

CARDIOCIRCULATORY RESPONSES TO UPRIGHT TILT AT SEA LEVEL AND HIGH ALTITUDE

Pages with reference to book, From 306 To 310

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ABSTRACT

A collaborative study was conducted to measure the cardiocirculatory responses to upright tilt in eight young men at sea level (SL); after 1h at 4300m simulated altitude (SA) and at 18h, 66h and 114h during residence at 4300m (HA). Heart rate (HR), stroke volume (SV), cardiac output (Ca), calf blood flow (CBF), blood pressure (BP) and total peripheral resistance (TPR) were obtained during supine rest and after 13 min of 60° head-up tilt using an impedance monitor and an electrospychmomanometer. SL to HA changes in blood volume (BV) were calculated from hematocrit and hemoglobin values. Supine HR, TPR and BP were increased while SV, CO and CBP were reduced SL to HA ($P < .05$). HR and BP in the upright position were increased SL to HA ($P < .05$). The responses to tilt (Asupine to upright) were unaltered SL vs SA. With prolonged exposure, SV, CO, TPR and CBP responses to tilt were reduced ($P < .05$). The reduced responses to tilt at HA were associated with a 10% decline in BV ($P < .01$). It was concluded that the reduction in SV during tilt at SL and SA was compensated for by increases in HR and TPR in order to maintain BP. After 18h HA, BP in the upright position was maintained only by an increase in HR (JPMA 41: 306, 1991).

INTRODUCTION

A rapid, passive change from the supine to an upright position causes venous pooling in the lower extremities. The resultant decreases in cardiac output and arterial blood pressure produce a reduction in the firing rates of the carotid sinus and aortic arch baroreceptors¹⁻³. The reductions in afferent signals from the baroreceptors to the medullary cardiovascular control centre trigger increased sympathetic and decreased para-sympathetic discharge. The changes elicit a peripheral venoconstriction which increases venous return and stroke volume. These responses along with cardiac acceleration and vasoconstriction result in increase in cardiac output and peripheral resistance and in a return of blood pressure towards normal. However, these adjustments to the change in position are not complete due to the increase in hydrostatic pressure in the legs, venous pooling and the resultant loss in blood and plasma volumes⁴. Stroke volume and cardiac output remain depressed while heart rate, peripheral resistance and arterial blood pressure remain elevated relative to the supine position^{5,6}. With high altitude exposure, the sympathetic nervous system becomes more active relative to the parasympathetic nervous system^{7,8}. The hyperactivity is evidenced by increased twenty-four hour urinary excretion levels of catecholamines. By the third to the fourth day of exposure to 3500m, catecholamines are increased as much as 78% above sea-level values and remain elevated for at least 3 weeks⁹. The increased sympathetic tone is associated with an increase in resting heart rate, blood pressure and arteriolar constriction^{5,9}. Exposure to high altitude has also been associated changes in resting stroke volume and cardiac output¹⁰⁻¹⁴. As time at altitude is extended, stroke volume tends to decrease^{10,14,15}, possibly due to reductions in plasma and blood volumes^{16,17}. The decrease in stroke volume is not totally compensated for by the increase in heart rate that occurs at altitude and therefore cardiac output is also reduced^{14,15}. Previous investigations have shown that altitude exposure alters vascular

responsiveness to a cardiocirculatory challenge¹⁶⁻¹⁸. However, the only circulatory variables reported were heart rate, blood pressure, forearm vascular resistance, forearm or calf blood flow or stroke volume and cardiac output. The effect of altitude-induced reductions in plasma and blood volumes on the maintenance of homeostatis during the cardiocirculatory challenges was not reported. The objective of the present investigation was to examine compensatory responses to upright tilt at sea level and after acute and prolonged exposure to high altitude,

PATIENTS AND METHODS

Eight healthy male subjects with an average age, height and weight of 21.6 years, 175.7 cm and 73.13 kg respectively were selected. None of the subjects had been exposed to high altitude for at least six months prior to initiation of this study and none was highly trained. All gave their informed consent and were medically evaluated prior to participation in the study. Each subject was tested on a tilt-table a total of five times: once at sea level (Natick, MA: 50m), once after 1h in a hypobaric chamber (4300m), and after 18h, 66h and 1 14h of residence on the summit of Pikes Peak Co (4300m). The ambient temperature was $23^{\circ}\text{C} \pm 2^{\circ}\text{C}$ during testing at all locations,

Testing protocol overview

Subjects were tested at least one h postprandial. Prior to each day's testing, calf volume was measured by water displacement and a micro-hematocrit was measured from a finger-tip blood sample. Impedance electrodes were applied and the subject rested quietly in a sitting position for 15 min. The subject then lay supine on a tilt table. Securing straps and a steel foot rest allowed the subject to remain passive when changing from one position to another. A blood pressure cuff was placed around the subject's right-upper arm and impedance monitor cables were connected to the electrodes. When tilted to the upright position, the right arm rested at heart level on a shelf situated next to the tilt platform. Blood pressure and heart rate were determined in the supine position every 3 minutes for 15 minutes. From minute 9 to 11, supine thoracic and peripheral impedance data were obtained. At minute 16, the subject was tilted (<2 s) to a head-up 60° angle. Blood pressure and heart rate were determined immediately and every minute for the first five and every two minutes thereafter. At the end of minute 5 and 13 of tilt, upright thoracic and peripheral impedance data were obtained.

Impedance

Impedance data were obtained using an impedance cardiograph (Minnesota; model 304B). A constant sinusoidal current (4mA) with a frequency of 100kHz, applied to electrodes located on the forehead and lateral malleolus, served as an excitation current source. The four pickup electrodes were located at the base of the neck (3 cm to the right of the first thoracic vertebrae), 30 cm directly below on the back and on the lateral segment of the calf 10 and 20 cm above the excitation electrode located on the lateral malleolus. Electrode sites were marked with indelible ink for consistency of placement from day to day. Thoracic impedance changes recorded via the b. electrodes were used to estimate stroke volume and cardiac output while the two lower limb electrodes were used to estimate calf blood flow and calf blood pooling.

To eliminate movement artifacts due to respiration during the collection of the impedance signals, subjects were instructed to hold their breath after a normal exhalation. A minicomputer (MINC; Digital Equipment Corp.) was used to digitize, store and later analyze the impedance signals. The calculations of volume, flow and pooling were made according to Nyboer¹⁹ and others^{2,20} using the systolic down stroke extrapolation method. Volume was calculated according to the equation:

$$V = \frac{PL^2}{Z_0^2} \Delta Z$$

where V is volume (ml); P represents blood resistivity at 100 kHz (ohms/cm); L is the distance between the two pickup electrodes (cm); Z₀ is base impedance (ohms) and ΔZ is pulsatile changes of

impedance (ohms). The impedance change Z is the value of an extrapolated systolic down stroke to compensate for venous run off. Most studies utilizing the impedance technique use a constant value for blood resistivity which assumes little or no change in hematocrit^{2,6,11,15}. However, a significant increase in hematocrit was expected during the altitude exposure. Therefore, a value for blood resistivity was determined prior to each test using a hematocrit obtained from a finger sample²¹. Heart rate was calculated from the impedance pulse recording. Cardiac output and peripheral blood flow were determined by multiplying heart rate by the volume values obtained from the back or calf electrodes, respectively. Changes in blood pooling were estimated according to equation 2.

$V_b = p \cdot (L^2/Z_o^2) \cdot \Delta Z_o$ (2) where V_b represents the degree of pooling (ml) and ΔZ_o is the change in base impedance (ohms). Pooling was expressed in ml/100 ml of body segment tissue relative to the supine position. Systolic and diastolic blood pressure were determined using an electrophygmomanometer (Vita-stat; model 900-s). Mean arterial pressure was calculated as 1/3 pulse pressure plus diastolic blood pressure. Total peripheral resistance was calculated as mean arterial pressure divided by cardiac output. Blood and plasma volumes were estimated using the equations of Dill and Costill²² from the hematocrit and a hemoglobin value obtained from a blood sample taken from an arm vein during rest at sea level, 66h and 114h of altitude. The cyanmethemoglobin procedure was utilized for measurement of hemoglobin (Hycel, Inc). The data were analyzed by analysis of variance with repeated measures, t-tests and where appropriate, Neuman-Keuls post-hoc test. Statistical significance was established at $p < 0.05$.

RESULTS

TABLE I. Cardiocirculatory responses to upright tilt at sea level (S.L.) and at altitude (A).

Variable	Position	S.L.	A (1h)	A (18h)	1 (66h)	A (114h)
Heart rate (beat/min)	Supine	60 ± 4	68 ± 3	72 ± 4*	75 ± 3*	76 ± 5
	13 min tilt	79 ± 5#	90 ± 5#	99 ± 7*#	103 ± 5*#	-
Stroke volume (ML/beat)	Supine	97 ± 9	89 ± 3	78 ± 5	63 ± 6*	63 ± 7*
	13 min tilt	56 ± 3#	58 ± 4#	61 ± 2#	53 ± 4	-
Cardiac output	Supine	5.68 ± .51	6.03 ± .38	5.58 ± .39	4.64 ± .36*	4.66 ± .35*
	13 min tilt	4.39 ± .33#	5.20 ± .41#	5.97 ± .44#	5.23 ± .44#	-
Total peripheral resistance (mmHg/1/min)	Supine	15.23 ± 1.10	13.42 ± .60	17.34 ± 1.28	19.46 ± 1.26*	20.93 ± 1.66*
	13 min tilt	20.78 ± 1.79#	16.28 ± 1.15*#	17.08 ± 1.46	19.39 ± 1.66	-

Values are mean (SE)

*P < 0.05 from sea level value

#P < 0.05 from supine value

TABLE II. Cardiocirculatory responses to upright tilt at sea level (S.L.) and at altitude (A).

Variable	Position	S.L.	A (1h)	A (18h)	A (66h)	A (114h)
Calf blood flow (ml/min)	Supine	63.21 ± 7.40	67.85 ± 14.00	44.23 ± 6.16*	43.04 ± 4.44*	36.54 ± 6.16*
	13 min tilt	25.22 ± 4.71#	30.54 ± 6.65#	27.03 ± 4.75#	21.94 ± 2.58#	30.41 ± 5.86
Blood pooling (ml/min)	13 min tilt	10.03 ± .88	7.84 ± 1.91	10.18 ± 2.27	7.48 ± 1.68	8.57 ± 2.12
Systolic blood pressure (mmHg)	Supine	119 ± 4	120 ± 5	131 ± 3*	123 ± 4	127 ± 3
	13 min tilt	115 ± 2	111 ± 3#	115 ± 3#	120 ±	117 ± 5
Diastolic blood pressure (mmHg)	Supine	65 ± 4	61 ± 6	75 ± 2*	70 ± 3	78 ± 4*
	13 min tilt	77 ± 3#	68 ± 4*#	81 ± 3	68 ± 2*#	83 ± 4
Mean arterial blood pressure (mmHg)	Supine	83 ± 2	80 ± 4	93 ± 1*	87 ± 3	94 ± 3*
	13 min tilt	89 ± 2#	82 ± 3	93 ± 2*	97 ± 2*#	94 ± 4

Values are means (S.E.); N=8

*P < .05 from sea level value

#P < .05 from supine value

Table I and II presents the physiologic parameters obtained from the test subjects while in the supine position and after 13 min of 60° upright tilt at sea level and during 1h, 18h, 66h and 1 14h of altitude exposure. Since no significant differences were found between the 5th and the 13th min of tilt in any of the parameters measured at sea level or altitude, only the 13th min was used for comparison (Table I). Supine heart rate increased steadily throughout the exposure from 60b/min at sea level to 76 b/mm at 1 14h altitude. Upright heart rate increased from 79 b/mm at sea level to 103 b/mm at 66h of altitude. Heart rate, stroke volume, cardiac output and total peripheral resistance were not measured during tilt at 114h of altitude exposure due to technical difficulties. A 35% reduction was observed in supine stroke volume from sea level to the 66h of exposure. Stroke volume in the upright position during altitude exposure was not statistically different from sea level during any of the testing times at altitude. Supine cardiac output tended to decrease from sea-level values after 1 h altitude, but did not change or increase slightly in the upright position. Total peripheral resistance in the supine position declined slightly at 1h altitude then steadily increased to 20.93 mmHg/l/min after 1 14h altitude. During upright tilt, total peripheral resistance was reduced 22% from sea level values after 1h altitude (20.78 mmHg)/l/min). At 18h and 66h altitude, total peripheral resistance in the upright position was not different from sea level (Table II). Supine calf blood flow declined steadily during the entire altitude exposure. The maximum reduction was observed after 1 14h altitude. Calf blood flow during tilt did not change significantly during exposure. Similarly, blood pooling estimations at altitude did not differ from sea level. Supine systolic blood pressure tended to be higher during the altitude exposure but was significantly different only at 18h altitude. There was no significant change at altitude from the sea-level value of 115 mmHg in the upright position. Supine diastolic blood pressure was increased 15% and 20% from sea-level after 18h and 1 14h altitude, respectively. In the upright position, diastolic blood pressure increased above the sea-level value, reaching statistical significance after 66h altitude. In the supine position, mean blood pressure tended to rise as the altitude exposure continued. Mean arterial pressure in the upright position declined slightly after 1h altitude and then increased significantly above sea-level values with continued exposure (Table III).

TABLE III. Hematocrit, hemoglobin, blood volume and plasma volume values at sea level and at 1h, 66h and 114h altitude (4300m)

		SL	1h	66h 114h
Hematocrit (%)	42.1 ± 1.0	42.1 ± 1.0	46.9* ± 0.6	47.9* ± 0.8
Hemoglobin (g/100 ml)	15.12 ± 0.33	A	16.84* ± 0.21	16.84* ± 0.31
Blood volume	100.0	100.0 (Est)	89.9*	89.8*
% of S.L.	± 0.0	± 0.0	± 2.3	± 1.2
Plasma volume	100.0	100.0 (Est)	83.2*	81.0*
% of S.L.	± 0.0	± 0.0	± 3.7	± 2.0

Values are mean ± S.E.

*P < .01 from sea level values

A = Not estimated

Est = Estimated

Blood measurements

Values for hematocrit, hemoglobin, blood and plasma volume at sea level and after 1h, 66h and 114h of altitude are presented in Table III. Hematocrit and hemoglobin increased significantly after 66h of altitude. Blood and plasma volume, calculated from hematocrit and hemoglobin were reduced significantly (p < .01).

DISCUSSION

In the present investigation, none of the circulatory parameters measured in the supine position during the first hour at altitude differed statistically from sea level. After 18h or more of altitude exposure, supine heart rate, total peripheral resistance, diastolic and mean arterial blood pressure were increased while stroke volume, cardiac output and calf blood flow were reduced from their respective sea level values. These results are similar to those reported in previous studies^{5,11,15,18,21}. What has not been reported previously was the response of these parameters to the cardiocirculatory challenge of upright tilt during the first week of altitude acclimatization. Total peripheral resistance, diastolic and mean arterial blood pressure measured in the upright position after 1h altitude were significantly reduced from sea level. However, the responses to upright tilt, i.e., the change in a parameter due to the change in position, in these as well as all of the other parameters measured were not altered from sea level. The similarity of response and the fact that the hematocrit was not different suggest that no significant fluid shift or reduction in plasma or blood volume occurred after 1h altitude exposure. With continued altitude exposure, the differences between the supine and upright values for stroke volume, cardiac output, total peripheral resistance and calf blood flow were reduced. These reductions were due almost entirely to changes in the supine values since the values obtained during upright tilt after 18h altitude were little altered. The reasons for the changes in the parameters measured while in the supine position are most likely related to either an altitude-induced reduction in plasma and blood volume or to increased stimulation of the sympathetic nervous system. In this study, Hct increased from 42.1% at sea level to 46.9% at 66h with a further increase to 47.9% at 114h. Likewise, Hb concentration rose from

15. 12g/100ml at sea level to 16.84g/100ml at 66h and 114h altitude. Blood and plasma volume were estimated to have decreased approximately 10% and 18% respectively after the first two days at altitude. These estimated values are similar to measurements using the Evans Blue dye method under conditions analogous to the present study^{23,24}. The reduction in blood volume was sufficient to reduce venous return which, in turn, decreased stroke volume. Although increased at altitude, heart rate only partially compensated for the reduction in stroke volume. Therefore, cardiac output was also reduced. The increase in sympathetic activity caused by increased plasma norepinephrine levels may also have contributed to the reduction in supine cardiac output. Increased sympathetic discharge causes a reduction in peripheral blood flow by increasing the resistance of the peripheral vessels⁹. In this study, the elevations in supine total peripheral resistance and the decrease in blood flow as time at altitude continued support to this view. Just as some of the changes in supine values can be explained on the basis of increased sympathetic activity, the lack of an increase in total peripheral resistance during tilt after 18h altitude may be due to the increased concentrations of norepinephrine. Upon tilt at sea level, there are increased sympathetic nerve activity and raised plasma levels of norepinephrine¹, resulting in a rise in heart rate, total peripheral resistance and diastolic and mean arterial blood pressure. The results of the present study suggest that because the catecholamine levels were already high due to the altitude exposure, the additional sympathetic nerve activity and release of norepinephrine during tilt did not result in any additional constriction of the resistance vessels. Arterial pressure is the product of three factors: heart rate, stroke volume and total peripheral resistance. At sea level and at 1h altitude, when blood volume was not diminished, the decrease in stroke volume during tilt due to a reduced venous return was primarily compensated for by a combination of increases in heart rate and total peripheral resistance resulting in the maintenance of an adequate blood pressure. The increase in venous tone at this time has been shown to be transient^{25,26}. After 18h altitude, when blood and plasma volumes were significantly reduced and when upright tilt did not raise total peripheral resistance above upright sea level values, the maintenance of blood pressure was provided entirely by an increase in heart rate. Because the values for calf blood pooling were not altered throughout this study, it is not likely that there was a greater venoconstriction during tilt at altitude. A greater and more prolonged venoconstriction would have aided the reduced venous return by causing more blood to move from the veins into the central circulation.

REFERENCES

1. Fluck, D.C and Salter, C Effect of tilting on plasma catecholamine levels in man. *Cardiovasc. Res.*, 1973; 7:823.
2. Shvartz, E., Gaume, S.O., White, R.T. and Reibold, R.C. Hemodynamic responses during prolonged sitting. *J. Appl. Physiol.*, 1983; 54:1673.
3. Ward, R.J., Danziger, F., Bonica, J.J., Allen, O.O. and Tolas, A.G. Cardiovascular effects of change of posture. *Aerospace Med.*, 1966; 257.
4. Hagan, R.D., Diaz, F.J. and Horvath, S.M. Plasma volume changes with movement to supine and standing positions. *J. Appl. Physiol.*, 1978; 45:414.
5. Malhotra, M.S. and Murthy, W.S. changes in orthostatic tolerance in man at altitude of 3500 meters. *Aviat. Space Environ. Med.*, 1977; 48:125.
6. Zambrano, S.S. and Spodick, D.H. comparative responses to orthostatic stress in normal and abnormal subjects. Evaluation by impedance cardiography. *Chest*, 1974; 4:294.
7. Malhotra, M.S. and Mathew, U Effect of prolonged stay at altitude (4000m) on autonomic balance. *Aerospace Med.*, 1974; 45:869.
8. Hoon, R.S., Sherma, S.C., Balanubramanian, V., Chandra, K.S. and Mathew, O.P. Urinary catecholamine excretion on acute induction to high altitude (3658 m). *J. Appl. Physiol.*, 1976; 41:631.

9. Malhotra, M.S., Murthy, W.S., Purkayastha, S.S., Mukberjee, A.K., Mathew, U and Dua, G.L Responses of the autonomic nervous system during acclimatization to high altitude in man. *Aviat. Space Environ. Med.*, 1976; 47: 1076.
10. Klauaen, K. cardiac output in man in rest and work during and after acclimatization to 3,800 m. *3. Appl. Physiol.*, 1966; 21:609.
11. Mori, S., Sakakibara, M., Takabayaahi, A, Takagi, S. and Mita rai, O. Cardiac output responses in rest and work during acute exposure to simulated altitudes of 3,000,4,500 and 6,000 m and during overnight sleep at 4,500 m. *Jpn. 3. Physiol.*, 1982; 32:337.
12. Sime, F., l'enaloz, O., Rutz, U, Gonzalis, N., Ctnvarruhiaa, E. and Postigo, It Hypoxemia, pulmonary hypertenaion and low cardiac output in newcomers at low altitude.). *AppL Phyaiol.*, 1974; 36:561.
13. Vogel, J.A. and Harris, C.W. cardiopulmonary responses of resting man during early exposure to high altitude.). *Appl. Physiol.*, 1967; 22:1124.
14. Vogel, J.A., Hartley, L.H., Cruz, J.C. and Hogan, R.P. Cardiacoutputduringexercisc in aea4level residents at aea level and high altitude. .2. *Appl. Physiol.*, 1974; 36:169.
15. Hoon, R.S., Balasubramanian, V., Methew, O.P., Tiwari. S.C., Sharma, S.C. and Chadha, K.S. Effect of high-altitude expoasure for 10 days on stroke volume and cardiac output. *3. Appl. Physi oL*, 1977; 42:722.
16. Cymerman, A., Fulco, C.S., Young, A.). and Maher, J.T. Acute mountain sickness (AMS): Relationship to forearmvaacular responses. *Fed. Proc.*, 1982; 41:1616.
17. Heiatad, D.D., Wheeler, R.C and Aoki, V.S. Reflex cardiovascular response after 36hr. of hypoxia. *Am.). Physiol.*, 1971; 220:1673
18. Sutton, JR., Houston, C.S. and Jones, N.L ed. Hypoxia, exercise and altitude. New York, AR. Usa, 1983, p. 454.
19. Nyboer, 3. Electrical impedance plethynmography. Springfield, Ill., Thomas, 1959.
20. Van De Water, J.M., Dove, G.B., Mount. BE. and Linton, LA Application of bicelectric impedance to the measurement ofarte rial flow. *J. Surg. Rca.*, 1973; 15:22.
21. Hill, D.W. andThompson, F.D. The importance of blood resistivity in the measurement ofcardiacoutputbythe thoracic impedance method. *Mcd. Biol. Eng.*, 1975; 12:187.
22. Dill, D.B. and Costill, DL Calculation of percentage changes in volumes of blood, plasma and red cells in dehydration. *J. Appl. Physiol.*, 1974; 37:247.
23. Hannon, J.P., Chinn, K.S. and Shields, J.L Effects of acute high-altitude exposure on body fluids. *Fed. Proc.*, 1969; 28:117&
24. Surks, ML. Chinn, K.S. and Matoush, LG. Alterations in body composition in man after acute exposure to high altitude. *J. Appl. Physiol.*, 1966; 21:1741.
25. Samueloff, S.L.. Browse, N.L. and Shcpherd, J.T. Response of capacityvessels in human limbs to head-up till and suction on lowerbody. *J. Appl Physiol.*. 1966; 21:47.
26. Denniston. J.C., Maher, J.T., Reeves, IT., Cruz., J.C., Cymerman, A. and Grover, RF. Measurement of cardiac output by electrical impedance at rest and during exercise. *J. Appl. Physiol.*, 1976; 40:91.