Plasma adrenocorticotrophin and cortisol responses to acute hypoxia at rest and during exercise

P. Bouissou¹, J. Fiet², C. Y. Guzezenece³, and P. C. Pesquies³

¹ Département de Physiologie, Faculté de Médecine, Créteil, France
² Hôpital Saint-Louis, Paris
³ CERMA, Paris, France

Summary. Plasma adrenocorticotrophin (ACTH) and cortisol (F) concentrations were studied in six male subjects under normoxic (N) and acute hypoxic (H) conditions (altitude 3000 m) in a hypobaric chamber. Comparisons were made at rest, at 15, 30, and 60 min of exercise (65% $V_{O_{2,max}}$), and after a 10 min recovery period. Mean (±SE) resting plasma ACTH levels were significantly higher in H (18.6±5.7 pmol·l⁻¹) than in N (9.6±1.6 pmol·l⁻¹) but no difference in resting plasma cortisol was observed between the two conditions. Both plasma ACTH and F concentrations were significantly increased at 60 min of exercise and during the recovery period under normoxic conditions. Hypoxia did not affect the ACTH response to exercise but reduced cortisol elevation. The changes in plasma cortisol concentration from rest to exercise were significantly correlated to ACTH under normoxic (r=0.89, p<0.001) but not under hypoxic (r=0.43, NS) conditions. Plasma lactate concentration was higher at the end of exercise in hypoxia (p < 0.01), and no correlation existed between plasma lactate and ACTH levels. These observations provide further evidence that at sea level the increase in plasma cortisol levels during exercise is the result of ACTH-induced steroidogenesis. The responses observed at rest and during exercise in hypoxia suggest that adrenal sensitivity for ACTH may be altered.

Key words: Adrenocorticotrophin — Plasma cortisol — Exercise — Acute hypoxia — Plasma lactate

Introduction

Adrenocortical response to hypoxia has long been of interest because its metabolic consequences and its possible implication in acclimatization to altitude (Hornbein 1962; Moncloa et al. 1968; Sutton 1977). Resting plasma cortisol concentrations have been reported to be increased (Humpleter et al. 1980; Moncloa et al. 1968) or unchanged (Bouissou et al. 1986; Sutton 1977) in humans exposed to acute hypoxia. During physical exertion at altitude or under simulated hypoxia, the cortisol response was found to be greater than at sea level (Sutton 1977). However, ACTH, which is held to be the primary stimulus for cortisol secretion, was not measured in any of these studies. As a consequence, it is not clear whether hypoxia truly stimulates the hypothalamic-pituitary-adrenocortical axis. On the other hand, the cortisol response to exercise was compared at the same absolute work loads under normoxic and hypoxic conditions, so that the decrease in maximal aerobic power ($V_{O_{2,max}}$) with altitude was not taken into account (Sutton 1977). Changes in plasma ACTH and cortisol with exercise, as for many hormones (Bouissou et al. 1986; Galbo 1983), are related to relative (% $V_{O_{2,max}}$) rather than absolute work loads.

Therefore, the purpose of this study was to assess plasma ACTH and cortisol levels at rest and during exercises performed at the same relative work load (65% $V_{O_{2,max}}$) in normoxic and acute hypoxic conditions. In addition, plasma lactate accumulation, which has been suggested as a possible stimulus for ACTH secretion (Farrell et al. 1983), was also evaluated.
Methods

The subjects in this study were six healthy male volunteers. The mean (±SE) age, weight and height for the group was 33 ± 2.9 years, 78 ± 1.8 kg, 178 ± 6 cm, respectively. The subjects were studied on two occasions within 15 days. Before each test session they refrained from food and exercise for 8 h. Each subject performed, at the same times (between 8 and 11 AM) 1 h submaximal exercise tests on an electrically braked ergocycle (Minijhardt KEM-2). The protocols for the two studies were identical except that the subjects were exposed to two different altitudes in a hypobaric chamber: sea level (758 mm Hg) and 3000 m (520 mm Hg). The order in which the experimental conditions were presented was randomized and unknown to the subjects. In both studies, the subjects remained in the hypobaric chamber for about 2 h. The work loads were selected to elicit 65% VO2max, each subject's VO2max having been previously determined at each altitude. Oxygen consumption (VO2) was continuously measured during the tests using a computerized exercise testing system (Beckman Horizon MMC) and heart rate was monitored from an electrocardiogram (Fukuda, HC 1). Hypoboric or sham decompression was achieved in 10 minutes. Then a indwelling catheter was inserted into a superficial forearm vein and the subjects rested for 30 min before the resting blood sample was collected. All subjects were familiar with catheterization procedures. Subsequently, blood samples were taken at 15, 30, and 60 min of exercise and after a 10 min recovery period following exercise. Each blood sample was immediately analysed for hematocrit value (Hct). After centrifugation of the remaining blood, the plasma was assayed for cortisol (Fiorelli et al. 1972) and ACTH (Yalow et al. 1964) using radioimmunoassay procedures. Plasma lactate (after deproteinization with cold perchloric acid) was measured by an enzymatic method (Hochorst 1962). The data (mean ± SE) were statistically analysed using analysis of variance for repeated measurements and Tukey's post hoc test (Fergusson 1981). The null hypothesis was rejected at p < 0.05.

Results

The metabolic and cardiorespiratory responses to exercise in normoxic and hypoxic conditions are presented in Table 1. At the same relative work load there was no difference in heart rate (Hr) and minute ventilation (VE) between the two conditions. A lower hypoxic VO2 resulted in a significantly lower submaximal VO2 under hypoxia. Plasma volume reductions with exercise (estimated from changes in Hct values) were similar in normoxic (4.3 ± 1%) and hypoxic (4 ± 1%) conditions. The mean resting plasma ACTH and cortisol concentrations in normoxia were 9.6 ± 1.6 pmol·l⁻¹ and 0.24 ± 0.01 µmol·l⁻¹, respectively. Such values are commonly reported for normal resting subjects (Beaulieu 1978). Plasma ACTH increased in 5 of the 6 subjects after hypoxic decompression, and the mean value of resting plasma ACTH levels was twice as high in H as in N. These increases were associated with a small and non-significant increase in resting plasma cortisol concentrations. The ACTH response to exercise is shown in Fig. 1. ACTH rose with exercise in both conditions, significant differences being observed at the end of exercise and during the post exercise period when compared with the resting values. No hypoxia main effect was measured between the two conditions. One exception to these response patterns was observed. In one subject, who showed the highest level of resting plasma ACTH (40 pmol·l⁻¹), adrenocorticotrophin declined by 34 pmol·l⁻¹ at the end of exercise. This subject also showed no change in plasma cortisol concentration with exercise. The corrected values of plasma cortisol were significantly increased at 60 min of normoxic exercise and continued to rise into the recovery period (Fig. 2). In hypoxic conditions the plasma cortisol concentration did not show significant elevation with exercise, and cortisol was found to be significantly lower during the post-exercise period when compared with normoxia. Plasma lactate concentrations measured at the end of exercise under hypoxic conditions were significantly higher than in normoxia (Table 2).

Table 1. Heart rate (HR), minute ventilation (VE), oxygen uptake (VO2) and relative work load (% VO2max) during exercise in normoxic and hypoxic conditions (means ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Normoxia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>148 ± 2</td>
<td>145 ± 3</td>
</tr>
<tr>
<td>VE</td>
<td>72.2 ± 3.2</td>
<td>73.3 ± 5.1</td>
</tr>
<tr>
<td>VO2</td>
<td>2.31 ± 0.08</td>
<td>1.90 ± 0.10</td>
</tr>
<tr>
<td>% VO2max</td>
<td>65</td>
<td>66</td>
</tr>
</tbody>
</table>

Fig. 1. Plasma ACTH concentrations (mean ± SE) at rest and during exercise under normoxic (□ □) and acute hypoxic (■ ■) conditions. (a: significantly different from rest, p < 0.05)