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EFFECT OF SIMULATED ASCENT TO 3500 METER ON NEURO-ENDOCRINE FUNCTIONS

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Abstract : Ascent to extreme High Altitude (HA) is in steps and it entails acclimatization at moderately HA locations. In terms of acclimatization, it is pertinent to understand the physiological changes, which occur on immediate ascent to moderate HA. The study aimed to evaluate the effect of ascent to 3500 m on neuro-endocrine responses in the first hour of induction. The plasma levels of catecholamines and cortisol were measured before and after one hour of ascent to high altitude. The peripheral oxygen saturation (SpO_2), Galvanic Skin Resistance (GSR), Heart Rate (HR) and Blood Pressure (BP) were simultaneously monitored. The plasma epinephrine, norepinephrine, dopamine and cortisol were increased after one-hour exposure to 3500 m altitude as compared to before exposure. The SpO_2 showed a significant decrease during & after high altitude induction. The heart rate and diastolic BP increased at 3500 m whereas the GSR did not show significant changes. There are changes in neuroendocrine responses, which reflect a sympathetic over activity in the first hour of exposure to 3500 m.

Key words : hypoxia simulated ascent cortisol catecholamines

INTRODUCTION

Ascent to high altitude causes alterations in neuro-endocrine responses in unacclimatized lowlanders. However, there is a paucity of information available on the changes in the first hour of ascent to moderate high altitude. Only one recent study (1) observed the effect on autonomic response in the first one hour of exposure to 4850 m and its correlation with acute mountain sickness. Another study on this aspect evaluated the effect of normobaric (not hypobaric) hypoxia using gas mixtures containing 11% oxygen (2) in the first 15 minutes of exposure.

The neuro-endocrine responses have a significant role in the physiological adjustments to high altitude hypoxia. The altered levels of catecholamines helps in the regulation of vital physiological functions like blood pressure (BP) and heart rate (HR). High altitude hypoxia activates the adrenergic system sometimes causing an

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increase in the levels norepinephrine (3) and dopamine (4). Hypoxia at high altitude stimulates the adrenal cortex. (5). It is suggested that blunting of adrenocortical response to altitude stress may contribute to the occurrence of high altitude pulmonary edema (6). There is no information on Galvanic Skin Resistance (GSR), an important measure of autonomic function at high altitude. Only one previous study (7) has evaluated the effect of hypobaric hypoxia on GSR.

In terms of acclimatization, it is pertinent to understand the physiological changes, which occur on immediate ascent to moderate high altitude. The present study aimed to evaluate the neuro-endocrine changes during the first one hour of ascent to 3500 m. Stress hormone changes are assayed in respect of epinephrine, norepinephrine, dopamine and cortisol by their estimation before and after the exposure.

MATERIAL AND METHODS

Subjects: The study was carried out on 17 normal healthy male participants from the Indian Army. They were of age 27.18 ± 3.283 yrs, height 170.06 ± 4.892 cm and weight 67.06 ± 6.398 kg (Mean ± SD). The guidelines of the Helsinki Declaration (1975) and the Ethics Committee on Human Experimentation of the Institute were followed in conducting the trials. The participants were explained the protocol of the experiment, and an informed consent was obtained from each of them.

The participants were examined by a physician. All of them were non-smokers with no history of neurological, cardiovascular or respiratory involvement. They were native lowlanders, with no exposure to high altitude in the last two years. The intake of alcohol, nicotine, caffeine and medication was restricted during the study period.

Protocol. Baseline recording: The subjects reported at 10 am to the laboratory. A single subject was studied in a session. The sea level (SL) recordings for all physiological parameters were carried out inside the Decompression Chamber. The decompression chamber offered the advantage of studying the effect of hypoxia under controlled conditions of temperature and relative humidity without the discomfort and the vagaries of the field conditions.

High altitude recordings: The subjects were inducted, one per session, to high altitude (HA) at a fixed rate of 152.4 $m.min^{-1}$, with a pause of 5 min at 1830 m. The subjects were finally inducted to 3500 m and exposed for one hour. Then they were deinducted (returned) to sea level (RSL) subsequently at the same rate as ascent. The recordings were carried out at SL and during induction (DI) for 30 min each, at HA for 60 min, during deinduction (DDI) and on RSL for 30 min each.

The experiments were carried out with the participants resting in comfortable supine posture. To ensure their safety and well being, a physician (a classified physiologist of the Army Medical Core) was present during the experiments in the Decompression Chamber. Two scientists were also present to record the observations. During the experiments, the Barometric pressure for SL (260 m) was 745 mm Hg & for 3500 m

altitude it was 483.3 mm Hg. The ambient temperature was 22–23°C and relative humidity was 65%.

Parameters. The following parameters were investigated :

Neuro-endocrinology : The blood sample was drawn before induction to high altitude (SL) and on return to sea level (RSL). The sampling took place at the same time of the day for every participant. The plasma was isolated for the estimation of catecholamines and cortisol.

The catecholamines (Epinephrine, Norepinephrine & Dopamine) in plasma were measured using Radioimmunoassay (8) following extraction and then acylation using combi-cat kit, OLD, Hamburg, GbBH. The sensitivity of the assay was 30 $pg.mL^{-1}$, 50 $pg.mL^{-1}$ and 750 $pg.mL^{-1}$ for Epinephrine (EPI), Norepinephrine (NE) & Dopamine (DA) respectively; whereas the intra-assay precision were 4.6%, 4.6% and 6.1% respectively and inter-assay precision were 8.2%, 6.1% and 13.4% respectively.

Plasma cortisol was measured using Radioimmunoassay (9). The quantitative measurement of cortisol in plasma was done using Immunotech RIA kit, Marseille, France. The sensitivity of the assay was 10 $nM.L^{-1}$, the intra-assay co-efficient of variation was less than 5.8%; the inter-assay co-efficient of variation was found to be 9.2%.

Autonomic Functions : For each parameter, 5 min interval readings were taken and averaged for every individual condition viz. SL, DI, HA, DDI and RSL. Systolic and Diastolic Blood Pressure (SBP & DBP respectively) and Heart Rate (HR) were recorded on an automated Digital BP Monitor (Model – UA 767-AND, A & D Co. Ltd., Japan) using the oscillatory method. The GSR was measured with the help of Biofeedback Instrument (Medicaid, GBI – 2000, India), by placing the surface electrodes on palmer aspect of the middle and index fingers. Peripheral Oxygen Saturation (SpO_2) was recorded with the help of a Pulse Oximeter (BCI Capnochek, USA) continuously by placing the probe on the tip of the index finger.

Statistical analysis

The data were subjected to repeated measure Analysis of Variance with different environmental conditions as one of the factors with five levels. After getting the significant results from ANOVA, Student Newman Keuls multiple range test was performed to test the pair wise significance in different environmental conditions. The paired t-test was done to compare sea level vs. after high altitude exposure for epinephrine, norepinephrine, dopamine and cortisol. The minimum significance level was fixed at 5%.

RESULTS

Neuroendocrinology : Fig. 1 depicts the changes in plasma catecholamines and cortisol at sea level vs. following one-hour hypoxic exposure at 3500 m altitude. As compared to sea level, there were significant increases in epinephrine levels ($P<0.001$), nor epinephrine levels ($P<.001$), dopamine

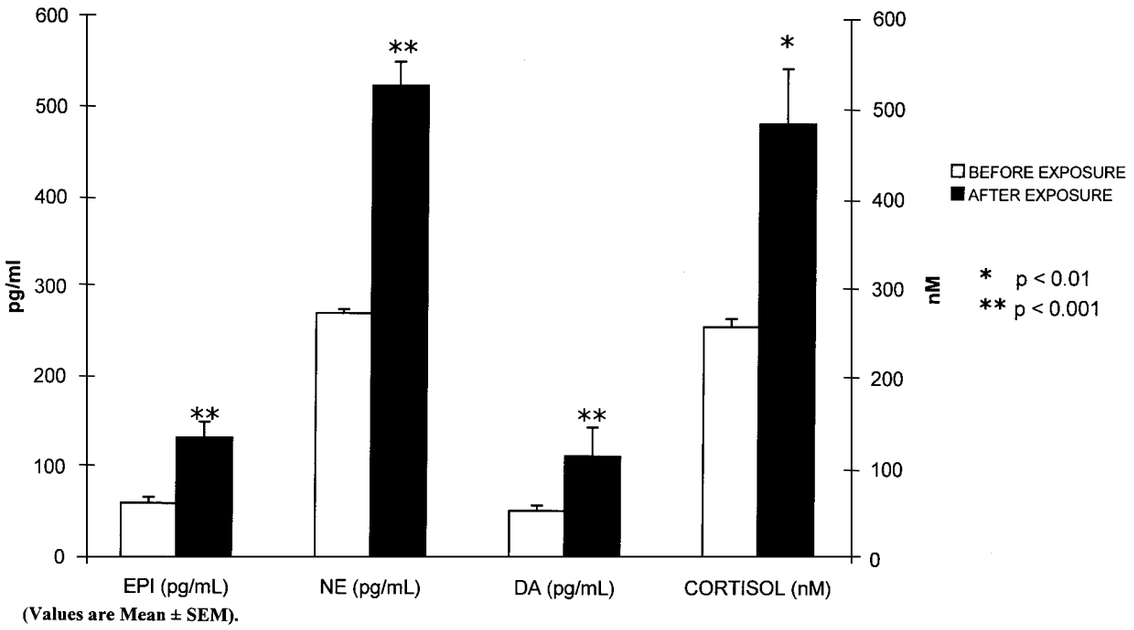

Fig. 1 : Effect of simulated ascent to 3500 m for 1 hour on Epinephrine (EPI), Norepinephrine (NE), Dopamine (DA) and Cortisol.

levels (P<0.001) and plasma cortisol levels (P<0.001) following exposure.

Autonomic functions : The effect of one hour of simulated ascent to 3500 m high altitude on autonomic functions is detailed in Table I. There was no significant effect of high altitude on systolic BP. There was a significant overall effect of high altitude on diastolic BP (P<0.001). As compared to SL, the values were elevated at HA although not statistically significant. However, they were significantly higher during deinduction and on RSL as compared to SL values (P<0.05 and P<0.01 respectively).

There was a significant overall increase in heart rate on ascent to 3500 m (P<0.001). Table I shows the average values in each phase and its pair-wise comparison. As shown, there was a significant increase at HA as compared to SL (P<0.01). The values were also significantly higher at HA as compared to DI heart rate values (P<0.01). The values decreased on DDI and decreased further on RSL. The heart rate was significantly lower during DDI (P<0.05) as compared to HA. The heart rate values were further reduced at RSL as compared to DDI values (P<0.01). There was no significant effect of high altitude on the GSR.

The SpO_2 levels showed significant increase in ascent to 3500 m altitude (P<0.001). The average value in each phase and its comparison is depicted in Table I. As compared to SL, the levels were significantly lower during DI (P<0.01) at HA

TABLE I: Effect of simulated ascent to 3500 m for one hour on autonomic functions.

Variable	SL	DI	HA	DDI	RSL	Overall significance	Pair-wise significance (p)									
							SL vs DI	SL vs HA	SL vs DDI	SL vs RSL	DI vs HA	DI vs DDI	DI vs RSL	HA vs DDI	HA vs RSL	DDI vs RSL
BP systolic (mm Hg)	118.89 ± 2.26	118.7 ± 2.09	120.04 ± 2.44	118.40 ± 2.46	118.26 ± 1.70	NS	–	–	–	–	–	–	–	–	–	–
BP diastolic (mm Hg)	69.74 ± 2.18	70.34 ± 2.03	71.94 ± 2.21	72.77 ± 2.22	74.35 ± 1.92	P<0.001	NS	NS	P<0.05	P<0.01	NS	NS	P<0.01	NS	NS	NS
GSR (kohm)	317.27 ± 61.41	365.70 ± 89.96	365.92 ± 72.40	340.73 ± 60.65	322.72 ± 46.47	NS	–	–	–	–	–	–	–	–	–	–
SpO_2 (%)	99.01 ± 2.30	96.49 ± 0.52	84.10 ± 0.90	90.99 ± 0.56	98.88 ± 0.27	P<0.001	P<0.01	P<0.001	P<0.001	NS	P<0.001	P<0.01	P<0.001	P<0.001	P<0.001	P<0.001
HR (bpm)	72.44 ± 2.30	73.15 ± 2.26	78.81 ± 2.33	75.59 ± 2.51	69.95 ± 2.18	P<0.001	NS	P<0.01	NS	NS	P<0.01	NS	NS	P<0.05	P<0.01	P<0.01

Values are Mean±SEM.; SL : Sea Level; DI : During Induction; HA : High Altitude; DDI : During Deinduction; RSL : Return to Sea Level.

(P<0.001), DDI (P<0.001). There was no significant difference in SL and RSL values. The SpO_2 levels at HA were significantly lower than DI (P<0.001), DDI (P<0.001) and (P<0.001).

DISCUSSION

The study aimed to evaluate the neuroendocrine responses on acute induction (one hr.) to simulated high altitude (3500 m). The alterations reflect a sympathetic over activity. The SpO_2 showed the expected decline at high altitude. Heart rate showed a significant increase. The systolic BP showed a marginal (but non significant) increase at 3500 m. The diastolic BP increased at 3500 m, during DDI and on RSL. The levels of plasma epinephrine, norepinephrine, dopamine and cortisol were elevated following exposure. The GSR remained unaltered upon ascent to high altitude.

The present study demonstrated an increase in HR in the first hour of ascent to 3500 m altitude. The finding is in agreement with the previous reports, which have observed that hypoxic exposure reduces the baroreflex responses causing an increase in HR but no significant change in systolic BP (2). The finding of an increase in diastolic BP is in agreement with a recent study in dogs (10). The increased levels of catecholamines at high altitudes are linked to increase in HR, BP arteriolar and venous tones (11, 12). In the present study too, the increased HR can be attributed to the rise in levels of epinephrine and norepinephrine.

The increase in catecholamines especially norepinephrine levels is likely to be due to an activation of the alpha-adrenergic system by hypoxia (3). In addition there may be a desensitization of beta-adrenergic receptors (13). The findings of the present study are also in line with the reported increase in dopamine levels at high altitude (4). A recent study (14) however, has reported a transient reduction in both parasympathetic and sympathetic activity during stepwise-simulated ascent to 4500 m.

Hypoxic exposure increased the plasma cortisol levels in the present study. There may be a stimulation of the adrenal cortex by hypoxia, causing a rise in ACTH and cortisol. Hypoxia at high altitude may increase the release of cortisol by influencing the pO_2 and blood flow to the adrenal glands. (15). The cortisol response to hypoxia could be mediated by a reflex action from the carotid bodies and also by non-chemoreceptors mechanisms (16, 17).

The present study revealed no significant change in GSR. A previous study has observed a decrease in GSR. However, the protocol of the mentioned study was different from ours in that the data was recorded 15 days before and 1 month after return from Antarctica and was in response to a cognitive stress. In the present study, the resting GSR was monitored at sea level, during ascent, at high altitude, during descent and after return to sea level in simulated conditions.

To conclude, the study clearly demonstrates a sympathetic over-activity in the first hour to simulated ascent to 3500 m as evidenced by increases in DBP, HR, plasma epinephrine, nor epinephrine, dopamine and cortisol.

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