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Physiology Section

Cold Pressor Response in High Landers Versus Low Landers

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ABSTRACT

Background: Native high landers face two main environmental challenges i.e. hypobaric hypoxia and low ambient temperatures. Both factors contribute to increased sympathetic stimulation and increased blood pressure. Despite these challenges, subjects living at high altitude have lower systolic and diastolic pressures as compared to subjects living in plains. Present study investigated cold pressor test (CPT) which is a potential predictor of future hypertension in high landers and low landers

Materials and Methods: Vascular reactivity in terms of changes in systolic and diastolic blood pressure and heart rate in response to cold pressor test has been compared in high lander (n=45) and low lander (n=46) population.

Results: Systolic and diastolic blood pressure changes and heart rate changes with cold pressor test are lower in high landers as compared to low landers. Females in both the groups in general exhibited greater cold pressor response than males.

Conclusion: Hypo-reactive cold pressor test is due to higher parasympathetic tone and lower sympathetic tone. Decreased cold pressor response in high landers reflects another adaptive modulation of sympatho-vagal activity that enables them to stay in hypobaric atmosphere and lower temperatures without undue autonomic stress.

Keywords: Altitude, Autonomic, CPT, Hypertension, Parasympathetic, Sympathetic

INTRODUCTION

Indian Northern mountainous terrain extends from west to east for thousands of miles; where people dwell perennially at and above 5000-6000 feet, with very low winter temperatures; and even in summers, temperature remains very cold. On the contrary low landers of Gangetic plains face winter with low ambient temperatures for a mere 2-3 months.

Native high landers are innately adapted for hypobaric atmosphere and have large barrel shaped chest, small bodies and polycythemia [1-3]. High landers face two main environmental challenges i.e. hypobaric hypoxia and low ambient temperatures. Hypoxia both acute and chronic is known to cause sympathetic stimulation [4-6]. Autonomic functions in general exhibit higher sympathetic tone as revealed by higher LF/HF ratio (Low Frequency / High Frequency ratio) both acute and chronic exposure to high altitude [7-9]. Apart from increased sympathetic stimulation due to hypoxia, cold exposure independently may also contribute to increased blood pressure [10,11]. Despite these two challenges the native populations at high altitudes have systolic and diastolic pressures lower than the population at low altitude. Heart rate have also been reported to be lower in natives at high altitudes, this is largely attributable to higher vagal tone [12-14].

This peculiar lower risk of hypertension and related adverse cardiovascular events in high landers and its physiological correlation needs to be investigated and compared with that of the low landers. The vascular reactivity in terms of blood pressure and heart rate response to cold pressor test is a marker of sympathetic tone [15]. Also vascular reactivity to cold pressor test, has been described as an useful indicator of future hypertension [16-18].

In the present study we have investigated vascular reactivity to cold pressor test in high landers and compared it with low lander population.

MATERIALS AND METHODS

Study Design: This was a cross-sectional experimental study done in two populations; High Landers and Low Landers.

Subjects: High Landers consisted of young males and females in age range of 18-25 years. Subjects were randomly selected from student population of Tehri – Garhwal division of Uttarakhand province of India. All subjects were residing in this region since birth. This hilly region is at around 1550 – 1950 m above sea level and has low ambient temperature ranges from 8-15°C in October-November months.

Low Landers consisted of young males and females in age range of 18-25 years. Subjects were randomly selected from the student population of King George's Medical University, Lucknow (ambient temperature ranges from 20-27°C in October-November months) and all were residing in plains since birth.

All subjects filled a detailed proforma regarding their clinical and personal history. Subjects taking any cardiac antihypertensive drug, bronchodilator, antihistaminic and analgesic agents, alcoholics and smokers were excluded from the study. General clinical examination was performed to rule out any systemic disorder. An informed written consent was obtained from volunteers of all the groups and non invasive nature of experimental protocol was explained to them. The study protocol was approved by ethical committee of the Institute King George's Medical University, Lucknow, India.

Experimental Protocol: We performed all the tests between 9:00 AM - 12:00 PM in the months of October-November to avoid diurnal and seasonal variation. Testing of high landers was done at high altitude while the testing of low landers was done at low altitude. The height and weight were recorded in all the volunteers and Body mass index (BMI) calculated. The Subjects were asked to relax in a chair for 15 min. In all subjects test was performed in sitting posture as described elsewhere [19]. Baseline heart rate was determined from radial pulse for one minute. Systolic (SBP) and Diastolic Blood pressure (DBP) were recorded from right arm by a Sphygmomanometer in mm of Hg. The subjects were then asked to immerse their left hand in a big bowl filled with commercial ice cubicles with some water (0 - 4°C) for 1 min. The SBP and DBP were recorded at the end of one minute from right arm. Simultaneously pulse rate for 15 s at the end of cold stress was determined by another observer.

STATISTICAL ANALYSIS

The results are presented in Mean ± SD and percentages. Normality of data was tested using Shapiro Wilk's test and equality of variance

Parameters	High Landers (n=45)	Low Landers (n=46)
Age in years	18.33 ± 1.33	19.67 ± 1.47
Male:Female	20:25	24:22
Height (cm)	161.17 ± 8.53	166.02 ± 10.17*
Weight (kg)	48.20 ± 7.26	57.36 ± 12.23*
BMI	18.50 ± 1.98	20.65 ± 3.06*
BSA	526.50 ± 49.83	578.41 ± 72.08*
Abdominal girth	64.20 ± 10.51	77.85 ± 10.71*

[Table/Fig-1]: Subject parameters, data presented as Mean ± SD. * represent statistically significant differences ($p < 0.05$)

Parameters	High landers	Low landers	p value
SBP Resting	111.6 ± 11.4	112.5 ± 10.5	0.689
SBP CPR	122.7 ± 11.2	124.4 ± 9.1	0.423
SBP % rise	10.2 ± 3.7	10.9 ± 4.0	0.386
DBP Resting	73.2 ± 8.0	73 ± 8.9	0.891
DBP CPR	83.6 ± 7.7	82.9 ± 8.3	0.692
DBP % rise	14.5 ± 4.4	14.0 ± 4.1	0.600
Pulse Rate Resting	77.2 ± 6.3	79.4 ± 8.3	0.240
Pulse Rate CPT	86.1 ± 8.0	93.4 ± 10.1	0.000
Pulse Rate % rise	11.8 ± 8.5	18.9 ± 13.7	0.004

[Table/Fig-2]: Cold pressure responses in high landers and low landers, values presented as Mean ± SD, p-values represent level of significance as derived from unpaired t-test

was tested using Levene's test. The continuous variables were compared using unpaired t-test and dichotomous parameters compared using Chi Square test between High and Low Landers. The paired t-test was used to compare rise from resting to CPR. Subgroup analysis was done with respect to gender in both high landers and low landers using unpaired t test. Correlation analysis was done using Pearson correlation test. The p-value less than 0. 05 was considered significant. All the analysis were carried out by using SPSS 21. 0 (Chicago, Inc., USA).

RESULTS

There were total of 45 subjects in High Lander group and 46 subjects in Low Lander group. The male and female ratio was similar in both the groups. There was no significant difference in the age between high and low lander subjects. The measured height and weight and abdominal girth were significantly lower among the High Landers as compared to Low Landers. Also the derived parameters body surface area (BSA) and Body Mass Index (BMI) are accordingly lower in highlanders [Table/Fig-1].

The cold pressor response was compared between highlanders and low landers [Table/Fig-2]. There was no significant difference in resting pulse rate, systolic and diastolic blood pressures between the high landers and low landers. With 1 minute cold stress there was a significant rise in pulse rate, systolic and diastolic blood pressures from resting state in both the groups. However there is no statistically significant difference between cold pressor response in terms of absolute rise and percent rise in systolic and diastolic blood pressure between high landers and low landers. Only the rise in pulse rate (both absolute and percent rise) after cold pressor test is significantly lower in highlanders.

Increase in SBP, DBP and pulse rate in response to cold pressor test is in general was lower in females in both high landers and low landers [Table/Fig-3]. Among high landers % SBP rise only reached statistical significance. Among low landers rise in DBP and Pulse rate (both absolute values and percent increase values) shows statistically significant difference between males and females.

Correlation analysis results are presented in [Table/Fig-4]. Resting DBP and rise in DBP correlated with weight of the subjects. Resting DBP also correlated with body surface area of subjects. This correlation was only a weak correlation (r ~ 4). Other statistically significant values of correlation coefficient were less than 4, therefore are not relevant. Derivation of prediction equations was not attempted in view of poor correlations or nil.

DISCUSSION

CPT is used to assess cardiovascular reactivity in normotensive and hypertensive subjects. Increased response to CPT is an potential marker for future hypertensive disease [17]. A 45 years follow up study by Wood et al., also suggests that cold pressor test is a potentially useful predictor of hypertension [18]. Traditionally, the cold pressor response is described only with BP changes, while the heart rate also increases due to sympathetic stimulation. Heart rate response may also provide insight into cardio-autonomic modulation during cold pressor test [20, 21].

High landers are exposed to hypobaric atmosphere along with low ambient temperatures. Low landers when are exposed to high altitude hypoxia and low temperature contribute to increase in sympathetic tone both in short term and in long term. In the present study we have compared the cold pressor response in high lander population and low lander population using both blood pressure changes and heart rate changes. There are no statistically significant differences in systolic and diastolic blood pressures between the two groups in present study. Several epidemiological studies have reported that at high altitudes subjects have typically lower levels of blood pressures both systolic and diastolic [22-24] High lander population in our group is residing at just 1550 – 1950 m height while earlier reports are for the populations at more than 3500 m height. Further both the study groups largely comprise of subjects belonging to almost similar socioeconomic strata and being students their lifestyle does not vary much.

Though there was lesser increase in systolic and diastolic blood pressure (non significant) but the increase in heart rate response in high landers is significantly lower than low landers. Also baseline heart rate is marginally lower in high landers. Autonomic function studies on subjects residing at high altitudes reported higher parasympathetic tone and lower sympathetic tone as reflected by lower LF/HF ratio as compared to subjects living in plains [25-27]. In contrast, the low landers when exposed to high altitude exhibits decrease in parasympathetic tone and increase in sympathetic tone [26-29]. High landers thus have inherently higher parasympathetic tone and lower sympathetic tone.

Baseline systolic and diastolic blood pressures are also a good predictor of future hypertension. In our study groups differences in baseline blood pressures were not statistically significant. Several studies on different groups of population in high altitude reported lower prevalence of blood pressure [30-32]. Fiori et al., particularly studied Asian population at low altitude, medium altitude and high altitudes. The residents at medium altitude did not exhibit lower blood pressures [32]. Our study population also does not corresponds to high altitude and our results are in accordance with medium altitude population blood pressures reported in this study.

Females in general in both high landers and low landers tend to have higher cold pressor response than their male counterparts. This is in accordance with previous reports [33-35]. Apart from inherent differences in sympathetic and parasympathetic modulation in males and females this is also in part explained by increased CPT pain perception in females [34,35].

The cold pressor response parameters didn't exhibited significant correlations with subject parameters. Weight and body surface are though revealed a significant relationship but the level of correlation is weak. Derivation of prediction equations was not attempted in view of poor correlations. Further the small size of the population studied was not expected to yield any meaningful conclusion regarding relationship between the response and subject parameters.

Parameters	High Landers			Low Landers		
	Male (n=20)	Female (n=25)	p Value	Male (n=24)	Female (n=22)	p Value
SBP Resting	111.7 ± 12.3	111.4 ± 10.9	0.333	116.3 ± 9	108.4 ± 10.6	0.599
SBP CPR	121.8 ± 12.6	123.4 ± 10.2	0.226	127.2 ± 8.4	121.5 ± 9.1	0.539
SBP % rise	9.2 ± 3.5	11 ± 3.8	0.008	9.5 ± 3.1	12.4 ± 4.4	0.386
DBP Resting	74.0 ± 8.2	72.6 ± 8	0.940	76.7 ± 8.6	68.9 ± 7.4	0.009
DBP CPR	83.9 ± 8.0	83.4 ± 7.6	0.632	86.2 ± 7.9	79.4 ± 7.3	0.0312
DBP % rise	13.6 ± 4.2	15.2 ± 4.5	0.113	12.8 ± 4.5	15.4 ± 3.3	0.014
Pulse Rate Resting	78.2 ± 6.3	76.4 ± 6.2	0.555	79.6 ± 9.6	78.3 ± 6.6	0.002
Pulse Rate CPT	84.5 ± 7.0	87.4 ± 8.6	0.817	92.5 ± 9.2	94.4 ± 11.2	0.004
Pulse Rate % rise	8.1 ± 3.6	14.7 ± 10.1	0.243	17.2 ± 13.9	20.7 ± 13.6	0.032

[Table/Fig-3]: Cold pressure responses in high landers and low landers according to gender
Values presented as Mean ± SD, p-values represent level of significance derived from unpaired t-test

	Age	Height	Weight	BMI	BSA	Abdominal Girth
SBP Resting	0.03	0.29*	0.35*	0.25*	0.36*	0.35*
SBP CPR	0.01	0.25*	0.34*	0.29*	0.34*	0.34*
SBP % rise	-0.06	-0.25*	-0.18	-0.04	-0.21*	-0.18
DBP Resting	-0.02	0.32*	0.418*	0.31*	0.41*	0.346*
DBP CPR	-0.01	0.28*	0.400*	0.33*	0.38*	0.30*
DBP % rise	0.02	-0.29*	-0.26*	-0.12	-0.28*	-0.30*
Pulse Rate Resting	0.14	0.09	0	-0.07	0.03	0.08
Pulse Rate CPT	.228*	0.01	0.02	0.03	0.03	0.2
Pulse Rate % rise	0.09	-0.06	0.03	0.1	0.01	0.15

[Table/Fig-4]: Correlation analysis between cold pressor test response and subject parameters,
Values represents the Pearson's correlation coefficient (r); * represents significant values (p<0.05)

Cold pressor test is a simple and useful marker for assessing the autonomic modulation of blood pressure response to cold stress. It is able to reflect the differences in high landers versus low landers and also between males and female population.

This study has limitations due to cross-sectional design and its smaller study groups. Studies with larger cohort and long term follow up are warranted for assessment of relationship between cold pressor test response and longitudinal profile of blood pressures in individuals.

CONCLUSION

In the present study we report that the cold pressor test tends to be hyporeactive in high landers as compared to low landers. This hyporeactiveness reflects another adaptive modulation of sympatho-vagal activity that enables them to stay in hypobaric atmosphere and lower temperatures without undue autonomic stress.

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