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AUGMENTED CHEMOSENSITIVITY AT ALTITUDE AND AFTER RETURN TO SEA LEVEL: IMPACT ON SUBSEQUENT RETURN TO ALTITUDE[1]

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SUMMARY. Augmentation of hypoxic (HVR) and hypercapnic (HVCR) ventilatory chemosensitivity is a component of acclimatization in lowlanders sojourning at high altitude. Previous studies suggest that the augmented ventilatory chemosensitivity declines upon return to sea level (SL) over one or more weeks. We hypothesized that some degree of ventilatory acclimatization would be retained upon reintroduction to altitude (RA) 8 days following return to SL due to retention of enhanced chemosensitivity. Ventilation (VE/VCO_2), arterial oxygenation (SaO_2), HVR ($\triangle VE/\triangle Sa-O_2$) and HCVR ($VE/PCO_2$) of 11 male lowlanders were measured during rest at SL, after 1, 2 and 14 days residence at 4300 m, and at 1, 3 and 7 days after return to SL and in 6 subjects during a 24 hr RA after 8 days at SL. Ventilatory acclimatization produced an increase ($P < 0.005$) in VE/VCO_2 (-12%), SaO_2 (-10%), HVR(-170%) and HCVR (-43%). After returning to SL, HVR and HCVR remained elevated ($P<0.05$) for at least 3 days. During RA, subjects demonstrated a retention of -90 and -67% of their acclimatization responses for VE/VCO_2 and SaO_2 respectively, even though HVR and HCVR were no longer statistically elevated. These measurements of ventilation and arterial oxygenation during re-exposure to high altitude clearly indicate the retention of ventilatory acclimatization, thus lessening the hypoxic stress during subsequent sojourns to altitude within that time period. However, the absence of augmented chemosensitivity to either hypoxia or hypercapnia in these subjects leaves the mechanism for this enhanced ventilatory response in question.

Keywords: acclimatization, deacclimatization, altitude, ventilation, control of breathing.

RESUMEN. El aumento de la sensibilidad de los quimioreceptores a la hipoxia (HVR) e hipercapnia (HCVR), es componente de la aclimatación en residentes del nivel del mar que ascienden a la altura. Estudios previos sugieren que esta mayor sensibilidad de los quimioreceptores declina al retornar a nivel del mar (NM) por el lapso de una a más semanas. Hemos formulado la hipótesis que algún grado de aclimatación ventilatoria se mantendría al re-ascender a la altura (RA) 8 días después del retorno a NM, debido a una retención de la hipersensibilidad de los quimioreceptores. La ventilación (VE/VCO_2), oxigenación arterial (SaO_2), HVR (VE/SaO_2) y HCVR (VE/PCO_2) de 11 hombres del nivel del mar se midieron en reposo a nivel del mar, después de 1, 2 y 14 días de residencia a 4300 m, a los 1, 3 y 7 días después de retornar a NM y en 6 sujetos que estuvieron durante 24 horas en RA, 8 días después a nivel del mar. La aclimatación ventilatoria produjo un incremento ($p<0.05$) en VE/VCO_2 (-12%), SaO_2 (-10%), HVR (-170%) y HCVR (-43%). Después de retornar a NM, HVR y HCVR permanecieron elevadas ($P<0.05$) por lo menos durante 3 días. Durante el re-ascenso, los sujetos demostraron una retención de -90 y -67% de sus respuestas de aclimatización para la VE/VCO_2 y SaO_2 respectivamente, a pesar que el HVR y HCVR ya no estaban estadísticamente elevadas. Estas mediciones de la ventilación y oxigenación arterial durante la re-exposición a la altura claramente apuntan a la retención de la aclimatación ventilatoria, y consecuentemente disminuyen el stress hipóxico durante subsecuentes reascensos a la altura en ese período. Sin embargo, la ausencia del aumento de la sensibilidad de los quimioreceptores a la hipoxia o a la hipercapnia en estos sujetos, deja en interrogante cual es el mecanismo para esta respuesta ventilatoria incrementada.

Palabras Claves: aclimatization, deaclimatization, altitud, ventilación, control of respiración.

INTRODUCTION

The time course and expression of a wide variety of physiological adaptations to altitude acclimatization have been well studied. However, the same cannot be said for the process of deacclimatization to high altitude (HA), or the physiological responses accompanying reintroduction to high altitude following recent residence at altitude. It is logical to assume that the physiological responses which accompany altitude acclimatization undergo a deacclimatization

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process of similar duration upon return to low altitude.

Ventilatory acclimatization to high altitude occurs over a period of several days to weeks. Upon return to sea level (SL), resting ventilation decreases toward sea level values but initially remains slightly elevated. Several studies have reported resting ventilation and ventilatory chemosensitivity to hypoxia (HVR) and hypercapnia (HCVR) to be elevated above pre-altitude exposure controls from a few days to as long as 45 days after return to SL (Forster et al., 1971; Lahiri et al., 1972; Sato et al.1992). For example, Sato et al. found that HVR, decreased approximately 40% over the first 7 days following return to SL from six days residence at 3,800 m. However, we are not aware of any studies which have longitudinally examined the ventilatory responses of lowlanders before, during and after high-altitude residence and upon subsequent reintroduction to high altitude following return to sea level. Therefore, the purpose of this study was to test the hypothesis that some degree of ventilatory acclimatization to altitude would be retained upon re-exposure to HA eight days following return to SL. Specifically, we hypothesized that enhanced hypoxic and/or hypercapnic ventilatory responsiveness would be retained for this period following return to SL and upon re-exposure to HA.

METHODS

Eleven healthy male lowland residents participated in this investigation. All were young (mean$\pm$SD) (29$\pm$1 y), very fit (peak oxygen uptake 56$\pm$2 ml/kg/min) members of the U.S. Army Special Forces. All studies were conducted with the subjects resting semisupine and fasted at least 2 hr. Resting ventilation and metabolic rate were acquired using a metabolic chart while subjects breathed room air thru a low deadspace facemask. Arterial oxygen saturation (SaO_2) was measured by finger pulse oximetry. Progressive isocapnic HVR was measured using a rebreathing system containing an initial concentration of 21% O_2 for sea-level studies and 36% O_2 for high-altitude studies. HCVR was measured by the rebreathing technique. Subjects rebreathed from a bag initially containing 7% CO_2 in oxygen. During both the HVR and HCVR tests, all variables were digitally sampled at 50 HZ by a computer and averaged over four breath intervals. HVR($\triangle VE/\triangle SaO_2$) and HCVR($\triangle VE/\triangle PCO_2$) were calculated using least squares regression.

Studies were conduced over a period of 30 days. Sea-level control studies were conducted during the first week. Subjects then ascended by plane and car to the 4,300 m summit of Pikes Peak, CO. They resided on the summit a total of 18 days while a variety of test were performed. Ventilatory measurements were made on HA days 1, 2 and 14. Following the HA residence, the subjects were rapidly transported back to Natick, MA where upon arrival they entered and spent the night in a hypobaric chamber at a barometric pressure of 446 torr. The next morning, subjects were released from the chamber and entered into the post altitude (PA) test period. Ventilatory measurements were made on PA days 1, 3 and 7 at sea level after return from HA. Finally, on PA day 8, six of the eleven subjects were re-exposed (RA) to a barometric presssure of 446 torr for approximately 36 hr in a hypobaric chamber.

RESULTS

The SaO_2 decreased ($P<0.05$) to 79$\pm$8% on HA1 but increased ($P<0.05$) to 89$\pm$2% by the 14th day of residence at HA. After seven days post HA residence at SL, in the 6 subjects re-exposed to high altitude, SaO_2 was similar (85$\pm$3%) to those measured on HA14 but higher ($P<0.05$) than those measured on HA1. This sustained elevation of SaO_2 suggested that ventilation was likewise enhanced during RA.

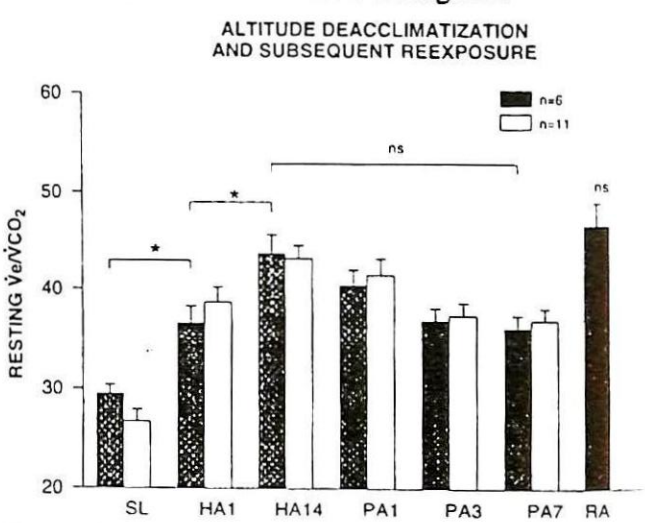

Figure 1: Resting minute ventilation, plotted as VE/VCO_2. Results are presented for the entire group of 11 subjects and also for the subgroup of 6 subjects who were subsequently re-exposed to altitude.

Resting minute ventilation, plotted as VE/-VCO_2 in Fig 1, demonstrated the expected acclimatization response, increasing by ~12% over 14 days residence at 4,300 m. Moreover, upon return to sea level, resting ventilation remained elevated throughout the seven day PA period and in the 6 subjects during RA. These results suggested that the ventilatory acclimatization response was retained over this period. Given that the mechanism of ventilatory acclimatization to altitude includes augmentation of ventilatory chemosensitivity to hypoxia and hypercapnia, we evaluated the HVR and HCVR across this same period.

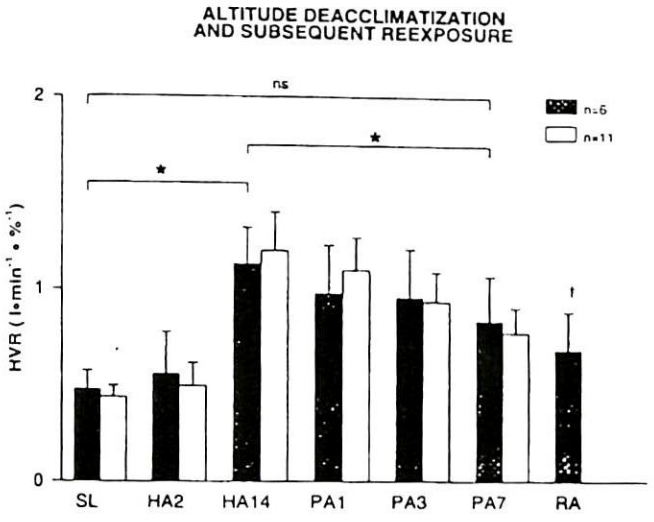

Figure 2: Hypoxic ventilatory response ($\Delta VE/\Delta SaO_2$) as a function of residence at altitude.

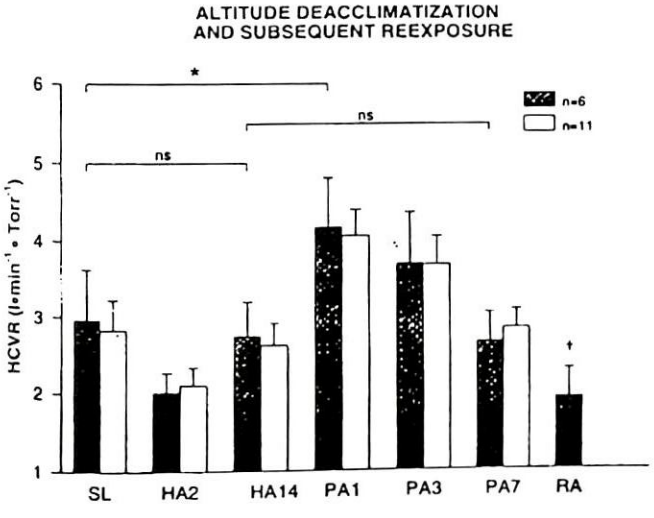

Figure 3: Hypercapnic ventilatory response ($\Delta VE/\Delta PCO_2$) as a function of residence at altitude.

HVR increased ($P<0.05$) ~170% by the 14th day at 4,300 m (Fig 2). Compared to the SL control period, HVR was elevated ($P<0.05$) during the first three days after return to SL from HA. In the six subjects during RA, HVR was not significantly different from their pre-acclimatization SL control. As ilustrated in Fig 3, somewhat similar results were observed with the subjects' HCVR. Although HCVR did not demonstrate any change from SL control (2.83 ± 1.33 l/min/torr) during the period of HA residence, upon return to sea level HCVR was elevated ($P<0.05$) on PA1 (4.06 ± 1.14 l/min/-torr) and PA3 (3.68 ± 1.22 l/min/torr), but returned to SL control values by PA7. During RA, HCVR was actually decreased ($P<0.05$) compared to the preacclimatization SL control value.

DISCUSSION

During 18 days residence at 4300 m, acclimatization produced an increase in resting ventilation, arterial oxygen saturation and ventilatory chemo-responsiveness. Upon return to sea level, elevated ventilation and enhanced HVR and HCVR persisted for approximately 1 week, such that on the seventh day the HVR retained about 45% of its acclimatization response. These results are similar those previously reported by Lahiri et al. (1972) and Sato et al. (1992). After eight days at SL, during re-exposure to altitude, subjects demonstrated a retention of approximately 90 and 67% of their acclimatization responses for ventilation and arterial oxygenation respectively. However, HVR and HCVR were no longer statistically elevated. These measurements of resting ventilation and arterial saturation during re-exposure to high altitude clearly indicate the retention of ventilatory acclimatization. However, the absence of augmented chemosensitivity to either hypoxia or hypercapnia in these subjects leaves the mechanism for this enhanced ventilatory response somewhat in doubt. With the exception of possible methodological errors in our measures of HVR and HCVR during reexposure, it is possible that other factors such as attenuation of hypoxic ventilatory depression may have contributed to the enhanced ventilatory response upon altitude rexposure. Nevertheless, we conclude that ventilatory acclimatization to altitude is retained for at least eight days following return to sea level, thus

lessening the hypoxic stress during subsequent reexposure to altitude within this time period.

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