Assessment of the Level of Burnout in Several Medical Fields by Studying the Diurnal Profile of Salivary Cortisol

Ioniță Alexandrina[1], Copotoiu Monica[2], Hutan Adina[3], Copotoiu Ruxandra[4]

[1] Department of Anaesthesia and Intensive Care, County Hospital, Tîrgu Mureș, Romania
[2] Clinic of Rheumatology, Emergency County Hospital, Tîrgu Mureș, Romania
[3] University of Medicine and Pharmacy, Tîrgu Mureș, Romania
[4] Clinic of Anaesthesia and Intensive Care, Emergency County Hospital, Tîrgu Mureș, Romania

Background: Occupational stress afflicts not only job performance, but also the physical status and the health of the working human being. Thus, methods to analyze the level of stress and burnout by laboratory measurements and different types of questionnaires were developed during the last years.

Aim: To determine the relationship between salivary cortisol variations and the individual self evaluation performed by physicians in several medical fields: general surgery, intensive care, internal medicine.

Material and method: A self assessment survey was undertaken by physicians in three specialties, investigating the place doctors find themselves in the collectivity, their integration and interpersonal relationships – all contributing to a burn-out potential inventory score, the BPI. The BPI score was correlated with the cortisol level found in 3 samples of saliva collected at awakening, immediately after the maximum stress of the day and at night, before sleeping.

Results: We found significant variations of the cortisol level between the early morning salivary level at awakening and the climax of the stress. There was a linear correlation between the maximal cortisol level and the BPI score.

Conclusion: Salivary cortisol, well correlated with serum levels is a consistent marker of the stress and the intensity of the reactivity to stress. Thus we promote it as a feasible, accessible and low cost measurement of the reactivity to stress, both for the individual and the professional group.

Keywords: occupational stress, salivary cortisol, BPI

Abbreviations
ACTH – adrenocorticotrophormone
BPI – Burnout Potential Inventory
CBG – Corticosteroid Binding Globulin
ED – Emergency Department
ELISA - Enzyme Linked ImmunoSorbent Assay
ICU – Intensive Care Unit
ng – nanograms

Introduction

Occupational stress affects job performance in any field, education, justice, economy, military service, sports, aviation and last but not least, in medicine [1].

In response to environmental stress, an increasing number of physiological processes change, including the output of stress hormones. The major role played by the activity of the hypothalamo-pituitary-adrenal axis in this adaptive process was acknowledged long ago [2,3,4,5].

A dysfunction in the activity of the adreno-hypothalamo-pituitary axis is associated with psychosomatic and psychiatric symptoms, such as hyperactivity in major depression and an increased risk of infectious disease. Also cardiovascular diseases and nutrition (obesity, diabetes) are commonly found, while hyporeactivity is commonly associated with autoimmune diseases, such as: lupus erythematosus, multiple sclerosis, neurodermatitis, fibromyalgia, chronic fatigue syndrome, shock and rheumatoid arthritis [6,7,8,9,10].

Following stimulation by ACTH (adrenocorticotropic hormone), the adrenal cortex synthesizes steroid hormones, among them the most important glucocorticoid hormone being cortisol. After release into the bloodstream, up to 90 to 95% of cortisol is bound to CBG (corticosteroid binding globulin), a globulin synthesized in the liver, and other non-specific seric agents with the role of carriers, who are considered reservoirs of cortisol in conditions of increasing demand. While the bound cortisol is inactive, the free circulating cortisol can exert physiological and pharmacological effects. For this reason, the half-life of circulating cortisol is 90 minutes [10]. Steroid hormones are inactivated by the liver and the byproducts are excreted in amounts of approximately 75% in the urine, the remaining 25% in the bile and faeces [9,10].

The biochemical properties of cortisol – low molecular weight and high lipophylicity facilitate the free entry of the hormone not only into the cells, but also in the body fluids, including saliva. Passively diffusing into the saliva, the cortisol reaches levels unaffected by the salivary flow. Thus the salivary levels of cortisol will not be biased by those factors that can alter the salivary output, be it by augmenting or decreasing it.

In addition, cells in the salivary glands oppose bound cortisol saliva penetration [11]. In order to describe corticosteroid hormone profiles, we use today either the blood level of cortisol or the urinary or blood levels of byproducts as reliable substitues [12,13,14]. We therefore hypothesized that cortisol salivary level would reflect the occupational stress intensity as assessed by a psychological validated method.

Materials and methods

The study plan was accepted by the Ethics Committee of the University of Medicine and Pharmacy of Tîrgu Mureș, number 28/2009.

We ran a prospective survey using a questionnaire based on BPI (Burnout Potential Inventory) criteria, to investigate the individual assessment of the activity, the place and integration in the team and interpersonal relationships of the subjects. The subjects were physicians working in the Tg.Mures County Hospital and the Emergency County Hospital, in different fields: general surgery, internal medicine, anesthesiology and intensive care.

We chose the BPI (Burn-out Potential Inventory) score to quantify the magnitude of the stress [15].

The BPI score is used in the individual evaluation of the own activity, the rate of integration in collectivity, or for comparable studies regarding different collectivities.

Inclusion in the study was made on a voluntary basis, the response rate being of 60 out of 90 questionnaires offered, that is an overall response rate of 66.66%. We included all the subjects who agreed to and succeeded to collect saliva samples in specific moments of their working day and to handle over both the filled in questionnaire and the saliva containers the next day. The questionnaires, respectively saliva collection containers were distributed to medical staff from several departments: medical, surgical and ICU (including The Emergency Department - ED), as follows: 40 for ICU and ED, 30 surgical specialties (general surgery, urology, and gynecology) and 20 for other medical specialties (cardiology, gastroenterology, oncology, infectious diseases).

Saliva harvested in containers of 5 ml was stored at -20°C until undergoing the ELISA test, a competitive quantitative method (enzyme linked immunosorbent assay) at the Central Laboratory of the Emergency County Hospital of Tîrgu Mureș. The values were expressed in ng (nanograms), produced by Nova Tec Immunodiagnostica GmbH.

We ended up with a number of 18 respondents from surgery included in the study, 12 subjects in the internal medicine group and 26 intensivists and emergency physicians.

The questionnaire applied is, in fact, a normative test. The subjects score a figure that is compared to the individual scores of a representative sample. Interpretation according to the score recorded is further detailed.

The BPI is to be interpreted as described by Potter [15]. A score of 45–180 points of the BPI is relevant for a low potential of occupational stress, provided preventive measures are taken. If one has scores between 181 and 270, one has a moderate potential. An interventional plan is needed in problem areas. The highest scores vary between 271 and 450 points, indicating an increased potential of developing occupational stress. It is vital to take action in these cases.

Respondents had to deliver demographic data, such as the age, sex, specialty, marital status, addiction and length of activity. Saliva samples were collected in three moments of an ordinary day: early in the morning at awakening, labeled as a, immediately after a stressful activity at work, labeled as b, and at night before sleeping, the c moment. The most stressful activity was selected by the subject itself as the b moment.

We distributed the participants in three groups according to their field of activity. All the groups included both physicians who passed the board evaluation and residents.

We named the first group, the critical care group. It comprised 26 subjects, intensivists and emergency medicine physicians.

The second group, the surgical one, comprised 18 general surgeons, urologists and gynecologists.

The third group was the smallest, the medical group, and included 12 internists, cardiologists, general practitioners, oncologists and infectionists. It was considered to be the least invasive group.

The questionnaires were filled in after saliva sampling. The individual scores thus obtained were correlated to the levels of salivary cortisol. We further studied the salivary cortisol variation correlated to the speciality and the sampling moment. Laboratory data obtained were correlated to the BPI score after completing the questionnaire.

Statistical analysis of all the results obtained from our respondents was performed with GraphPad Prism 5.0 program. Data were submitted to the normality tests (Gaussian distribution) before any analysis. Comparing more than two groups, that did not pass the normality tests due to scarce numbers, we performed oneway ANOVA analysis with Friedman test. Spearman test was used for corelation analysis.

Results

The responses have been patchy, and after exclusion of incorrect laboratory study evidence collected, we could compare the following groups:

- 26 respondents in the intensive care and emergency medicine group;
- 18 general surgeons, urologists, gynecologists;
- 12 internists, cardiologists, gastroenterologists, oncologists, infectious disease specialists and residents.

The scores obtained were correlated with the levels of salivary cortisol and general data of the responders.

In the surgical group, the morning levels of cortisol at scores over 180 were over 6.5 ng/ml, with an evening decrease. In the medical group, there was a single score of

Table I. Demography of the research subjects

Variable	Critical care	Surgery	Internal medicine
Age (years, mean±SD)	32.92±7.42	40.41±10.82	38.72±12.57
Male	7	13	4
Female	19	5	8
On duty (mean±SD)	5.11±3.92	3.33±1.41	2.62±1.70
Experience (mean±SD)	6.29±6.60	11.85±8.45	12.38±13.38
Cortisol a (ng/ml, mean±SD)	8.43±4.85	7.51±4.13	15.60±26.88
Cortisol b (ng/ml, mean±SD)	3.40±2.12	4.51±2.45	4.36±2.19
Cortisol c (ng/ml, mean±SD)	3.44±3.78	3.19±2.99	10.84±28.11
BPI (mean±SD)	127±12	112.5±4.5	147±2

Table II. Correlation between BPI score and cortisol levels – p values.

Specialty	Cortisol a	Cortisol b	Cortisol c
Critical Care			
Total	0.998	0.536	0.004
Male	0.661	0.782	0.109
Female	0.448	0.571	0.016
Surgery			
Total	0.829	0.639	0.046
Male	0.469	0.952	0.240
Female	0.930	0.208	0.241
Internal medicine			
Total	0.561	0.030	0.686
Male	0.720	0.078	0.673
Female	0.010	0.187	0.894

195 points, with a higher evening cortisol level, while the anesthesia – intensivists group scored in 5 cases over 180 points. In other 3 cases, the evening cortisol values were less than the morning levels, with the tendency to return to basal values, while in 2 cases the evening values were higher than the morning ones. In all cases, the cortisol levels after a stressfull activity were less than in the morning and evening samples of the same individual. Concomitantly we found higher levels of cortisol without real signs of burnout or stress to the female subjects.

When correlating the burnout score to the a, b and c values (meaning for the morning, after stress and evening cortisol level), the results failed to issue a significant correlation for any specialty between the maximal stress value and the initial value at awakening as seen in table II.

Figure 1 reflects the cortisol salivary levels of the three targeted moments (a, b, c) for each group, as compared to the curve of all the subjects.

We found that cortisol variations for all the groups were significant – $p < 0.05$ – when considering the morning values (a) compared to the values of the most stressful moment (b). Moreover, for the surgeons, the morning cortisol level is significantly correlated to the burn-out score, while for the intensivists, it is the evening score that significantly correlates to the burn-out score. These differences do not appear in the internal medicine group. We can only speculate that the stress is there for the surgeons and certainly anticipated for the day, while for the intensivists, at the end of the day the stress was hardly if not even tapered down. The most stable group as to the intensity of stress was the internal medicine group.

Discussions

The complex response to stress includes high blood levels of cortisol, an increased sympathetic activity, a decline in the parasympathetic output and an augmented cytokine release. Sleep deprivation as a consequence of stress is associated with an increased evening cortisol blood level, along with insulin and glucose, a high blood pressure, a lower parasympathetic driving and obviously, increased levels of cytokines, intestinal hormones and ghrelin. Ghrelin is

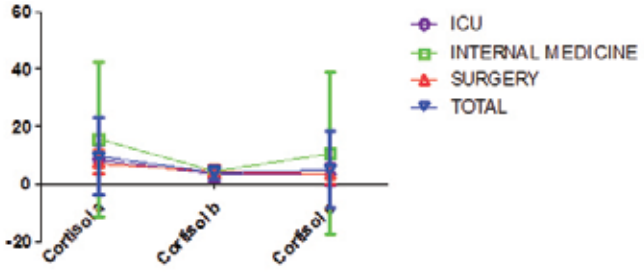

Fig. 1. Variation of the cortisol diurnal levels in 3 specialities

credited with augmenting appetite and hunger. Excess food intake is associated with cognitive and food disorder [16].

The biochemical properties of cortisol, such as low molecular weight and high lipophilicity facilitates the free entry not only into the cells, but also into the body fluids, including saliva. In addition, cells in the salivary glands oppose bound cortisol saliva penetration [2,11].

Important enough, the salivary cortisol level, apparently due to passive diffusion, seems to be unaffected by the flow rate of saliva. Thus salivary cortisol levels are not biased by those factors that cause hypo- or hypersalivation [11,12].

Salivary cortisol assessment as an alternative to the blood concentration, is not only convenient and stress-free for patients, especially for children, but also for the medical staff.

The diurnal profile of salivary cortisol allows for establishing correlations between daily blood level variations and the physical well-being. Thus Lasikiewicz et al. while studying the diurnal profile of basal salivary cortisol in middle-aged adults have established that an abnormal diurnal profile is predictive of health or is associated with certain diseases, including AIDS [17,18]. They showed flat profiles in breast cancer, their subsequent mortality preceding close. In contrast, elevated levels of cortisol following awakening occur in chronic diseases, stress or burnout, but constantly in type II diabetes mellitus [18,19,20]. Cortisol values depend on the quality of sleep and the sleep-wake rhythm. Low values immediately upon awakening are consistent with frequent awakenings and reduced quality of sleep. Diurnal cortisol disorders can be associated with metabolic disorders (endocrine disorders, central type obesity [17]. Working in continous stress triggers the rise of catecholamine and glucocorticoid blood levels for several hours after the stressor activity. This suggest a prolonged effect, sometimes even the failure to return to basal levels the following day or loss of the diurnal variations [21].

Cortisol values are fluctuating. They usually peak in the morning, upon awakening, depending on the level of secreted ACTH. At 30–45 minutes after awakening, cortisol reaches approximately 50–75% of the maximum level. The minimum level was noted at night, with amendments to those with night work [8,19,20].

The use of cortisol in determining the effects of stress on the individual involves monitoring of the basal conditions, during both stress and the recovery phase. Cortisol failure to return to basal level, is evocative for a chronic stress, even for a chronic, stress induced disease.

One can advocate for salivary cortisol sampling: a stable, noninvasive, non stressful procedure, the possibility to collect saliva anytime, anywhere, even by the subject. If we add to it the observation that four weeks spent at room temperature do not alter the value of the results, despite evidence that agglutination might occur, and therefore samples have to be preserved at -20°C, we understand why salivary cortisol is accepted as a diagnosis method in pediatrics and research [5,14,22,23].

The cortisol assessment must consider the psychosocial factors that might alter cortisol secretion (seen in the individual personality variations depending on the degree of introversion, intensity and exposure to stress) [18,19,20]. Differences between the morning and evening values can provide information on the functioning of adreno-hypothalamo-pituitary axis [10].

Normal serum cortisol levels vary between 20 and 50 micrograms/dl. Still, it was found that the values at awakening for an ordinary working day were higher for women, that they correlated with the workplace requirements, although this association was less pronounced at elite [8,9,24,25].

The release of stress hormones, such as cortisol, when exposed to professional stress, can manifest in various symptoms, both somatic and psychological causing high levels of emotional exhaustion and depersonalization and low personal achievement, with the onset of fatigue, physical and mental exhaustion, depression, cynicism and negative emotions, inability to concentrate, anxiety and insomnia, apathy and irritability [8,9,25]. The prolonged exposure to stress can lead to failure to return to the basal values of catecholamine and glucocorticoid hormones. Thus diurnal cortisol variations may vanish.

We are not aware of similar studies on the medical staff in our country.

Conclusions

Differences between salivary cortisol levels assessed upon awakening in the morning, when the professional stress is minimal and at the climax of stress are significant.

Salivary cortisol concentration gradient between morning and evening is also significant, as the maximum stress gradient – evening value.

Lack of significant differences between the salivary cortisol values of maximum stress and the evening values, evoke slow and incomplete reduction of cortisol triggered by stress at the end of the day, when the reaction to stress is not completely blunted.

Salivary cortisol, well correlated with serum levels is a consistent marker of stress level and we promote it as a feasible and accessible, low-cost measure of individual and professional group reactivity to stress, very significant for its intensity.

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