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Effects of hyperbarism on central respiratory drive and respiratory pattern in humans

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Rocco M, Pelaia P, Conti G, Malpieri R, Cottini F, Bortone C, Gasparetto A. Effects of hyperbarism on central respiratory drive and respiratory pattern in humans. Undersea Hyperbaric Med 1994; 21(3):315–319.—The aim of our study was to evaluate the effects of increasing pressure (from 1 to 3 and 6 atm abs) on respiratory drive, respiratory pattern, and inspiratory impedance of the respiratory system. Seven healthy volunteers were studied during a dry compression to 6 atm abs in a hyperbaric multiplace chamber. We observed a significant increase in tidal volume, $P_{0.1}$ (the pressure generated in the airway after 100 ms of inspiration against a closed inspiratory line), T_{tot}, and T_i, and a significant respiratory rate reduction with increasing pressure from 1 to 3 atm.abs; $P_{0.1}$ also increased significantly when comparing 3 and 6 atm abs measurement with 1 atm abs. The $P > 0.01$ and $P_{0.1}/(VT/T_i)$ showed a significant progressive increase compared with 1 atm abs. In conclusion, the passage from 1 to 3 and 6 atm abs causes, in healthy subjects at rest, an increase in the central respiratory drive activity, evaluated with $P_{0.1}$ measurement. The response to the respiration system is an increase in tidal volume and T_i with a decrease in respiratory rate.

hyperbaric air, respiratory drive, respiratory pattern, inspiratory occlusion pressure, impedance of the respiratory system

As demonstrated by Whitelaw et al.(1), neuromuscular respiratory drive can be evaluated easily from the analysis of $P_{0.1}$ (the pressure generated in the airway after 100 ms of inspiration against a closed inspiratory line) provided that the occlusion is rapid, noise free, and not perceived by the subject. This procedure has been validated by many authors both in normal humans in various conditions (1–6) and in pathologic situations (7, 8).

The aim of the present study was to evaluate the effects of the hyperbaric environment on $P_{0.1}$ and on the respiratory pattern and inspiratory impedance in healthy humans.

MATERIALS AND METHODS

The study was performed on seven healthy, non-smoking human volunteers (age 34.4 ± 5.3 yr; mean ± SD; three women and four men) during a dry compression to 6 atm abs in our hyperbaric multiplace chamber. Informed consent was obtained from the volunteers. All subjects were familiar with exposure to raised ambient pressure; moreover, they were trained in breathing via a mouthpiece to minimize the artifacts linked to this specific condition of breathing. All measurements were done in a noise-free environment and the subjects were blindfolded during the whole procedure. During the study they were comfortably sitting upright and rested at least 10 min between each series of measurements.

A specific breathing device fitted with an occlusor was built; it was composed of a spirometry mouthpiece (Hewlett Packard, Palo Alto, CA) connected through a central luminal airway pressure line to a pressure transducer (Bentley-Trantec, UK) located in the chamber and connected to the outside through a specific channel to register pressure at the airways opening (PAO) on a Kontron 3100 polygraph. No appreciable shift or alteration in amplitude up to 20 Hz was observed with this pressure measure system.

The mouthpiece was connected through a breathing valve with a Venturi flow meter positioned in the expiratory line, calibrated at each pressure, to obtain airflow tracings and ventilation values by integration of the flow signals. The resistive pressures of the inspiratory line at a flow value of 1 liter/s were 1 and 3 cmH_2O at 1 and 6 atm abs, respectively; the resistive pressures of the expiratory line at the same flow rate were 1.3 and 3.1 cmH_2O at 1 and 6 atm abs, respectively. The inspiratory line end allowed connection to a unidirectional, low-resistance valve (DAR Lab, Mirandola, Italy) to obtain rapid, noise-free, hand-driven occlusion of the inspiratory line. Basically, the valve consists of a cylinder containing an inflatable rubber valve that was activated during expiration. In this way, the subjects started an inspiration against a closed inspiratory line, and occlusion pressure was recorded.

Baseline values of tidal volume (VT), respiratory rate (RR), minute ventilation (VE), inspiratory time (T_i), expiratory time (T_e), total breathing cycle (T_{tot}), t_i/T_{tot}, mean inspiratory flow (VT/T_i), occlusion pressure $P_{0.1}$, and effective inspiratory impedance [$P_{0.1}/(VT/T_i)$] were obtained in the chamber at 1 atm abs. Respiratory pattern was calculated on 10 breaths, $P_{0.1}$ values, and derived variables were obtained as a mean of three measurements repeated in at least 30-s intervals. The same variables were also recorded at 3 and 6 atm abs. In four subjects the sequence of measures was 1, 3, and 6 atm abs, whereas in three the sequence was 3, 6, and 1 atm abs.

All data, expressed as mean (±SD), were statistically evaluated with the analysis of variance test for repeated measurements. Values of $P < 0.05$ were considered significant. The gas density was evaluated according to the formula: (specific gravity $O_2 \times \%O_2 \times$ atm abs) + (specific gravity $N_2 \times \%N_2 \times$ atm abs) = total gas density (9).

RESULTS

The progressive increase of pressure from 1 to 3 atm abs produced a significant increase in $P_{0.1}$, VT, and T_{tot} in our healthy subjects (Table 1). Respiratory rate

Table 1: Modification of Respiratory Variables in Seven Healthy Volunteers Breathing Air at 1, 3, and 6 atm abs

	1 atm abs (T0)	2 atm abs (T1)	3 atm abs (T2)
R.R., breath/min	15 ± 4.16	12.9 ± 4.47[a]	12.5 ± 3.87[a]
VT, liter	0.54 ± 0.18	0.60 ± 0.27	0.77 ± 0.31[a]
VE, liter/min	7.8 ± 2.4	7.27 ± 2.20	7.97 ± 1.97
P0.1, cmH_2O	1.77 ± 0.40	2.50 ± 0.62[a]	3.33 ± 0.46[a,b]
VT/Ti, liter/s	0.35 ± 0.10	0.29 ± 0.08	0.35 ± 0.05
Ttot, second	4.27 ± 1.2	5.04 ± 1.65[c]	5.09 ± 1.28[c]
Ti, second	1.51 ± 0.25	2.19 ± 0.80[c]	2.13 ± 0.69[c]
Te, second	4.44 ± 1.84	4.86 ± 1.59	4.63 ± 1.29
Ti/T_{tot}	0.27 ± 0.07	0.29 ± 0.06	0.31 ± 0.07
P0.1/(VT/Ti), cmH_2O/liter/second	5.20 ± 1.24	8.90 ± 2.52[a]	9.46 ± 2.28[a]

[a] $P < 0.01$ vs. T0; [b] $P < 0.05$ vs. T0; [c] $P < 0.01$ vs. T1; [d] $P < 0.05$ vs. T1.

showed a significant decrease at 3 atm abs. Respiratory rate at 6 atm abs was not modified in comparison to 3 atm abs values. As a new result of the inverse modifications of RR and VT, the VE did not show significant variations at 3 or at 6 atm abs.

The T_i was significantly increased in comparing both 1 and 3 atm abs and 1 and 6 atm abs. $P_{0.1}$ showed a significant increase both comparing 1 and 4 atm abs measurements and comparing 3 atm abs with 6 atm abs measurements. $P_{0.1}/(VT/T_i)$ ratio, a measure of the effective impedance of the respiratory system, showed a significant progressive increase comparing the base values with 3 and 6 atm abs results. As shown in Fig. 1, the best fit describing the relationship between $P_{0.1}/VT/T_i)$ and air density was the equation: $y = 10{,}473 + (-594.217/\times)$ with $R = -0.69$.

DISCUSSION

The aim of this investigation was to analyze the effects of hyperbarism on respiratory pattern, inspiratory impedance, and central respiratory drive (evaluated from

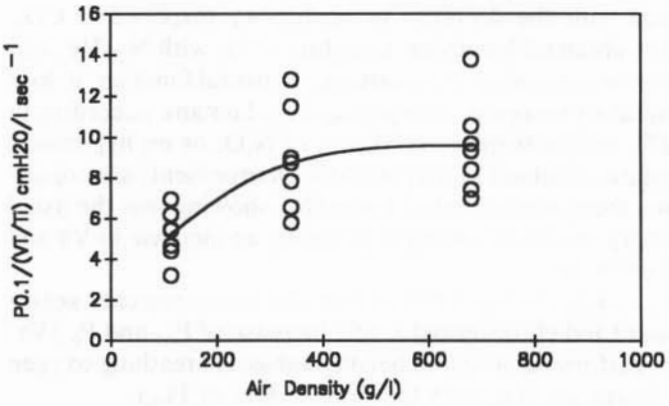

FIG. 1—Relationship between $P_{0.1}$ (VT/T_i) and inspired air density at 1, 3, and 6 atm abs.

$P_{0.1}$ values) in healthy humans. Since its introduction in clinical use (1), $P_{0.1}$ has been extensively studied in spontaneously breathing patients (1, 4, 5, 9–11) and shows, at least in patients with acute respiratory failure, a correlation with inspiratory and expiratory work of breathing (12). As $P_{0.1}$ measurement requires no sophisticated devices and is a simple procedure, it can also easily be used in hyperbaric environments to analyze the ventilatory demand of subjects at different pressures (2). Our results are consistent with those obtained in previous studies.

Linnarsson and Hesser (13) studied the ventilatory responses to CO_2 and exercise in high P_{N_2} environments by evaluating the $P_{0.1}$; they excluded any role for narcotic depression in the modification of central respiratory drive observed during their study. Hesser and Lind (2) evaluated $P_{0.1}$ and related variables in normal subjects breathing 100% O_2 at 1.3 atm abs and breathing air at 6 atm abs; they suggested that the respiratory drive was enhanced in response to an increase of inspiratory loading due to high gas density. Saltzman et al. (14), evaluating the effects of pressure on ventilation and gas exchange in a group of healthy subjects, observed a progressive reduction of respiratory rate that was inversely related to ambient pressure and inspired gas density and an increase in V_T directly, which was related both to pressure and density. The authors concluded that this correlation may reflect the correlation between gas density and pressure or may be an indication of a direct independent effect of pressure. Linnarsson and Hesser (13) studied the difference between raised ambient pressure and mechanical loading on the function of the respiratory centers by comparing the responses of ventilation and central respiratory drive to progressive hypercapnia at two levels of N_2 pressure. Their results (13) showed that $P_{0.1}$ progressively increased the pressure, although not sufficiently to prevent a reduction of ventilation, which was probably due to the increase of gas density. Moreover, comparing their data with those obtained by Camporesi et al. (15) in subjects breathing 1–5.6 atm abs He–O_2 mixture, the authors proposed that the increased airway resistance was responsible for the observed increase in respiratory center activity. The study by Camporesi et al. (15) allowed the exclusion of an independent effect of pressure per se on central respiratory drive.

The preeminent role played by gas density modifications has been underlined by Gelfand et al. (16), who compared V_T, respiratory rate, $\dot{V}$, and Pa_{CO_2} modifications of two subjects who breathed mixtures of O_2 with N_2, Ne, and He over a gas density range of 0.24–22 g/liter and a pressure range of 1–37 atm abs. The analysis of $\dot{V}/Pa_{CO_2}$, as functions of pressure and inspired gas density, showed that the increase of gas density was associated with the decrease of ventilatory response to CO_2; moreover, comparing the data obtained breathing a mixture of O_2 with N_2, He, and Ne, the authors hypothesized that even when N_2 is narcotic to mental function, it does not produce a depressant ventilatory response to hypercapnia in humans, according to studies on breath holding (17), on the respiratory effects of N_2O, or on hyperbaric Ne inhalation (18). These results, obtained in a hyperbaric environment, are consistent with data obtained from a study performed at 1 atm abs, showing that the usual response at rest to an inspiratory resistive loading is generally an increase in V_T and a decrease of respiratory rate (19, 20).

The role of increased P_{O_2} values during 3 and 6 atm abs measurements seems negligible, because Hesser and Lind (3) observed a 40% increase of $P_{0.1}$ and $P_{0.1}(V_T/T_i)$ comparing measurements performed at rest in healthy subjects breathing oxygen at 1 and 4 atm abs or air at 6 atm abs (i.e, with the same values of Pi_{O_2}).

In conclusion, our study has shown that a pressure increase from 1 to 3 and 6 atm abs in healthy subjects at rest causes an increase in central respiratory drive activity. The functional respiratory response observed is an increase in V_T and T_i with a decrease in respiratory rate. These responses are probably due to an increase in airway resistance as a consequence of air density increase (about 6 times from basal 1 atm abs value) and to the need to minimize the inspiratory work of breathing.

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