Biology of Sport, Vol. 22 N°3, 2005

SHORT REPORT

IS EXERCISE CORTISOL RESPONSE OF ENDURANCE ATHLETES SIMILAR TO LEVELS OF CUSHING'S SYNDROME?

W. Daly, A.C. Hackney
Endocrine Section – Applied Physiology Laboratory, Dept. of Exercise and Sport Science, University of North Carolina, USA

Abstract. Several theories exist as to the mechanism causing the development of the Overtraining Syndrome in athletes. One theory proposes hypercortisolemic states (e.g., "pseudo" Cushing's Syndrome type-condition) brought on by intensive exercise training and the stress of sporting competitions results in neuroendocrine dysfunctions and subsequent physiological compromise. We wondered whether stressful exercise could provoke changes in cortisol to the magnitude of that seen in Cushing's Syndrome patients. Therefore we conducted a study to determine if the cortisol levels in highly trained endurance athletes in response to a stressful exercise bout compared to that found in Cushing Syndrome patients. Cortisol levels were examined in physically active men at rest, and after intensive, prolonged exercise (~85 min at 75% VO_2max) and compared to that of Cushing's patients at rest. Results showed exercise does significantly ($p<0.001$) and substantially elevate cortisol to near Cushing's Syndrome levels. However, the cortisol response to exercise in athletes is highly transient and abates rapidly. The present findings support that cortisol responses to exercise such as what endurance athletes might encounter in their sporting competition (or during an intensive exercise training session) can elevate cortisol to the levels seen in Cushing Syndrome patients (i.e., for only a short period of time).

(Biol.Sport 22:209-214, 2005)

Key words: Endocrine - Exercise Training - Steroid hormones

Reprint request to: Dr. Anthony C. Hackney, Director Applied Physiology Laboratory, Fetzer Building - CB # 8700, Chapel Hill, NC 27599-8700, USA
e-mail: thackney@med.unc.edu

Introduction

The Overtraining Syndrome is a medical condition that develops in elite athletes and results in their physical performance and psychological well-being becoming impaired [3]. Many sports medicine clinicians and athletic trainers attempt to prevent the development of this condition because of the devastating effects it can have upon competition in critical sporting events, such as the Olympic Games, World Cup or the World Championships. The etiology of this syndrome has not been completely elucidated; but manifests several distinct neuroendocrine characteristics, in particular development of hypothalamic-pituitary-adrenal (H-P-A) axis dysfunction [3]. Several theories exist as to the cause of the Overtraining Syndrome; one theory proposes hypercortisolemic states brought on by intensive exercise training and the stress of sporting competitions result in the development of neuroendocrine abnormalities and subsequent physiological compromise [3,4]. Specifically, some investigators have proposed that a "pseudo" Cushing's Syndrome type-condition may develop in athletes [3]. We were intrigued by this hypothesis and wondered whether stressful exercise could provoke changes in cortisol to the magnitude of that seen in Cushing's Syndrome patients. Therefore we conducted a study to determine if the cortisol levels in highly trained athletes in response to a stressful exercise bout compared to that found in Cushing Syndrome patients at rest.

Materials and Methods

Cortisol levels were measured in healthy physically active men (n=39; age range = 18 - 36 yr) who had all been involved in exercise training and competitive sport (e.g., running, cycling) for a number of years. Their average maximal aerobic capacity (>60 ml/kg/min) rated all subjects as highly trained [4]. The subjects were divided into control resting (n=17) and experimental exercise (n=22) groups. The physical and training characteristics of these subjects have been reported in detail elsewhere, no significant differences existed between the groups [1,2]. In accord with the Declaration of Helsinki all subjects approved and signed an informed consent prior to voluntary participation in the study.

Serial blood specimens were collected from all subjects for ~3 hr at mid-day following a 12 hr fast, and with no physical activity for the previous 24 hr. Subjects also followed a controlled diet for the previous 72 hours. During the 3 hr mid-day period the experimental exercise group simulated an athletic competition by running on a treadmill at ~75% of their maximal aerobic capacity until reaching

volitional exhaustion; (i.e., 84.8±3.8 min; mean running time), and then rested quietly for an additional 90 min. An antecubial venous catheter was placed 30 min prior to the beginning of the exercise for blood sampling, which occurred at pre-exercise (Rest), at exhaustion (EXH), at 30, 60, 90 min into recovery from the exercise terminating (i.e., 30R, 60R, 90R) for the experimental group. During recovery the experimental group rested quietly (supine) and consumed water freely. The control group, meanwhile, rested quietly (supine) in our laboratory for this exact time period with bloods collected (as above) at comparable time points. Additionally, both groups provided a single blood specimen 24 hr after the initial Rest blood draw (i.e., 24 hr). During this latter 24 hr period the subjects were asked to refrain from physical activity, avoid stressful personal events and replicate their diet of the previous day.

The blood samples were all treated appropriately to insure viable hormonal analysis (details reported elsewhere) [1,2]. Plasma cortisol concentration was measured in duplicate and was analyzed with an ultra-sensitive, single-antibody, solid phase methodology radioimmunoassay technique (DPC Inc., Los Angles, CA, USA). All within and between coefficients of variation for the assays were less than 10%.

Statistically, the hormonal results were analyzed with a mixed-model parametric analysis of variance, and Fisher post hoc procedures (Statistica software v6.0, Statsoft Inc., Tulsa, OK, USA). The significance level was set at $p \leq 0.05$.

Results

Fig. 1 depicts the cortisol concentrations for the control and experimental groups as well as the reported cortisol levels for untreated Cushing's Syndrome patients (n=150) [6]. The cortisol levels at Rest in both the control and experimental group are within normal expected values for males [4,5].

The running exercise resulted in significant ($p<0.001$) cortisol elevations from Rest at EXH, 30R, 60R, and 90R for the experimental group (Fig. 1). Also, the EXH, 30R, 60R, and 90R cortisol concentrations of the experimental group were all significantly greater than the control group resting responses at corresponding times ($p<0.001$). These hormonal responses to exercise for the experimental group were as expected and within typical ranges of values for this type of physical activity [4,5]. At the 24 hr measurement, the cortisol of the experimental group was significantly less ($p<0.05$) than its own Rest concentration, as well as significantly less ($p<0.01$) than the control group concentration at 24 hr.

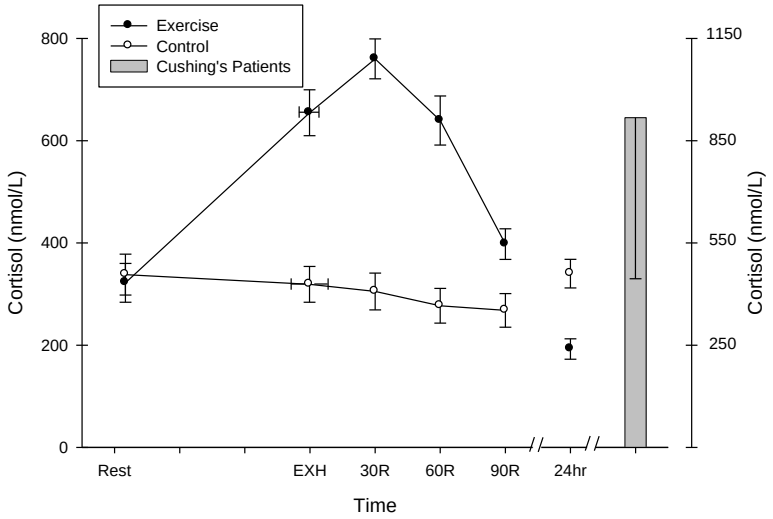

Fig. 1
The cortisol concentrations (mean ± SE, using the left Y-axis scaling) of the exercise group (n=22) and control group (n=17) at comparable time points over an approximately 3 hour period, and 24 hr later. Between Rest (basal, resting) and EXH (point of exhaustion) the exercise group performed running exercise until volitional exhaustion. During this same period of time the control group rested quietly. Each group had blood sampling at 30, 60 and 90 min (i.e., 30R, 60R, 90R) following the EXH sampling, during this time the subjects rested quietly. The filled bar represents the cortisol for Cushing's Syndrome patients as reported in reference 6 (mean ± SD, using the right Y-axis scaling)

Inspection of Fig. 1 reveals that at the end of exercise (EXH) and for the first hour of recovery from that exercise, the cortisol levels of the experimental group were nearly at the mean levels found in Cushing patients. Furthermore, from EXH until the 90R point into recovery the cortisol concentrations of the experimental group were at a level found in approximately 66% of the Cushing's patients (i.e., mean ± 1 SD).

Discussion

The data suggest that strenuous, intensive exercise can result in elevations in cortisol that are substantial and of the magnitude observed in Cushing's Syndrome patients. These elevations, however, appear to be relatively transient as they had nearly subsided by 90 min after the exercise was terminated. This rapid return of levels during recovery to nearly that of Rest values suggest cortisol is not persistently or chronically elevated in healthy athletes, as is seen in many Cushing's patients. On the contrary, our laboratory group has previously noted that daytime exercise can results in significantly suppressed cortisol release in athletes and such a suppressed release may persistent for many hours after exercise ends [2]. This may be the case in the present data since the 24 hr cortisol concentrations of the experimental group were lower than those observed in control subjects at the same time, as well as their own Rest values from the previous day. It is unclear why this occurred, but it may represent a negative feedback regulation response in the H-P-A axis due to the high cortisol initially observed after the exercise [5].

As noted, some investigators postulate a hypothetical scenario linking the Overtraining Syndrome to the development of a pseudo Cushing's Syndrome type-condition in athletes [3]. Our purpose was not to test this linkage directly, only to see if stressful exercise caused changes in cortisol to the level observed in Cushing Syndrome. Our findings do most certainly support that this can occur in response to exercise that endurance athletes might encounter in their sporting competition (or during intensive exercise training sessions); although, only for a short period of time. Other studies are necessary, however, to examine whether such cortisol changes in athletes can result in chronic disruptions of the H-P-A axis as has been associated with the Overtraining Syndrome.

References

1. Daly W., C.Seegers, S.Timmerman, A.C.Hackney (2004) Peak cortisol response to exhaustive exercise: effect of blood sampling schedule. *Med.Sportiva* 8:17-20

2. Hackney A.C., A.Viru (1999) Twenty-four-hour cortisol response to multiple daily exercise sessions of moderate and high intensity. *Clin.Physiol.* 19:178-82

3. Lehmann M., C.Foster, J.Keul (1993) Overtraining in endurance athletes: a brief review. *Med.Sci.Sports Exerc.* 25:854-62

4. McArdle W.D., F.I.Katch, V.L.Katch (1996) Exercise Physiology: energy, nutrition, and human performance. Williams & Wilkins, Philadelphia

5. McMurray R.G., A.C.Hackney (2000) Endocrine responses to exercise and training. In: W.Garrett (ed.) Exercise and Sport Science. Lippincott Williams & Wilkins, Philadelphia, pp. 35-62

6. Newell-Price J., P.Trainer, L.Perry, J.Wass, A.Grossman, M.Besser (1995) A single sleeping midnight cortisol has 100% sensitivity for the diagnosis of Cushing's syndrome. *Clin.Endocrinol.* 43:545-50

Accepted for publication 20.05.2005