

METABOLIC SYNDROME AND CORTISOL/DHEAS RATIO IN PATIENTS WITH BIPOLAR DISORDER AND SCHIZOPHRENIA

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SUMMARY

The cortisol/DHEAS ratio has been found to predict different health outcomes. We examined the association between cortisol/DHEAS ratio and metabolic syndrome (MetS) in patients suffering from bipolar disorder and schizophrenia. The only subcomponent of MetS positively associated with the cortisol/DHEAS ratio was diastolic blood pressure. Possible reasons for this finding, as well as study limitations, are discussed.

Key words: metabolic syndrome – MetS - cortisol/DHEAS ratio - bipolar disorder - schizophrenia

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INTRODUCTION

Metabolic syndrome (MetS) is a cluster of symptoms with higher prevalence in psychiatric patients compared to general population (Britvic et al. 2013, Jakovljević et al. 2007, Oreski et al. 2012, Vuksan-Ćusa et al. 2013, Wysokinski et al. 2012).

There is a long history of research into the role of the hypothalamo-pituitary-adrenal axis (HPA) in the aetiology of different psychiatric disorders (Maric & Adzic 2013). The overlap between some clinical features of the MetS and Cushing disease has prompted the hypothesis that adrenal steroids may be associated with the development of MetS (Anagnostis et al. 2009). However, previous studies investigating the role of cortisol and DHEAS in MetS showed conflicting results (Pasquali et al. 2006, Weigensberg et al. 2008). Alterations in cortisol and dehydroepiandrosteron sulfate (DHEAS) levels are thought to play a role in the pathophysiology of schizophrenia and bipolar disorder (Gallagher et al. 2007).

Patients with schizophrenia and bipolar disorders have reduced life expectancy compared to general population (Laursen 2011). The cortisol/DHEAS ratio has been found to predict health outcomes better than the level of either hormone alone as well as all-cause mortality (Butcher et al. 2005).

To the best of our knowledge, only one study (Phillips et al. 2010) investigated the association of cortisol/DHEAS ratio and the presence of MetS, in the population of Vietnam army veterans. The aim of our study was to determine the association between cortisol/DHEAS ratio and the presence of MetS in patients with bipolar disorder and schizophrenia.

SUBJECTS AND METHODS

This study included patients with bipolar disorder (n=60) and schizophrenia (n=62) who were treated at the University Hospital Centre Zagreb between July

2009 and June 2010. The diagnoses were confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al. 1998). Gender distribution for whole sample was roughly equal, with 52.2% males and 47.8% females.

All bipolar patients were in the euthymic phase defined with HDRS-17 (Hamilton 1960) score 7 or less and YMRS (Young et al. 1978) score 5 or less. All schizophrenic patients had to fulfill the following inclusion criteria: stable clinical picture (assessed by the treating psychiatrist), stable dose of an antipsychotic for at least 4 weeks, good general physical health, and the absence of drug and alcohol abuse. All patients were treated with the second generation antipsychotics (SGA). In addition, 89% patients with bipolar disorder and 22% patients with schizophrenia received mood stabilizers. Written informed consent was obtained from all the participants, under procedures approved by the Local Ethics Committee.

Venipuncture was performed for all subjects between 8 and 9 a.m. after 12 hours overnight fast. MetS was defined according to the NCEP ATP III criteria (Expert Panel 2001) and parameters were assessed as described in our previous work (Vuksan-Ćusa et al. 2011). Factors that are known to influence morning cortisol levels were controlled for: time of morning awakening, morning activity and exercise, as well as caffeine consumption and smoking. Participants were instructed to abstain from unusual physical activity or stress for a period of 24 hours prior to the blood sampling. Basal cortisol and DHEAS were assessed using a competitive immunoanalysis method on COBAS E601 device. Referent interval for morning cortisol was 138-690 nmol/l and for DHEAS 3-11 μmol/l.

Statistical analyses

Statistical analyses were performed using the SPSS version 17.0. Data are presented as mean ± standard deviation (SD) or as median. Independent t-test, Mann-Whitney U-test or Pearson's chi-square test were used

Table 1. Demographic, clinical and biological parameters for patients with and without metabolic syndrome (MetS)

	MetS (n=43)	Non-MetS (n=80)	
Age (years)	42.8±13.7	38.6±13.3	t=1.7, P=0.10
Gender (m:f)	25:18	38:42	χ ² =1.3, P=0.26
Duration of illness (years)	10.0	9.0	U=1547.0, P=0.36
MetS subcomponents			
Waist circumference (cm)	99.6±11.6	86±10.3	t=6.7, P=0.000
Triglycerides (mmol/l)	2.2	1.4	U=680.5, P=0.000
HDL (mmol/l)	1.2±0.38	1.4±0.42	t=-2.1, P=0.046
Blood glucose (mmol/l)	6.5	4.9	U=864.5, P=0.000
Systolic pressure (mmHg)	130.0	120.0	U=917.0, P=0.000
Diastolic pressure (mmHG)	85.0	80.0	U=1057.5, P=0.000
Cortisol (nmol/l)	479.6.5±131.7	456.2±149.5	t=0.9, P=0.39
DHEAS (nmol/l)	4962.8±2277.74	5398.8±2388.08	t=-0.9, P=0.33
Cortisol/DHEAS ratio (nmol/l)	10.7	8.9	U=1446.0, P=0.15

Values are Mean ± Standard deviation (SD) for normally distributed and Median for asymmetrically distributed continuous variables

to compare demographic, clinical and biological variables between patients with and without MetS. Multiple regression analysis was performed to examine the relationships between the subcomponents of MetS and the cortisol/DHEAS ratio. The cortisol/DHEAS ratio was calculated as cortisol/DHEAS (*100). Statistical significance was set at two-tailed $P < 0.05$.

RESULTS

Demographic, clinical and biological characteristics of patients with and without MetS are shown in Table 1. Forty three patients (35%) met criteria for MetS. There were no group differences in demographic (age and gender) and clinical (duration of psychiatric illness) parameters.

There were no significant associations of baseline cortisol levels, DHEAS levels and the cortisol/DHEAS ratio with the presence of MetS in this psychiatric sample. Furthermore, diastolic blood pressure was the only subcomponent of MetS significantly positively related to the cortisol/DHEAS ratio ($\beta=0.416$, $P=0.004$). The association between systolic blood pressure and the cortisol/DHEAS ratio remained only a trend ($\beta=-0.259$, $P=0.072$).

DISCUSSION

Although the majority of studies showed higher cortisol concentration (Pasquali et al. 2006) and generally lower DHEAS concentration (Muller et al. 2005) in individuals with MetS, our study did not confirm these results.

Furthermore, the cortisol/DHEAS ratio was not associated with the presence of MetS. This is the first study to evaluate the relationship between MetS and cortisol/DHEAS ratio in psychiatric patients. Our results do not support the findings from study of Phillips et al. (2010) who reported positive association between cortisol/DHEAS ratio and MetS in Vietnam army veterans. It is noteworthy that their sample included subjects with no specific psychiatric diagnoses mentio-

ned. While in our study the only subcomponent of MetS significantly related to cortisol/DHEAS ratio was diastolic blood pressure, Phillips et al. (2010) showed significant association of this ratio with four out of five MetS subcomponents.

We hypothesize that the lack of stronger associations in our study may be related to the presence of psychiatric disorder itself or prescribed pharmacotherapy. Female patients with schizophrenia were found to have increased cortisol levels compared to healthy females (Muck-Seler et al. 2004) and cortisol/DHEAS ratio was higher in schizophrenic patients (Ritsner et al. 2004), although this has not been confirmed in all the studies (Gallagher et al. 2007). Also, it has been reported that low dose quetiapine and olanzapine, mostly prescribed antipsychotics in our patients sample, decrease cortisol levels in schizophrenic patients (Cohrs et al. 2006). Furthermore, the study of Phillips et al. (2010) included only male participants who are known to have higher cortisol levels compared to females (Purnell et al. 2004). Finally, there is evidence that DHEAS levels show complex associations with psychosis, depending on the phase of disease as well as psychopharmacological treatment and age (Strous et al. 2009).

The limitations of our study are a relatively small psychiatric sample, cross sectional design and single morning measurement of serum cortisol and DHEAS. Different clinical and psychopharmacological influences on those parameters also need to be explored.

CONCLUSION

In conclusion, the cortisol/DHEAS ratio was positively associated with only one subcomponent of MetS - diastolic blood pressure, in the sample of bipolar and schizophrenia patients. Given the high prevalence of MetS in psychiatric patients and the role of cortisol/DHEAS ratio in health outcomes, it would be worthwhile to further examine this relation in larger psychiatric samples. Different clinical and psychopharmacological influences on those parameters also need to be explored.

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Conflict of interest : None to declare.

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