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Noninvasive Assessment of the Vasoconstrictive Effects of Hyperoxygenation

J.W. Dooley and W.J. Mehm

Division of Altitude and Hyperbaric Physiology, Department of Scientific Laboratories, Armed Forces Institute of Pathology, Washington, DC 20306-6000

Dooley JW, Mehm WJ. Noninvasive assessment of the vasoconstrictive effects of hyperoxygenation. J Hyperbaric Med 1989; 4(4):177–187—Eleven healthy volunteers were assessed for changes in mean arterial pressure (MAP), Doppler ankle-arm pressure index, calf arterial blood flow (CABF), and transcutaneous partial pressures of oxygen and carbon dioxide ($P_{tc}O_2$-CO_2) during 30-min periods, breathing air (control) at 1.0 atmosphere absolute (ATA) and 100% oxygen (O_2) at 1.0, 2.0, and 3.0 ATA. Measurements were performed with automated pressure cuffs and strain gauge devices, modified for hyperbaric conditions, to assess regional (calf) vasoconstriction relative to changes in partial pressures of inspired O_2 (PI_{O_2}). Additionally, $P_{tc}O_2$-CO_2 measurements were continuously monitored from the chest (Ch_{O_2} and Ch_{CO_2}) and calf (Cf_{O_2} and Cf_{CO_2}) and were evaluated as a regional perfusion index (RPI). Significant increases in MAP and decreases in both CABF and RPI at 1.0 ATA O_2 were strong indicators of vasoconstriction. The lack of significant changes from 1.0 ATA O_2 responses in both MAP and CABF at 2.0 and 3.0 ATA O_2 suggests vasoconstriction throughout all levels of PI_{O_2}. RPI at 2.0 and 3.0 ATA O_2 did not differ significantly from control RPI. We conclude that 1.0 ATA O_2 elicits sufficient regional vasoconstriction at the calf to reduce extremity cutaneous oxygenation (Cf_{O_2}) relative to central tissue oxygenation (Ch_{O_2}). At 2.0 and 3.0 ATA O_2, despite indications of vasoconstriction, extremity cutaneous oxygenation relative to central tissue oxygenation is not reduced. Our data indicate that hyperbaric oxygen at 2.0 and 3.0 ATA results in an increase in peripheral tissue O_2 delivery, despite vasoconstrictive reductions in peripheral (calf) blood flow.

arterial blood flow, hyperbaric oxygen, mean arterial pressure, transcutaneous oxygenation, strain gauge plethysmography

Introduction

Vasoconstriction resulting from hyperoxygenation is well documented. Cerebral (1–3), retinal (4, 5), renal (6), and skeletal muscle (7–9) vasoconstriction have been reported in humans with elevated partial pressures of arterial oxygen (Pa_{O_2}). Despite the reduction in blood flow associated with vasoconstriction, the hyperoxygenation of arterial blood has been demonstrated to increase tissue O_2 tensions (2, 10–12). This generally accepted increase in tissue oxygenation relative to increased partial pressures of oxygen (PI_{O_2}) is

the basis of hyperbaric oxygen (HBO) therapy. Despite the general acceptance of increased tissue oxygenation, systematic investigation to establish specific dosage effects of $P_{I_{O_2}}$ on regional blood flow and target tissue O_2 tensions has been lacking.

Currently used noninvasive clinical devices allow investigation of extremity blood flow and tissue oxygenation under normobaric conditions. Data obtained from use of these devices under hyperbaric conditions may enhance scientific understanding of tissue oxygenation during HBO therapy.

The purpose of this study was to determine the effects of elevating $P_{I_{O_2}}$ on various physiologic vasoconstrictive and tissue oxygenation indicators. Specifically, mean arterial pressure, the Doppler arm-pressure index, calf arterial blood flow, and calf cutaneous oxygenation were measured as a function of $P_{I_{O_2}}$, using noninvasive vascular assessment and $P_{tc}O_2$-CO_2 monitoring devices under both normobaric and hyperbaric conditions.

Materials and Methods

General

Eleven healthy male volunteers, ranging in age from 21 to 41 yr (mean: 35 yr), were noninvasively monitored for physiologic responses to 30-min sessions of breathing air or 100% O_2 at 1.0 ATA and 100% O_2 at 2.0 and 3.0 ATA, inside a hyperbaric chamber. All subjects were examined and found medically qualified for hyperbaric exposures. Subjects were nonsmokers with normal lungs (radiograph), hematocrit, and hemoglobin (mean: 15.6 $g \cdot dl^{-1}$). Hemoglobin values were also used for calculation of "ideal" arterial blood O_2 content (vol% O_2) at all $P_{I_{O_2}}$ levels (13).

All data were collected from subjects at least 2 h postprandial or before any morning meal was consumed. Subjects breathed air (control) or 100% O_2 from a clear vinyl head tent (hood) assembly supplied by a standard U.S. Air Force A-14 oxygen regulator in the nondiluter (100% O_2) setting. For assessments at 1.0 ATA, exhausting of the hood was assisted by an exhaust boost pump. Concentrations of O_2 and CO_2 inside the chamber were maintained below 23 and 0.05%, respectively, by the chamber air-conditioning system. Except for slight variances during compression and decompression, chamber air temperature was maintained at approximately 22°C with a 55% relative humidity.

Assessments

Brachial systolic (SYS) and diastolic (DIA) pressures were determined by the auscultation method. Mean arterial pressure (MAP) was calculated as DIA + ⅓ (SYS-DIA). Additionally, Doppler arm (ARM) and ankle (ANK) segmental pressures were determined from the use of components from a Vasculab Noninvasive Vascular Diagnostics System (MedaSonics, Inc.), including a bidirectional Doppler, a 5 MHz probe, arm and ankle segmental pressure cuffs,

and an automated system controller modified for hyperbaric use (manuscript in preparation). MAP and an ANK/ARM pressure index (A/PI) were calculated and used as indicators of vasoconstriction. A/PI responses to the various levels of hyperoxia were measured to assess changes in peripheral pressures (ANK) relative to central (ARM) pressures.

Calf arterial blood flow (CABF) was determined from strip chart recordings of repeated strain gauge plethysmographic measurements of arterial inflow to the calf. This required use of the Vasculab strain gauge plethysmograph, with a 33-cm strain gauge and contoured thigh cuff, and a standard ankle pressure cuff. Tests for CABF were performed according to slight modifications of published methods (14, 15). CABF was calculated as percent slope (% slope) and represents percent change in calf volume over time. Transcutaneous partial pressures of O_2 and CO_2 ($P_{tc}O_2$-CO_2) were continuously monitored throughout all experimental sessions from two TCM3 Transcutaneous O_2-CO_2 Monitoring Systems (Radiometer, Copenhagen). Chest $P_{tc}O_2$ (Ch_{O_2}) and $P_{tc}O_2$ (Ch_{CO_2}) and calf $P_{tc}O_2$ (Cf_{O_2}) and $P_{tc}CO_2$ (Cf_{CO_2}) were continuously monitored from outside the chamber. A regional perfusion index (RPI) was derived from Cf_{O_2}/Ch_{O_2} (16). CABF and RPI, like MAP and A/PI, were calculated and assessed as indicators of vasoconstriction.

Normobaric Sessions

Subjects completed a 30-min supine rest period on a gurney inside the unpressurized hyperbaric chamber before initiating 30-min experimental breathing sessions (Fig. 1). Transcutaneous electrodes, heated to 45°C, were

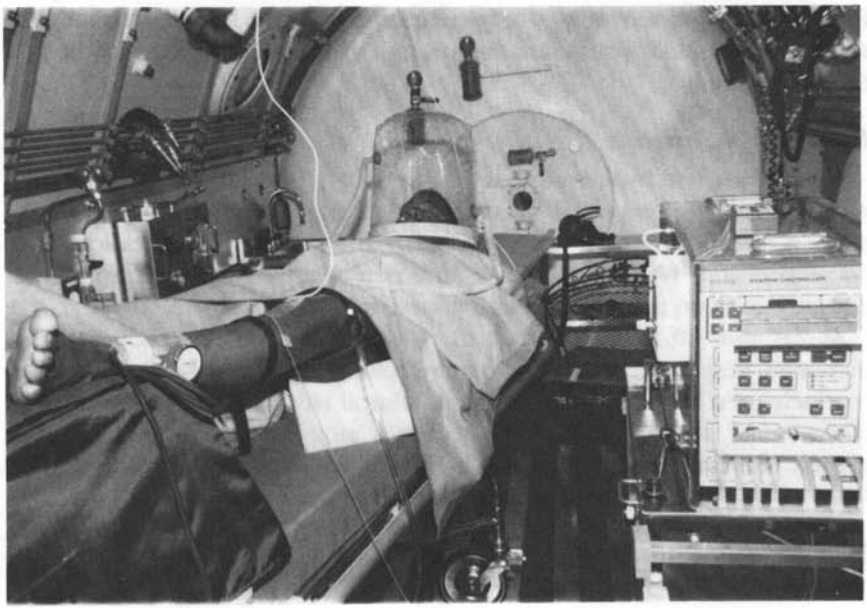

FIG. 1—Subject resting supine on a gurney awaiting assessment of CABF, breathing air (0.21 ATA O_2) or oxygen (1.0, 2.0, or 3.0 ATA O_2) from hood assembly.

applied to the subject's chest, 5 cm inferior to the middle third of the left clavicle and to the posterior-medial aspect of the left calf, just proximal to the predetermined strain gauge site. Before electrode application, the skin was partially decornified by shaving, repeated application and removal of surgical tape (17), and wiping with alcohol. The $P_{tc}O_2$-CO_2 electrodes were connected to adhesive fixation rings applied to the prepared sites. To avoid any cold-induced cutaneous vasoconstriction, subjects were covered with a blanket throughout all sessions.

During the two consecutive 30-min normobaric experimental sessions, subjects breathed unnebulized air (0.21 ATA O_2), then 100% O_2 (1.0 ATA O_2). Midway through each experimental period, two measurements of left arm SYS and DIA were obtained. After these measurements, two Doppler systolic pressures were also obtained at the left brachial (ARM) and left posterior tibial (ANK) arteries. All pressure measurements were completed between Minutes 19 and 22 of each experimental period. The means of the two pressure readings for SYS, DIA, ARM, and ANK were used for statistical analysis. At the end of the final ANK measurement, Ch_{O_2} and Cf_{O_2} were also recorded from $P_{tc}O_2$-CO_2 monitors outside the chamber.

After blood pressure measurements, the subjects were assessed for CABF with the Vasculab system. Strain gauge plethysmograph (SPG) tracings were recorded during the final 5–7 min of each 30-min experimental period. SPG tracings represent percentage calf volume increase due to arterial inflow during above-knee venous occlusion (14). Five, 20–30-sec trials were performed, with approximately 30 sec venous flow recovery between trials. CABF was calculated and expressed as the mean percent slope (% slope) of the last three SPG tracings.

Hyperbaric Sessions

Normobaric and hyperbaric sessions were conducted in the same fashion, with the exception of actual chamber pressurization during hyperbaric sessions. A rate of 0.45 ATA (15 fsw) • min^{-1} for chamber compressions and decompressions was used to lessen the potential for detrimental pressure change effects on the monitoring equipment.

At 2.0 and 3.0 ATA, regulator O_2 supply pressure was progressively increased. Respective regulator pressure settings were consistent with those routinely used by the U.S. Air Force for clinical HBO therapies conducted at 2.36 (wound healing) and 3.0 ATA (carbon monoxide poisoning, gas gangrene). However, exact breathing gas flow rates and CO_2 levels inside the hood assembly during breathing periods were not measured.

Statistical Analysis

Student's t statistic was used to test for statistical significance ($P < 0.05$) of paired treatment comparisons. Critical t values for determining statistical significance were corrected for simultaneous multiple mean comparisons,

according to Boniferroni (18). The Pearson Product Moment Correlation Coefficient was used to test for statistically significant relationships ($P < 0.05$) between variable means within treatments. Data are expressed with bar graphs to indicate that experimental findings at each treatment level represent discontinuous events (Figs. 2–4).

Results

Mean values (± SD) of measured and derived variables representing cutaneous oxygenation, blood pressure, and blood flow responses to 0.21 (control), 1.0, 2.0, and 3.0 ATA O_2 are listed in Table 1. Mean differences between experimental groups for SYS, DIA, and MAP were not significant. Statistically significant differences in MAP at all levels of PI_{O_2} relative to controls are depicted in Fig. 2. Doppler ARM, ANK, and A/PI were not significantly affected by increases in PI_{O_2}. Consistent differences were observed between SYS and ARM at all levels of PI_{O_2}, apparently related to lag time inherent in the remote control procedure of recording Doppler pressures.

In addition to the expected correlations between actual and derived pressure values, statistically significant correlations were observed between SYS and RPI at 3.0 ATA O_2 (Table 2).

Dramatic increases were observed in Ch_{O_2} and Cf_{O_2} as PI_{O_2} was increased, with Cf_{O_2} being lower than Ch_{O_2} at every level of PI_{O_2} (Table 1). The ratio of Cf_{O_2} to Ch_{O_2} (RPI) remained virtually constant except for a significantly lower RPI at 2.0 ATA O_2 relative to RPI at 1.0 ATA O_2 (Fig. 3). Ch_{O_2} and Cf_{O_2} were not

Table 1: Dependent Variable Mean Values (± SD)

	PI_{O_2}, (ATA)							
Variable	0.21		1.0		2.0		3.0	
SYS, mmHg	119.4	(10.3)	124.0	(10.5)	126.1	(15.6)	128.5	(13.2)
DIA, mmHg	78.1	(7.3)	82.8	(8.5)	83.8	(10.9)	86.6	(9.1)
MAP, mmHg	91.9	(7.5)	96.5	(8.3)	97.9	(12.0)	100.6	(9.9)
ARM, mmHg	116.0	(10.7)	116.5	(9.6)	114.9	(12.2)	117.4	(15.4)
ANK, mmHg	127.2	(12.2)	131.1	(11.3)	130.6	(13.4)	129.7	(16.1)
A/PI, ratio	1.16	(0.05)	1.13	(0.07)	1.14	(0.05)	1.15	(0.13)
Ch_{O_2}, mmHg	76.0	(15.3)	523.8	(51.4)	1178.0	(92.5)	1944.5	(134.3)
Cf_{O_2}, mmHg	63.2	(9.5)	374.5	(52.4)	1031.6	(107.1)	1628.4	(126.0)
RPI, ratio	0.85	(0.17)	0.72	(0.10)	0.88	(0.13)	0.84	(0.07)
Vol% O_2	20.8	(0.9)	23.0	(0.9)	25.4	(0.9)	27.8	(1.0)
Ch_{CO_2}, mmHg	42.1	(3.1)	39.1	(3.5)	37.2	(3.1)	36.1	(2.5)
Cf_{CO_2}, mmHg	42.8	(2.6)	40.4	(2.6)	39.9	(2.7)	38.5	(2.9)
CABF, % slope	11.5	(4.1)	8.4	(3.7)	7.7	(2.2)	8.4	(2.9)

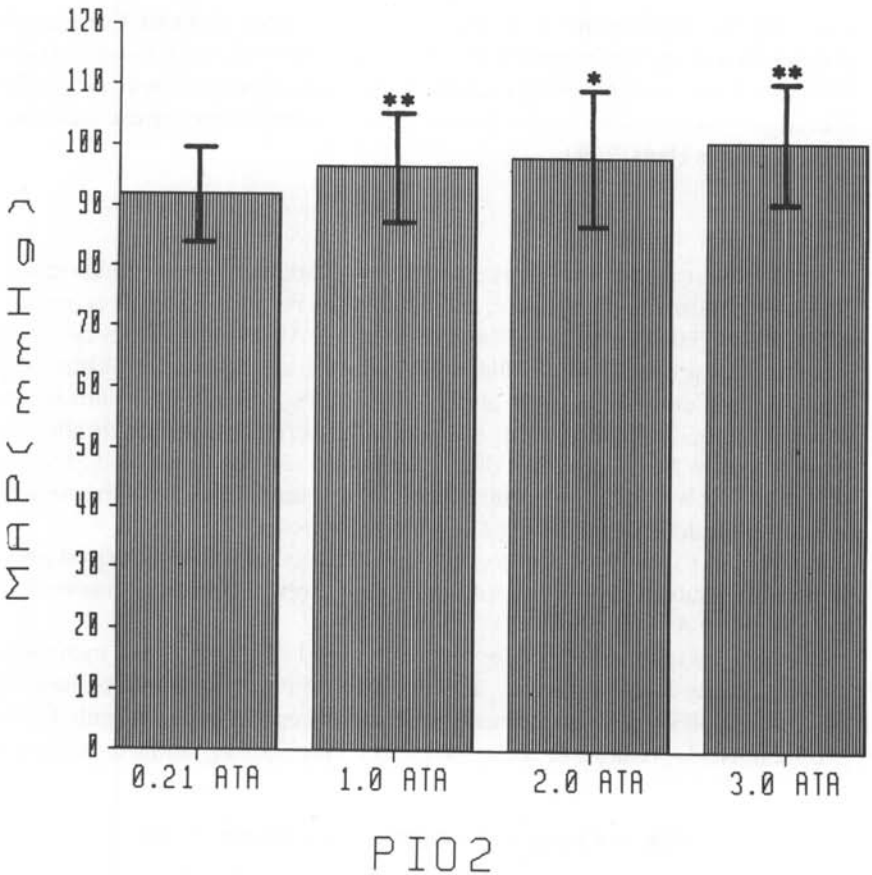

FIG. 2—Mean arterial pressure means (± SD) at 0.21, 1.0, 2.0, and 3.0 ATA O_2 ($n = 11$). *Asterisk* denotes $P < 0.05$; *double asterisks* denote $P < 0.01$ level of significance for comparisons to the control (0.21 ATA O_2) mean.

Table 2: Selected Significant Correlations

PI_{O_2}	Variables	Correlation	*P* Value
0.21 ATA	vol% O_2 vs. CABF	−0.661	0.027
	Ch_{O_2} vs. RPI	−0.757	0.007
1.0 ATA	vol% O_2 vs. CABF	−0.659	0.027
	Cf_{O_2} vs. RPI	0.752	0.008
3.0 ATA	RPI vs. Cf_{O_2}	0.662	0.027
	Ch_{CO_2} vs. Cf_{CO_2}	0.829	0.002

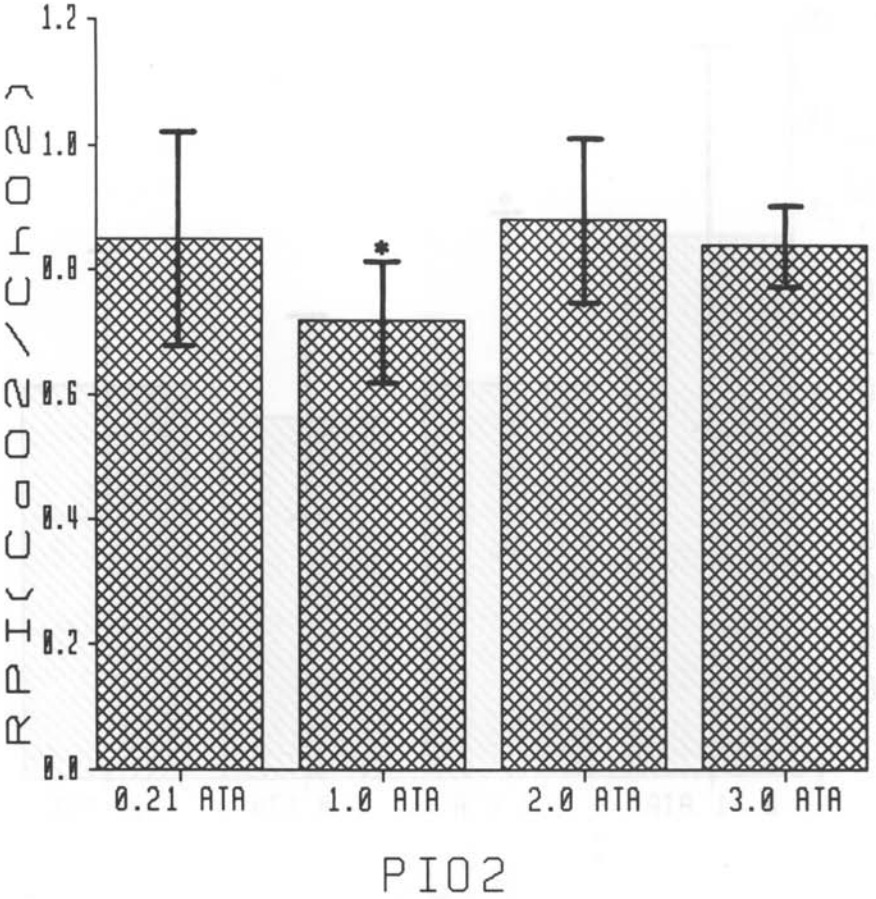

FIG. 3—Regional perfusion index means (± SD) at 1.0, 2.0, and 3.0 ATA $P_{I_{O_2}}$ (n = 11). *Asterisk* denotes $P < 0.05$ level of significance for comparison to 2.0 ATA O_2.

significantly correlated at any level of $P_{I_{O_2}}$. There were several significant correlations between RPI and both Cf_{O_2} and Ch_{O_2}. However, these correlations were expected because of the derivation of RPI from mean values of these Ptc_{O_2} measurements.

Except for an insignificant decrease in Cf_{CO_2} at 2.0 ATA O_2, decreases in Ch_{CO_2} and Cf_{CO_2} were significant at all treatment levels of $P_{I_{O_2}}$. Ch_{CO_2} and Cf_{CO_2} were significantly correlated at 0.21 and 3.0 ATA O_2.

The 27% reduction in CABF at 1.0 ATA O_2 was significant, but substantial reductions in CABF at 2.0 and at 3.0 ATA O_2 were not significant (Fig. 4). Significant correlations were observed between CABF and vol% O_2 for 0.21 and 1.0 ATA O_2 (Table 2) but not for 2.0 or 3.0 ATA O_2.

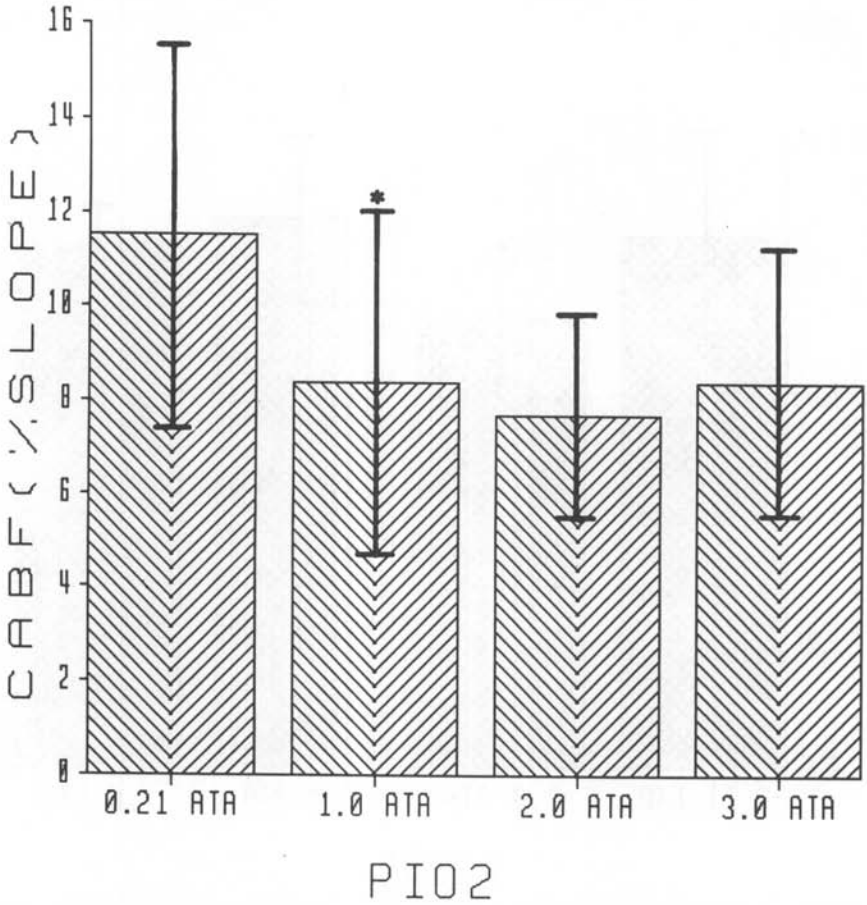

FIG. 4—Calf arterial blood flow means (± SD) at 1.0, 2.0, and 3.0 ATA $P_{I_{O_2}}$ ($n = 11$). *Asterisk* denotes $P < 0.05$ level of significance for comparisons to control (0.21 ATA O_2) mean.

Discussion

Mean arterial pressure, RPI, and CABF were all significantly affected by subjects' inhalation of 100% O_2 at 1.0 ATA. Analysis of responses suggests that all three variables responded as indicators of vasoconstriction. However, changes at 2.0 and 3.0 ATA O_2 were variable and more difficult to interpret. Therefore, discussion of our findings will be made relative to level of $P_{I_{O_2}}$.

0.21 ATA O_2

Control Ch_{O_2} was consistent with previously published data (16, 19–21), as was Cf_{O_2} (16, 19). The slightly lower Cf_{O_2} in our subjects is also consistent with previous findings of a decreasing gradient from central to peripheral monitoring sites (16, 21). Similarly, the 0.85 RPI calculated from Cf_{O_2}-Ch_{O_2} was consis-

tent with a previously reported RPI of 0.89 (16). The transcutaneously measured Ch_{CO_2} and Cf_{CO_2} (Table 1) were consistent with expected changes at all experimental levels of PI_{O_2}, although 0.21 ATA O_2 values were slightly higher than previously reported directly measured Pa_{CO_2} values (2, 22).

1.0 ATA O_2

The significant increase we observed in MAP at this PI_{O_2} (Fig. 2) has been reported previously (1, 22). However, others have reported no significant increase in MAP at PI_{O_2} levels from 1.0 to 3.0 ATA (2, 6, 8, 9, 13). Our finding of increased MAP strongly suggests vasoconstriction.

The significantly lower RPI at 1.0 ATA O_2 (Fig. 3) was due to a proportionally smaller rise in Ca_{O_2} relative to Ch_{O_2} (Table 1). This diminished cutaneous oxygenation in the calf relative to the chest strongly suggests regional vasoconstriction (16) and leads us to conclude that concurrent changes in MAP and RPI are valid indicators of peripheral vasoconstriction during inhalation of 100% O_2 at 1.0 ATA.

Reduction in cardiac output occurring during O_2 breathing at 1.0 ATA O_2 (6, 22–24) confounds the interpretation of the statistically significant decrease in CABF (Fig. 4) and the correlation of CABF to vol% O_2 (Table 2) observed in our subjects. However, at 1.0 ATA O_2 we observed a 27% reduction in CABF, proportionately much greater than the 5–17% reductions previously reported in cardiac output (6, 22–24). This response of CABF suggests a vasoconstrictive component that is independent of and additive to a concurrent reduction in cardiac output. The significant increase (5%) in MAP concurrent with reduction in cardiac output further suggests vasoconstriction.

The significant reductions in Ch_{CO_2} ($P < 0.001$) and Cf_{CO_2} ($P < 0.05$) we observed at 1.0 ATA O_2 are consistent with directly measured changes in Pa_{CO_2} values reported elsewhere (2, 22). Reported increases in venous pressures of CO_2 during O_2 breathing seem to be proportional to decreases in Pa_{CO_2} (2, 13), with no indications of tissue accumulation of CO_2 (2).

2.0 and 3.0 ATA O_2

Mean arterial pressure and CABF values at 2.0 and 3.0 ATA O_2 were not significantly different from those at 1.0 ATA O_2 (Figs. 3 and 4). That MAP was significantly elevated at both 2.0 and 3.0 ATA O_2 strongly suggests vasoconstriction. Despite this apparent vasoconstriction, the RPI at 2.0 and 3.0 ATA O_2 was not altered from the control (0.21 ATA O_2) value of RPI (Fig. 3). This response suggests that, although convective O_2 delivery is reduced with reduction in blood flow to the calf, calf cutaneous tissue O_2 delivery is substantially increased during HBO because of increases in diffusive O_2 delivery.

The significant reduction of Ch_{CO_2} at 2.0 and 3.0 ATA O_2 ($P < 0.01$) and Cf_{CO_2} at 3.0 ATA O_2 ($P < 0.05$) is consistent with previous findings (2, 25). Again, as at 1.0 ATA O_2, reported increases in venous pressures of CO_2 (2, 13)

are apparently proportional to decreases in Pa_{CO_2} and do not result in tissue accumulation of CO_2 (2).

Conclusions

We have found that MAP, RPI, and CABF are useful, noninvasive indicators of extremity vasoconstriction. Responses of these vasoconstrictive indicators to varying levels of PI_{O_2} lead us to conclude that the major portion of the vasoconstrictive response to PI_{O_2} occurs between 0.21 and 1.0 ATA O_2. Further, we conclude that increases in diffusive O_2 delivery during HBO are greater than reductions in convective O_2 delivery associated with observed decreases in CABF. Our findings support the efficacy of HBO in elevating extremity cutaneous oxygen delivery.

Additionally, we conclude that automated strain gauge plethysmographic and transcutaneous O_2/CO_2 monitoring devices are useful in assessing vasoconstrictive effects of normobaric and hyperbaric oxygenation. However, to differentiate the contributions of regional vasoconstriction and cardiac output to the total reduction in extremity blood flow, we suggest the assessment of cardiac output in future investigations.

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James W. Dooley is an aerospace physiologist in the United States Air Force Biomedical Science Corps. Correspondence should be addressed to Major Dooley at DGMC/SGPH, Travis Air Force Base, CA 94535-5300.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Departments of the Army or Air Force or of the Department of Defense.

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