Ceylon J. Med. Sci. 33 (No. 2, December) 1990, pp 67-77

INTRA-INDIVIDUAL AND DIURNAL VARIATION OF LUNG FUNCTION MEASUREMENTS IN HEALTHY SRI LANKANS

M. Udupihille[1]

Summary. Maximum expiratory flow-rates in the latter part of the flow-volume curve are considered to be useful in the diagnosis of early small airways obstruction. For this objective, it is essential to determine the degree of intra-subject and diurnal variation of these variables in healthy individuals. This study measures intra-individual variation of dynamic lung function tests, including indexes derived from the flow-volume curve, in a group of healthy Sri Lankans.

Eleven subjects (4 women) of age range 22 to 48 years were studied. Spirometric tests (FVC, FEV_2, and $FEF_{25-75\%}$) peak expiratory flow rates (using the mini-Wright peak flow meter) and flow-volume curves were peformed in the morning and in the afternoon on 10 consecutive days. The mean morning-afternoon differences and mean coefficients of variation were calculated for each test.

There was no morning-afternoon variation in any of the tests. The intra-individual variations detected for FVC and FEV_1 and the the peak expiratory flow rate were of the order of 3 to 4%. The variations of the maximum expiratory flow rates at 50% and 25% lung volume and the the forced mid-expiratory flow rate ($FEF_{25-75\%}$) were about 7to 10%. The results were similar to those reported in other populations.

It is concluded that the indexes derived from a volume-time tracing during a forced expiratory manoeuvre were more reproducible and therefore more suited for population screening. The high variability inherent in the indexes derived from the flow volume curve may limit their usefulness in detecting early airways obstruction.

Key words: Lung function measurements, adults, diurnal variation

INTRODUCTION

One of the purposes of lung function testing is to identify early airways disease, specially those involving the small airways of the lungs which constitute the "silent zone". For this purpose, it is essential not only to establish normal values for a given population, but also to investigate the variability of the tests concerned and to establish whether a diurnal variation is present; and if so, to find out the extent of this variation.

John Hutchinson was the first to report the existence of a day-to-day variation of lung fnnction with respect to vital capacity (l). Since then, several studies of reproducibility of some spirometric measurements have appeared in the

1. Head, Department of Physiology, Faculty of Medicine, University of Peradeniya, Peradeniya.

literature (2, 3, 4). Some reports (5) are available with regard to intra-ndividual variation of indexes derived from the flow-volume curve. No data are available for Sri Lankans.

The aim of this investigation was to determine the morning:evening and day-to-day variation of a number of lung function tests in a group of healthy Sri Lankan subjects, both men and women.

METHOD

Fourteen normal subjects (4 women) of age range 22 to 48 years, volunteered for the study. They were employees of the department of Physiology at the Faculty of Medicine, Peradeniya, familiar with the testing procedure and accustomed to performing forced expiratory manoeuvres. The subjects had no history of upper respiratory infection in the three weeks immediately preceding the test. None gave a past history of chronic respiratory illness. Three of the male subjects developed upper respiratory tract infections during the test period and were excluded from the final analysis.

The mean age and height of the 7 remaining men were 32.3 (SD 8.96) years and 159.8 (SD 1.84) cm respectively. They had a mean smoking history of 0.9 paek years (the pack-year indicates the number of cigarettes smoked per day divided by 20 and multiplied by the number of years the subject has been smoking). Five were never-smokers and one, an ex-smoker. The mean age of the four women was 29.3 (SD 2.50) years and the mean height was 151.6 (SD 4.53) cm. None of the women smoked.

As the subjects chosen were highly motivated, familiar with the testing procedure and experienced in the performance of lung function tests, the effect of training and learning on the results was minimized.

To eliminate inter-observer error, all the tests were carried out by a single operator.

The following tests were performed:

1. Peak expiratory flow rate (PEFW)
2. Indexes derived from the forced expiratory spirogram which included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced mid-expiratory flow rate ($FEF_{25-75\%}$) and the FEV_1/FVC ratio
3. Indexes derived from the flow-volume curve which were instantaneous peak expiratory flow rate (PEF), flow rate at 50% lung volume ($V_{max\,50}$) and the flow rate at 25% lung volume ($V_{max\,25}$).

A new mini - Wright peak flow meter was used to measure peak expiratory flow rate as the instrument had been observed to lose calibration with time(6). A single instrument was used to obtain all the readings in order to eliminate differences in readings between instruments. Measurements were taken with the subjects in the standing position and the flow meter held horizontally The subjects were watched for faults in technique such as acceleration of air-flow at the mouth which is known to give spuriously high readings (7). They were exhorted to perform the test to the best of their ability and the highest result of three acceptable blows was taken as the correct reading, as recommended in the ACCP Scientific Recommendations (8).

The forced expiratory manoeuvres were performed using Morgan "Spiroflow" spirometer (obtained from PK Morgan Ltd., 4, Bloors Lane, Rainham, Gillingham, Kent, United Kingdom). The spirometer conformed to the recommendations of the American Thoracic Society 1987 Update (9). Tests were performed with the subject seated and without a nose-clip, as stated in the ACCP Scientific section recommendations (8), the largest value of three acceptable readings which varied by less than 5% of the highest reading was selected as the correct reading. The "end of test" criteria were as recommended by the American Thoacic Society (9). The FEV_1 was calculated using the back - extrapolation method (10).

A Rikedensky X-Y recorder (obtained ftom Rikedensky Mitsui Electronics Ltd., Oakcroft Road, Chessington, Surrey, England) was used in series with the spirometer to record flow-volume curves. The curve resulting from the forced expiratory manoeuvre giving the largest sum of FVC and FEV_1 was selected for calculating forced expiratory flow rates (9).

The ambient temperature of the laboratory recorded to an accuracy of $\pm 1°C$ was between 24 to 29°C. The results were converted to BTPS using a nomogram (10).

Tests were peformed between 7.30 and 8.30 in the morning following a 30 minute period of rest after arriving in the laboratory, and between 4.00 and 4.30 in the afternoon following a 30 minute rest period after the day's work. Those who were smokers did not smoke for 2 hours prior to the test.

RESULTS

The readings obtained for eleven subjects for each lung function test (expressed as the mean of the readings for the 10 test days) for the morning and afternoon separately, were used to calculate the mean morning and afternoon difference. These values (and SD and 95% confidence intervals of the diffe-ences) with respect to each lung function test, are shown in Table 1. The

Table 1. Morning: afternoon variation of respiratory function tests

Test	Morning and afternoon difference Mean (SD)	95% confidence intervals of the difference	t	P
PEF (Wright) (l/min)	-2.70 (8.08)	8,10 to -2.70	1.10	0.293 (NS)
FVC (l)	0.021 (0.043)	0,05 to -0.01	0.621	0.136 (NS)
FEV_1 (l)	-0 001 (0.028)	0.02 to -0.02	0.107	0.917 (NS)
FVC/FEV_1 %	-0,688 (1.198)	0.11 to -1.50	1.905	0.086 (NS)
$FEF_{25-75\%}$ (l/s)	-0.007 (0·145)	0.09 to -0.11	1.660	0.871 (NS)
PEF (l/s)	-0.113 (0.185)	-0.08 to -0.17	2.018	0.071 (NS)
V_{max} 50 (l/s)	-0.055 (0,106)	-0.02 to -0.09	1:736	0.113 (NS)
V_{max} 25 (l/s)	-0.054 (0.084)	-0.03 to -0.08	2.119	0.060 (NS)

Means (and SD) of the morning and afternoon differences for eleven subjects for ten days are given in column 2. NS = not significant; PEF (Wright) = peak expiratory flow rate measured by the mini-Wrght peak flow meter.

peak expiratory flow rate recorded by the flow meter, FEV_1, the FVE_1 / FVC ratio and the indexes derived from the flow-volume curve were observed to have afternoon readings which were marginally higher than the readings obtained in the morning. The data obtained in the afternoons gave slightly lower readings for FVC. The differences, however, were very small and were not statistically significant.

The "within-subject" coefficients of variation (CV) for each test were calculated as the means of all the readings obtained for the ten days for all eleven subjects; The mean coefficients of variation (and 95% confidence intervals) are shown in Table 2. The within-subject CV was lowest (being of the order of 3%) for FEV_1 and the FEV_1 / FVC ratio. High coefficients of variation (of the order of 10%) were seen in $FEF_{25-75\%}$, and Vmax25 measurements,

Table 2. "Within-subject" coeffcient of varation of respiratory function

Test	Coefficient of variation % (SD)	95% confidence intervals
PEF (Wright) l/s	3.03 (1.41)	3.34 to 2.72
FVC (l)	3.48 (1.70)	3.85 to 3.11
FEV (l)	4.01 (2.06)	4.46 to 3.56
FVC/FEV_1 (%)	2.49 (0.73)	2.65 to 2.33
$FEF_{25-75\%}$(l/s)	10.09 (2.69)	10.6 to 9.76
PEF (l/s)	5.46 (2.74)	6.06 to 4.86
Vmax50 (l/s)	7.74 (2.35)	8.25 to 7.23
Vmax25 (l/s)	10.32 (3.63)	11.1 to 9.53

Mean coefficients of variation (and SD) obtained for 10 days for eleven subjects are given in column 2. NS = not significant; PEF (Wright) = Peak expiratory flow rate obtained by the mini-Wright peak flow meter

DISCUSSION

A small group of subjects was studied as it was impracticable to repeatedly test a large group over a one hour period in the mornings and evenings daily, Since the results of this study confirmed the findings of other authors (who also tested small groups of subjects) in other population groups, it was decided not to extend the study to a larger group.

The study showed no significant variation in respiratory function (as measured by FVC, FEV_1, $FEF_{25-75\%}$, $\dot{V}_{max50}$, $\dot{V}_{max25}$ and PEF estimated by flow-volume curves and the mini-Wright peak flow meter) between the morning hours (7,30 to 8.30 am) and the afternoon hours (4.00 to 4.30 pm). This is in agreement with the results of Cochrane, Prieto and Clark (5) and Hruby and Butler (11) who showed that there was no consistent statistically significant pattern of variation of FVC, FEV_1 and $FEF_{25-75\%}$ between the hours of 9 am and 6 pm in normal individuals, although a diurnal variation was demonstrable in patients (11, 12). The latter authors showed that the above findings were also applicable to vital capacity and airways resistance.

The existence of a variation between the morning hours and the late evening hours cannot be ruled out in the present study. Patients are generally tested during working hours (between 8 am and 4 pm). Within these times, this study shows that there is no significant morning: afternoon difference in the measurements. Therefore it can be concluded that respiratory function tests can be carried out in the laboratory throughout a working day without loss of precision.

Several studies are available concerning the day-to-day variability in lung function tests in normal subjects. Table 3 shows the coefficient of variation for repeated measurements of FEV_1 in various studies reported in the literature. Rozas, Allen and Goldman (21) have reported coefficients of variation observed in five subjects with regard to FVC and FEV_1 for five days to be 2.8 (SD 1.7)% and 2.8 (SD 2.1)% respectively. Recent studies that have reviewed the existing data have suggested that the "within subject" coefficients of variation for FVC and FEV_1 are between 3-4% (23, 24). Hankinson and Paterson (17) have reported that the "intra-subject" coefficient of variation over a one to two year period was less than 3% for FVC and 3.68% for FEV_1. These results compare favourably with the present study where the coefficients of variation were 4.01 (SD 2.06)% and 3.49 (SD 1.41)% respectively.

The coefficients of variation of the tests show considerable variation from person to person (Table 4). This is in agreement with the findings of Black, Offord and Hyatt (24) and McCarthy, Craig and Cherniack (4). The significance of this variability is unclear. Longitudinal studies are necessary to determine whether there may be implications such as increased susceptibility to lung damage in response to environmental pollutants, cigarette smoke and other noxious stimuli.

The results of the present study show that the more sensitive tests of airways obstruction such as $FEF_{25-75\%}$ and tests of small airways obstruction such as V_{max50} and V_{max25} have large intra-subject variations (of the order of 8-10 per cent). It has been shown that the maximum expiratory flow rate is effort-independent over the latter half of the FVC, due to the fact that airway compression and collapse occurs with increasing effort, which causes progressive increase in intra-thoracic pressure (25). Thus, tests such as $FEF_{25-75\%}$, V_{max50}, and V_{max25} would be expected to be highly reproducible. However, tests that are considered effort-dependent such as FVC and FEV_1 demonstrated much less variability. These findings are in agreement with Dawson (2), Leuallen and Fowler (26) and Clement and Van de Woestijne (27). It is possible that slight differences in FVC on successive expirations may contribute to the variability noted in effort-independent flow rates (27). The high variability inherent in these tests may limit their usefulness in clinical practice. The considerably smaller coefficients of variation for FEV_1, FVC and FEV_1 /FVC ratio reported here suggest that these measurements may be more useful for routine screening of patients than the more modern tests of airway dysfunction.

Table 3. Intra-individual variation of FEV_1 values reported in the literature

Reference	CV%
Dawson (2)	3.0
Carey, Dawson & Merrett (13)	1.6-4.9
Guberan, Williams & Smith (14)	4.1
Stebbings (15)	8.2
Lapp, Hankinson, Burgess & O'Brian (16)	9.1
Hruby & Butler (11)	3.0
McCarthy, Craig & Cherniack (4)	3.0
Cochrane, Prieto & Clark (5)	2.7
Hankinson & Peterson (17)	3.68
MacDonald & Cole (18)	3.8
Pennock, Rogers & McCaffree (19)	6.7-8.1
Pham et al (20)	5.1
Rozas, Allen & Goldman (21)	2.8
Groth, Dirksen, Dirksen & Rossing (21)	4.7

CV = Coefficient of variation

Table 4. Within - subject coefficient of variation (%) (with respect to each subject for each lung function measurement) in 11 healthy subjects

Subject	PEF Wright	FVC	FEV_1	FVC/ FEV_1	FEF $_{25-75\%}$	PEF	V_{max50}	V_{max25}
1	3.79	2.62	3.67	2.65	9.28	3.06	9.59	10.3
2	3.90	2.89	2.26	2.70	7.61	3.24	4.95	12.1
3	2.12	2.97	3.61	3.53	14.45	3.17	8.98	13.33
4	2.49	2.03	2.41	2.27	8.97	3.20	4.86	8.55
5	3.17	3.08	4.21	2.75	8.89	5.01	6.53	9.98
6	2.30	3.67	3.06	3.17	10.73	5.27	8.89	7.21
7	2.79	5.85	5.24	2.25	11.15	10.52	10.24	10.24
8	1.45	4.43	4.46	1.84	11.48	7.45	9.81	10.32
9	2.69	4.15	3.54	3.34	6.90	6.77	7.72	4.17
10	2.11	2.13	2.27	1.90	11 5	3.41	4.91	12.0
11	3.67	4.50	9.36	2.29	10.01	8.96	9.63	9.80

Mean coefficients of variations for 10 days for each subject are given for each lung function test

ACKNOWLEDGEMENTS

I thank the members of the staff of the Department of Physiology who volunteered to take part in this study, A researeh grant from the University of Peradeniya is gratefully acknowledged. This study formed a part of a thesis submitted by the author to the University of Peradeniya for the degree of Ph.D.

REFERENCES

1. Hutchinson J. On the capacity of the lungs, and on the respiratory functions, with a view of establishing a precise and easy method of detecting disease by the spirometer. Medico-Chirurgical Transactions, Series 2, 1846;29:137–252.
2. Dawson A. Reproducibility of spirometric measurements in normal subjects. American Review of Respiratory Diseases 1966;93:264–268.
3. Gilson JC, Hugh-Jones P. The measurement of the total lung volume ond breathing capacity. Clinical Scieuce 1949;i:185–216.
4. McCarthy D, Craig DB, Cherniack RM. Intraindividual variability in maximal expiratory flow-volume and closing volume in asymptomatic subjects. American Review of Respiratory Diseases 1975;112:407–411.
5. Cochrane GM, Prieto F, Clark TJH. Intra-subject variability of the maximal expiratory flow volume curve. Thorax 1977;32;171–176.
6. Oldham HG, Bevan MM, McDermott M. Comparison of the new miniature Wright peak flow meter with standard Wright peak flow meter. Thorax 1979;34:807–809.
7. Connolly CK. Falsely high peak expiratory flow readings due to acceleration in the mouth. British Medical Journal 1987;294:285.
8. ACCP Scientific Section Recommendations. Statement on spirometry; a report of respiratory pathophysiology. Chest 1983;83;547–550.
9. American Thoracic Society. Standardization of spirometry – 1987 Update. American Review of Respiratory Diseases 1987;136:1285–1298.
10. Cotes JE. Lung function. Assessment and applications in medicine. 4th ed. Oxford:Blackwell scientific publications 1979.
11. Hruby J, Butler J. Variablity of routine pulmonary function tests. Thorax 1975;30:548–552.
12. Guyatt AR, Alpers JH, Hill LD, Bramley AC. Variability of plethysmographic measurements of airways resistance in man. Journal of Applied Physiology 1967;22:383–389.
13. Carey GCR, Dawson TAJ, Merrett JD. Daily changes in ventilatory capacity in smokers and non-smokers. British Journal of Preventive and Social Medicine 1967;21:86–89.
14. Guberan, E Williams M.K, Smith MJ. Circadian variation of FFV1 in shift workers. British Journal of Industrial Medicine 1969;26:121–125.
15. Stebbings JH Jr. Chronic respiratory disease among non-smokers in Hagerstown, MD 2. Problems in the estimations of pulmonary function values in epidemiological surveys. Environmental Research 1971;4:163–192.
16. Lapp NL, Hankinson JL, Burgess DB, O'Brian R. Changes in ventilatory function in coal miners after a work shift. Archives of Environmental Health 1972;24:204–298.
17. Hankinson JL, Peterson MR. Data analysis for spirometry instrumentation standards. American Review of Respiratory Diseases 1977;115 (suppl):116.
18. MacDonald JB, Cole TJ. The flow-volume loop: reproducibility of air and helium-based tests in normal subjects, Thorax 1980;35:64–69,
19. Pennock BE, Rogers RM, McCaffree DR. Changes in measured spirometric indices: What is significant? Chest 1981;81:97–99.

20. Pham QT, Mur JM, Cavelier C, Meyer-Bisch C, Chan N, Huong ND, Indices fonctionnels respirations; variabilite valuers de reference et pouvoir discriminant. Bulletin Europeen de Physiopathologie Respiratorie 1981; 17: 949-961.

21. Rozas CJ, Allen L, Goldman AL. Daily spirometric veriability. Normal subjects and subjects with chronic bronchitis with and without airflow obstruction. Archives of Internal Medicine 1982; 14:2 1287 - 1291.

22. Groth S, Dirksen A, Dirksen, H, Rossing N. Intraindividual variation and effect of learning in lung function examinations. A population study. Bulletin Europeen de physiopathologie Respiratorie 1986; 32: 35 - 42.

23. Nickerson BG, Lemen RJ, Gerdes CB, Wegmann MJ, Robertson G. Within subject variability and percent change for significance of spirometry in normal subjects and in patients with cystic fibrosis. American Review of Respiratory Diseases 1980; 122:859 - 866.

24. Black LF, Offord K, Hyatt RE. Variability in the maximum expiratory flow volume curve in asymptomatic smokers and in nonsmokers. American Review of Respiratory Diseases 1974; 110: 228-292.

25. Fry DL, Hyatt RE. Pulmonary mechanics: a unified analysis of the relationship between pressure volume and gas flow in the lungs of normal and diseased human subjects. American Journal of Medicine 1960;29: 672 - 689.

26, Leuallen EC, Fowler WS. Maximal mid-expiratory flow. American Revew of Tuberculosis and Pulmonary Disease 1955; 72 783—800.

27. Clement J, Van de Woestijne KP. Variability of maximum expiratory flow curves and effor independency. Journal of Applied Physiology 1971; 31: 55-62