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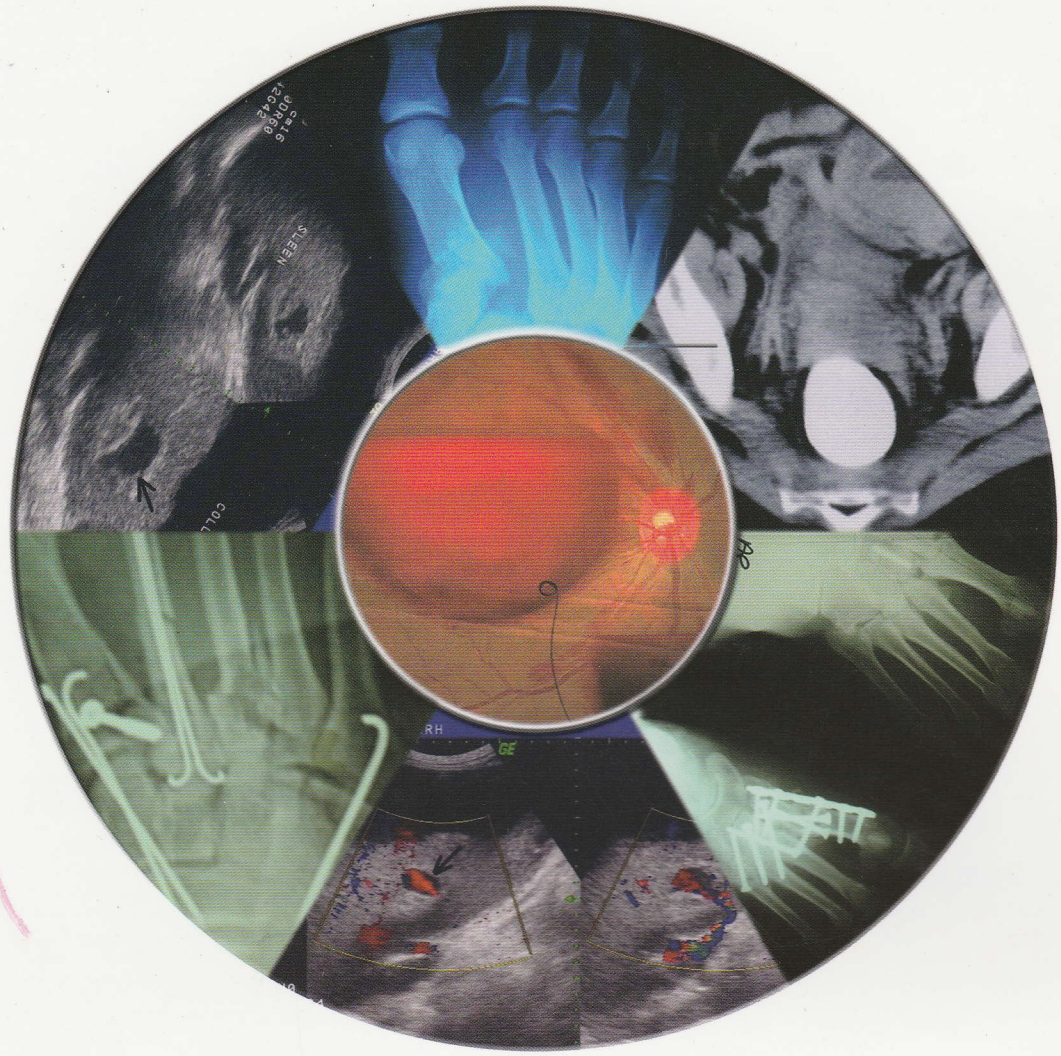

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ORIGINAL STUDY

Relationship Between Anxiety and Stress Hormones : A Study on Doctors Working in Emergency Department

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Abstract

Objective: The aim of this study was to analyse the relationship between anxiety and stress hormones including cortisol, prolactin, and insulin, of the internship doctors working in Emergency Department (ED).

Material and Method: Among 37 doctors coming to ED for medical training, 22 were chosen for the study group and 15 for the control group. Anxiety scores, several hormones and serum glucose levels of the groups were studied.

Results: Anxiety scores, glucose and cortisol levels were higher but insulin levels were lower in the study group compared to the control group ($p< 0.05$). An increase in the prolactin level was also observed but it was not statistically significant ($p> 0.05$). While a positive correlation between Spielberger State Anxiety Score (SSAS) and cortisol level ($r = 0.430$, $p<0.01$) was observed, negative correlation was observed between SSAS and insulin level ($r = -0.402$, $p<0.05$).

Conclusions: This study shows that there are some stress hormone changes in the metabolic reactions of the body to stress and supports the hypothesis that there is a relationship between metabolic and anxiety evaluation parameters.

Key words: Anxiety, Stress Hormones, Emergency Department.

Introduction

Stress, which is one of the important health problems in this time, is an underlying cause of many diseases. Stress was mostly researched in the patients applying to ED and particularly in trauma and metabolic responses of the body to trauma[1,2]. There are a small number of studies of anxiety (stress) on some patients' relatives[3]. While stress experienced by patients and their relatives when they apply to ED is generally accepted by many, doctors reactions to the events are mostly ignored. Understanding the way doctors, who are bio-psychosocial beings, perceive the stress they experience and their emotional metabolic reactions will allow the responses of the doctors, (who are not patient or patients' relatives) to stress, to be understood much better.

In the present study, the relationship between metabolic and emotional reactions of the doctors who have newly started working at ED was studied. We thought there would be a relationship between stress hormone levels and level of anxiety in doctors. Anxiety levels were analyzed using various tests and also metabolic changes were assessed using measurements of serum hormones and glucose. We claimed difference between the control and study groups. As a result, comparing metabolic and psychological findings. We mainly aimed at investigating the relationship between metabolic and psychological parameters.

Material And Method

This prospective clinical study was conducted by cooperation between the Medical Emergency and Biochemistry Departments in Şahinbey Hospital in the Medical Faculty of Gaziantep University, and the Departments of Endocrinology and Metabolism Disease and Biochemistry in Gevher Nesibe Hospital in Medical Faculty of Erciyes University, at the time of doctors change during the 2003- 2004 academic year. Doctors in study and control groups were chosen from the doctors who joined the ED of Medical Faculty in Gaziantep University. In this research, while the study group was 22 (16 males and 6 females) out of 37 intern doctors initiated for training course, the control group consisted of 15 (11 males and 4 females) out of 37 intern doctors, who had completed a training course at ED (Table 1). In the formation of the groups, certain criteria were taken into consideration. These were: ages of the subjects were between 22-26, they had no endocrinological and/or psychological disease, they didn't use any psychotropic medication (antianxiety, antidepressant) before the study, and female subject had no menstrual cycle problems, not pregnant or lactating. Subjects were not informed about the content of the research in detail but they accepted to take part in the research by signing a consent form. In order to obtain similar prolactin levels, the percentage of the women both in study and control groups and the females' menstrual cycle phases coinciding with follicular phases were strictly taken into consideration. In order to reduce the changes in

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Table 1 : Age and sex dispersion of groups

	Study Group				Control Group			
Age	Women	Man	Total	%	Women	Man	Total	%
22	1	1	2	9	0	1	1	7
23	2	11	13	59	1	3	4	27
24	1	2	3	14	0	5	5	32
25	2	2	4	18	2	2	4	27
26	0	0	0	0	1	0	4	7
Total	6	16	22	100	4	11	15	100
%	27	73	100		27	73	100	

serum insulin and glucose levels, subjects who had their lunch in the dining hall of the hospital and did not eat/drink anything but water were included in the study. At around 15:30 hrs, the study and control groups were given Beck, Spielberger State-Trait Anxiety Inventory (SSTAI) tables of 60 questions to answer in different places. Later, at about 14:00 hrs, 6-7 cc of blood were taken from the two groups to measure cortisol, prolactin, insulin and blood sugar. Blood glucose was studied immediately. Serum was separated to study hormone levels and stored at -20 ^{0}C in the Biochemistry Department. In the formation of the control group, subjects were chosen from doctors who had completed ED training. Considering the absence of difference in hormonal interactions and in glucose levels during the day, the control group was studied in another room concurrently. Control group comprised the doctors with different (excluding those who have just started working in ED) criteria from the study group like sex, age, but the times for taking blood samples were strictly followed when individuals were chosen for the control group.

Beck anxiety tests were used in this study consisting of 21 questions with no time limitation in providing the answers for adults. Score range is between 0-63. For this test high scores indicate the severity of anxiety. There are 4 choices of responses for the SSTAI. In these two tests there are both negative and positive statements. The total scores of positive expressions are subtracted from that of negative expressions. To this score 50 points were added to SSAS and 35 to Spielberger Trait Anxiety Score (STAS). The final score is accepted as the anxiety score of the subject. In both tests, scores above 60 indicate high level of anxiety [4,5,6]. Blood samples were brought into room temperature for study 10 days after they were taken. Three hormones were studied in the Biochemistry Laboratory of the Faculty of Medicine in Gaziantep University. Serum cortisol (Immunotech France) and insulin (Diagnostic System Labaratories, USA) levels were measured by RIA method and serum prolactin (Bayer, Germany) level by Automated Chemiluminescence system. The tool which measured hormones was Roche Hitachi Moduler E-170-Menheim (Germany). Intra and interassay variation coefficient (CV) analyses and sensitivities of the kits were 6.44 µgr/dl 2.8% and 5.7% for cortisol and 8 ulU/ml 10% and 7.2% for insulin. Statistical analyses were performed in SPSS statistics programme. Mean and standard deviation were calculated for glucose, cortisol, prolactin, and insulin obtained from both study and control groups. The relationship between anxiety tests (Beck, SSTAI) and metabolic parameters (glucose, cortisol, prolactin, and insulin) was analyzed using Pearson-Correlation Coefficient test. P value lower than 0.05 was accepted as statistically significant.

Results

Anxiety scores of the doctors in Emergency Unit, mean and standard deviation of metabolic parameters, are listed in Table 2. Of the metabolic parameters, glucose (87.9±11.8 mg/dl and 77.7±11.2 mg/dl) and cortisol (12.9±5.2 µg/dl and 7.4±2.4 µg/dl) levels were, statistically, significantly higher; insulin (13.1±9.4 uIU/m) and (25.6±7.3 ulU/ml) wase statistically, significantly lower in the study group compared to the control ($p<0.05$). Beck, SSAS, and STAS scores were respectively (4.0±3.9, 33.1±8.9 and 36.4±7.3 points) in study group and (1.7±1.2, 26.5±5.9 and 30.3±4.7

points) in control group. Clearly, these three scores were, statistically, significantly higher in the study group compared to the control. There was an increase in prolactin level in the study group, too, but it was statistically insignificant ($p>0.05$). There was a positive correlation between SSAS and cortisol ($r=0.430$, $p<0.01$) and a negative one between SSAS and insulin ($r = -0.402$, $p<0.05$)(Table2).

Table 2 : The relations of parameters in study and control groups

Paramter	Study Group (n=22) (X ± SD)	Control Group (n=14) (X ± SD)	t	p
Glucose (mg/dl)	87.9 ± 11.8	77.7 ± 11.2	2.564	.015*
Cortisol (µg/dl)	12.9 ± 5.2	7.4 ± 2.4	3.704	.000*
Prolactin (ng/ml0	15.1 ± 7.9	12.3 ± 3.17	1.245	.152*
Insulin (uIU/ml)	13.1 ± 9.4	25.6 ± 7.3	-4.164	.000*
Bech (Point)	4.0 ± 3.9	1.7 ± 1.2	2.087	.018*
Stait (Point)	33.1 ± 8.9	26.5 ± 5.9	2.475	.011*
Trait (Point)	36.4 ± 7.3	30.3 ± 4.7	2.749	.005*

* Statstically significant

Discussion

The term anxiety is derived from the Indo-Germanic root of "angh" which means "troubled" and "being in trouble". The term anxiety is commonly used in English speaking countries and it is used in the world literature in this way. In Turkish it can be described as "depression", a state of anxiety which is boring or unpleasant and which causes "excitement". When we study the correlation between anxiety and stress, we notice that there is an increasing state of consciousness which reminds us of a biological warning system like an increase in blood pressure, heart rate, and blood sugar in the cases of potential danger which occurs with some changes in the body. This concept was defined as "response to stress". Anxiety is a part of the response to stress. Stress and physiological and behavioral symptoms of anxiety are interrelated. The main components of the response to stress are Corticotrophin Releasing Factor (CRF) and limbic system, hypothalamic-pituitary-adrenal axis (HPA), locus seruleus-noradrenalin and autonomic nervous system which are related to it. Central and peripheral components of this system work interactively and clinical and neuroendocrinological changes are observed in the relations between these systems in cases of stress and anxiety [5,7,8].

In literature we see that the levels of serum cortisol, prolactin and blood sugar are examined in cases of stress [6]. While most of the studies found that levels of serum glucose, cortisol and prolactin increased in cases of stress, some studies found that stress didn't affect the levels of these hormones and serum level of glucose [6,9].

Cortisol is secreted freely from the adrenal cortex into the blood stream and this secretion occurs in a rhythm concurrent with the episodic and circadian rhythm of ACTH secretion (diurnal rhythm, difference in diurnal-nocturnal secretion). ACTH and cortisol are at the highest levels in blood in the early hours of the morning (between the sixth and eighth hours of sleep). Their secretion progressively decreases during the day and reaches the lowest level in the blood in evening hours. ACTH and cortisol secretion follows several stresses (anxiety, surgical intervention, hypoglycemia, etc) and increases within minutes and so there is a considerable increase in plasma levels. Stress response occurs in the central nervous system (CNS). Neural stimulation stimulates ACTH secretion with the increase in CRH secretion [10]. In our study, serum cortisol level was determined to be at a considerably high level in the study group (12.9±5.2 µg/dl) compared to the control (7.4±2.4 µg/dl). This high level is in agreement with literature. Blood was taken at the same time in study and control groups. Even at this time slice which is

concurrent with the hours when cortisol is secreted at the lowest levels, serum cortisol levels in the doctors were far above the levels taken at the same hours from the control group (an increase of 74 %). We observed that serum cortisol level increased considerably with stress or, in other words, increase in cortisol level was the most noticeable response of the hormones to stress.

Normal secretion of prolactin, which is one of the anterior pituitary hormones, occurs at regular intervals within 24 hours. Intervals between release is about 95 minutes. Secretion starts immediately after sleep and reaches its peak halfway through sleep. While it makes a trough at lower levels at around midday, the lowest peak level is in the evening hours. Serum prolactin level is higher in women than in men, but depends on estrogen. Daytime peak of prolactin secretion is more noticeable in the luteal phase in the menstrual cycle compared to the follicular phase. Prolactin secretion in humans increases with stress. Increases in prolactin levels is higher in women than in men in every case of stress. It increases five times as much within the first hours following surgery. Opiate peptides, and particularly beta-endorphin, mediates stress-related prolactin increase. Melatonin stimulating hormone (MSH) is also considered to have an inhibitor effect in stress related prolactin increase. So, there is a dual control by both beta endorphin and MSH. Prolactin levels decrease as a result of being subject to the same repetitive stressor [11,12,13]. Serum prolactin level was found to be higher in female doctors (18.1±8.9 ng/ml) than in male doctors (12.4±4.7 ng/ml) and in the study group (15.1±7.9 ng/ml) than in control group (12.3±3.17 ng/ml). That serum prolactin level increased with stress, but more so in women, was consistent with literature. Yet, both increases were found to be statistically insignificant. We are of the opinion that the results were closer to reality since we were careful about the factors closely related to prolactin secretion like sex, secretion of prolactin within the first 10 days following menstruation, absence of lactation and pregnancy.

Basal insulin is secreted from the pancreas in a healthy individual in an amount which will produce an average of 10-15 microU/ml blood level. Glucose is the most important factor regulating the release of insulin. After the use of oral and/or intravenous glucose, insulin secretion increases. The insulin value obtained for the study group was 13.1+9.4 uIU /ml. This value was lower than that in the control group (25.6±7.3 uIU/ml). This decrease in the serum-insulin levels of the doctors who have just started working in ED and who were considered to have stress was found statistically significant (p= .000). Under stress, catecholamins increase and insulin release is inhibited as in the case of adrenalin-noradrenalin given as an infusion. Therefore, we can suggest that stress decreases the release of insulin. Again, in response to stress, there is an increase in the release of ACTH and glucocorticoids as well as in catecholamins, and the sympathetic system is stimulated if insulin release is inhibited. However, in cases of prolonged stress basal insulin levels may be normal or increased [14,15,16,17]. The level of insulin in our doctors was found to be low as we expected.

We observed a statistically significant increase in serum glucose level in the study group (87.9±11.8 mg/dl) compared to the control (77.7±11.2 mg/dl). Literature mentions frequent increases in blood sugar in stress [17,18]. Yet, in literature there are also studies which found no increase in serum glucose level in stress [19,20]. Studies which found no increase in serum glucose level in stress are studies carried out before 1975. In those studies, blood samples might have been kept for some time after they were taken or developments in the methods of studying blood sugar might have been insufficient. We know that blood cells use up glucose and reduce the level of blood sugar during the storage. The increase observed in the doctors who came to ED for the first time and whom we considered to be stressed is consistent with overall literature. Again this increase is in agreement with the decrease in serum insulin level.

Beck Anxiety Score was, statistically, significantly high in the study group (4.0±3.9 points) compared to the control (1.7±1.2 points). SSAS in the study group (33.1+8.9 points) compared to the control (26.5±5.9 points) and STAS in the study group (36.4±7.3 points) compared to the control (30.3±4.7 points). These results show us that anxiety levels at that time increased in the study group. Particularly, increases in Beck and SSAS were found to be in agreement with acute stress and the literature. Since STAS shows a higher general level of anxiety, there might not have been a difference between the groups. However, scores which showed trait type of anxiety in the study group, which was considered much more stressed, was found high, too. We can ascribe this to the mutual interaction between the two types of anxiety [5,6].

When we look at the correlation between stress hormones and anxiety which is one of the main purposes of our study, we notice a considerable positive correlation between SSAS and serum cortisol level and also a negative correlation between insulin and the same anxiety score ($p<0.01$, $p<0.05$). Although we saw some studies in the literature which found a correlation between anxiety scores and cortisol, we have not found any studies which found a negative correlation between insulin and anxiety score [21]. We observed that with the increase in anxiety (in SSAS) in the doctors in ED, cortisol, which accompanies this metabolically and which is an important stress hormone, increased, and insulin decreased. Correlation found between the SSAS and cortisol and insulin support this finding. Consequently, this study reveals the anxiety experienced by the doctors in ED by showing that there are hormonal changes in the body to stress, and this supports the hypothesis that there is a relationship between metabolic and anxiety evaluation parameters. We consider that our study will provide basis for more comprehensive and new research in future and new studies must be conducted in this field.

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