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The predictive value of serum cortisol and DHEA-S, and their ratio, for antipsychotic response in acute schizophrenia

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Προγνωστική αξία της τιμής της κορτιζόλης και των DHEA-S στον ορό και η σχέση τους ως προς την αντιψυχωσική απάντηση στην οξεία σχιζοφρένεια

Περίληψη στο τέλος του άρθρου

OBJECTIVE **To compare the serum levels of cortisol, and the sulfated form of dehydroepiandrosterone (DHEA-S) and their ratio in patients with schizophrenia and healthy control subjects, and to evaluate their association with the response to antipsychotic treatment.** METHOD **In this clinical prospective study, 60 patients with schizophrenia and 40 healthy age- and sex-matched control subjects participated. Clinical evaluation of patients was conducted using the Positive and Negative Symptom Scale (PANSS), and a questionnaire on socio-demographic and clinical data was used. All the patients had experienced an acute exacerbation of the illness (PANSS: P1 and P3 ≥4). Serum levels of cortisol, DHEA-S, and their ratio, were measured at baseline in all participants and after 3 and 6 weeks of antipsychotic treatment in the patients with schizophrenia. For the purposes of the study, the patients were divided into two subgroups: responders and non-responders to antipsychotic medication.** RESULTS **Patients with schizophrenia had significantly higher mean serum cortisol and DHEA-S levels than subjects in the control group. Responders had significantly higher serum cortisol and DHEA-S levels compared with non-responders. Elevated serum cortisol levels were associated with a positive response to antipsychotic therapy. The subgroup of responders showed greater reduction of the PANSS positive and negative scale scores at all three assessment points.** CONCLUSIONS **Elevated serum cortisol levels may have predictive value for a positive response to antipsychotic medication in the context of acute schizophrenia exacerbation.**

Key words

Cortisol
DHEA-S
Schizophrenia
Treatment response predictor

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Schizophrenia is a severe, heterogeneous chronic mental disorder with diverse clinical manifestations, influenced by various genetic risk factors and with complex interplay between environmental risk factors, such as stress exposure and gene-environment interactions.[1]

According to the vulnerability-stress concept, patients with schizophrenia display increased sensitivity to stress. The hypothalamo-pituitary-adrenal (HPA) axis is one of the major hormonal systems mediating the physical and psychological stress response. Evidence is accumulating for disturbances in HPA activation and abnormal HPA regulatory mechanisms in psychiatric illnesses. A body of evidence has accrued demonstrating dysfunction of the HPA axis leading to elevated peripheral cortisol levels in a proportion of patients.[2] Recently, there has been increased interest in the role of neurosteroids, particularly dehydroepiandrosterone (DHEA) which, in its sulfated form (DHEA-S), is the most abundant in humans.[3] It is considered both a neurosteroid, being produced in the brain, and a neuroactive steroid, produced in the adrenals and gonads, and exerting an effect on the brain.[2,4]

The onset of schizophrenia is often associated with a stressful period in life, indicating that stress can trigger the onset in individuals with a genetic predisposition to the disease. The HPA axis is a crucial system in maintaining homeostasis and adapting to stress. When stress is acute, the adaptive biochemical responses include increased adrenocortical secretion of stress hormones, prominently cortisol and DHEA. Cortisol (glucocorticoid) is a major mediator of the physiological stress response and impacts on many physiological systems to allow the body to react to a stressor. DHEA exerts mainly anabolic effects (i.e., promotion

of growth and repair), thus repairing catabolic damage so long as the levels remain sufficiently high in the circulation. In humans, 99% of circulating DHEA is in its sulfated form DHEA-S. Serum DHEA-S levels are 100 or more times higher than those of DHEA, and DHEA-S has a much longer life and shows no diurnal variations. From a practical point of view, therefore, estimation of DHEA-S is preferable to DHEA, as its levels are more stable. Neuroactive steroids, such as cortisol, DHEA, and its sulfate ester, are the steroid hormones that have several notable roles in the central nervous system (CNS).[5] DHEA-S has multiple effects in the CNS, mediated through its non-genomic actions on several neurotransmitter systems, such as γ-amino butyric acid type A (GABAA), N-methyl-D-aspartate (NMDA) and sigma receptors.[6] Animal experiments show that DHEA-S has profound psychotropic effects, such as memory enhancement, antidepressant, anxiolytic and antiaggression.[7] Moreover, DHEA-S has potent antiglucocorticoid and neuroprotective actions on the brain and can protect hippocampal neurons from glucocorticoid induced neurotoxicity. In healthy subjects, administration of DHEA rapidly reduces the cortisol level. The concomitant release of DHEA-S in the acute stress response is considered to protect the brain against the potentially damaging effects of excessive cortisol activity. These acute adaptive responses to stress are designed to increase survival, yet the dysfunctional stress responses, i.e., over- or underactivity of the HPA axis, may be damaging to an individual. Failure to deactivate these stress responses within a dysfunctional stress system may result in imbalance of these steroid hormones, which may lead to overexposure to the effects of glucocorticoids and increased sensitivity to brain insult.[8]

The HPA axis abnormalities in schizophrenia are indicated by elevated basal cortisol levels, non-suppression of cortisol after the dexamethasone suppression test, and blunted cortisol awakening response. Increased cortisol levels observed in schizophrenia have been proposed as endophenotypic markers of illness.[1]

It has been reported, although inconsistently, that the levels of DHEA and DHEA-S may have an impact on the psychopathological manifestations of schizophrenia.[9–15]

In the last 3 decades, several authors have reported a link between neuroactive steroids and the pathophysiology or therapeutics of schizophrenia. The relationship between blood levels of DHEA, DHEA-S and cortisol, and the onset, prognosis, symptom severity, and treatment response of schizophrenia has been investigated in a number of studies.[13,16–18]

Early treatment response is one of the strongest predictors of long-term symptomatic and functional outcome in psychosis. Unfortunately, we do not have reliable predictors of early treatment response in schizophrenic psychosis, which makes it impossible to tailor psychiatric care to the needs of the individual patient. Biomarkers of stress hold great potential as clinical predictors of treatment response; stress plays a recognized role in precipitating the onset and relapse of psychosis, and the cortisol stress response is already abnormal at psychosis onset.[19]

We therefore decided to conduct a study of serum levels of cortisol, DHEA-S and their ratio in patients with schizophrenia, in terms of clarifying their role in the pathophysiology of the disorder and their potential as biomarkers for the efficacy of antipsychotic therapy in these patients.

The aim of our study was to compare serum cortisol and DHEA-S levels, and their ratio in patients with schizophrenia and healthy control subjects, and to evaluate their association with the response to antipsychotic treatment in the patients with schizophrenia.

MATERIAL AND METHOD

In this clinical prospective study, we included 60 patients with schizophrenia of both genders, aged 18–50 years, treated as inpatients or outpatients at the University Psychiatry Clinic, Skopje, North Macedonia. All the patients had experienced an acute exacerbation of the illness according to the Positive and Negative Symptom Scale (PANSS): P1-delusions and P3-hallucinatory behavior ≥4. Patients who suffered from major physical illness, drug or alcohol abuse, epilepsy and other organic brain syndromes were excluded. All the patients underwent physical examination and routine laboratory tests to rule out physical illness. Clinical evaluation of the patients was performed using the PANSS. As a control group, 40 matched healthy subjects were enrolled. A non-standardized questionnaire was used for collection of socio-demographic (gender, age, education, employment, marital status) and clinical data (age of onset of the disorder, duration of illness, number of relapses, number of hospital treatments, type of antipsychotic agents, treatment adherence, family history). We collected all the data in the period of one year (January 2016 to January 2017).

At the end of the study, the patients with schizophrenia were divided in two groups according to the antipsychotic therapy response: (a) Subjects suffering from schizophrenia classified as responders who had no ratings of >3 on items P1, P2, P3, P5 and P6 of the PANSS and had a ≥30% reduction from baseline in the PANSS total score; and (b) subjects suffering from schizophrenia who did not meet these criteria and who were defined as non-responders.

All participants in the study provided written informed consent to participate in this prospective study, after having received a detailed explanation of the study procedures. The study was ap-

proved by the Ethics Committee of Medical University in Skopje and by the Board of the University Clinic of Psychiatry.

Steroid determination

Serum cortisol and DHEA-S levels were measured at the Institute of Clinical Biochemistry at the Medical University in Skopje, North Macedonia. Serum samples for cortisol and DHEA-S were collected between 8 a.m. and 9 a.m. hours after 20 min of rest. All participants were instructed to abstain from unusual physical activity or stress for a period of 24 hours prior to blood sampling. Blood samples were collected at baseline in all participants and after 3 and 6 weeks of the antipsychotic treatment in the patients with schizophrenia. Cortisol and DHEA-S levels were measured by the IMMULITE 2000, competitive chemiluminescent enzyme immunoassay.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) for windows, version 17.0 was used for statistical analysis of the data. The statistical methods used for analysis of the data included non-parametric methods (Chi-square test, Mann-Whitney U test, Friedman ANOVA), and parametric methods (t-test for independent samples). Correlation between parameters was examined with Pearson and Spearman Rank correlation coefficients. Of the multivariate methods we used MANOVA. Binary Logistic Analysis was used to determine the predictive value of serum cortisol, DHEA-S and their ratio for antipsychotic treatment response. Values of $p<0.05$ were considered statistically significant.

RESULTS

Table 1 shows the sociodemographic characteristics of the patients with schizophrenia and the control group. The patients with schizophrenia had significantly higher mean serum levels of cortisol (t=6.07; p<0.001) and DHEA-S (t=7.66; p<0.001) levels than the control group. Mean cortisol/DHEA-S ratio was no different in the two groups (Z=-1.57; p=0.11).

The two subgroups of patients with schizophrenia, classified as responders and non-responders to antipsychotic treatment, did not differ significantly in terms of gender (men/women: 29/8 and 15/8, respectively; Pearson Chi-square=1.26; df=1; p=0.26), age (t=0.34; p=0.73), marital status (Pearson Chi-square=1.41; df=2; p=0.49), education (Pearson Chi-square=4.21, df=3; p=0.24), age of onset of the disorder (Z=0.15; p=0.88), duration of illness (Z=0.32; p=0.75), number of relapses (Z=0.11; p=0.9), number of hospital treatments (Z=0.68; p=0.49) and the type of antipsychotic agents administered – typical/atypical (Pearson Chi-square=0.86; df=1; p=0.35).

Table 1. Sociodemographic characteristics of patients with schizophrenia and control subjects.

Variables	Patients (n=60)	Control subjects (n=40)	p-level
Gender			
Male	44 (73.33)	25 (62.5)	X^2=1.32; p=0.25 ns
Female	16 (26.67)	15 (37.5)	
Age			
Mean±SD	35.30±9.19	36.67±7.13	t=0.79; p=0.43 ns
Education			
Elementary school	11 (18.33)	0	
Secondary school	42 (70.0)	20 (50.0)	X^2=22.05; p=0.00006 sig
Higher education	3 (5.0)	7 (17.5)	
High education	4 (6.67)	13 (32.5)	
Employment			
Employed	11 (18.33)	31 (77.5)	
Unemployed	12 (20.0)	9 (22.5)	X^2=44.74; p=0.00000 sig
Previously employed but not anymore	37 (61.67)	0	
Marital status			
Not married	40 (66.67)	15 (37.5)	
Married	16 (26.67)	20 (50.0)	X^2=8.25; p=0.016 sig
Divorced	4 (6.67)	5 (12.5)	

X^2 Pearson Chi-square, t (t-test for independent samples)

Ns: Non significant, sig: Significant

Table 2 shows the levels of serum cortisol, DHEA-S and the cortisol/DHEA-S ratio in the group of responders compared with the group of non-responders at baseline assessment point.

We used MANOVA analysis to compare the difference in serum levels of cortisol, DHEA-S and their ratio between responders and non-responders during the 6 weeks period of examination.

Table 2. Serum levels of cortisol, sulfated dehydroepiandrosterone (DHEA-S) and cortisol/DHEA-S ratio at baseline in responders and non-responders to treatment with antipsychotics.

Hormone	Responders (n=37)	Non-responders (n=23)	Test	p-value
Cortisol	640.6±116.4	419.1±121.2	7.05	0.000000
DHEA-S	375.6±114.4	255.4±106.2	4.06	0.00014
Cortisol/DHEA-S	2.08±1.8	2.1±2.2	0.09	0.93

t-test for independent samples

Across all three assessment points (baseline, after 3 and after 6 weeks), the responders had a significantly higher level of serum cortisol (p<0.001) and DHEA-S (p=0.002) compared with non-responders, while cortisol/DHEA-S ratio did not differ significantly between the two groups (p=0.7). Hormonal levels decreased significantly during the study period of 6 weeks in both groups. Significant "group"×"time" interaction was found for hormone cortisol (p=0.002) (tab. 3).

We used binary logistic analysis to determine the predictive value of serum cortisol, DHEA-S and cortisol/DHEA-S ratio for positive/negative respond to antipsychotic therapy in patients with schizophrenia (tab. 4).

Of the three factors analyzed, only serum cortisol was a significant factor for antipsychotic treatment response; elevated serum cortisol levels were associated with a positive response to antipsychotic therapy.

According to the PANSS scores, responders scored significantly higher on the positive PANSS scale (F=6.06; df=1.58; p=0.017), delusions (F=7.41; df=1.58; p=0.009) and suspiciousness (F=12.509; df=1.58; p=0.001) than non-responders at baseline.

The responders showed greater reduction of the PANSS positive and PANSS negative scale scores across all three assessment points (baseline, after 3 and after 6 weeks of antipsychotic therapy) than the non-responders (figures 1 and 2).

Correlation between serum cortisol and DHEA-S levels

Table 3. Comparison of hormonal concentrations and ratio between responders and non-responders to antipsychotics across three assessment points (MANOVA).

Serum stress hormones	t-value	Df		F	P
Responders versus non-responders					
Hotelling-Lawley test	0.62	3	56	11.46	0.000
Cortisol	1054548.030	1	58	28.683	0.000
DHEA-S	366603.017	1	58	10,747	0.002
Cortisol/DHEA-S	0.977	1	58	0.120	0.730
Across the three examinations					
Hotelling-Lawley test	0.862	6	226	16.24	0.000
Cortisol	576305.421	2	116	44.38	0.000
DHEA-S	77337.031	2	116	10.08	0.000
Cortisol/DHEA-S	3.853	2	116	2.18	0.19
Interaction					
Hotelling-Lawley test	0.147	6	226	2.77	0.013
Cortisol	87261.088	2	116	6.72	0.002
DHEA-S	16020.123	2	116	2.09	0.13
Cortisol/DHEA-S	1.090	2	116	0.62	0.54

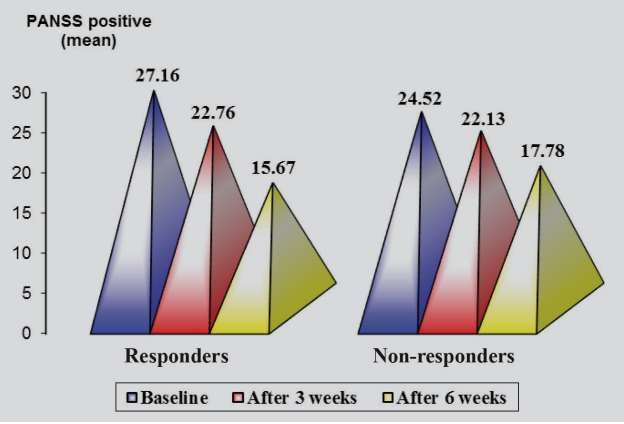

Figure 1. Positive and Negative Symptom Scale (PANSS) positive scale scores across three assessment points in responders and non-responders to antipsychotic treatment.

Table 4. Binary logistic analysis of serum hormonal concentrations and ratio cortisol/DHEA-S between responders and non-responders to antipsychotic treatment (at baseline data).

	-2 Log likelihood=39.893 Nagelkerke R Square=0.661 percent correct=85.0							
	B	SE	Wald	Df	Sig	EXP(B)	95% CI for EXP(B)	
							Lower	Upper
Cortisol	-0.014	0.005	8.513	1	0.004	0.986	0.977	0.995
DHEA-S	-0.008	0.005	2.558	1	0.110	0.992	0.981	1.002
Cortisol/DHEA-S	-0.188	0.395	0.227	1	0.633	0.828	0.382	1.796
Gender	1.241	1.240	1.002	1	0.317	3.459	0.305	39.301
Constant	9.679	2.624	13.603	1	0.000	15978.441		

Dependent variable: Without positive response/with positive response

95%CI: 95% Confidence interval

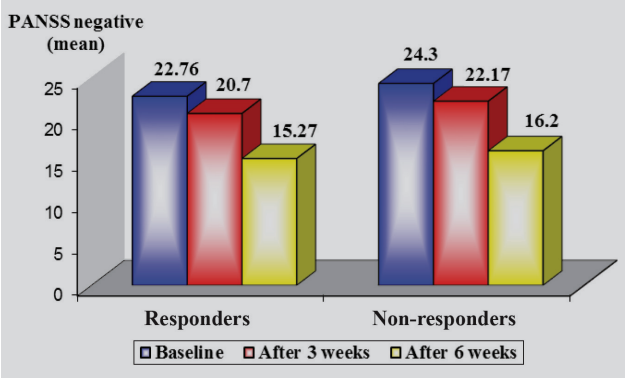

Figure 2. Positive and Negative Symptom Scale (PANSS) negative scale scores across three assessment points in responders and non-responders to antipsychotic treatment.

and PANSS scores across all three assessment points in the two groups was examined with Spearman rank-order correlations, which showed statistically significant correlation between serum cortisol and PANSS positive scale score at the third assessment point ($R=-0.35$; $p<0.05$). The correlation was negative; higher serum cortisol levels significantly correlated with lower PANSS positive scale score. Investigation of correlation between serum DHEA-S levels and PANSS scores in the responders group showed statistically significant positive correlation between hostility and the DHEA-S level at the second assessment point ($R=0.38$; $p<0.05$); higher serum DHEA-S levels are associated with higher hostility scores.

Examination of correlation between serum cortisol and DHEA-S levels and PANSS scores across all three assessment points in the group of non-responders showed statistically significant positive correlation between cortisol and item delusions on the PANSS positive scale at the baseline ($R=0.5$; $p<0.05$); higher serum cortisol levels are associated with higher scores for delusions. Investigation of correlation between serum DHEA-S levels and total PANSS item scores in this group showed no statistically significant correlation across all three assessment points.

DISCUSSION

Recent studies on schizophrenia have focused increasingly on potential causative factors, such as structural and functional brain abnormalities. The assumption that alterations in cortisol and DHEA-S levels may have a role in changes in clinical presentation of several neuropsychiatric disorders, including schizophrenia, has been emphasized.[20]

Our study showed that plasma cortisol levels were significantly elevated in the patients with schizophrenia compared with the control group, which is in agreement with the results of most of the studies.[1,8,10,19–28] Some studies report no significant differences between patients with schizophrenia and healthy control subjects in terms of cortisol levels[14,17,29] or lower cortisol levels in patients with schizophrenia.[30,31]

The serum DHEA-S levels in this study were significantly higher in patients with schizophrenia compared with control subjects, which coincided with the results of most of the studies,[9,10,13,14,20,32] although some studies found lower serum DHEA-S levels[33] or no difference[17] in patients with schizophrenia compared with healthy control subjects.

According to our results, we can conclude that elevated serum cortisol and DHEA-S levels in patients with schizophrenia may play a role in the pathophysiology of schizophrenia, and they could be used as a biological marker for the diagnosis of this disorder.

Current and lifetime stress are widely acknowledged to contribute to the risk for, and to the variation in symptom severity in mental health disorders. The neural diathesis-stress model of schizophrenia has been proposed as a framework for the development of schizophrenia as the consequence of an interaction between a genetic susceptibility and stress triggered by stressful or traumatic experiences.[34–36] Briefly, this theory is based on findings that the HPA axis is activated after stress exposure, and that cortisol is one of many secretagogues and glucocorticoids released throughout the brain. One systematic review highlights recent evidence of blunting of cortisol response following experimentally induced psychosocial stress. The authors concluded that, while there was some evidence of this blunted response across illness types and stages, the strongest evidence was observed for those with chronic schizophrenia.[37]

The authors of one recent study compared symptom severity and testosterone, DHEA-S and cortisol levels in premenopausal women with schizophrenia and an age- and sex-matched control group. They concluded that DHEA-S might be a potential biological marker for schizophrenia, because there is evidence of an association between DHEA-S and the pathophysiology of schizophrenia.[14]

In our study, we evaluated the association between serum cortisol and DHEA-S levels and response to antipsychotic treatment in patients with schizophrenia. At the baseline assessment point, the subgroup of responders showed significantly higher serum cortisol and DHEA-S levels compared with the subgroup of non-responders.

Across all the three assessment points, the responders had significantly higher serum cortisol and DHEA-S levels compared with non-responders, which is in agreement with the results of another study.[11] Responders also showed greater reduction of the PANSS positive and negative scale scores across all the three assessment points compared with non-responders.

Early treatment response is one of the strongest predictors of long-term symptomatic and functional outcome in psychosis. Biomarkers of stress hold great potential as clinical predictors of treatment response, while stress plays a recognized role in precipitating the onset and relapse of psychosis.[19]

The authors of one longitudinal study investigated the ability of cortisol as a biomarker to predict treatment response at 12 weeks follow-up in first episode psychosis. Their findings showed that blunted cortisol awakening response predicted poor treatment response at the onset of psychosis. They concluded that cortisol should be considered as possible predictor of treatment response, and an optimal target for the development of novel therapeutic agents.[19]

The authors of one prospective study investigated the association between serum cortisol and DHEA-S levels, and their molar ratios, with the response to antipsychotic treatment in patients with schizophrenia during exacerbation of the disorder. Their findings suggest that the molar ratio of cortisol to DHEA-S may have predictive value for response to antipsychotic medications in the context of exacerbation of chronic schizophrenia. Elevated cortisol levels and an elevated cortisol-DHEA-S ratio in this study were shown to be predictive of a positive short-term response to antipsychotic treatment, with a clear advantage of cortisol/DHEAS ratio over serum cortisol concentrations for prediction.[11]

The authors of a recent study evaluated serum cortisol and DHEA-S levels in terms of clarifying their role in the pathophysiology of schizophrenia and the possibility of using them as potential biomarkers of the efficacy of antipsychotic therapy. They concluded that hormonal predictors of the effectiveness of antipsychotic therapy in patients with the first psychotic episode and chronic schizophrenia may include minor changes in high cortisol levels at week 3–4 of therapy, high rates of DHEA-S before and 3–4 weeks of therapy, unidirectional changes in cortisol and DHEA-S, and their ratio at 3–4 weeks of therapy.[10]

The present study was designed to investigate association between serum cortisol and DHEA-S levels, and their ratio, and the response to antipsychotic treatment during an exacerbation of schizophrenia.

We tested the relationship between serum cortisol and DHEA-S levels and the cortisol/DHEA-S ratio, and positive response to antipsychotic treatment during acute exacerbation of schizophrenia.

Of the three factors analyzed, only serum cortisol was significant for antipsychotic treatment response; elevated cortisol levels were associated with a positive response to antipsychotic therapy. We can conclude that elevated serum cortisol levels may have predictive value for positive response to antipsychotic therapy in the context of acute schizophrenia exacerbation.

The authors of one study investigated serum cortisol and DHEA-S levels in two groups of patients with schizophrenia divided according to their responsivity to antipsychotic treatment.[11] They examined correlation between changes in serum levels of cortisol and DHEA-S and changes in PANSS dimensions, and demonstrated that among responders, increased serum DHEA-S and cortisol levels were significantly correlated with improvement in activation and with the PANSS total score. In their study, reduction over time of the PANSS total scores showed significant association with increased DHEA-S levels. Among non-responders, on the other hand, no significant correlation was observed between changes in any hormonal measures and symptom severity.

In our study, we also examined the relationship between these hormones and clinical symptoms (evaluated with PANSS) in patients with schizophrenia with different responses to antipsychotic treatment.

Examination of the association between serum cortisol and DHEA-S levels with psychopathology in the responders in our study showed significant correlation between serum cortisol and the PANSS positive scale score, and significant correlation between hostility and serum DHEA-S.

Investigation of the correlation between serum cortisol and DHEA-S with psychopathology in the non-responders showed statistically significant correlation between serum cortisol and delusions, but no correlation between serum DHEA-S levels and psychopathology.

Our results suggest that serum cortisol and DHEA-S levels are associated with different schizophrenia symptoms in patients with schizophrenia, according to their responsivity to antipsychotic treatment.

Our study has some limitations, one of which is related to assessment of diurnal rhythmicity of hormones. Future

studies should collect blood samples taken at different points during the day. Another limitation is the possible influence of menstrual status, use of oral contraceptives and hormone replacement therapy, which might affect cortisol levels. Smoking also influences serum cortisol levels and is more prevalent in patients with schizophrenia; excluding smokers may have provided better results. Assessment over a longer period of time should be performed in future studies.

The limited number of studies that have investigated the role of serum cortisol and DHEA-S levels as potential biomarkers of the efficacy of antipsychotic therapy in patients with acute exacerbation of schizophrenia is a reason to propose similar future research with large sample numbers.

In conclusion, our study provides evidence that serum levels of cortisol and DHEA-S may serve as biomarkers for diagnosing schizophrenia. Elevated serum cortisol and DHEA-S levels may play a role in the pathophysiology of schizophrenia. The subgroup of responders to antipsychotic treatment had significantly higher serum cortisol and DHEA-S levels than the subgroup of non-responders, respectively. Elevated serum cortisol levels may have predictive value for positive response to antipsychotic therapy in the context of acute schizophrenia exacerbation. The group of responders showed greater reduction of the PANSS positive and PANSS negative scale scores across all three assessment points. Serum cortisol and DHEA-S levels were associated with different symptoms in patients with schizophrenia, according to their responsivity to antipsychotic treatment. The results from this study add to our existing knowledge about the pathophysiology of schizophrenia, but the complex interaction between neurosteroids and their possible role as biomarkers in schizophrenia demand further investigation.

ΠΕΡΙΛΗΨΗ

Προγνωστική αξία της τιμής της κορτιζόλης και των DHEA-S στον ορό και η σχέση τους ως προς την αντιψυχωσική απάντηση στην οξεία σχιζοφρένεια

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ΣΚΟΠΟΣ Σύγκριση των επιπέδων κορτιζόλης και του DHEA-S στον ορό και η σχέση τους αφ' ενός μεταξύ ασθενών με σχιζοφρένεια και υγιών μαρτύρων και αφ' ετέρου με την ανταπόκριση στην αντιψυχωσική θεραπεία. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Σε αυτή την κλινική προοπτική μελέτη συμπεριλήφθηκαν 60 ασθενείς με σχιζοφρένεια και 40 υγιείς με ανάλογη ηλικία και φύλο ως ομάδα ελέγχου. Όλοι οι ασθενείς παρουσίασαν οξεία επιδείνωση της νόσου (PANSS: P1 and P3 ≥4). Η κλινική αξιολόγηση των ασθενών έγινε με την κλίμακα θετικών και αρνητικών συμπτωμάτων. Χρησιμοποιήθηκε ένα ερωτηματολόγιο για τη συλλογή κοινωνικο-δημογραφικών και κλινικών δεδομένων. Για τους σκοπούς της μελέτης, η εξεταζόμενη ομάδα χωρίστηκε σε δύο υποομάδες: σε αυτούς που ανταποκρίθηκαν και σε εκείνους οι οποίοι δεν ανταποκρίθηκαν. Τα επίπεδα της κορτιζόλης και του DHEA-S στον ορό, καθώς και η σχέση τους μετρήθηκαν κατά την έναρξη σε όλους τους συμμετέχοντες και μετά από 3 και 6 εβδομάδες, αντίστοιχα, κατά τη διάρκεια της αντιψυχωσικής θεραπείας σε ασθενείς με σχιζοφρένεια. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Οι ασθενείς με σχιζοφρένεια είχαν σημαντικά υψηλότερα επίπεδα κορτιζόλης και DHEA-S στον ορό σε σύγκριση με την ομάδα ελέγχου. Αυτοί που ανταποκρίθηκαν είχαν σημαντικά υψηλότερα επίπεδα κορτιζόλης και DHEA-S στον ορό, σε σύγκριση με εκείνους που δεν ανταποκρίθηκαν. Τα αυξημένα επίπεδα κορτιζόλης στον ορό συσχετίστηκαν με θετική ανταπόκριση στην αντιψυχωσική θεραπεία. Η ομάδα αυτών που ανταποκρίθηκαν έδειξε μεγαλύτερη μείωση των θετικών και των αρνητικών βαθμολογιών κλίμακας PANSS και στα τρία σημεία αξιολόγησης. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Τα αυξημένα επίπεδα κορτιζόλης στον ορό μπορεί να έχουν προγνωστική αξία για τη θετική ανταπόκριση στην αντιψυχωσική θεραπεία στο πλαίσιο της οξείας επιδείνωσης της σχιζοφρένειας.

Λέξεις ευρετηρίου: DHEA-S, Κορτιζόλη, Πρόβλεψη απόκρισης θεραπείας, Σχιζοφρένεια

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