to 6 Hz frequency, it signifies the function of airways till the terminal airways and the parameter of R6 – R20 which denotes the resistance of airways at 6 Hz subtracted to that of 20 Hz, and it signifies the function of terminal and distal airways which are usually the first one to get affected by hazardous effect of smoking as per the previous studies conducted earlier evaluating the physiology of respiratory airways using FOT. Jetmalani et al.,[14] also observed changes in FOT parameters in smokers compared to non-smokers but in this study, none of the parameters gave a significant difference, where the present study findings differ from it, since there is a significant comparitive difference in FOT parameters. As per Faria et al.,[15] the FOT is a good tool to detect airway changes in individual with pack years <20 and it was observed in the present study also that FOT is useful in detecting early airway changes that too in early smokers.

Limitations of the study

The study carried the limitation of a small sample size which got further shrinked due to the pandemic, and hence, a smiliar study in a larger group of subjects can help to generate further useful data. The technique of FOT is not readily available at many centers yet, and hence, further research on the reference values of FOT parameters in various ethnic population groups is needed for the comparisons, as are already available for the spirometry.

CONCLUSION

Hence, the present study concludes that standalone spirometry is not adequate in detecting early airway changes in smokers in young and initial smokers with a lower SI who are still asymptomatic. but on the other hand, FOT has proved as a good diagnostic modality in detecting early airway changes in smokers compared to non-smokers by yielding significant difference of values in FOT parameters like R6 and R6 – R20 which are suggestive of the involvement of distal airways that are considered to be the earliest site affected in smokers. A combined approach of FOT along with spirometry can increase the efficacy of diagnosing early airway changes in even initial smokers having a low SI.

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Author's Contribution:
KB- Literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, manuscript preparation; **SKB-** Concept, design, protocol preparation, manuscript editing; **AJ-** Manuscript preparation, data analysis; **VP**- Manuscript review; **BBP-** Manuscript review; **BP**- Study design, implementation of study protocol, statistical analysis, manuscript preparation and submission of article, coordination.

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