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Work-related stress and cortisol levels: is there an association? Results of an observational study

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Abstract. – OBJECTIVE: Chronic exposure to work-related stress (WRS) stimulates the hypothalamic-pituitary-adrenal (HPA) axis to increase glucocorticoid secretion, including cortisol, and these hormones can be measured both in serum and urine. The Health Safety Executive Toolkit (HSE) questionnaire is used to assess WRS risk objectively. The scope of our study is to investigate whether serum or urinary cortisol levels could be used as alternative objective indicators of WRS, specifically in those subjects who are chronically exposed to it.

PATIENTS AND METHODS: 130 patients (75 males and 55 females, mean age 47.7 ± 11.3 years) were evaluated at a specialized Centre for Secondary Hypertension, where both their serum (8 AM) and 24-hours urinary cortisol were measured and they were asked to complete two questionnaires: one questionnaire to collect data about their socio-demographic and job characteristics, and the HSE questionnaire to evaluate WRS.

RESULTS: Multiple linear regression analysis showed an association of urinary cortisol with several variables: tobacco smoke (β = 69.6; *p* = 0.003); female gender (β = -37.3; *p* = 0.041); exposure to physical risks (β = 51.8; *p* = 0.032); control score (β = -22.7; *p* = 0.039); role score (β= 39.3; *p* = 0.020). Age was the only variable associated with serum cortisol levels (β = -3.6; *p* = 0.042).

CONCLUSIONS: Urinary cortisol levels, but not serum levels, are associated with variables linked to WRS (score control and role) and to socio-demographic variables, namely gender and tobacco smoke. Thus, urinary cortisol can be considered a useful and non-invasive biological indicator to quantify WRS.

Key Words:
Urinary, Blood, Cortisol, Work-related stress, Occupational medicine.

Introduction

The concept of stress was introduced in 1926 by Hans Selye[1] to define the organism response to environmental stimuli. In its most recent "Selyan sense", stress can be interpreted as the non-specific response of the body to each request. According to a transactional approach introduced in 1984 by Richard Lazarus, stress is a two-way process that involves the production of stressors by the environment and the response of an individual subjected to these stressors[2-4]. In its modern definition, work-related stress (WRS) is defined as the perception of imbalance felt by the worker when the demands of the working environment exceed the individual capacities to cope with such requests. WRS is associated with exposure to certain working conditions, both physical and psycho-social, and with worker's awareness of having difficulty in dealing with major aspects of their work, which may lead to changes in cognitive, environmental and physiological status[5,6].

WRS results from exposure to both psychosocial risks, such as those aspects related to the planning, organization and management of work and their environmental and social contexts, which have the potential to generate physical, social and psychological damages[7-9].

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Excessive workloads, work rhythms perceived as too tight, a lack of control over one's own work, low support level from colleagues or superiors, the presence of unacceptable behavior in the form of verbal or physical harassment, not being involved in organizational changes or having a poorly defined role within the company are some of the psychosocial risks that threaten the worker[10].

It should be noted though that WRS is not always an undesirable phenomenon. In fact, WRS is also capable of promoting psychological[11] and physical well-being[12], which is defined as "eustress". The concept of stress response, referring to a highly adaptive process, was originally described by Selye[1] and Cannon[13], who identified the primary role of the sympathetic nervous system (and its effectors, e.g. catecholamines) and the endocrine system (regulated by the hypothalamic-pituitary-adrenal axis). These physiological reactions are triggered to promote mental alertness and mobilize body's energy resources[14]. Even though it is true that these physiological reactions and hormones may help the organism in the short-term, they are also directly responsible for those long-term detrimental consequences that a sustained stress response has on the organism and increase the risk for some stress-related diseases. The hypothalamic-pituitary-adrenal axis is an important neuroendocrine system, which not only orchestrates stress reactions, but also controls the immune system, mood, emotions and metabolism[15,16], representing the system that mediates the so-called General Adaptation Syndrome (GAS)[17].

Being cortisol the most important effector of this complex physiological response, it is proposed to be used as an objective biological maker to quantify the amount of stress. In fact, exposure to a stressor will stimulate the hypothalamic-pituitary-adrenal axis to increase the secretion of stress-related glucocorticoid hormones, including cortisol[18], responsible for the numerous detrimental health consequences brought on by a sustained stress response[19-21]. Both urinary and serum levels can be measured with appropriate laboratory tests and their sampling takes into account their daily oscillations[22]. Cortisol secretion follows a circadian rhythm. Its serum concentration peaks right after awakening, as the result of retinal stimulation by light. Cortisol levels begin to drop later in the morning, while adrenaline and serotonin continue to be released. From the middle of the day, cortisol levels start to decrease and lethargy slowly sets in. During sleep, cortisol secretion resumes and its serum concentration rises again slowly. This prepares the body for awakening and the cycle repeats. Many studies investigated the relationship between cortisol levels and WRS (evaluated by questionnaires tools based on the strongest theoretical models of WRS). Thus, we aim to assess whether a correlation exists between serum and urinary levels of cortisol and the scores of the questionnaire developed by the Health Safety Executive (HSE)[23,24], to assess those variables suspected to cause WRS and whether serum or urinary cortisol levels could be used as alternative objective indicators of WRS. This questionnaire was also modified to be adopted in our country[25].

Patients and Methods

Patients

The study was carried out from January 2017 to December 2017 and comprises 130 workers (mean age 47.7 ± 11.3 years), 75 (57.7%) males and 55 (42.3%) females, enrolled at a Specialized Center for Secondary Hypertension of the Teaching Hospital "Umberto I", "Sapienza" University of Rome. The study was evaluated and approved by the Sapienza University of Rome Ethics Committee, in accordance with the Italian law. Patients provided written informed consent and our research conforms to the principles of the Declaration of Helsinki. Cortisol levels were measured in all subjects, both in the serum (in the morning, at 8 am) and in urine samples of the previous 24 hours (24-hour urinary free cortisol excretion). Serum cortisol was measured by enzyme-linked immunosorbent assay (ELISA). The intra-assay coefficient of variation was 1.7% for cortisol at 129 nmol/L. The inter-assay coefficient of variation was 4.7% for cortisol at 102 nmol/L and 2% for cortisol at 940 nmol/L. Urinary cortisol concentration was measured by immunoassay after extraction with a solvent (ethyl acetate). The analytical sensitivity was 27 nmol/L. The inter-assay coefficient of variation was 13.1% for cortisol at 38 nmol/L, and 5.7% for cortisol at 323 nmol/L.

Questionnaires

Each participant was surveyed with two questionnaires. The first questionnaire collected information about their sociodemographic, job characteristics and blood pressure status. In particular, it focused on the kind of job, smoking habit and blood pressure of participants. The second questionnaire was the Health Safety Executive Toolkit (HSE) questionnaire, administered to quantify the amount of stress that they perceive at work. The HSE questionnaire also adheres to the WRS assessment guidelines set out by EU regulations and presented in the Circular dated 18/11/2010 of the Italian Ministry of Labour and Social Policy (pursuant to Legislative Decree No. 81/2008 and subsequent modifications and supplements).

The HSE questionnaire consists of 35 items measured with a 5-point Likert scale. Higher scores indicate better work conditions and consequently a lower stress risk. It defines 7 different domains:

- **Demand:** workload, work schedule and work environment;
- **Control:** how much control workers have on their job;
- **Support:** subdivided into "support from managers" and "support from peers". It includes the encouragement, sponsorship and resources provided by the organization, line management and colleagues;
- **Relationships:** good practices implemented to avoid conflicts and deal with unacceptable behaviors;
- **Role:** whether workers understand their role within the organization and whether the organization ensures that no conflicts occur;
- **Change**: how organizational changes (either large or small) are managed and communicated within the organization.

Statistical Analysis

Descriptive statistics was carried out using frequency distribution (contingency tables, mean and standard deviation). Univariate analysis was carried out using chi-square test for categorical variables and Mann- Whitney test for quantitative variables. Bivariate analysis was conducted using the Spearman *rho*-correlation coefficient. Multivariate analysis was performed using a linear model in which serum and urinary cortisol levels were the dependent variables and the HSE questionnaire domains were the independent variables. The analysis was adjusted for age, gender and smoking habits. The software used was the SPSS® software, 25.0 release (SPSS Inc., Armonk, NY, USA). Statistical significance was set at $p < 0.05$.

Results

In relation to their job, 26 patients (20%) were healthcare workers, 53 (40.8%) white collars, 23 (17.7%) blue collars, 13 (10%) consultants, 15 (11.5%) artisans. Moreover, 60 patients (46.2%) suffered from primary hypertension, 48 (36.9%) from secondary hypertension, and the remaining 22 (16.9%) had a normal blood pressure. The distribution of serum and urinary cortisol levels of are reported in Figure 1.

Univariate Analysis Results

Results are reported in Table I. Urinary cortisol is higher in smokers and male participants. *p*-values are 0.032 and 0.001, respectively.

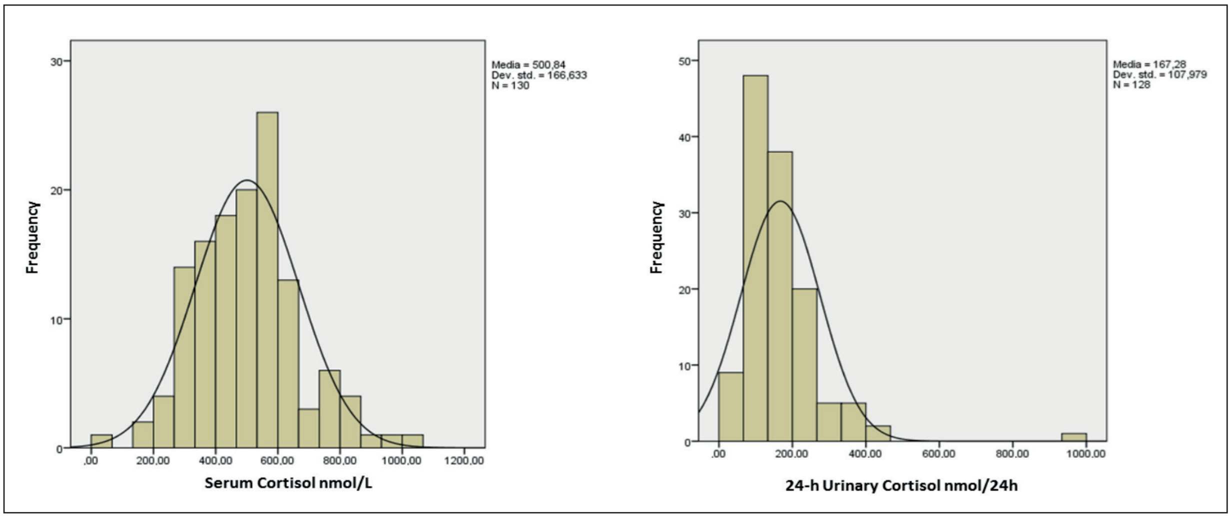

Figure 1. Distribution of serum and urinary cortisol level.

Table I. Univariate analysis results.

		Serum cortisol median (range)	24-h urinary cortisol median (range)
Gender	Females	498.8 (245.6-875.4)	114.2 (46.5-971.2)
	Males	501.7 (64.6-1038.6)	168.7 (28.6-444.5)
		***p* value = 0.656**	***p* value < 0.001**
Smoking	No	497.7 (64.6-1038.6)	140.2 (28.6-444.5)
	Yes	533.5 (187.8-828.8)	201.5 (46.5-971.2)
		***p* value = 0.432**	***p* value = 0.032**
Job	Healthcare workers	474.7 (262-1038.6)	127.0(46.5-416.0)
	White collars	533.7 (64.6-860.3)	127.2(46.5-395.2)
	Blue collars	498.8 (187.8-786.6)	168.8 (88.9-971.2)
	Consultants	501.7 (348.4-875.4)	163.2 (96.0-282.3)
	Artisans	497.2 (317.2-964.9)	146.7 (28.6-444.5)
		***p* value = 0.676**	***p* value = 0.246**
Blood pressure status	Normal blood pressure	534.3 (262-964.9)	140.45 (28.6-444.5)
	Primary hypertension	506.9 (64.6-1038.6)	141.3 (46,5-373,7)
	Secondary hypertension	496.65 (187.8-875.4)	150.4 (46,5-971,2)
		***p* value = 0.722**	***p* value = 0.340**

Bivariate Analysis Results

Results are reported in Table II. Age shows a negative correlation with both blood (*rho* = -0.224, p = 0.011) and urinary (*rho* = - 0.201, p = 0.023) cortisol levels. None of the domains of the HSE questionnaire show a correlation with either serum or urinary cortisol levels.

Multivariate Analysis Results

Results are reported in Table III. Multiple linear regression analysis shows a positive association between urinary cortisol and the following variables: tobacco smoke (β = 69.6; p = 0.003) and HSE Role score (β = 39.3; p = 0.020). A negative association exists between urinary cortisol

Table II. Bivariate analysis results.

Variable	Serum cortisol rho (p)	24-h urinary cortisol rho (p)
Age	-0.224 (0.011)	-0.201 (0.023)
Demand	0.002 (0.985)	0.002 (0.817)
Control	0.014 (0.879)	0.073 (0.416)
Support from managers	0.151 (0.09)	0.052 (0,567)
Support from peers	0.125 (0.162)	-0.003 (0.976)
Relationship	0.070 (0,432)	0.125 (0.163)
Role	-0.023 (0.796)	0.084 (0.354)
Change	0.039 (0.670)	0.149 (0.100)

Table III. Multivariate analysis of urinary cortisol levels.

Variable	All patients β coefficient (*p*)	Males β coefficient (*p*)	Females β coefficient (*p*)
Female gender	-37.33 (0.041)	-	-
Smoking	69.63 (0.03)	53.72 (0.028)	66.74 (0.090)
HSE Control score	-22.73 (0.039)	-	-59.76 (0.03)
HSE Role score	39.30 (0.020)	-	58.59 (0.058)
HSE Relationship score	-	-	47.23 (0.069)
Age	-	-1.61 (0.065)	-
R^2 of the model	0.204	0.179	0.386

and the following variables: female gender (β = -37.3; p = 0.041) and HSE Control score (β = -22.7; p = 0.039). Given the differences noted between males and females, gender acts as an effect modifier, effect modification that occurs when the magnitude of the effect of the primary exposure on an outcome differs depending on the level of a third variable.

Discussion

In our study, we found that urinary cortisol level is higher in the participants who are active smokers or reported higher scores on the Role domain of the HSE questionnaire. We also found that urinary cortisol is lower in female participants and in those who reported lower scores on the Control domain of the HSE questionnaire. However, these findings apply to urinary cortisol. In fact, serum cortisol seems to be associated with age only (its level decreases with age). Other studies already tried to explore an association between serum cortisol level and the amount of stress, but results have been inconclusive so far. Hansen et al[26] explored the association between Karasek's Job content questionnaire and cortisol level - both serum and urinary - without reaching any conclusive result. Other investigations[27-30] did not show any correlation between cortisol level and stress at work, but this might be due to inadequate sampling errors. As mentioned previously, cortisol level varies throughout the day. Therefore, the most accurate determination of cortisol levels can be performed either on a blood specimen collected at 8AM - when serum cortisol concentration is expected to be at its highest - or on a specimen of urine collected in the previous 24 hours. Schnorpfeil et al[31] reported an association between poor social support and high overnight urinary cortisol excretion; no correlation with either the HSE Demand or HSE Role scores was noted. Conversely, our study shows that urinary cortisol level is inversely correlated with HSE Control score, among female participants. Therefore, gender acts as an effect modifier.

Conclusions

In consideration of our results, we suggest that measuring urinary cortisol can potentially improve the accuracy of the HSE questionnaire in quantifying the amount of stress that employees experience at work. Given the detrimental effects of sustained high levels of cortisol[32-34], we regard of utmost importance that we continue to explore the relationship between cortisol and WRS.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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