Testosterone and DHEA-S levels with chronic tic disorder in children

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ABSTRACT

The neurobiological basis of tic disorders is thought to be a series of interactions including genetic, environmental and gender related factors. Being male is thought to be an especially important risk factor in the pathogenesis of tics. Our aim in this study was to investigate gender-related hormones such as testosterone, dehydroepiandrosterone sulfate (DHEA-S) and cortisol in tic patients. A total of 26 patients who had not entered puberty and had been diagnosed with chronic tic disorder and 25 healthy children were included in the study. Serum total testosterone, cortisol and DHEA-S levels were measured and the relationship with clinical data was investigated. The testosterone and DHEA-S levels of the patient group were higher than that of the control group (P = 0.019, P = 0.025) but no statistical difference was found between the cortisol levels (P = 0.642). No statistical correlation was found between total tic severity, general disturbance, movement tic subscale scores and the DHEA-S (P = 0.77, P = 0.45, P = 0.819 respectively) and testosterone levels (P = 0.954, P = 0.669, P = 0.909 respectively). The results of this study reveal an elevation of testosterone and DHEA-S levels in patients. Future studies with a larger number of patients are likely to help elucidate the importance of these androgens in tic disorder.

1. Introduction

Tic disorder (TD) is a common neuropsychiatric disorder with childhood onset, characterized by non-rhythmic, rapid, intermittent, involuntary, and repetitive muscle spasms (Leckman, Peterson, & Cohen, 2002). Tourette’s syndrome (TS) is a chronic tic disorder (CTD), characterized by motor and vocal tics, lasting a cumulative total of at least 1 year, in the absence of a known medical cause (American Psychiatric Association, 2000). TS and CTD have been shown to be related, with TS being a more severe form of CTD (Spencer, Biederman, Harding, Wilens, & Faraone, 1995).

The neurobiological basis of this disorder is thought to be a series of interactions between genetic, environmental and gender-dependent factors (Singer, 2005). Male gender and exposure to psychosocial stress have been emphasized as important risk factors in CTD and TS pathogenesis. Furthermore, genetic studies have disproven the hypothesis that X-related inheritance patterns may be the reason for the male predominance (Santangelo et al., 1994). Also, it has been suggested that exposure to androgens during critical periods of fetal development may play a role in the development of the disorder (Alexander & Peterson, 2004). It is well known that tic disorder starts in childhood and improves during adulthood (Santangelo et al., 1994). Considering that androgens cause tics to worsen in males (Leckman & Scahill, 1990) and some drugs with an anti-testosterone effect show an anti-tic effect (Peterson, Campise, & Azrin, 1994; Izmir, & Dursun, 1999), androgens may be a factor that affects the severity of the tics and plays a role in the pathogenesis of the disorder both in males and females.

Although all these findings suggest that androgens may have a role in the pathophysiology of the disease. These androgens are also a part of the HPA axis and increase together with cortisol in response to stress. The role of stress and cortisol in CTD and TS has been investigated in previous studies.

In this study, we aimed to investigate the testosterone, DHEA-S and cortisol levels in children with TS and CTD.

2. Materials and methods

2.1. Subjects

26 patients aged 7–12 years who presented to the Child and...
Adolescent Psychiatry Department of the Faculty of Medicine at Inonu University between 2012 and 2014 were included in the study. They had been diagnosed with CTD or TS, but had not entered puberty and had not received treatment. Patients and the control group were selected by random sampling methods. The control group consisted of 25 healthy children of similar age and gender. The study procedures were approved by the Inonu University Ethics Committee and written consent was obtained from the parents of the participants. The diagnoses were made by an experienced child and adolescent psychiatrist using the Diagnostic and Statistical Manual, Fourth Edition (DSM - IV) criteria and the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K – SADS - PL) (Kaufman et al., 1997). Patients with other concurrent psychiatric, neurological, endocrine or chronic disorder or history of drug use were excluded from the study. We excluded 7 patients with ADHD comorbidity and 4 patients with OCD comorbidity.

A voluntary control group of similar age and gender was created from the children of hospital staff. Those with a psychiatric, neurological, endocrine or chronic disorder and with a history of drug use were excluded according to the study inclusion criteria.

Physical examinations of all children in the patient and control groups were performed by the family physician. Tanner staging was used to evaluate pubertal development in all children (Marshall & Tanner, 1970, 1969). Children with Tanner stage 1 or more breast and pubic hair development for girls or genital and pubic hair development for boys were considered to have entered puberty and were not included in the study.

2.1.1. Data collection tools

2.1.1.1. Sociodemographic data form. This provided the sociodemographic data of the patient and the family and the developmental history of the patient.

2.1.1.2. Yale Global Tic Severity Scale (YGTSS). This is a clinical interview containing 11 items on the severity of motor and sound tics completed by a clinician (Leckman et al., 1989). The five indicator scores are total motor tics score, total phonic tics score, total tic score, whole disturbance grading and general severity score.

2.1.1.3. K – SADS - PL. The K – SADS - PL is a semi-structured diagnostic interview designed to assess current and past episodes of psychopathology according to DSM - IV for psychiatric disorders in school-aged children and adolescents (Kaufman et al., 1997).

Venous blood samples from the patient and control groups were obtained at 09:00 in the morning after 12 h of fasting and a 30 min rest. After the collected bloods were centrifuged, the obtained samples were kept in polypropylene tubes at −80 °C until the time of analysis.

2.2. Serological techniques

All biochemical analyses were performed at the Research Laboratory of Inonu University, Faculty of Medicine, Division of Biochemistry. A highly sensitive and specific commercial ELISA kit (DiaMetraDK0002, DK0001, DK0005DiaMetraS.r.l., Milano, Italy) was used for the analysis of testosterone, cortisol and DHEA - S in the serum samples. The kit principle is based on the competition between the serum samples to the standard and sample wells, respectively. After that, 100 μL of testosterone and DHEA - S conjugate and 200 μL of cortisol conjugate was added, mixed and incubated at 37 °C for 1 h. Following the incubation, the content of each well was removed and washed twice with 300 μL of distilled water. After washing, 100 μL of TMB - substrate was added to each well and incubated for 15 min at room temperature in the dark. The reaction was stopped in each well by the addition of 100 μL of stop solution. The amount of testosterone, cortisol and DHEA - S in serum samples was determined by measuring optical density at 450 nm on a multimode microplate reader (BioTek synergy H1M, BioTek Instruments, Winooski, VT, USA). The testosterone, cortisol and DHEA - S concentrations were calculated from the standard calibration curve. Testosterone and cortisol results were expressed as ng / mL while DHEA - S results were expressed as μg/mL.

2.3. Statistical analysis

Statistical analyses were performed with the Statistical Program for Social Sciences (SPSS) for Windows, version 17.0. Descriptive statistics for continuous variables are presented as mean and standard deviation, while number and percentage were provided for categorical variables. The normal distribution of data was tested using the Shapiro–Wilk test. The demographic characteristics of the patient and control groups were compared with the unpaired t test. Pearson’s chi-square test was used to compare the groups in terms of gender. When evaluating any differences between the groups for testosterone, DHEA – S, cortisol and DHEAS/Cortisol, the Mann Whitney U test was used that did not show a normal distribution and Paired t test used that showed a normal distribution. Spearman’s rank correlation test was used to assess the strength of the relationship between the testosterone, DHEA - S and cortisol levels and the severity of the disease. A value of P < 0.05 was considered to be statistically significant. A power analysis showed that in order to detect medium sized effects (alfa=0.05) with 80% power, for each group at least 25 children had to be included.

3. Results

A total of 51 children aged 7–12 years who had not entered puberty were evaluated in this study. The study group consisted of 9 (34.6%) females and 17 (65.4%) males with a mean age of 11.5 years. The control group consisted of 9 (36%) females and 16 (64%) males with a mean age of 11.2 years. There was no significant difference between the 2 groups in terms of mean age and gender (p=0.135, p=0.654, respectively) (Table 1).

The testosterone, DHEA – S and DHEAS/Cortisol levels of the patient group were statistically significantly higher than the control group (p=0.022, p=0.011, p=0.018 respectively). No statistically
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