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ORIGINAL ARTICLE

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Metabolic responses during initial days of altitude acclimatization in the Eastern Himalayas

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Abstract The study was carried out on 16 men (aged 20–30 years) to evaluate daily metabolic responses during the early phase of altitude acclimatization at moderate altitudes between 3100 and 4200 m in the Eastern Himalayas. Resting (R) and submaximal exercise (E) oxygen consumption ($\dot{V}O_2$) at 100 W at sea level (SL) were 3.25 (SEM 0.15) and 20.31 (SEM 0.77) ml/kg per min respectively. On day 1 at 3110 m both R and E $\dot{V}O_2$ decreased ($P<0.001$) and subsequently remained constant. At 3445 m these values tended to increase over the 3110 m values but were lower than the SL values. At 4177 m the decline in $\dot{V}O_2$ was significantly greater ($P<0.01$) than at the preceding altitudes. Pulmonary ventilation ($\dot{V}E$) increased consistently ($P<0.001$) with increase in altitude. The arterial oxygen saturation (S_aO_2) at different altitudes was lower ($P<0.001$) than SL values. The cardiac frequency (f_C) at R and E was higher ($P<0.001$) at altitude; the values at 3110 and 3445 m were significantly lower ($P<0.001$) than at 4177 m. Blood pressure (BP) increased ($P<0.001$) on the first day at each altitude. The systolic BP tended to decline towards SL values but the diastolic BP remained high ($P<0.001$) throughout. The resting blood lactic acid concentration, $[la^-]_{bl}$, showed a decline ($P<0.001$) only at 4177 m. The $[la^-]_{bl}$ at E was similar at 3110 and 3445 m but was higher ($P<0.01$) at 4177 m. These observations suggest that acclimatization to a mid-altitude of 3445 m can be safely avoided where rapid ascent to higher altitude is required.

Key words High altitude · Acclimatization · Metabolic changes

Introduction

Several physiological functions have been shown to be involved in the process of acclimatization of man to high altitudes (HA). The acute responses include hyperventilation, improvements in haemodynamic function, O_2 transport and its delivery and utilization (Ward et al. 1989; Monge and Leon-Velarde 1991). Ascent to HA is made either by road or by air; since air ascent is more rapid and acute, the changes in physiological functions are very prominent. Most of the studies on metabolic responses at HA have been done on air ascent, and no attempts at measurement have been made during the gradual ascent by road to HA (Malhotra et al. 1976; Mathew et al. 1977; Sengupta et al. 1978; Selvamurthy 1988; Wolfel et al. 1991; Reeves et al. 1993). Likewise, studies on exercise responses at HA have been performed several days after arrival, but daily resting and exercise responses have not been monitored from the first day of the sojourn at different altitudes (Klausen et al. 1966; Sengupta and Goyle 1980; Wolfel et al. 1991; Reeves et al. 1993).

There is also a paucity of information on metabolic responses in men transported by road at altitudes ranging from 3100 to 4200 m. However, recent studies by Banderet and Burse (1991) have recommended an initial slow ascent up to 3000 m followed by a gradual climb of 500 m allowing 1–2 days to acclimatize at each altitude before undertaking a trek at extreme altitude. The present study was carried out to evaluate the daily metabolic responses at rest and during exercise in men transported by road during the early phase of acclimatization at altitudes of 3110, 3445 and 4177 m in the Eastern Himalayas. The hypothesis to be tested is whether a mid-altitude (3445 m) acclimatization is required, as suggested by Banderet and Burse (1991).

Methods

Subjects

Sixteen healthy men with mean age of 25.1 (SEM 0.87) years, height 171.5 (SEM 1.14) cm, body weight 62.1 (SEM 1.90) kg and body surface area 1.70 (SEM 0.03) m^2 volunteered to participate in the study. The subjects had no previous experience of ex-

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posure to simulated or natural hypoxic stress. All the subjects were briefed about the experimental procedure. The study protocol was approved by the Institute's Ethical Committee. Each subject signed an informed consent statement prior to participation and could withdraw without prejudice at anytime.

Protocol

The studies at sea level (SL) were performed during two consecutive days at Meerut (220 m) where the laboratory temperature was maintained between 18 and 20° C. These subjects were taken to HA in the Eastern Himalayas by road and were re-evaluated daily during 4 days at 3110 m, 2 days at 3445 m and 4 days at 4177 m. The gradual ascent from SL to 3110 m was completed in 36 h, from 3110 to 3445 m in 2 h and from 3445 to 4177 m in 4 h respectively. During their stay at HA, the subjects were confined to their dwellings and did not undergo any physical exertion. At HA, the various parameters were monitored every day in a make-shift laboratory where the temperature was maintained between 17 and 20° C.

Physiological variables

All subjects reported to the laboratory at 0800 hours and rested in a supine position for about 30 min before the physiological measurements were made. The cardiac frequency (f_c in beats/min) from the standard configuration of limb lead ECG and blood pressure (BP in mm Hg) using the oscillometric method, were monitored on a multiparameter recorder (Propaq 102, Protocol Systems, USA). The arterial oxygen saturation (S_aO_2) was measured by otpical plethysmography and spectrophotometric techniques using a pulse oximeter model N-10 (Nellcor, USA). Resting oxygen consumption (lVO_2) was determined while the subjects were seated quietly on the cycle ergometer and expired gas samples were collected for 4 min for subsequent analyses. Both at SL and at HA each subject exercised for 10 min at a submaximal intensity of 100 W on a cycle ergometer (model SK 4000, Speigel Keller Co., Germany). However at HA, cycle ergometry was terminated when the f_c reached 180 beats/min or due to fatigue whichever ensued earlier.

Gas samples were collected every minute throughout the exercise bout or before the cessation of exercise due to fatigue. Resting (R) and submaximal exercise (E) lVO_2 was measured using a Servomex O_2 analyzer (Taylor Instrument, Rochester, NY, USA) and expired CO_2 by Capnograph mark III (Gould Medical BV, The Netherlands). Pulmonary ventilation (lV_E) was monitored using a Koffrani-Michaelis respiration gasometer (Max Planck Institute, Dortmund, Germany). Blood lactic acid concentration, ($[la^-]_{bl}$ in mmol/l) was measured using a YSI model 23L lactate analyzer (Yellow Spring Instrument Co., Ohio, USA). Capillary blood by finger prick was obtained for determination of $[la^-]_{bl}$ in R and 2 min after the termination of submaximal exercise on day 2 of arrival at each altitude. All the equipment was calibrated at each altitude before performing any test.

Statistics

Statistical analysis of the data was performed by analysis of variance using the Newman-Keuls multiple range test. If the F-value was significant a paired t – test was applied for inter-group comparison.

Results

Cardiac frequency

The resting f_c increased on day 1 of arrival at 3110 m ($P<0.001$) (Fig. 1). There was a slight decline ($P>0.05$) of the succeeding values compared to day 2 but the value remained higher ($P<0.01$) than the SL values up to day 4. The submaximal exercise caused a significant increase in f_c in all subjects at all three altitudes. However at 3110, 3445 and 4177 m, the increase in exercise f_c above resting f_c (Δf_c) was significantly higher than the SL values but there were no significant differences ($P>0.05$) between them.

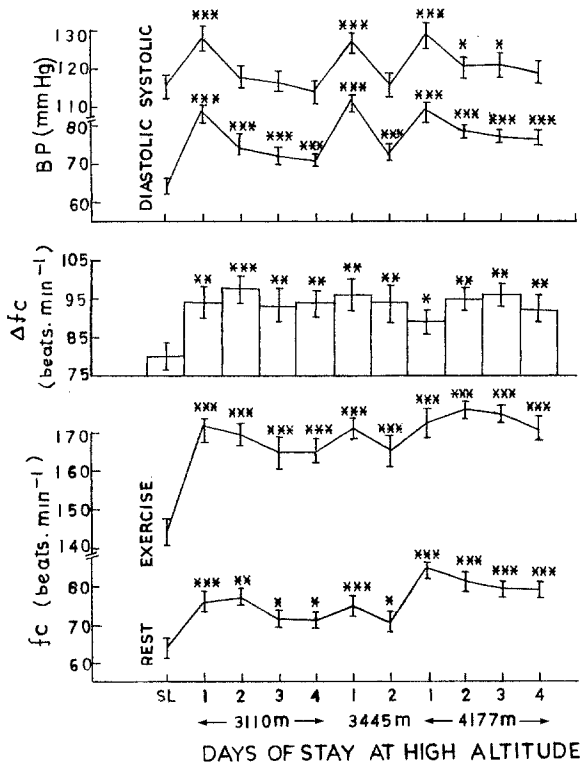

Fig. 1 Resting diastolic and systolic blood pressure (BP), heart rate (f_c), exercise f_c and exercise-rest f_c (Δf_c) at sea level (SL) and on different days of acclimatization at 3110, 3445 and 4177 m. Significances vs SL values: *** $P<0.001$, ** $P<0.01$, * $P<0.05$

Blood pressure

Both diastolic and systolic BP showed a significant increase ($P<0.001$) on arrival at 3110 m (Fig. 1). The diastolic BP decreased ($P<0.001$) on day 2 of the stay at 3110 m but was maintained at values higher than at SL during the entire period of stay at this altitude ($P<0.001$). The systolic BP returned to SL values on day 2. On day 1 at 3445 m, both diastolic and systolic BP again showed a significant ($P<0.001$) increase over the preceding values and a similar pattern of ensuing response to the previous high altitude. The BP response at 4177 m was also comparable to the other two HA locations.

Pulmonary ventilation

R lV_E increased on arrival at 3110 m ($P<0.001$); (Fig. 2). E lV_E also showed a significant increase ($P<0.001$) over the

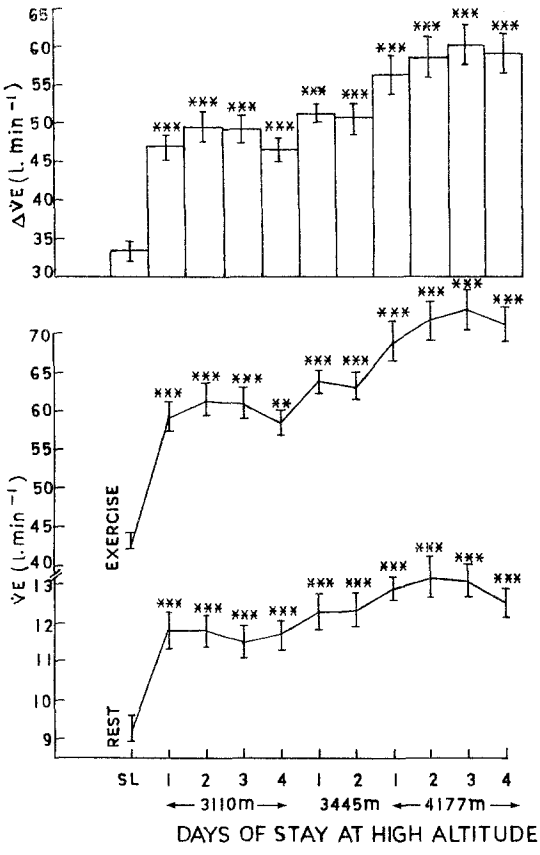

Fig. 2 Pulmonary ventilation (IV_E) at rest, during submaximal exercise and exercise-rest IV_E (ΔIV_E) at SL and on different days of acclimatization at 3110, 3445 and 4177 m. Significances vs SL: *** $P<0.001$, ** $P<0.01$, * $P<0.05$

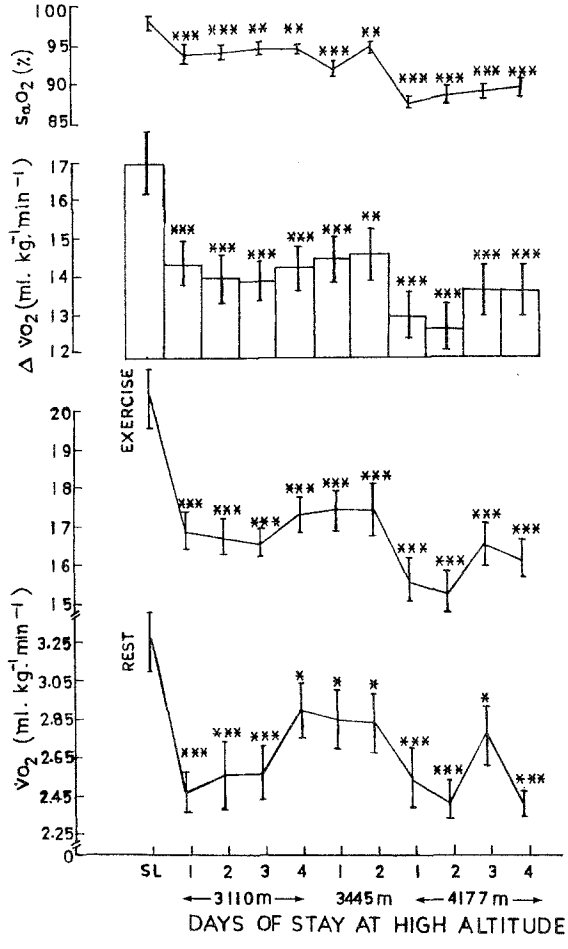

Fig. 3 Arterial oxygen saturation (S_aO_2), oxygen consumption (IVO_2) at rest, submaximal exercise IVO_2 and exercise-rest IVO_2 (ΔIVO_2) at SL and on different days of acclimatization at 3110, 3445 and 4177 m. Significances vs SL: *** $P<0.001$, ** $P<0.01$, * $P<0.05$

SL values from day 1 to 3 at 3110 m. A similar increase was also noted at 3445 m. R and E IV_E at 4177 m showed a significant increase ($P<0.05$) over those at the preceding altitudes and continued to rise up to day 3 but tended to decline subsequently. The ΔIV_E at all the altitudes was higher ($P<0.001$) than at SL. The ΔIV_E on different days of the stay was not significantly different ($P>0.05$) between 3110 and 3445 m but was higher at 4177 m ($P<0.001$).

Oxygen consumption

The R and E values of IVO_2 showed a significant decrease ($P<0.001$) on day 1 at 3110 m and remained at a lower level until day 3 of the stay at this altitude (Fig. 3). On arrival at 3445 m both R and E IVO_2 did not show any significant decline ($P>0.05$) compared to the values on day 4 of the stay at 3110 m. At 4177 m, R and E IVO_2 decreased significantly ($P<0.01$) from the values at 3445 m and remained at a lower level. Similarly to E IVO_2, ΔIVO_2 was significantly lower ($P<0.001$) at all altitudes studied. The ΔIVO_2 on different days of the stay at 3110 and 3445 m was not significantly different. The ΔIVO_2 on day 1 and 2 of the stay at 4177 m was significantly lower ($P<0.01$) than the preceding altitude values and tended to increase subsequently.

Arterial oxygen saturation

The S_aO_2 at SL declined ($P<0.001$) from mean SL values of 97.8% (SEM 0.25) to 94.6% (SEM 0.45) on day 1 of arrival at 3110 m, remained low until day 4 of the stay ($P<0.001$) at 3110 m, and showed a greater fall at higher altitudes (Fig. 3). The S_aO_2 showed a gradual increase with increase in the duration of the stay at 4177 m but was still maintained at lower levels compared to SL or the values at 3110 and 3445 m ($P<0.001$).

Lactic acid

The resting $[la^-]_{bl}$ on arrival at 3110 and 3445 m was not significantly different ($P>0.05$) compared to the SL values but was found to have decreased ($P<0.01$) on day 2 at 4177 m (Fig. 4). At 3110 and 3445 m, the exercise-induced increase in $[la^-]_{bl}$ and $\Delta[la^-]_{bl}$, although not significantly different from each other, was significantly higher ($P<0.001$) than the SL values. At 4177 m the exercise-induced increase in $[la^-]_{bl}$ and $\Delta[la^-]_{bl}$ were significantly

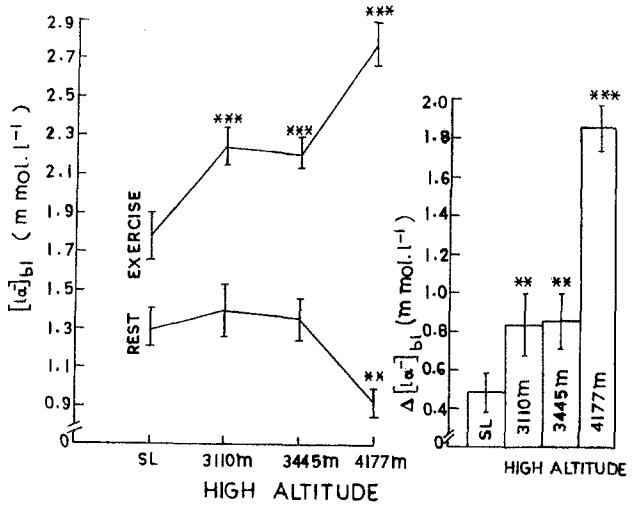

Fig. 4 Blood lactic acid concentration ($[la^-]_{bl}$) at rest, during submaximal exercise and exercise-rest $[la^-]_{bl}$, $\Delta[la^-]_{bl}$, at SL and day 2 of arrival at 3110, 3445 and 4177 m. Significances vs SL: *** $P<0.001$, ** $P<0.01$, * $P<0.05$

higher ($P<0.001$) not only from SL values but also from those at 3110 and 3445 m.

Discussion

Cardiovascular response

The unique aspects of this study concerned the evaluation of daily variations in the physiological responses of sojourners moved by road during their acclimatization at altitudes ranging from 3100 to 4200 m in the Eastern Himalayas. The initial response to the decrease in S_aO_2 on immediate arrival at HA has been shown to be a higher f_c mediated via chemoreceptors and the sympathoadrenal axis (Mathew et al. 1983; Mazzeo et al. 1991). The greatest increase in diastolic and systolic BP was seen on the first day of arrival at each altitude. Although the systolic BP tended to decline to SL values with increased duration of the stay at all three altitudes, the diastolic BP remained elevated. Similarly to BP, R and E f_c also remained elevated at all altitudes. Despite a significant decline in S_aO_2 at 3110, 3445 and 4177 m by about 3.2, 5.3 and 9.5% respectively, the maximal Δf_c was more or less identical at all altitudes. The percentile increase in systolic and diastolic BP and E f_c on the first day of arrival at each altitude was also more or less of the same magnitude. The results indicate that having achieved acclimatization to a lower altitude, the cardiovascular response on the first day of arrival at subsequently higher altitudes does not apparently seem to be related to the degree of hypoxia or decline in S_aO_2 at least between 3100 and 4200 m.

Sympathoadrenal activity

Our observations on the maintenance of higher BP and f_c values during the process of acclimatization to altitude are consistent with the findings of earlier investigators (Malhotra et al. 1976; Norboo 1986; Robinson and Haymes 1990; Grubbstrom et al. 1993). The acute exposure to hypoxia has been shown to cause stimulation of the sympatho-adrenomedullary system and activation of the renin-angiotensin-aldosterone system resulting in vasoconstriction and increase in peripheral vascular resistance (Johnson et al. 1983). The hypoxia-induced decline in vagal tone and reciprocal excitation of the sympathetic system in man (Malhotra et al. 1976) have been shown to be additional contributory factors towards elevation in f_c and BP at high altitude.

Acute Mountain Sickness (AMS)

The signs and symptoms were assessed of AMS, such as headache, nausea, vomiting, giddiness, anorexia, muscular weakness, sleeplessness and depression. About 35% of the subjects in our study showed symptoms of AMS. These subjects showed a marked increase in BP and f_c. The symptoms were pronounced during the first 72 h of the ascent to 3110 m, and the symptoms gradually subsided thereafter.

Respiratory changes

The consistent increase in $\dot{V}_E$ with increase in altitude indicates that the hypoxic ventilatory response is directly proportional to the fall in partial pressure of oxygen. This HA hyperventilation is an important adaptive mechanism to keep the alveolar partial pressure of O_2 high (Lahiri 1974; Sato et al. 1992). The observation that the increases in R and E $\dot{V}_E$ during the entire period at 3110 and 3445 m were of the same magnitude suggest that for rapid ascent to higher altitudes, acclimatization at 3445 m could be safely avoided. The significant increase in $\dot{V}_E$ over the values of the preceding altitude on arrival at 4177 m appeared to be due to a substantial decline in S_aO_2 at this altitude (Easton et al. 1984). The S_aO_2 declined by 8.4% at 4177 m compared to a decline of 3–3.5% at 3110 and 3445 m.

Metabolic responses

On arrival at 3110 m, the initial decline in R and E $\dot{V}O_2$ would have been mainly due to a reduction in cardiac output and stroke volume (Fulco et al. 1988; Wolfel et al. 1991). Consolazio et al. (1966) had also observed a similar decrease in $\dot{V}O_2$ at rest and during exercise at HA. Sime et al. (1974) similarly found a decrease in $\dot{V}O_2$ of 10% at rest and 7% during exercise at HA. With increasing duration of the stay at 3110 m the resting $\dot{V}O_2$

showed a considerable recovery and increased by about 19% on day 4 at 3110 m. Since the S_aO_2 at 3445 m was not substantially altered, R and E $\dot{V}O_2$ remained more or less constant during the entire period of stay at this altitude. A standard exercise intensity (100 W) performed at SL and during acute exposure to 3445 m elicited a higher f_c and $\dot{V}O_2$ since the subjects would have been working closer to their $\dot{V}O_{2max}$ (Drinkwater et al. 1982). Nevertheless, further reduction in S_aO_2 on arrival at 4177 m again caused a decline in $\dot{V}O_2$, which was even lower than at 3110 m. The maintenance of slightly higher $\dot{V}O_2$ at 3445 m compared to 3110 m appears to be a consequence of pre-acclimatization at 3110 m. These observations of higher $\dot{V}O_2$ at 3445 m are in agreement with the findings of Bender et al. (1988): no compromise of $\dot{V}O_2$ during exercise at HA was observed though the $[la^-]_{bl}$ showed a marked elevation.

Lactic acid build-up

The higher $[la^-]_{bl}$ accumulation following submaximal exercise at HA is indicative of a state of anaerobic metabolism during the initial days of acclimatization to the hypoxic stress. Robinson and Haynes (1990) suggested that hypoxia mandates an increased reliance on the anaerobic catabolism of blood glucose and intra-muscular glycogen as energy substrates for muscular work, with a concomitant increase in lactic acid formation by working muscle and its subsequent appearance in the circulation. The resting blood lactic acid concentration at 3110 and 3445 m was of the same magnitude; therefore the degree of hypoxaemia attained at these altitudes was also identical, again suggesting that acclimatization at 3445 m could be avoided. However, to perform the same work load at 4177 m the $[la^-]_{bl}$ build-up was significantly higher than at lower altitudes suggesting an accentuated degree of hypoxaemia at this altitude. The exact mechanism leading to higher $[la^-]_{bl}$ during the initial days of arrival at HA remains speculative and may be due to activation of the adrenergic system leading to a higher rate of lactate appearance (Brooks et al. 1991; Reeves et al. 1992).

In conclusion, the ascent from 3110 to 3445 m did not cause any deleterious effects on cardiopulmonary performance. The metabolic responses at 3110 and 3445 m were similar, indicating that the ascent was not stressful. If the individuals are acclimated to lower altitudes, acclimatization to mid-altitude (3445 m) apparently may be safely avoided for a rapid ascent to higher altitudes.

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