Original Research Paper

Volume-8 | Issue-8 | August-2018 | PRINT ISSN No 2249-555X

Physiology

PULMONARY FUNCTION TESTS AND EFFECT OF BRONCHODILATORS IN NATIVE HIGHLANDERS AND ACCLIMATIZED LOWLANDERS

Dr Surbhi Vashisht	MD, Asst Prof, Dept of Physiology, AFMC, Pune-40, India
Dr Deepak Vashisht*	MD, Asst Prof, Dept of Dermatology,Command Hospital,Pune-40, India*Corresponding Author
Dr Rajneesh Kumar Joshi	MD, Associate Prof, Dept of Community Medicine, AFMC, Pune-40, India

ABSTRACT

Background: Differences in dynamic lung function exist between native highlanders and acclimatized lowlanders. Present study was undertaken to compare ventilatory function in both these groups as also to assess and their response to bronchodilators.

Methods: The study was conducted on fifty healthy native highlanders (NHL) (age 25.96 + 5.67) yrs permanently living at high altitude and fifty acclimatized lowlanders (ALL) (age 28.52 + 5.85) yrs staying at high altitude for more than 12 weeks . Spirometry was performed before and after short acting bronchodilators and the results were analyzed.

Results: Baseline lung volumes were higher in NHL as compared to ALL indicating an inherited adaptive response to the hypoxic environment. There was no significant difference in baseline flow rates (PEFR, FEF25, FEF50, MMF and FEF75) between the two groups. Most measurements of pulmonary function assessed after bronchodilator administration were lower in ALL but the difference was statistically not significant.

KEYWORDS : Pulmonary function tests, Highlanders, Acclimatized lowlanders, bronchodilators

INTRODUCTION

High altitude is characterized by reduced barometric pressure, low air density, severe cold, low humidity and a hypoxic environment. Altitude affects the respiratory mechanics due to low air density and effect of hypoxia. 1, 2 .Physiological adaptation to high altitude amongst various ethnic groups has been studied earlier.3 High altitude natives have increased lung volumes accompanied by larger airways and improved lung mechanics. This together with reduced air density results in higher flow rates and better adaptation to the hypoxic environment.4 Increased ventilation at high altitude is a feature of adaptation of sojourners to high altitude, though this is not often seen in high altitude natives except for the Tibetans and Nepalese Sherpas.5,6 Spirometry is a versatile test to assess pulmonary physiology, normal values have been defined for different age-groups, gender, height and ethnicity. Flow volume loops are useful in assessing the flow as a function of volume during the Forced Vital Capacity (FVC) maneuver. The degree of bronchodilation can be assessed by measuring the changes in airway resistance or flow rates after bronchodilator administration. Maximal expiratory flow-volume (MEFV) and Partial expiratory flow-volume (PEFV) loops are practical and useful to evaluate bronchodilation and airway responsiveness. Bronchodilators especially the selective beta-2 agonists like salbutamol having a rapid onset of action are an important tool for assessing airway responsiveness.

Studies have demonstrated significantly higher lung volumes and greater effort independent airflow rates in native highlanders compared to acclimatized lowlanders. 7, 8. The present study was undertaken to compare the ventilatory function and assess the bronchodilator responsiveness in the native highlanders and compare it with the acclimatized lowlanders. To our knowledge this is the first study of its kind and further studies are required to objectively assess the bronchodilator responsiveness at high altitude.

Material and Methods

This study has been conducted at an altitude of 3450 m in the western part of Indian Himalayas. Fifty healthy native highlanders (NHL) permanently staying at high altitude and fifty healthy acclimatized lowlanders (ALL) who had stayed continuously at this altitude for a period of more than 12 weeks were enrolled for the study. Protocols were reviewed by the appropriate institutional review committees and written consent was obtained from all subjects. All subjects were interviewed and underwent thorough clinical examination to rule out any condition that could affect lung function. Anthropometric parameters including age, sex, height and weight were recorded. All tests were carried out on portable Spirometer (Spiro screenTM 2120, Gould Japan) and the equipment was calibrated daily using a standard 3-liter syringe.

All subjects performed the FVC maneuver conforming to the American thoracic society (ATS) criteria in the sitting position. Lung function tests (FVC, FEV1, MMF, PEFR and flow rates like FEF25, FEF50 and FEF75 were measured before and after salbutamol administration at BTPS. Subjects had rest of 15-20 mins before being subjected to the test.

The procedure was explained to subjects in the language they understood and then spirometry was carried out after 2-3 practice maneuvers. They first inhaled air till the total lung capacity (TLC) and then breathed out as fast and as forcibly as they could to residual volume (RV) and this maneuver was computed to trace the (MEFV) curve. Three such recordings were obtained with at least 5 minutes interval between the readings. The best of the three maneuvers recorded by each subject was included in this study. They repeated the same maneuver again fifteen minutes after the inhalation of 200µg salbutamol from a metered dose inhaler (Asthalin, 100µg/puff) under supervision. Subjects held the inhaler and activated it at the start of full inspiration from residual volume this was followed by a 10 sec breath hold at total lung capacity. All values were expressed as Mean+ SD. Statistical analysis was carried out using paired t-test to analyze the effect of the bronchodilator in the same group and unpaired t-test to compare values between the two groups. A p-value less than 0.05 was considered statistically significant.

Results

Physical characteristics and Baseline Lung Function Parameters- Table 1

	Age (yrs)	Height (cm)	Weight (Kg)	Mean FEV1	Mean FVC	Mean PEFR	Mean FEF25	Mean FEF50	Mean FEF75
NHL	25.96 + 5.67	165.90 + 5.15	62.85 + 5.76	3.52 + 0.54	4.19 + 0.57	8.93 + 1.28	7.66 + 1.77	4.61 + 1.92	1.71 + 0.53
ALL	29.24 + 7.18	171.45 + 4.94	65.98 + 6.98	3.22 + 0.29	3.69 + 0.38	8.87 + 1.03	7.57 + 1.54	4.32 + 1.88	1.52 + 0.54
P value				**0.0005**	**<0.0001**	0.7863	0.7825	0.4333	0.0674

There is a significant difference in values of FVC and FEV1 observed between the two groups. FVC in NHL was significantly higher [4.19(0.56) vs 3.69(0.38)] in the ALL (p<0.01). Similarly, FEV1 was also significantly higher in the NHL group 3.52(0.55) vs 3.22(0.29) (p<0.01) (Table1).

Effect on Lung volumes & Flow rates:: Post-inhalation values of PEFR, FEF 25, FEF 50, FEF 75 were higher in NHL as compared to ALL but the difference between the two groups is not statistically significant (p>0.05). Post-inhalation MMF was 3.45+ 0.94 L/sec and 3.12+0.89 L/sec in NHL and ALL respectively. Post inhalational value of FEF 25 is significantly more in the NHL group (<0.01) (Table 2). Other values are higher in the NHL but difference is not statistically significant (p>0.05) (Table 4).

The pattern of bronchodilator responsiveness: Post inhalational lung volumes were significantly higher in NHL as compared to ALL (<0.01) (Table 4) but there is no significant difference in the post inhalational flow rates. Magnitude of change in lung volumes and flow rates after bronchodilator administration was greater in the NHL group as compared to ALL group but the difference is not statistically significant. Bronchodilator responsiveness was lower in ALL than in NHL but this has not attained statistical significance as depicted in (Table 5).

Bronchodilator response in NHL (Table 2)

	Pre inhalation	**Post inhalation**	**p value**
Mean FVC (sd)	4.19+0.57	4.24+0.58	0.2531
Mean FEV1(sd)	3.52+0.55	3.55+0.56	0.3635
Mean PEFR (sd)	8.93 + 1.28	9.12 + 1.27	0.1278
Mean FEF25(sd)	7.66 + 1.77	8.04 + 1.46	**0.0145**
Mean FEF50(sd)	4.61 + 1.92	4.64 + 1.82	0.3201
Mean FEF75(sd)	1.71 + 0.53	1.79 + 0.63	0.3073
Mean MMF(sd)	3.26 + 0.96	3.35 + 0.94	0.2251

Bronchodilator response in ALL (Table 3)

	Pre inhalation	Post inhalation	p Value
Mean FVC (sd)	3.69+0.38	3.71+0.42	0.5927
Mean FEV1(sd)	3.22+0.29	3.23+0.33	0.6019
Mean PEFR (sd)	8.87 + 1.03	9.04 + 1.02	0.174
Mean FEF25(sd)	7.57 + 1.54	7.82 + 1.37	**0.0537**
Mean FEF50 (sd)	4.32 + 1.88	4.40 + 1.88	0.3122
Mean FEF75 (sd)	1.52 + 0.54	1.52+ 0.56	0.9763
Mean MMF(sd)	3.09 + 0.84	3.12 + 0.89	0.6288

Comparison of Post inhalation - Lung volumes and Flow rates (Table 4)

	NHL	**ALL**	**p Value**
FVC	4.24 + 0.58	3.71 + 0.42	**<0.0001**
FEV1	3.55 + 0.56	3.23 + 0.33	**0.0005**
Mean PEFR (sd)	9.12 + 1.27	9.04 + 1.02	0.7172
Mean FEF25 (sd)	8.04 + 1.46	7.82 +1.37	0.4424
MeanFEF50 (sd)	4.44 + 1.82	4.40 + 1.88	0.9162
MeanFEF75 (sd)	1.79 + 0.63	1.52 + 0.63	0.02
Mean MMF	3.45 + 0.94	3.12 + 0.89	0.8897

Table 5: Comparison of bronchodilator responsiveness

	NHL	**ALL**	**p value**
FVC (L)	47.17 (297.13)	21.57 (286.14)	0.6554
FEV1 (L)	29.81(236.73)	15.29 (208.04)	0.7402
PEFR (L/S)	0.19 (0.88)	0.17 (0.86)	0.9042
FEF25 (L/S)	0.37 (1.08)	0.25 (0.92)	0.537
FEF50 (L/S)	-0.17 (1.21)	0.09 (0.6)	0.179
FEF75 (L/S)	0.08 (0.58)	0.01 (0.28)	0.3646
MMF (L/S)	-0.12 (0.69)	0.03 (0.49)	0.2034

Though the bronchodilator responsiveness is more in the NHL group the difference has not attained statistical significance (p>0.05) and further studies are required to establish the same.

Discussion

Hypoxia at high altitude affects not only the static lung volumes but at the same time low air density decreases the airway resistance and reduces the dynamic work of breathing translating into better flow rates4. At the same time there are changes in bronchomotor tone on exposure to high altitude 9.

Resting bronchomotor tone in normal individuals is mediated by vagal motor activity 10, 11. There is dense parasympathetic innervation of the bronchial wall as compared to the sympathetic innervation which is relatively sparse and results obtained by beta-adrenergic receptor blockade with propranolol are conflicting.12

Salbutamol is a selective, rapidly acting beta- 2 agonist which results in relaxation of airway smooth muscle13. The advantage of using aerosols for drug delivery is the high local concentration of drug delivered to the small airways. The ATS/ ERS defines a positive bronchodilator response as an increase in FEV1 and/or FVC greater than or equal to 12% or 200 mL from baseline 14,15.

Modern Spiro metric equipment is computerized based on turbine principle to integrate the flow generated to describe the flow volume curves. FVC, FEV1, and FEF25–75 are commonly used parameters for assessing lung function16 and FEF50, FEF25–75 reflects small airway flow rates17.

In this study as expected all lung volumes are significantly higher in native highlanders and superior lung mechanics are an important adaptation to lifelong sustained increase in resting ventilation. Values of FVC and FEV1 observed in this study are higher than values reported by Wood et al in their study [FVC: 3.2 (0.29) and FEV1: 2.79(0.76)] in the age group of 58 + 17.3 yrs8. Our values are slightly lower than those reported by Apte et al. in their study in a similar age group. Both FVC and FEV1 were significantly higher in their study [FVC: 5.02 (0.51); FEV1: 4.27 (0.47)] 7.

Values observed in acclimatized lowlanders in age group (20-40 years) in our study were [FVC: 3.69 (0.38) and FEV1: 3.22 (0.29)] and are similar to values recorded by Kamat et al in their study [FVC: 3.61(0.51)] and [FEV1: 2.89 (0.52)] 18. Our results are also similar to those of Goyle et al.19 Flow rates at larger lung volumes (PEFR, FEF25, and FEF50) were similar in the two groups (p>0.05) (table 1). Flow rates in effort dependent portion of MEFV loop in ALL in our study are lower compared to values obtained by Apte et al. who had reported PEFR as 10.20 L/s and FEF25 as 8.57L/s in similar conditions7. This is also in variation to the results obtained by Apte et al. who had observed a significant increase in effort independent flow rates in NHL as compared to the ALL [FEF75: 2.23 (0.72) vs. 1.73(0.52) L/s; FEF75–85%: 1.54 (0.51) vs. 1.08 (0.35) L/s,] 7

Although inhaled bronchodilators are routinely used in clinical practice there are very few studies conducted on their effects in normal subjects 20. Earlier studies have confirmed that bronchodilation increases airway conductance even in normal subjects21. Thus, relaxation of airway smooth muscle appears to increase airway caliber when airflow rates and transmural pressure across airway wall is low22. During forced expiration, airway geometry alters markedly because of dynamic compression of the airways. Studies have shown that changes found in maximum flow are smaller than the changes in airway conductance22.

Maximum expiratory flow rate reflects changes in airway caliber due to alteration in bronchomotor tone and is affected by changes in lung recoil pressure and airway collapsibility22. No significant change in the maximum expiratory flow rate was observed in our study akin to other studies.23 This is due to two opposing factors. Firstly, there is an increase in airway caliber and conductance with bronchodilators which would increase the flow rates. At the same time, large airways become more compliant and collapse at lower transmural pressures thus limiting the maximum expiratory flow rates. Airway resistance is influenced by changes in larger airways whereas maximum expiratory airflow reflects changes in smaller airways.24

Furthermore, tests of maximum flow are usually preceded by full inspiration which itself may reduce the bronchomotor tone25. Changes in maximum expiratory flow after bronchodilators are maximum when forced expiration is started from low lung volumes22. This has been seen in earlier studies when larger changes were observed in PEFV curves than MEFV curves after bronchodilators were given to normal subjects22.

We assessed the response of short-acting bronchodilator salbutamol on lung volumes and flow rates in native highlanders and acclimatized low landers. Firstly all baseline lung volumes were higher in NHL as compared to ALL, indicating an inherited adaptive response to the hypoxic environment. Though there was no significant difference in the baseline flow rates (PEFR, FEF25, FEF50, MMF and FEF75) between the two groups. Most measurements of pulmonary function assessed after bronchodilator administration were significantly lower in acclimatized lowlanders than the native highlanders. The second notable difference between NHL and ALL was in bronchodilator responsiveness. Bronchodilator responsiveness was lower in the ALL than in NHL but this has not attained statistical significance. This study may help in assessment of bronchodilator responsiveness to short acting bronchodilators at high altitude and further studies are required to establish the same.

REFERENCES

1. Cruz JC. Mechanics of breathing at high altitude and sea level subjects. Respir Physiol 1973; 17:146-61.
2. Hackett PH, Reeves JT, Reeves CD, Grover RF, Reenie D. Control of breathing in Sherpas at low and high altitude. J ApplPhysiol 1980; 49: 374-9.
3. Beall CM. Tibetan and Andean patterns of adaptation to high-altitude hypoxia. Human Biology 2000; 72(1): 201-28.
4. Brody JS, Lahiri S, Simpser M, Motoyama EK, Velasquez T. Lung elasticity and airway dynamics in Peruvian natives to high altitude. J Appl Physiol1977; 42: 245-51.
5. Beall CM, Strohl KP, Blangero J, Blangero WS, Almasy LA, Decker MJ, Worthman CM, et al. Ventilation and hypoxic ventilatory response of Tibetan and Aymara high altitude natives. Am J Phys Anthropol 1997; 104: 424-47?
6. Havryk AP, Gilbert M, Burgess KR. Spirometry values in Himalayan high altitude residents (Sherpas). Respir Physiol Neurobiol 2002; 132(2): 223–232.
7. Apte CV, Rao KS. The maximum expiratory flow-volume loop in natives of Ladakh and acclimatized lowlanders. High Altitude Medicine & Biology 2005; 6(3):209-214.
8. Wood S, Norboo T, Lilly M, Yoneda K, and Eldridge M. Cardiopulmonary Function in High Altitude Residents of Ladakh. High Altitude Medicine & Biology2004; 4(4): 445-454.
9. Wilson CM, Bakewell SE, Miller MR, Hart ND, McMorrow RCN, Barry PW, Collier DJ, Watt SJ, A J Pollard AJ. Increased resting bronchial tone in normal subjects acclimatized to altitude. Thorax 2002; 57:400-404.
10. Barnes P J. Neural control of the human airways. Am Rev Respir Dis 1986; 134:1289-1314.
11. Widdicombe J G and Sterling G M. The autonomic nervous system and breathing. Archives of Internal Med 1970; 126:311-329.
12. Gayrard P, Orehek J, Grimaud C, Charpin J. Beta-adrenergic function in airways of healthy and asthmatic subjects. Thorax1975; 30: 657-662.
13. Paterson JW, Evans R, Prime FJ. Selectivity of bronchodilator action of salbutamol in asthmatic patients. British journal of diseases of the chest. 1971; 65:21-28.
14. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R,Coates A et al. Standardization of spirometry. update. Eur Respir J 2005; 26(2):319-38.
15. Pellegrino R,Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R et al. Interpretative strategies for lung function tests. Eur Respir J 2005; 26(5):948-68.
16. Dikshit MB, Raje S, Agrawal M J. Lung functions with Spirometry : An Indian Perspective-II: on the Vital Capacity of Indians. Indian J Physiol Pharmacol 2005; 49 (3): 257–270.
17. McFadden E R, Linden D A. A reduction in maximum mid-expiratory flow rate. A spirographic manifestation of small airway disease. Am J Med1972; 52: 725-737
18. Kamat SR, Tyagi NK, Rashid SS. Lung function in Indian adult subjects. Lung India 1982; 1:11–21.
19. Goyle B R, Venkataraman C, Rastogi S K, Lakhera S C, Gautam R K. Normal standards and prediction of lung function tests in Indian Armed Forces Personnel. Med J Armed Forces India 1984; 40: 151-156.
20. Lehmann S, Bakke PS, Edie GE, Humerfelt S, Gulsvik A. Bronchodilator reversibility testing in an adult general population; the importance of smoking and anthropometrical variables on the response to a beta2-agonist. Pulm Pharmacol Ther 2006; 19(4):272–280.
21. Skinner C, Palmer KNV. Changes in specific airways conductance and forced expiratory volume in one second after a bronchodilator in normal subjects and patients with airway obstruction. Thorax 1974; 29(5): 574-577.
22. Bouhuys A, Van DeWoestijne KP. Mechanical consequences of airway smooth muscle relaxation. J ApplPhysiol 1971; 30: 670 - 676.
23. Tattersfield AE, Leaver DG, Pride NB. Effects of beta-adrenergic blockade and stimulation on normal human airways. J ApplPhysiol 1973; 35: 613-619.
24. McFadden E R, Howes N J, Pride NB. The acute effects of inhaled isoproterenol on the mechanical characteristics of lungs in normal man. J Clin Invest 1970; 49: 779-790.
25. Nadel JA, Tierney DF. Effect of a previous deep inspiration on airway resistance in man. JApplPhysiol 1961; 16: 717-719.