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SHORT COMMUNICATION

COMPARISON OF SINGLE BREATH AND STEADY STATE METHODS FOR MEASUREMENT OF LUNG TRANSFER FACTOR FOR CO IN NORMAL SUBJECTS AND SMOKERS

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Abstract : Pulmonary diffusing capacity (lung transfer factor for carbon monoxide) has been assessed by the single breath ($TLCO_{SB}$) and steady state ($TLCO_{SS}$) techniques in well matched 90 females, 31 non-smoker and 29 smoker males, 18-50 years of age. Both $TLCO_{SB}$ and $TLCO_{SS}$ are significantly lower in females compared to non-smoker males (P<0.001). Tobacco smoking statistically significantly reduces $TLCO_{SB}$ as well as $TLCO_{SS}$ in smokers as compared to non-smokers. There is a statistically significant correlation of age with $TLCO_{SB}$ and $TLCO_{SS}$ in all the three groups (r = –0.702, –0.360 and 0.300 for $TLCO_{SB}$ and r = –0.481, –0.355 and 0.380 for $TLCO_{SS}$ in non-smoker males, smoker males and females respectively). $TLCO_{SB}$ is 30.43±4.89, 27.29±4.54 and 26.13±3.60 ml/mmHg/min, while $TLCO_{SS}$ is 19.47±5.26, 16.69±3.27 and 18.24±3.78 ml/mmHg/min in non-smoker males, smoker males and females respectively. A fairly good correlation between the $TLCO_{SB}$ and $TLCO_{SS}$ in male, both non-smoker and smoker, as well as the female subjects was observed. $TLCO_{SS}$ is lower than $TLCO_{SB}$ in all the three groups. Even in smokers of moderate intensity both of these tests are influenced to a nearly similar extent.

Key words : TLCO by single breath method
TLCO by steady state method
TLCO in smokers and non-smokers
TLCO in females

INTRODUCTION

Study of lung transfer factor for CO (TLCO) is recommended as a sensitive index of pulmonary gas exchange to detect structural and functional lung diseases (1, 2). TLCO measurement has been generally made using either single breath ($TLCO_{SB}$) or steady state ($TLCO_{SS}$) methods. Both $TLCO_{SB}$ and $TLCO_{SS}$ are influenced by regional non-homogenous distribution of ventilation and perfusion. Many authors have reported difficulty of measuring TLCO in patients exhibiting unequal ventilation (1, 3) The single breath method is thought to be inadequate in such cases. The steady state method however gives a more even distribution of test gas in lung and is therefore less sensitive to unequal ventilation. Earlier, measurement of TLCO steady state was not much popular due to technical difficulties involved in its measurement and complex calculations. Now recent technical developments have made

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this method more feasible for routine measurements.

Smoking is known to affect TLCO adversely, hence needs to be taken into consideration in the study of TLCO. At present, still there is no unanimity as to which method, $TLCO_{SB}$ or $TLCO_{SS}$, is a more valid index of gaseous diffusion within the lung (4). To understand the differences between $TLCO_{SB}$ and $TLCO_{SS}$ measurement in patients with lung diseases, one needs to have a better understanding of the differences obtained when the methods are applied to healthy subjects. The present study was undertaken to compare $TLCO_{SB}$ and $TLCO_{SS}$ in normal subjects in order to generate the normal values for subjects in this area. Further, the effect of tobacco smoking on TLCO was also assessed.

METHODS

One hundred and fifty normal individuals, 60 healthy sedentary male subjects (31 non-smokers and 29 smokers) and 90 females, 18-50 years of age, volunteered for this study. Healthy subjects were either healthy relatives of patients or medical students or employees working at Pandit B.D. Sharma PGIMS, Rohtak (India). In the smokers, tobacco consumption amounted to 10-15 pack years (moderate smokers). All of them were free from any cardiorespiratory disease, as assessed by history and clinical examination of subjects. The smokers were asked to abstain from smoking for at least two hours before reporting to the Respiratory Laboratory at 9 AM in the morning. Smokers were not allowed to smoke till the study was completed on that day. The tests were performed in a sitting position between 9-11 AM at least one hour after a light breakfast. Subjects with hemoglobin less than 12 gm/dl were excluded from this study. Routine pulmonary function tests including FVC, $FEV_1\%$, PEFR and $EFR_{25\text{-}27}$ were measured in each subject from flow volume curve using Morgan Transfer Test Model C and Computer Magna 88 (P.K. Morgan U.K.) to confirm whether any significant airway obstruction had already set in.

Two measurements of TLCO using single breath technique were made at an interval of 15 min between them (5). This was followed by measurement of transfer factor for CO by steady state technique ($TLCO_{SS}$) (6), using Rahn and Otis end-tidal sampling device for obtaining alveolar air (7), in the same subjects, on the same apparatus (Morgan Transfer Test Model C and Computer Magna 88).

All the results were expressed under STPD conditions. Correlation coefficient between age and $TLCO_{SB}$, age and $TLCO_{SS}$ were calculated using standard statistical methods.

RESULTS

Ninety females, 31 non-smoker and 29 smoker males, matched for age (±1 year), height (±2 cms), socio-economic status and physical activity, completed this study. Mean ± SD of

TABLE I : Ventilatory functions and transfer factor for CO in males and femals.

Parameter	Males		P value	Females	P value
	Non-smokers (I)	*Smokers (II)*	*(I vs. II)*	*(III)*	*(I vs. III*
n	31	29		90	
Age (yrs)	29.54 ± 8.87	30.08 ± 7.74	NS	29.24 ± 9.61	NS
FVC (L)	3.90 ± 0.78	3.80 ± 0.62	NS	2.87 ± 0.48	<0.001
FEV_1 %	88.71 ± 5.30	83.30 ± 6.21	<0.01	82.79 ± 8.50	<0.001
PEFR (L/sec)	8.76 ± 1.97	7.96 ± 1.62	<0.05	4.79 ± 1.68	<0.001
$EFR_{25\text{-}75}$ (L/sec)	4.00 ± 0.62	3.82 ± 0.58	NS	2.94 ± 0.91	<0.001
$TLCO_{SB}$ (#)	30.43 ± 4.89	27.29 ± 4.54	<0.01	26.13 ± 3.60	<0.001
$TLCO_{SS}$ (#)	19.47 ± 5.26	16.69 ± 3.27	<0.01	18.24 ± 3.78	<0.05

Values are Mean ± S.D. Statistical analysis using unpaired t-test. # - (ml/mmHg/min).

data for age and transfer factor for carbon monoxide (both $TLCO_{SB}$ and $TLCO_{SS}$) of subjects under study is shown in Table I. Correlation of age with $TLCO_{SB}$ and $TLCO_{SS}$ and between $TLCO_{SB}$ and $TLCO_{SS}$ is shown in Table II. Fig 1 shows the correlation of $TLCO_{SB}$ with $TLCO_{SS}$ in female as well as male subjects. We observed that performing $TLCO_{SS}$ by subjects was easier than measurement of $TLCO_{SB}$.

TABLE II : Correlation coefficient (r) between different parameters.

	$TLCO_{SB}$	P value	$TLCO_{SS}$	P Value
Males (n = 60)				
Non-smokers (n = 31)				
Age	–0.702	<0.001	–0.481	<0.01
$TLCO_{SB}$	–	–	0.349	<0.05
Smokers (n = 29)				
Age	–0.360	<0.05	–0.355	<0.05
$TLCO_{SB}$	–	–	0.383	<0.05
Females (n = 90)				
Age	0.300	<0.01	0.380	<0.01
$TLCO_{SB}$	–	–	0.340	<0.001

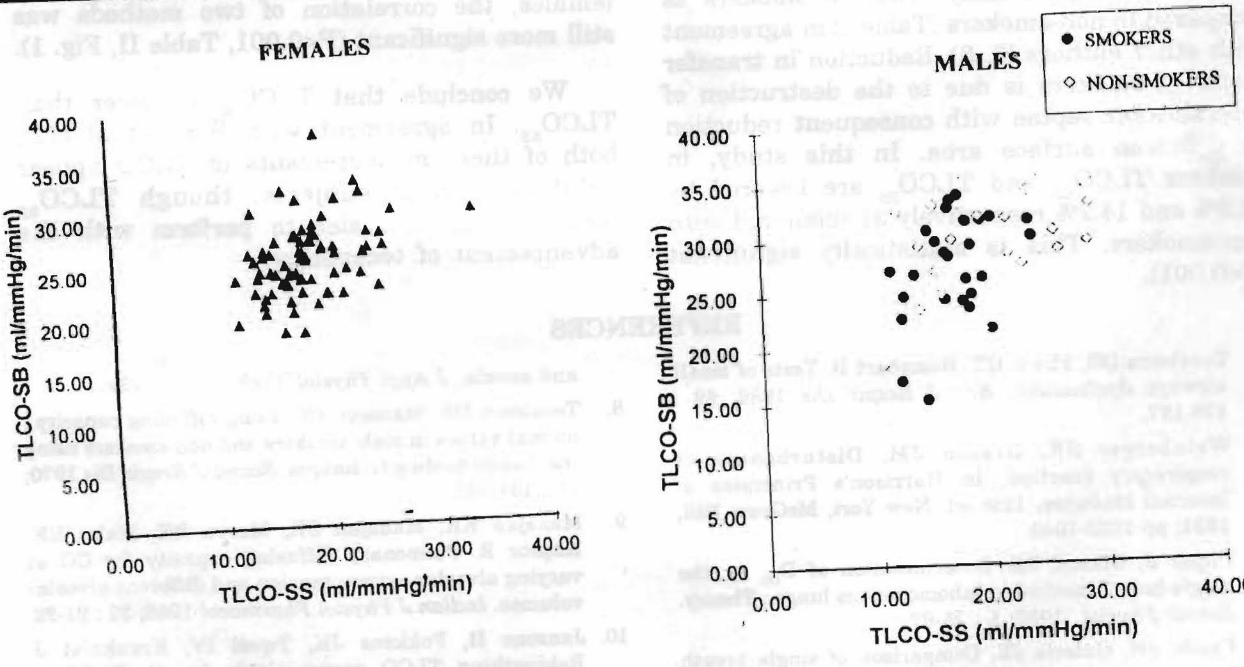

Fig. 1 : Comparison of $TLCO_{SB}$ with $TLCO_{SS}$ in both male and female subjects.

DISCUSSION

Measurement of $TLCO_{SB}$ is commonly used as a part of diagnostic lung evaluation. A lack of uniform technique and standard values has led different investigators to recommend that each lab must establish its own normal values (1, 2, 8). Mahajan et al (9) reported that for satisfactory inter-laboratory comparison of values of $TLCO_{SB}$, it must be measured at maximal alveolar volume and should be expressed as $TLCO_{120}$ (at constant pO_2 of

120 mmHg) by using a correction factor. $TLCO_{SS}$ is measured during spontaneous breathing at whatever lung volume the subject adopts under conditions of measurement. Therefore the latter may be more relevant to normal physiological conditions of gas exchange than obtained by single breath technique which requires breath-holding at total lung capacity (5, 9).

In this series, diffusion capacity measured by $TLCO_{SB}$ is statistically greater than $TLCO_{SS}$ values (Table I). It is well documented that smoking promotes unequal ventilation (3); hence increasing unequal ventilation causes an increasing underestimation with single breath method. This results in $TLCO_{SB}$ gradually being equal to $TLCO_{SS}$ at vital capacity (10).

FEV_1%, PEFR, $TLCO_{SB}$ and $TLCO_{SS}$ are statistically significantly lower in smokers as compared to non-smokers (Table I) in agreement with other authors (5, 8). Reduction in transfer factor in smokers is due to the destruction of interalveolar septae with consequent reduction in diffusion surface area. In this study, in smokers $TLCO_{SB}$ and $TLCO_{SS}$ are lowered by 10.3% and 14.2% respectively as compared with non-smokers. This is statistically significant ($P<0.001$).

In female subjects, both $TLCO_{SB}$ and $TLCO_{SS}$ are significantly lower as compared to non-smoker males while $TLCO_{SB}$ is still lower than that seen in even smoker males (Table I). Table II shows that in males a statistically significant negative correlation of age with TLCO was observed similar to earlier report (11); maximal TLCO was attained at the age of 18-20 years which gradually declined later. On the other hand, in female subjects a statistically significant positive correlation of age with TLCO was observed, as diffusion functions showed a small rise with age to attain maximal value in 31-35 years age group and then started declining with advancing age (unpublished observations). In this series, a good correlation was observed between two methods measuring TLCO in both non-smoker and smoker males ($P<0.05$). In females, the correlation of two methods was still more significant ($P<0.001$, Table II, Fig. 1).

We conclude that $TLCO_{SS}$ is lower than $TLCO_{SB}$. In agreement with Bore et al (12), both of these measurements of TLCO appear valid in normal subjects, though $TLCO_{SB}$ measurement is easier to perform with the advancement of technology.

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