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Chemoreceptor Sensitivity 'in Women Mountaineering Trainees of Different Altitudes Inducted by Trekking to 4350 m

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ABSTRACT

This study was conducted on women mountaineering trainees to evaluate the hypoxic and hypercapnic ventilatory responses, and the precise nature of changes in the sensitivity of chemoreceptors on induction by trekking to 4350 m. Two groups of women belonging to different ethnic origins and residents of different altitudes, ie, moderate-altitude women (MAW-Mongolians) and low-altitude women (LAW-Caucasians) were the subjects in this study. Tests of sensitivity to hypoxia and hypercapnia were carried out initially at 2100 m, then during 4 to7 days of sojourn at 4350 m following induction by trekking, and re-tested on return to 2 100 m. The results indicate that there is a significant difference ($P < 0.05$) of hypoxic ventilatory response in women of two different ethnic groups: Both hypoxic and hypercapnic ventilatory responses increased significantly ($P < 0.05$) on induction to high altitude. On descent, hypoxic values reverted back to pre-induction levels, whereas hypercapnic ventilatory response showed relatively higher values ($P < 0.05$).

Keywords: Hypoxic ventilatory response, hypercapnic ventilatory response, high altitude, chemoreceptor sensitivity

1. INTRODUCTION

Hyperventilation produced as a result of exposure to high altitude is an essential feature of hypoxic tolerance and altitude acclimatisation. However, there is considerable variation among individuals in the extent of, and the time required, for ventilatory acclimatisation to altitude. Studies, pertaining to chemoreceptor sensitivity changes to short-term exposure to high altitude, have been carried out extensively but work on gradual ascent to hypoxia is scanty. Present knowledge about the role of chemoreceptor sensitivity for high altitude adaptation is based mostly on studies on men. It is possible that women may respond differently than men because of the higher level of hormone progesterone, a known respiratory stimulant, found in women[1-3]. Recently, Muza[4] and his co-workers observed that in unacclimatised low-lander women, who rapidly-ascended to 4350 m in either the luteal or follicular phases of menstruation, had similar level of alveolar ventilation and chemosensitive responses.

There have been few studies of women's responses to high altitude[5-7]. Recent studies conducted at the Defence Institute of Phsiology & Allied Sciences (DIPAS), Delhi, on physical performance in hypobaric hypoxia have demonstrated better fitness for the native women of moderate altitude compared to their plain's counterparts*. However, it is not known whether there exists any difference in ventilatory chemoreceptor sensitivity to high altitude between

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these two ethnic groups. Further, no field study appears to have been carried out to evaluate the changes in chemosensitivity in women of two different altitude residents on exposure to high altitude.

The present study was conducted to evaluate normal values of hypoxic and hypercapnic ventilatory responses and the changes in the responses of chemoreceptor sensitivity in women mountaineering trainees of two different ethnic origins and residents of different altitudes, resulting from induction by trekking to 4350 m under similar ascent conditions.

2. METHODOLOGY

Out of the total number of 63 women trainees, who came to Himalayan Mountaineering Institute (HMI), Darjeeling (2 100 m), for a basic mountaineering course, 20 volunteers were randomly selected as subjects of this study. They all were Indians and belonged to middle class socio-economic status. Out of the total of 20, 10 women were moderate altitude residents, born and brought up at altitudes ranging between 2000 m to 2 100 m, and the remaining 10 women belonged to the plain regions (altitude not more than 260 m) of India. The two groups were comparable in terms of their physical attributes. The mean ± SD values of age and height for the two groups were 20.2 ± 2.6 yr and 150.5 ± 5.6 cm and 21.1 ± 3.4 yr and 156.5 ± 4.1 cm, respectively. Body surface area was similar in both the groups. Body weight showed negligible fluctuations. The values being 46.4 ± 6.4 kg, 46.7 ± 6.3kg and 47.0 ± 6.4 kg for MAW and 47.5 ± 5.6 kg, 47.4 ± 5.4 kg and 47.4 ± 5.7 kg for LAW, respectively at 2100 m, 4350 m and again at 2100 m. No further grouping of the subjects was done on the basis of their menstrual phase status as there is no effect of different phases of menstruation on chemosensitive responses on induction to high altitude[4]. All the volunteers gave their informed consent. They were also aware of their rights to withdraw from the study at any time. The protocol was approved by the Ethics Committee of the Himalayan Mountaineering Institute (HMI), Darjeeling. All the subjects were medically examined to rule out any systemic illness. The study was conducted in the following three phases:

Phase 1

Initial pre-training recording of the physiological parameters was carried out at the HMI (2 100 m, barometric pressure 586 mm *Hg*), in the temperature maintained (16-20 °C) MI room at the commencement of their mountaineering course. All the tests were completed three days after arrival at the HMI.

Phase 2

Measurements at the high altitude were done between 4 to 7 days of induction to high altitude at the base camp of the HMI (4350 m, barometric pressure 435 mm *Hg*), inside the silver hut, where the temperature was maintained between 17-20 °C.

Phase 3

Re-tests were conducted again in the MI room of the HMI (2100 m) within 48 h of return from high altitude on completion of the course. All the tests were performed in the morning between 5-7 am before breakfast by the same group of observers with the same set of equipment in all the situations.

At Darjeeling, the subjects had to undergo a rigorous training of mountaineering activities for 1 week, from early morning till late evening, with intermittent breaks. A stringent programme was formulated by the HMI for the entire course including ascent / descent and the period of sojourn at 43 50 m. After a week's training, they set their journey to the base camp (4350 m). The trainees were transported (160 km) by bus (day 8) from Darjeeling to Yoksom (2200 m). Next morning (day 9) all the trainees trekked for about 15 km and reached Bhakim (2750 m), where they stayed the next day (day 10).

On day 11, the subjects ascended on foot to Zamlingaon (3660 m) after crossing over a height of 4500 m, covering a distance of 12 km, and halted there the next day (day 12) for acclimatisation. On day 13, the trainees trekked for about 14 km and reached the base camp of the HMI at Chaurikhang (4350 m, barometric pressure 440 mm *Hg*), in the Eastern Himalayas. The subjects trekked at about 2-3 km/h for 5-6 h each day at increasing altitude, while carrying about 15 kg load on their bodies. During stay at intermittent altitudes of 2750 m and 3660 m, as well as during sojourn at 4350 m, the subjects were made to proceed to higher elevation and brought back to the Chaurikhang base camp. They were also engaged in different mountaineering activities for 4-5 h each day, which was an integral part of the training schedule for acclimatisation.

From day 14 to day 23 (10 days), all the subjects stayed at 4350 m in a hut made of metal sheets fitted with bunks. They undertook intense mountaineering activities like glacier-marching, ice cutting, peak assault, back packing, repelling, rock climbing, and were engaged in snow-bound field areas at higher elevations in the forenoon, and nearby camp areas in the afternoon. On the penultimate day of training, they climbed a peak of about 5550 m height. The maximum and minimum ambient temperatures at the base camp during the period of study were +10 °C and -7 °C, respectively. Sunshine and partial cloudiness during the day with occasional snowfall and high-velocity winds were the general features of the climate. Hypoxic and hypercapnic ventilatory response tests were completed between 4 to 7 days of the stay at 4350 m. After 10 days of sojourn at 4350 m, they returned to 2100 m, which involved trekking for 2 days (day 24 and day 25) and motor journey for 1 day (day 26). Re-tests were conducted from the following morning onwards and completed within 48 h of return, ie on day 27 and day 28.

3. RE-TESTS ON DESCEND TO PLAINS

3.1 Assessment Of Chemoreceptor Sensitivity

Studies were carried out in the early morning before breakfast, after the subjects rested in the temperature maintained (16-20 °C) room for 30-35 min. Hypoxic and hypercapnic sensitivity. tests were performed on two different days on subjects after they were comfortably seated.

3.1.1 Hypoxic Ventilatory Response Test

The hypoxic sensitivity test was carried out on the basis of the method described by Rebuck and Campbell[9]. The hypoxic ventilatory response (HVR) test was measured using a progressive isocapnic hypoxia protocol for 7-10 min. Subjects breathed from an 8 litre closed circuit spirometer through a low resistance-breathing valve fitted with a mouthpiece. The spirometer was filled with room air. With this re-breathing system, isocapnia was maintained by regulating the amount of expired air shunted through a canister of CO, absorber. Continuous monitoring of the end-tidal CO, and oxygen was done by rapid response zirconium oxygen and infrared carbon dioxide gas analysers (P.K.Morgan, England). The hypoxic ventilatory response test was terminated when the oxygen saturation decreased to 75-80 per cent. Minute ventilation was measured using pre-calibrated ventilation monitor (P.K.Morgan, UK) and converted into BTPS. Pulse arterial oxygen saturation (SaO_2) was measured every minute during the test by a portable finger-pulse oxymeter (N-20 SA, Nellcor, USA). The HVR was noted as slope relationship of V_E and SaO_2 ,described by the slope (AV, $/\Delta SaO_2$) expressed in litres per minute per unit per cent fall in oxygen saturation.

3.1.2 Hypercapnic Ventilatory Response Test

The CO, sensitivity test was carried out by the re-breathing technique of Read[10]. A 6 litre re-breathing bag fitted inside a perspex chamber was used. This bag-in-box setup was arranged in such a way that the subjects could breathe back and forth from the bag or the atmospheric air. The re-breathing bag was filled to an initial volume of 5 litre with 100 per cent medical oxygen. The subjects fitted with mouthpiece and nose clip initially breathed ambient air for about a minute, after which they were connected to the re-breathing bag (during inspiratory phase) by turning the stop cock of the valve. Rf and V_E were recorded and the end-tidal air was analysed for CO, and oxygen. Pulse arterial oxygen saturation (SaO_2) was monitored continuously which measured 100 per cent saturation throughout the test. Re-breathing was continued until the end-tidal CO, reached 10 per cent, which took about 4-5 min, while oxygen percentage remained more than 40 per cent at the end of experiment. Using the values of V_E (BTPS) versus end-tidal CO, ($P_{ET}CO_2$ mm *Hg)*, the sensitivity curves were drawn for each individual. The relationship was linear. From each CO, response curve, the intercept (B) and the value of the corresponding $P_{ET}CO_2$ were noted. The slope S of the curve was calculated as per the formula $V_E = S\ (P_{ET}CO_2 - B)$ of Lloyd[11] and co-workers, where B is the extrapolated intercept, and S is the slope of the line expressed as ventilation per unit change in $P_{ET}CO_2$.

3.2 Analysis of Hypoxic & Hypercapnic Variables

The analysis of hypoxic and hypercapnic variables at different altitudes has been done by two-way analysis of variance, the two factors being ethnicity and altitude. The ethnicity had two levels, ie, MAW and LAW. The altitude had three levels, ie, 2100 m, 4350 m, and back to 2100 m. Post-hoc test has been done by Student Newman Keuls multiple range test. Results are presented in Table 1. Post-hoc test results have been presented separately along with mean ± S.D. for various parameters [Table. 2(a) and 2(b)] and $p < 0.05$ was used as the level of significance.

4. RESULTS & ANALYSIS

4.1 Hypoxic Ventilatory Response

The resting value of ventilation showed a significant increment ($P < 0.01$) on induction to high altitude. Ventilatory response to hypoxia has been expressed by plotting V_E against arterial SaO_2. The changes in V_E divided by the changes in oxygen saturation ($\Delta V_E/\Delta SaO_2$), expressed in liters per minute per 1 per cent fall in oxygen saturation, was calculated. It is evident from the data that ventilator-y response test to hypoxia shows significant improvement ($P < 0.01$) at high altitude. There was a significant differences of HVR ($P < 0.05$) between the two different ethnic groups of women [Table 2(b)]. The MAW group showed a higher value of HVR (0.49 ± 0.17) in comparison to LAW group

Table 1. Hypoxic and bypercapnic ventilatory variables of different groups at different locations

Ethnicity	Altitude	Variables				
		V_E (l/min)	$\Delta V_E/\Delta SaO_2$ (l/min/ 1% fall in SaO_2)	Intercept (mm/*Hg*)	Slope (l/min/mm*Hg*)	$\Delta V_E/\Delta PCO_2$ (l/min/mm *Hg* change in PCO_2)
MAW	Initial (2100 m)	9.75 ± 1.44	0.40 ± 0.13	32.50 ± 3.98	0.71 ± 0.12	1.16 to.19
	Base camp (4350 m)	12.25 ± 1.88	0.66 ± 0.14	27.70 ± 3.16	1.38 ± 0.41	1.77 ± 0.35
	Re-test (2100 m)	9.80 ± 1.65	0.44 ± 0.11	33.10 ± 3.48	0.86 ± 0.19	1.33 ± 0.19
LAW	Initial (2100 m)	9.70 ± 1.77	0.36 ± 0.08	32.90 ± 4.41	0.74 ± 0.13	1.11 ± 0.27
	Base camp '(4350 m)	12.35 ± 2.20	0.57 ± 0.12	27.60 ± 3.89	1.35 ± 0.27	1.83 ± 0.36
	Re-test (2100 m)	9.70 ± 1.44	0.36 ± 0.08	33.70 ± 2.45	0.92 ± 0.21	1.33 ± 0.29
Main effect: Altitude (a)	F value	14.32	26.09	15.04	38.10	29.28
	P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Main effect: Etlmicity (b)	F value	0.001	5.37	0.103	0.131	0.005
	P value	0.971	0.024 (< 0.05)	0.749	0.719	0.982
Interaction effect: (a)x(b)	F value	0.018	0.246	0.050	0.161	0.206
	P value	0.982	0.782	0.952	0.85 1	0.814

Table Z(a). Post-hoc comparison for various parameters at different locations

Variables	Environmental conditions			Significance		
	Initial (2100 m) (A)	Base camp (4350 m) (B)	Re-test (2100 m) (C)	A vs B	A vs C	B vs C
V_E (l/min)	9.73 ± 1.57	12.30 ± 1.99	9.75 ± 1.51	P < 0.001	NS	P < 0.001
$\Delta V_E/\Delta SaO_2$ (l/min/ 1 % fall in SaO_2)	0.38 ± 0.11	0.61 ± 0.13	0.40 ± 0.10	P < 0.001	NS	P < 0.001
Intercept (mm Hg)	32.70 ± 4.09	27.65 ± 3.45	33.40 ± 2.95	P < 0.001	NS	P < 0.001
Slope (l/min/mm Hg)	0.73 ± 0.12	1.36 ± 0.33	0.89 ± 0.19	P < 0.001	P < 0.05	P < 0.001
$\Delta V_E/\Delta PCO_2$ (l/min/mm Hg change in PCO_2)	1.13 ± 0.23	1.80 ± 0.35	1.33 ± 0.24	P < 0.001	P < 0.05	P < 0.001

(0.43 ± 0.14). On descent, HVR values reverted back to pre-induction level.

4.2 Hypercapnic Ventilatory Response

The values of the slope of CO, response curves can be considered as the index of CO, sensitivity. The changes in CO, sensitivity response to hypoxia at 4350 m are given in Table 2(a). On exposure to high altitude the intercept recorded significant ($p < 0.01$) reduction, while the slope values showed significant increment ($p < 0.01$). However, there was no significant difference in the values of intercept and slope between the two different ethnic groups. On return to 2 100 m, the slope of the CO, response curve (index of CO, sensitivity) showed slightly higher values than the pre-induction values ($P < 0.05$), which is similar to the previous findings from this group[12].

Table 2(b). Post-hoc comparison between MAW and LAW group for $\Delta V_E/\Delta SaO_2$

	MAW	LAW	MAW vs LAW
$\Delta V_E/\Delta SaO_2$ (l/min/ 1 % fall in SaO_2)	0.49 ± 0.17	0.43 ro.14	P < 0.05

5. DISCUSSION

In this study, hypoxic and hypercapnic ventilator-y responses were evaluated in the two groups of females of different ethnic origins and residents of.different altitudes from the same batch of trainees at the HMI, Darjeeling. However, a comparative analysis of the two different ethnic groups responses indicated that they behaved similarly in terms of the values of chemoreceptor sensitivity response per se and also in the pattern of change in chemoreceptor sensitivity during acclimatisation at higher altitude except in $\Delta V_E/\Delta SaO_2$ ($P < 0.05$). The interaction effect between altitude and ethnicity was found to be not significant for all the parameters. The higher value of $\Delta V_E/\Delta SaO_2$ among MAW indicates the higher HVR in comparison to LAW. This observation corroborates with the findings of Reeves,‘* *et al.*, where they have found that persons residing at moderate altitudes can acclimatise to a higher altitude faster than that of sea-level residents by virtue of their effective higher HVR. The results obtained in the study also demonstrated significant increment in the responses of HVR in women on induction to high altitude and during acclimatisation at high altitude. HVR responses reverted back to their pre-induction levels promptly on descent. The hypercapnic ventilatory responses (HCVRs) also showed a significant increase on induction to high altitude, and on descent, it showed relatively higher values than the pre-induction values, which is similar to earlier findings from this group[13].

From these results, it has been suggested that there is a definite increase in the hypoxic sensitivity due to acclimatisation at high altitude. This finding overrides the earlier observation on men that there is no change of hypoxic sensitivity at high altitude among sea-level residents as well as in low landers, who were staying at high altitude for more than one year[13]. In the present study, the samples of end-tidal air were analysed for oxygen by rapid response zirconium oxygen analyser, which is not affected by barometric pressure, and hence, is suitable for high altitude studies. The earlier study used servomax oxygen analyser based on paramagnetic sensor that is pressure (altitude) dependent, The results of the present study on women are in confirmation with the previous evidences on men that peripheral chemo-receptor sensitivity, as measured by HVR, increases during acclimatisation at high altitude[13-18].

The observation of increased CO_2 sensitivity with acclimatisation is qualitatively similar to the earlier results on men carried out by DIPAS, Mathew[19], *et al.* studied CO_2 sensitivity response in 20 young men subjects at sea level, during acclimatisation at 3500 m and on return to sea level. The CO_2 sensitivity increased significantly in sojourners at high altitude,[19] which corroborates with the current findings. In the present study, relatively higher values of slope and intercept have been found at high altitude as compared to the earlier study[19]. These higher values may be due to different modes of induction, varying duration of stay at high altitude, and different ethnicity. It is also possible that the subjects of the present study had undergone mountaineering training at 2100 m for 1 week and thereafter inducted to 4350 m by trekking which took 6 days including 1 day by motorable road. These observations indicate that both peripheral (carotid body) chemoreceptors (responsible for hypoxic ventilatory response) and central (superficial ventral medullary) chemoreceptors (responsible for hypercapnic ventilatory response) increased their sensitivity during acclimatisation to high altitude. Forster and Demsey[20] reviewed this and hypothesised that in some way, central nervous system sensitivity to carotid body is increased by altitude, accounting for the gradual fall of PCO_2 at high, altitude called acclimatisation. However, the interaction of central and peripheral chemoreceptors drives at altitude suggests that the carotid chemoreceptors, by stimulating ventilation, initiate and maintain the acclimatisation process, while the fall of $[H^+]$ in extracellular fluid in ventral medulla (central cemoreceptors) limits the ventilatory increase[21]. On return to sea level, there is an acute elevation of O_2 tension, which eliminates the hypoxic stimulus arising from the peripheral chemoreceptors, and thus, depresses ventilation, Hyperventilation continues by the increased sensitivity of central chemoreceptor and it gradually disappears on return to sea level. The current study for the first time reports on women of two different ethnicity and different altitude residents on HVR and HCVR on induction and during acclimatisation at high altitude.

6. CONCLUSIONS

Two groups of women belonging to different ethnic origins and residents of different altitudes responded similarly in chemoreceptor sensitivity responses at high altitude as well as in the nature of changes in chemoreceptor sensitivity except the high HVR among moderate-altitude natives.

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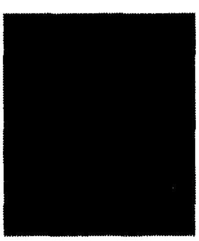

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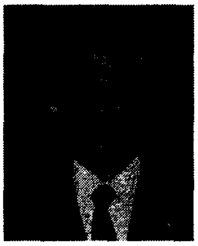

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