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HEART RATE VARIABILTY CHANGES DURING FIRST WEEK OF ACCLIMATIZATION TO 3500 m ALTITUDE IN INDIAN MILITARY PERSONNEL

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Abstract : Acute exposure to hypobaric hypoxia induces the changes in autonomic control of heart rate. Due to emergencies or war like conditions, rapid deployment of Indian military personnel into high altitude frequently occurs. Rapid deployment to high altitude soldiers are at risk of developing high altitude sickness. The present study was conducted to evaluate the acute exposure to high altitude hypobaric hypoxia (3500 m altitude) on the autonomic nervous control of heart rate in Indian military personnel during first week of acclimatization Indices of heart rate variability (viz; R-R interval, total power, low frequency, high frequency, ratio of low to high frequency) and pulse arterial oxygen saturation were measured at sea level and 3500m altitude. Power spectrum of heart rate variability was quantified by low frequency (LF : 0.04-0.15 H_Z) and high frequency (HF : 0.15-0.5 H_Z) widths. The ratio of LF to HF was also assessed as an index of the sympathovagal balance. Mean R-R interval decreased significantly on day 2 on induction to altitude which tended to increase on day 5. Total power (TP) decreased high altitude and tended to recover within a week. Both HF and LF power showed decrement at 3500m in comparison to sea level. The ratio of LF to HF (LF/HF) at 3500m was significantly higher at 3500m. SpO_2 values decreased significantly ($P<0.05$) at high altitude on day-2 which increased on day-5. We conclude that autonomic control of the heart rate measured by heart rate variability was altered on acute induction to 3500m which showed a significant decrease in parasympathetic tone and increase in sympathetic tone, then acclimatization seems to be characterized by progressive shift toward a higher parasympathetic tone.

Key words : heart rate variability, spectral analysis, acclimatization, high altitude

INTRODUCTION

High altitude (HA) is defined as 9000 ft and above because at this altitude most of the people develop sign and symptoms which are associated with acute mountain sickness

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(AMS). If AMS is untreated, this may lead to life threatening High Altitude Pulmonary Edema (HAPE) or High Altitude Cerebral Edema (HACE). Due to advancement of the technology, people visit to the HA regions without the acclimatization. As a result some of them are at risk for physical problems related to high altitude disorders, which could be unpleasant and may even lead to fatal casualties (1). In our earlier study we have presented the effect of altitude on cardiovascular system (2-3), respiratory system (4), chemoreceptor sensitivity (5-6), exercise responses (7-8) during initial days of acclimatization at different altitudes. At high altitude, hypoxemia triggers a series of pulmonary and cardiovascular adjustments to maintain an adequate oxygenation of the different organ systems. In the heart, the major adjustments are an increase in heart rate, cardiac contractility and cardiac output. At the vascular level, the main initial adaptive mechanisms to altitude induced hypoxemia are pulmonary artery vasoconstriction and peripheral and cerebral artery vasodilation. The hypoxia mediated stimulation of cardiovascular system reaches its maximum effects during the initial few days of exposure and thereafter it established a new steady state condition. Indeed, once these adjustments have reached their optimal effect, any further stimulation may have detrimental effects and induce specific high altitude related diseases like HAPE (exaggerated pulmonary hypertension) or HACE (exaggerated cerebral vasodilation). Hypoxia significantly alters the autonomic regulation of cardiovascular functions at high altitude (9-13). The changes in autonomic control of cardiovascular system during acclimatization to high altitude have been extensively studied by electrical nerve activity (14), beta adrenergic blockade (15), pharmacological interventions (16). It has also been known that beta-receptors is responsible for most electrocardiographic (ECG) changes at altitude. This is also shown that beta adrenergic blockade lowers the level of cardiovascular changes without any effect on hypoxia induced hyperventilation (17). At high altitude, sympathetic activity and vagal (parasympathetic) withdrawal act synergistically to increase heart rate, blood pressure and cardiac output. Increased sympatho-adrenal activity in combination with decreased parasympathetic tone at high altitude accounts for most of the cardio-vascular and ECG related changes (18-19). Heart rate variability which is the beat to beat alterations of the R-R intervals in an ECG is generally used to monitor the autonomic nervous system activities and power spectrum analysis of HR variability (HRV) is being considered as a new tool to assess the sympathovagal balance (18, 20). In fact, heart rate variability (HRV) is the consequence of heart rate modulation by both branches of the autonomic nervous system. The study on autonomic control of the cardiovascular system during acclimatization to high altitude is limited and few attempts have been made to monitor the changes in autonomic nervous control of heart rate during initial days of sojourn at high altitude (16, 21-23). Due to emergencies or war like conditions, rapid deployment of Indian military personnel into high altitude frequently occurs. Rapid deployment to high altitude soldiers are at risk of developing AMS, HAPE or HACE. The autonomic control of heart rate during acute ascent to 3500 m altitude in Indian military population has not been studied yet. The present study was conducted to evaluate the acute exposure to high altitude hypobaric hypoxia (3500 m altitude) on the autonomic nervous control

of heart rate in Indian military personnel during first week of acclimatization

METHODS

Six young healthy Army male soldiers (sea level residents) with (mean±SD) age of 24.83±2.93 yrs, height 172.17±6.94 cm, body weight were 64.33±4.32 kg were the subjects of the study. Clinical examinations were conducted to rule out any systemic illness. The study protocol was approved by the Institute's Ethical Committee and each subject signed an informed consent statement prior to participation and could withdraw without prejudice at any time. The sea level study was carried out at Chandigarh (barometric pressure 740 mm Hg) in the month of October where the laboratory temperature was maintained between 20 and 24°C with a relative humidity range of 55-60%. After recording the different physiological parameters at SL, the subjects were flown to an altitude of 3,500 m at Leh (barometric pressure 483 mmHg) in the Western Himalayas, India in 55-60 min by pressurized aircraft. The subjects reached at 3500 m altitude in the forenoon and the day of arrival was taken as day 0 at 3500 m. The ambient temperature at this altitude 3500 m varied between 10- 20°C during the period. During their stay at HA, the subjects were confined to their dwelling units and did not undergo any type of physical exertion. At 3500 m altitude all the tests were monitored in a makeshift laboratory where the temperature was maintained between 20 and 25°C. The first recording of HRV, Electrocardiograms (ECG) were collected on day 2 (within 48 hrs of arrival) and day 5 using standard limb lead II by telemetric physiological monitoring system (Nexsus-10, Netherlands). Data were collected for 10 minutes after getting stable electrocardiographic baseline. R-R interval (time duration between two consecutive R waves of ECG) was used for the HRV analysis. These intervals were processed using Kubois HRV analysis 2.0 software (University of Kuopio, Kuopio, Finland) (24). This software calculates time-domain metrics like the mean and standard deviation of the R-R intervals and frequency domain metrics like LF, HF, total power and LF/HF. A finger pulse Oximeter probe was set on the right index finger to measure pulse oxygen saturation level (Model MU 300, China). All the measurements were recorded when the subjects in resting quietly supine position. It is known that specific characteristics of the power spectrum of the HRV can be used to quantify sympathetic and parasympathetic control on the heart. The two frequency bands were considered i.e; low frequency (LF) band (0.04-0.15 Hz) and the high frequency band (0.15 Hz – 0.40 Hz). The low frequency was considered as marker of both sympathetic and parasympathetic activity and the high frequency was considered solely with cardiac parasympathetic activity (25-26). Both LF and HF were presented in form of absolute units to determine their power (LFau, HFau ms^2) as well as in normalized units (LFnu, HFnu, %) to determine the relative part of each component in the total power. The ratio of LF power to HF power (LF:HF) was chosen as an index of the sympathovagal balance.

Statistics

All data were expressed as mean±SEM. The changes in different indexes of HRV from sea level to day-2 and day-5 were analyzed

by one way repeated measure analysis of variance (ANOVA) followed by multiple comparison by Bonferroni t-test. A P-value of <0.05 was considered as statistically significant.

RESULTS

There were statistically significant increase in heart rate and decrease in SpO_2 values in all the subjects. In HRV, the R -R interval was significantly lower at 3550 m than at sea level (Table-I). None of the subjects showed any sign of electro-cardio graphic abnormalities both at sea level and high altitude locations. Total power (TP) of heart rate variability decreased on acute induction to 3500 m altitude on day-2 and then tended to return towards normoxic value with the acclimatization on day-5 without any significant changes. Both low frequency (LF) and high frequency (HF) of heart rate variability considerably decreased at 3500m altitude. Low frequency power decreased from sea level to day-2 at high altitude and to increase towards sea level value at day-5. High frequency power showed the significant fall on day-2 and then increase during acclimatization on day-5. HFnu decreased significantly on day-2 and tended to increase on day-5 during the course of acclimatization. LFnu also showed the significant increase on day-2 and then tended to decrease on day-5 without reaching the sea level value. The ratio of LF/HF (marker for sympatho-vagal balance) showed the significant increase on day-2 and then decrease on day-5 but remained elevated above the sea level value (Fig. 1).

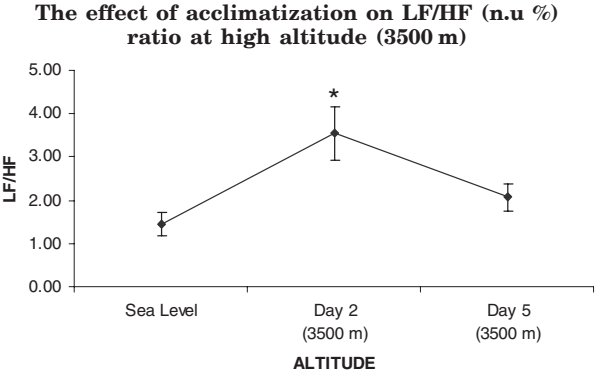

Fig. 1: The effect acclimatization on low-frequency (LF) to high frequency (HF) ratio. The LF/HF ratio was significantly different from that of sea level.

TABLE I: Spectral analysis of heart rate.

	Sea level	*Altitude (3500 m)*	
		Day-2	*Day-5*
R-R interval, msec	911±45.09	753.25±40.67*	801±32.4
Total power ms^2	4686.17±1229	2728.17±415	4532±565.7
LF au ms^2	1656.83±562	1259.17±100	1013.17±223.7
HF au ms^2	1040±159.7	329.3±48.3*	560.6±128.6*
LF n.u%	56.65±4.3	75±4.7*	64.97±2.9
HF n.u%	43.35±4.3	25±7.7*	35±2.9
LF/HF	1.44±0.289	3.54±0.61*	2.07±0.32
SpO_2 %	8.33±0.2	92.83±0.47*	96.5±0.22*
HR bpm^{-1}	167±3.8	81.19±411*	75.7±6.9

Values are mean±SEM at sea level and high altitude 3500 m (day-2 and day-5). LF au, low frequency power (in absolute units); HF au, High frequency power (in absolute units); LF nu, Low frequency (in numeric unit) as a marker of cardiac sympathetic activity; HFnu, High frequency (in numeric unit) as a marker of vagal activity; LF/HF, low frequency-to-high frequency (LF/HF) as a marker of the sympathovagal balance. *(P<0.05) signifies day 2 and day 5 at HA Vs SL.

DISCUSSION

Due to advancement of the modern transport system and proliferation of military activities, soldiers are being inducted to different heights by air within hours of departure and they are devoid of acclimatization. Acute exposure to high altitude alters the different physiological parameters to adapt in hypoxic environmental condition. The result of this present study demonstrate that heart rate variability, an indicator of the activity of the autonomic nervous system on heart rate was altered on exposure to high altitude of 3500m above sea level. The ratio of LF/HF which has been considered as an index of sympathetic nerve activity showed the significant increment on day -2 and tended to decrease afterwards. On arrival at high altitude HR value showed higher than the sea level value at rest and this is agreement with the other observations (27-28). Decrease in autonomic control of the heart can be assessed by decrease in total power (TP) which occurs in various pathological conditions like myocardial infraction (29). It has been reported that hypoxia significantly decrease the total power (28, 30-31). The decrease in total power could serve as a possible marker of the decrease in the autonomic control on the heart resulting the reduction in the absolute value of both spectral components (16).

The decrease in R-R interval coupled with a decrease HF on initial days at high altitude may be due to vagal withdrawal (25). The increase in LF:HF ratio at day-2 showed a maximum dominance of adrenergic control and was mainly due to the greater decrease in HF power than LF power. Because LF power is considered as marker of both sympathetic and parasympathetic activities and lack of increase of LF power initial days have been caused by the vagal withdrawal (20). Hyperactivity of the sympathetic nervous system and the down regulation of beta adrenergic receptor activity has already been reported earlier (32). This alteration is found to be an important adaptive mechanism to protect the vital organs including the heart from long term stimulation of high altitude induced hypoxic stimulation.

The result of this study indicates that the heart rate variability as an indicator of the autonomic nervous system activities was altered by exposure to altitude 3500 m. The changes in different index of heart rate variability like LF, HF, LF/HF showed that these parameters increased on day-2, which shifted to reverse and attained a stable value on day-5 during acclimatization. The maximum rise of heart rate also occurred on initial 72 hours days of exposure to high altitude and thereafter attained a relatively stable value on day 6. Our earlier study in air and road inductees at 3500 altitude indicated that to achieve a relatively stable value of different physiological parameters took at least 5 days for air inductees and at least 3 days for road inductees to overcome the initial hypoxic stress (2). The mode of induction to high altitude plays an important role in the process of acclimatization. It has been mentioned that decrease in heart rate variability at high altitude indicates a reduction in the autonomic nervous system responsiveness. It has also been reported that reduction of autonomic nervous system is linked with development of acute mountain sickness and physical fitness of an individual at high altitude (33-37). The limitation of our study is that we could not measure heart rate variability on daily basis

during stay at 3500m altitude as well as the number of subjects were also limited. The day to day measurements of HRV at 3500m would have given the clear picture of daily changes in spectral analysis of HRV. It can be concluded form this study on the basis of HRV analysis on day 2 and day 5 that autonomic nervous control of heart rate was altered on acute induction to 3500m altitude characterized by a significant decrease in parasympathetic tone and increase in sympathetic tone which shifted to reverse within a week.

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REFERENCES

1. Gertsch JH, Lipman G S, Holck PS . Prospective, double-blind, randomized, placebo-controlled comparison of acetozolaminde versus ibuprofen for prophylaxis against high altitude headache: The headache evaluation at altitude trial (HEAT). *Wilderness Environ Med* 2010; 21: 236–243.
2. Purkayastha SS, Ray US, Arora BS et al. Acclimatization at high altitude in gradual and acute induction. *J Appl Physiol* 1995; 79: 487–492.
3. Purkayastha S S, Bhaumik G, Sharma R P et al. Effects of mountaineering training at high altitude (4350 m) on physical work performance of women. *Aviat Space Environ Med.* 2000; 71: 685–691.
4. Basu CK, Selvamurthy W, Bhaumik G et al. Respiratory changes during initial days of acclimatization to increasing altitudes. *Aviat Space Environ Med.* 1996; 71: 685–691.
5. Bhaumik G, Sharma RP, Dass DK et al. Hypoxic ventilatory response changes of men and women 6 to 7 days after climbing from 2100 m to 4350 m altitude and after descent. *High Alti Med Biol* 2003; 4: 341–348.
6. Bhaumik G, Purkayastha SS, Sharma RP et al. Chemoreceptor sensitivity in women mountaineering trainees of different altitudes inducted by trekking to 4350m. *Defence Science journal* 2005; 55 : 427–435.
7. Bhaumik G, Purkayastha SS, Selvamrthy W et al. Oxygen saturation responses to exercise VO_2 at 2100m and 4350 m in women mountaineering trainees. *Indian J Physiol Pharmacol* 2003; 47: 43–51.
8. Bhaumik G, Dass DK, Lama H et al. Maximum exercise responses of men and women mountaineering trainees on induction to high altitude by trekking. *Wilderness Environ Med* 2008; 19: 151–156.
9. Wille M, Mairer K, Gatter H, Philippe M, Burtscher M. Changes in cardiac autonomic activity during a passive 8 hour acute exposure to 5500 m normobaric hypoxia are not related to the development of acute mountain sickness. *Int J Sports Med* 2012; 33: 186–191.
10. Prabhakarn P, Tripathi KK. Autonomic modulations during 5 hours at 4574 m (15,000 ft) breathing 40% oxygen. *Aviat Space Environ Med* 2011; 82: 863–870.
11. Vigo DE, P{erez Lloret S, Videla AJ et al . Heart rate nonlinear dynamics during sudden hypoxia at 8230m simulated altitude. *Wilderness Environ Med* 2010; 21: 4–10.
12. Zupet P, Princi T, Finderle Z. Effect of hypobaric hypoxia on heart rate variability during exercise: a pilot field study. *Eur J Appl Physio*l 2009; 107: 345–350.
13. Chen YC, Lin FC, shiao GM, Chang SC. Effect of rapid ascent to high altitude on autonomic cardiovascular modulation. *Am J Med Sci* 2008; 336: 248–253.
14. Halliwill JR, Minson CT. Effect of hypoxia on arterial baroreflex control of heart rate and muscle sympathetic nerve activity in humans. *J*

Appl physiol 2002; 93: 857–864.

15. Richalet JP, Kacimi R, Antezana AM. The control of cardiac chronotropic function in hypobaric hypoxia. *Int J Sports Med* 1992; 13: S22–S24.
16. Cornolo J, Mollard P, Brugniaux JV et al. Autonomic control of cardiovascular system during acclimatization to high altitude : effects of sildenefil. *J Appl Physiol* 2004; 97: 935–940.
17. Boutellier U, Koller EA. Propanolol and the respiratory, circulatory and ECG responses to high altitude. *Eur J Appl Physiol* 1981; 46: 105–119.
18. Koller EA, Bischoff M, Buhrer A. Respiratory, circulatory and neuropsychological responses to acute hypoxia in acclimatized and non-acclimatized subjects. *Eur J Appl Physiol* 1991; 62: 67–72.
19. Roche F, Reynaud C, Garet M, Picholet V, Costes F, Barthelemy JC. Cardiac baroreflex control in humans during and immediately after brief exposure to simulated high altitude. *Clin Physiol Funct Imaging* 2002; 22: 301–306.
20. Parati G, Saul JP, De Rienzo M, Mancia G. Spectral analysis of blood pressure and heart rate variability in evaluating cardiovascular regulation. *Hypertension* 1995; 25: 1276–1286.
21. Kanai M, Nishihara F, Tatsuya S. Alterations in autonomic nervous control of heart rate among tourists at 2700 and 3700 m above sea level. *Wilderness Environ Med* 2001; 12: 8–12.
22. Iwasaki K, Ogawa Y, Aoki K et al. Cardiovascular regulation response to hypoxia during stepwise decreases from 21% to 15% inhaled oxygen. *Aviat space Environ Med* 2006; 77: 1015–1019.
23. Perini R, Milesi S, Biancardi L, Veicsteinas A. Effects of high altitude acclimatization on heart rate variability in resting humans. *Eur J Appl Physiol* 1996; 73: 521–528.
24. Schultz DM, Zhou X, Singal A, Musley S. Cardiovascular effects of spinal cord stimulation in hypertensive patients. *Pain Physician* 2011; 14: 1–14.
25. Pagani L, Lombardi F, Guzzetti S et al. Power spectrum analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. *Cir Res* 1986; 59: 178–193.
26. Kamath MV, Fallen EL . Power spectrum analysis of heart rate variability: a non-invasive signature of cardiac autonomic function. *Crit Rev Biomed Eng* 1993; 21: 245–311.
27. Povea C, Schmitt L, Brugniaux J et al. Effects of intermittent hypoxia on heart rate variability during rest and exercise. *High Alti Med Biol* 2005; 6: 215–225.
28. Hughson RL, Yamamoto Y, McCullough RE et al. Sympathetic and parasympathetic indicators of heart rate control at altitude studied by spectral analysis. *J Appl Physiol* 1994; 77: 2537–2542.
29. Kleiger RE, Miller JP, Bigger JT Jr, Moss AJ. Decreased heart rate variability with increased mortality after acute myocardial infarction. *Am J Cardiol* 1987; 59: 256–262.
30. Bernardi L, Passino C, Wilmerding V et al. Breathing pattern and cardiovascular autonomic modulation during hypoxia induced by simulated altitude. *J Hypertension* 2001;19: 947–958.
31. Akselrod S. Components of heart rate variability: basic studies. In :*Heart Rate Variability*, edited by Malik M and Camm AL. Armonk, NY: Futura, 1995, p. 147–163.
32. Mahar JT, Manchanda SC, Cymerman A et al. Cardiovascular responsiveness to beta-adrenergic stimulation and blockade in chronic hypoxia. *Am J Physiol* 1975; 228: 477–481.
33. Huangh HH, Tseng CY, Fan JS, Yen DH, Kao WF, Chanj CS, Kuo TB, Huang CL, Lee CH. Alterations of heart rate variability at lower altitude in the prediction of trekkers with acute mountain sickness at high altitude. *Clin J Sports Med* 2010; 20: 58–63.
34. Koehle MS, Guenette JA, Warburton DE. Oximetry, heart rate variability and the diagnosis of mild top moderate acute mountain sickness. *Eur J Emerg Med* 2010; 17: 119–122.
35. Schmitt L, Fouillot JP, Millet GP, robach et al. Altitude, heart rate variability and aerobic capacities. *Int J Sports Med* 2008; 29: 300–306.
36. Cornolo, Brugniaux JV, Macarlupu JL, Privat C, Leon-Velarde F, Rrichalet JP. Autonomic adaptations in Andean trained participants to a 4220 m altitude marathon. *Med Sci Sports Ererc* 2005; 37: 2148–2153.
37. Lanfranchi PA, Colombo R, Cremona, Baderna et al. Autonomic cardiovascular regulation in subjects with acute mountain sickness. *Am J Physiol Heart Circ Physiol* 2005; 289; H2364–H2372.