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Effect of Altitude and Duration of Stay on Pulmonary Function in Healthy Indian Males

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ABSTRACT

The study was carried out with the objective to investigate the effect of varying altitude and duration of exposure on blood pressure, heart rate and lung function parameters in healthy Indian soldiers after adopting proper acclimatization schedule. For this purpose 17 soldier of Indian Army, weight and height matched, were studied after obtaining written consent. Recording of blood pressure (systolic and diastolic), heart rate, AMS, SpO_2 and lung function variables (FVC, FEV1, FEV1/FVC %, MVV, FEF25-75 %, MEF 25 %, MEF 50 %, MEF 75 %, PEF) were done at basal (290 m), 800 m, 3200 m (day 10 and day 20) and upon de-induction. Our results demonstrate that with increasing altitude FVC declined, FEV1 did not change and due to these changes FEV1/FVC per cent increased. Expiratory flow rates including MEF 25 %, MEF 50 %, MEF 75 %, PEF and mean expiratory flow rate (FEF 25-75 %) increased upon induction to high altitude. This increase may be due to reduction in air density causing less air resistance which accelerates lung emptying. Though the increase upon induction in all the values was transient and returned to baseline values after de-induction. MVV reflecting respiratory muscle function increased significantly upon induction to altitude in our study and returned to basal values upon de-induction. Understanding respiratory system in mountainous regions and its further correlation with other systems pertaining to acclimatisation could help in laying step in unveiling mechanism of human high altitude adaptation.

Keywords: High altitude; Pulmonary function; Forced vital capacity; Maximum voluntary ventilation

1. INTRODUCTION

A number of individuals travel to high altitude terrains either for work or for recreational activities[1,2]. Mountain climate is a unique challenge to human body due to reduction in barometric pressure which in-turn leads to decrease in oxygen per breath. Reduced breathable oxygen causes low blood and tissue oxygen saturation[3-5]. A number of compensatory responses occur in the body that enable humans to tolerate this reduced oxygen availability, which comes under acclimatisation process. Increase in heart rate and ventilation is an important feature of high altitude acclimatisation. Lung plays an indispensable role in this process and is one of the primary organs in the series of physiological response. Role of lung in altitude exposure came to light in 1893, where changes in lung volume and ventilation were discussed[6]. Respiratory system is variably affected at high altitude and plays a significant role during high altitude hypoxia. To measure changes in lung function; spirometry is known to be the most common and widely employed test[7,8]. It is used to measure timed inspired and expired volumes and is most common of pulmonary function tests. Forced vital capacity (FVC) has been shown to decrease, both at high altitude and using simulated high altitude conditions. A few airflow parameters have been shown to improve upon high altitude exposure, which may be due to reduction in air density[9]. There have been contradicting studies in the trend of forced expiratory volume in 1 s (FEV1) and maximum voluntary ventilation (MVV) upon high altitude exposure[1].

Effect of altitude and duration of exposure on lung function variables on healthy male volunteers with the purpose of understanding respiratory function in mountainous regions has been investigated.

2. MATERIAL AND METHODS

2.1 Study Volunteers and Protocol

Initially 20 healthy male of the age group 21-30 years, height 1.73 m ±0.07 m and weight 66.72 kg ±1.4 kg of Indian Army were selected randomly for the study. The volunteers conformed to the procedure and an informed written consent was obtained from each of them after explaining detailed protocol of study. All the volunteers were non-smokers and non-alcoholic and were not exposed to high altitude environment previously. No previous history of respiratory disorder was there in any of the volunteer. During the study three volunteers were excluded due to mild cough and data were not considered for analysis. The study procedure was approved by Defence Institute of

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Physiology and Allied Sciences, Delhi, Ethical Committee and were carried out in strict compliance with the approved guidelines. The baseline studies were carried out initially at Delhi (~290 m, B), thereafter all the volunteers were flown to Bishkek, Kyrgyzstan (~800 m, A1). All variables were studied after 3 days of stay at 800 m. This was followed by induction to an altitude of 3200 m (Tuya Ashu Pass, Kyrgyzstan, A2) by a road journey and variables were recorded there at day 10 (A2-D10) and day 20 (A2-D20) of high altitude exposure. All the volunteers were provided with proper winter clothing and got involved in mild indoor activities with room temperature at 22 $^oC \pm 2$ ^oC. After induction to altitude, proper acclimatisation schedule was followed before starting any measurements. Thereafter all the volunteers were de-induced to 800 m (DI-A1) by road and to 290 m (DI-B) by air. All the variables were again repeated after 3 days of de-induction. All measurements were performed at approximately similar time during each test day and by the same instructor.

2. ACUTE MOUNTAIN SICKNESS

Lake Louise Score system was used to assess acute mountain sickness (AMS) which is based on presence of following symptoms: headache, dizziness, gastrointestinal distress (loss of appetite, nausea, or vomiting), fatigue and insomnia. Each item was scored on a scale between 0 and 3 by the volunteers (0 = none, 1 = mild, 2 = moderate, 3 = severe).

3. BLOOD PRESSURE AND HEART RATE MEASUREMENT

Systolic and diastolic blood pressure along with heart rate was measured in volunteers using mercury free BP instrument (OMRON®, USA). Measurements were taken in supine position after volunteers were rested for at least 15 min. Blood pressure (BP) and heart rate (HR) were taken at similar time at each time point during the study.

4. BODY WEIGHT AND HEIGHT MEASUREMENT

Body weight was measured in the morning before breakfast after voiding using electronic balance (Deca 770, Seca Corporation, USA). Body weight was taken at similar time at each time point during the study. For height measurement, a calibrated height rod was used (Medical Scale and Measuring System, Birmingham, UK) and proper instructions were given before recording.

5. ARTERIAL OXYGEN SATURATION MEASUREMENT

Saturation of peripheral oxygen (SpO_2) was measured using finger pulse oximeter (Nonin Medical Inc. USA).

6. LUNG FUNCTION TESTS

Portable Spirometer (Pony FX, COSMED, Italy) was used for measuring forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FEV1/FVC ratio, average mid expiratory flow (FEF 25 % - 75 %), maximal expiratory flow rate when 25 per cent of FVC remains to be exhaled (MEF 25 %), maximal expiratory flow rate when 75 per cent of FVC remains to be exhaled (MEF 75 %), peak expiratory flow (PEF) and maximum voluntary ventilation (MVV). The test was performed at least two hours after a meal. Instructions were clearly explained to each volunteer and were made to rest for minimum 15 m before starting the procedure. All measurements were done in standing position with nose clip. Total of three manoeuvres were obtained of which minimum two meet repeatability criteria (<0.15 L variability for FVC and FEV1). A good seal around mouthpiece, no obstruction to the mouthpiece, no glottis closure, no premature termination and wearing nose clips were ensured during each effort.

7. STATISTICAL ANALYSIS

Data were represented as Mean ± SEM. The data were analysed using Prism 5 software (Graph Pad Prism 6, USA). To compare the changes in same group in different phases, data was analysed using one way analysis of variance (ANOVA) with repeated measure and Post hoc testing with Bonferroni multiple comparison test. P value <0.05 was considered significant.

8. RESULTS

Systolic blood pressure increased significantly ($p<0.01$) upon HA induction at day 10 (122 mm Hg ± 1.71 mm Hg) and day 20 (120 mm Hg ±2.05 mm Hg) compared to basal (117 mm Hg ±1.72 mm Hg) and 800 m (117 mm Hg ± 1.85 mm Hg). Similarly, diastolic blood pressure increased significantly ($p<0.001$) upon HA induction at day 10 (76 mm Hg ±1.41 mm Hg) and day 20 (72 mm Hg ±1.63 mm Hg) compared to basal (66 mm Hg ±1.41 mm Hg) and 800 m (66 mm Hg ±1.52 mm Hg). Both systolic and diastolic BP returned to normal after de-induction. HR increased significantly ($p<0.05$) upon HA exposure at day 10 (68 beats/min ±1.75 beats/min) compared to basal (63 beats/min ±1.73 beats/min) and 800 m (64 beats/min ±1.81 beats/min) and returned to similar values as basal upon de-induction (64 beats/min ±1.7 beats/min). SpO_2 decreased significantly upon high altitude inductionand restored upon de-induction as shown in Fig. 1. Additionally, the AMS score based had all values less than 2 for all the volunteers.

FVC decreased upon HA induction to day 10 (4.72 litres ± 0.18 litres) compared to basal (4.81 litres ± 0.18 litres) and returned to basal values upon de-induction. FEV1/FVC ratio increased at day 10 (80.29 % ±1.42 %) of exposure compared to basal (79 % ± 1.34 %). FEF25-75 per cent increased upon day 10 (3.92 L/s ± 0.25 L/s) and day 20(4.23 L/s ± 0.42 L/s) of induction to mountain compared to basal (3.57 L/s ± 0.24 L/s) and 800 m (3.68 L/s ± 0.21 L/s) and returned to basal values upon de-induction. MVV values increased upon induction to high altitude by 16.8 per cent and 18 per cent at day 10 and 20 respectively compared to basal and returned to basal three days after de-induction as shown in Fig. 2.

MEF 25 % increased upon HA induction with significant increase at day 20 (1.86 L/s ± 0.15L/s) compared to basal (1.68 L/s ± 0.12 L/s). MEF 50 per cent increased significantly upon induction to day 10 (4.84 L/s ± 0.36 L/s) and day 20 (4.96 L/s ± 0.37 L/s) of HA compared to basal (4.50 L/s ± 0.32 L/s)and 800m (4.60 L/s ± 0.32 L/s) and returned to basal values upon de-induction. MEF75 per cent increased significantly upon

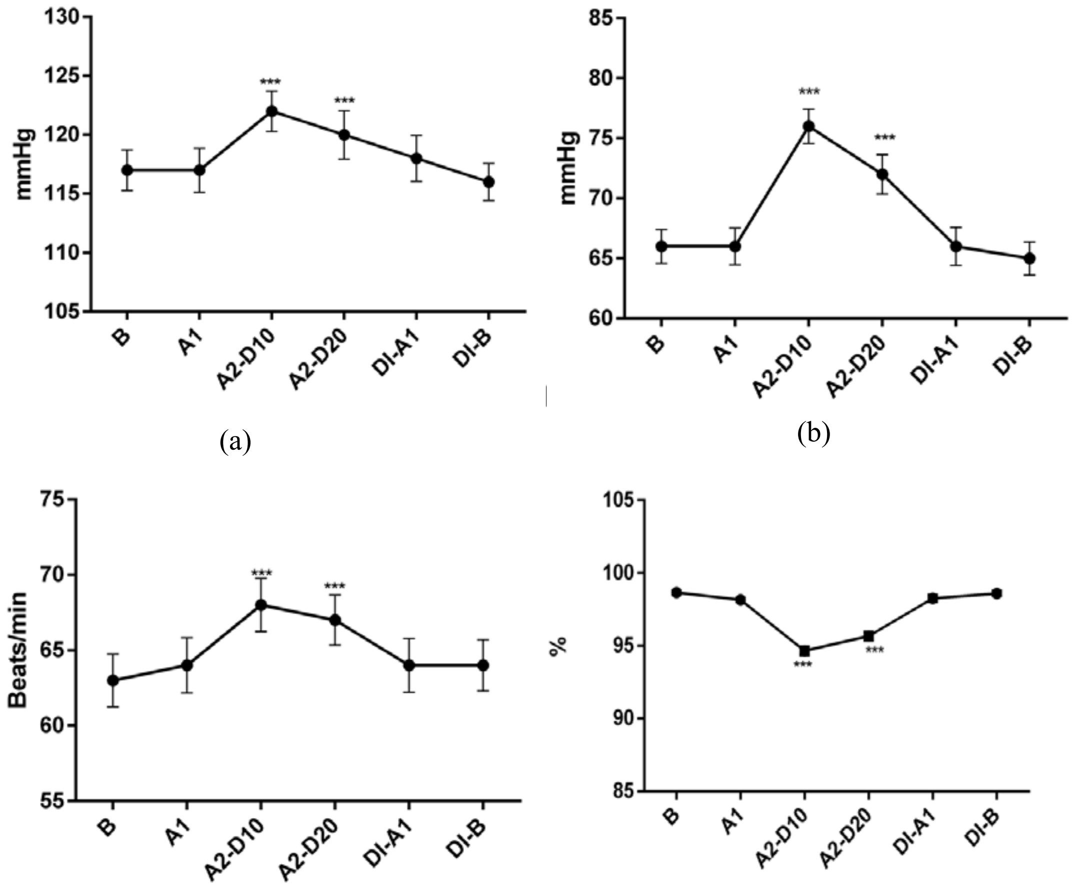

Figure 1. Changes in (a) Systolic blood pressure, (b) Diastolic blood pressure, (c) heart rate, (d) SpO_2 at different time points in Indian volunteers. Values are mean ± SEM and *** = p≤ 0.001 as compared to basal.

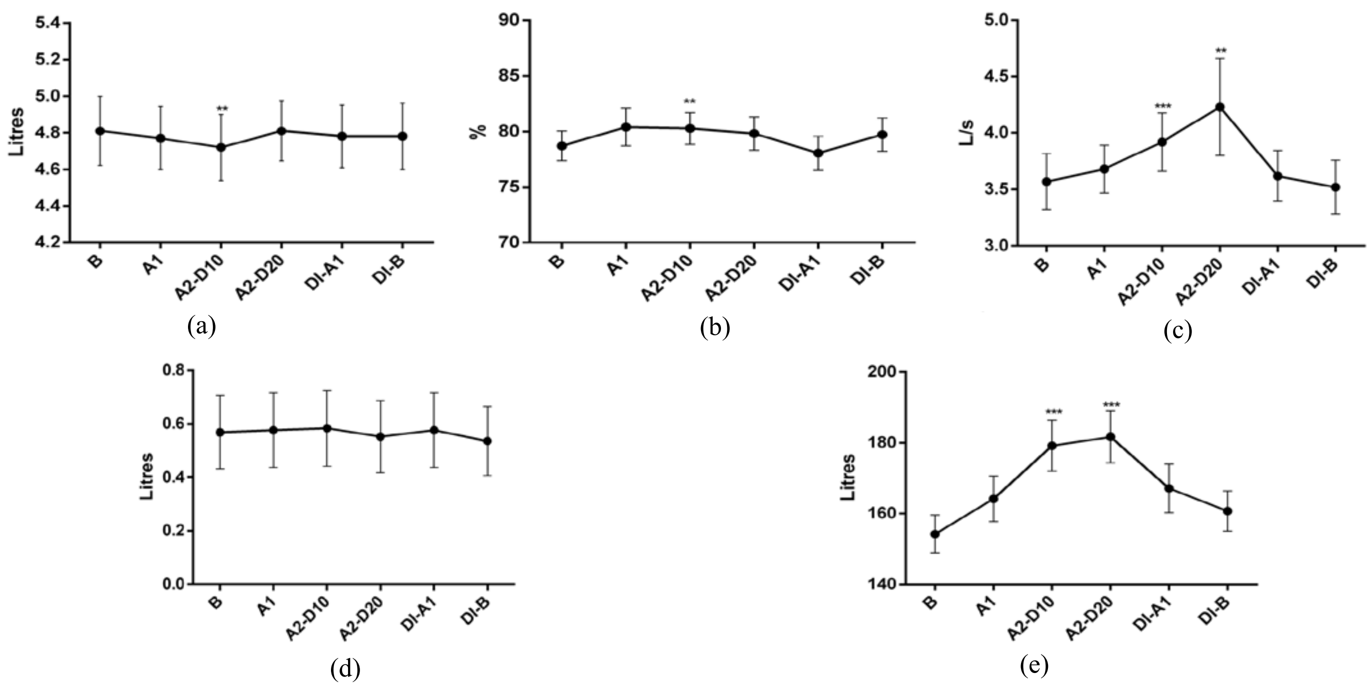

Figure 2. Changes in (a) FVC, (b) FEV1/FVC, (c) FEF 25-75%, (d) FEV1, (e) MVV at different time points in Indian volunteers. Values are mean ± SEM and ** = p≤0.01 and *** = p≤ 0.001 as compared to basal.

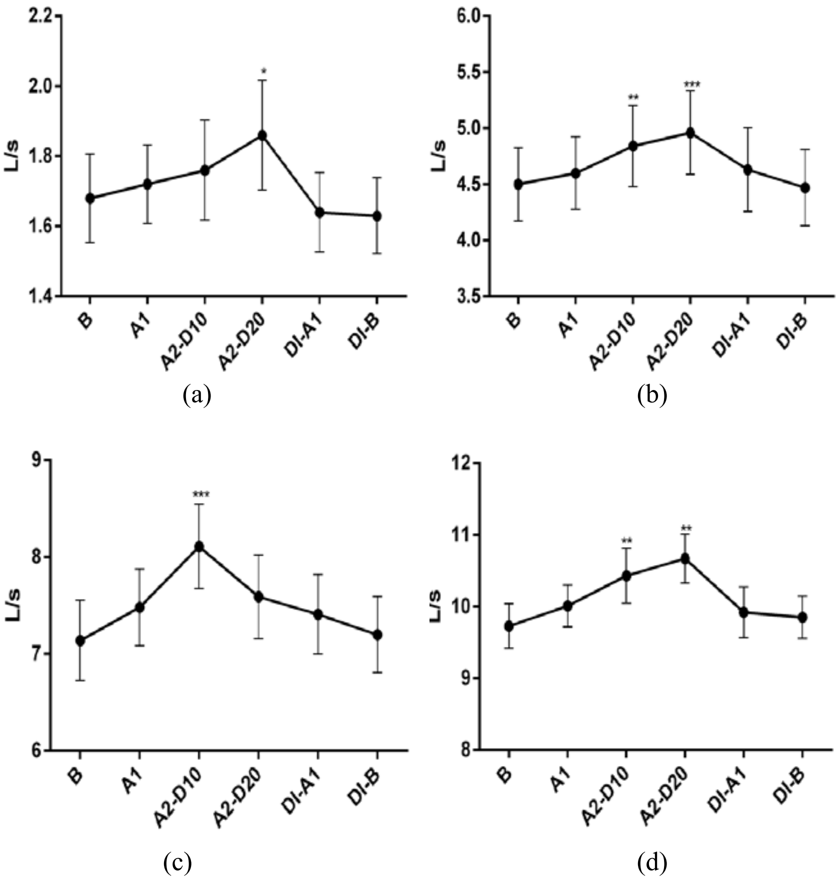

Figure 3. Changes in (a) MEF 25 %, (b) MEF 50 %, (c) MEF 75 %, (d) PEF at different time points in Indian volunteers. Values are mean ± SEM and * = p≤0.05, ** = p≤0.01 and *** = p≤ 0.001 as compared to basal.

day 10 (8.11 L/s ± 0.43 L/s) of exposure to HA compared to basal (7.14 L/s ± 0.41 L/s) and 800 m (7.48 L/s ± 0.4 L/s) and returned to baseline upon de-induction. Peak expiratory flow too increased at day 10 (10.43 L/s ± 0.38 L/s) and 21 (10.67 L/s ±0.34 L/s) and returned to baseline upon de-induction (9.85 L/s ± 0.3 L/s) as shown in Figs. 3 (b) - 3(d).

9. DISCUSSION

In the present study we have reported changes in BP, HR, FVC, FEV1, FVC/FEV1, FEF 25 % -75 %, MEF 25 %, MEF 50 %, MEF 75 %, MVV and peak expiratory flow in lowlanders at basal and at different altitude durations of high altitude stay. This is one of the few studies where measurements of variables in Indian soldiers are done in a different geographical region at different altitudes. These kinds of studies could be helpful for understanding respiratory function in the soldiers who are posted or visit different altitudes for various purposes. Pulmonary function tests (PFTs) include spirometry which measures the function of lung and is an important respiratory function parameter. It measures emptying and filling of lungs during a slow or forceful manoeuvre and also tests respiratory muscle strength[1,7]. It generates pneumotachographs from volume and flow of inspired and expired air. FVC is the maximum amount of air which can be inspired or expired during a maximal effort. FEV1 is the volume which expired by the person in one second after a maximal inspiration. FEV1 reflects both small and larger airway function[10] and did not change much upon altitude induction[11], which is also reflected in our study. FEV1/FVC ratio gives an index for airflow limitation[8]. Low FEV1/FVC ratio indicate an obstructive abnormality like in case of asthma or emphysema. Higher or normal FEV1/FVC ratio with lower FVC indicates restrictive ventilation abnormality like in respiratory muscle weakness, interstitial lung disease[7,8]. In the past, studies (both field and simulated) have shown to decrease FVC in high altitude regions of Nepal and Alps[12]. At 4559 m a decrease has been found in FVC in both normal and HAPE patients as compared to basal[13]. Acute mountain sickness has been known to decrease FEV1, FEF25 per cent -75 per cent and FVC upon high altitude exposure[14]. A number of studies have shown that high altitude environment reduces FVC, FEV1 and MVV, but there have been contradictions too[6,9,11,12,15-17]. FVC and FEV1 at an altitude of 3110 m did not change upon initial exposure and declined upon further exposure to 3445 m and 4177 m[1]. In our study we have found a decrease in FVC upon HA exposure with significant decrease at day 10 and returned almost normal upon de-induction which may be due to early closure of airways. FEV1/FVC increased significantly upon day10 of HA induction as compared to basal, but no change when compared to 800 m. This increase in the FEV1/FVC ratio is due to no change in FEV1 upon high altitude and fall in FVC. FEF25 per cent - 75 per cent is the mid maximal expired air flow and is measure of small airway function and in our study its value increased upon HA induction and returning to normal after de-induction. Forced expiratory flow values have increased upon high altitude exposure in our study probably due to reduced airway resistance. If FEV1/FVC ratio is less than 5th percentile of predicted value in the volunteer, then it's a possible marker of a ventilatory obstructive effect. In our study none of the case was found within this criterion. MEF 25 per cent is the flow rate when 25 per cent of FVC is remaining in the lungs and is an indicator of small airway function. MEF 75 per cent is the flow rate when 75 per cent of FVC is remaining and it reflects fairly large to medium size bronchi condition[10]. MEF 50 per cent is the flow rate when half of FVC is remaining and is indicative of small to medium airway function[10,18]. Wolf[19], *et al*. reported MEF 50 per cent and MEF 75 per cent increased with increasing altitude of 1580 m as compared to 171 m with a mean 11 per cent and 15 per cent rise respectively[19]. Similar results are reflected in our study upon altitude induction. MEF 25 per cent shows decrease upon initial exposure to high altitude and increased upon further stay at 3500 m[12]. This increase may be due to reduction in air density causing less air resistance which accelerates lung emptying[15]. In the present study no significant change in MEF 25 per cent was observed at day 10 of induction, though value increased upon HA induction to day 20 and returned to normal upon de-induction. This increase at day 20 may be due to respiratory adaptation pertaining to greater duration of stay at high altitude. PEF is the maximal expiratory flow rate in a forced manoeuvre[18,20]. PEF has been reported to be consistently improved at 2800 m, 4267 m, and 5300 m compared to basal[16,21,22]. At a similar altitude (3200), PEF is known to linearly increase[12] which is also reflected in our study. MVV is also called as maximum breathing capacity and is generally measured for 12 s to 15 s to evaluate respiratory muscle endurance. It correlates to FEV1 multiplied by 35 and can be used if the person is not comfortable in performing MVV test oxygen cost of breathing at high altitude is 26 per cent of maximal oxygen capacity, which is only 5.5 per cent at basal[23]. This means that work of breathing increases at high altitude which also affects respiratory muscles and it's a marker of respiratory muscle endurance. There has been contradicting studies in MVV upon high altitude exposure. While few field and hypobaric hypoxia chamber studies have found an improved MVV[24-27], some have reported a decrement in its value[1,11]. In our present study we found increased maximum voluntary ventilation which may be due to us following of proper acclimatization in the volunteers and taking the first measurement after 10 days at altitude. Consequences of high altitude on lung and spirometry variables in human soldiers in different altitude regions are essential and interesting area of research and can be correlated further with other important acclimatisation parameters.

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She has contributed towards planning and coordination of study and in reviewing and drafting of the manuscript.