Journal of Psychiatric Research 47 (2013) 1831–1834

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Oxidative imbalance in child and adolescent patients with obsessive compulsive disorder

Hasan Kandemir [a,*], Mahmut Abuhandan [b], Nurten Aksoy [c], Emin Savik [d], Cemil Kaya [b]

[a] Harran University School of Medicine, Child and Adolescent Psychiatry, Sanliurfa, Turkey
[b] Harran University School of Medicine, Pediatric Department, Sanliurfa, Turkey
[c] Harran University School of Medicine, Biochemistry Department, Sanliurfa, Turkey
[d] Sanliurfa Pediatric State Hospital, Biochemistry, Sanliurfa, Turkey

ARTICLE INFO

Article history:
Received 14 May 2013
Received in revised form
13 August 2013
Accepted 13 August 2013

Keywords:
Child and adolescent obsessive compulsive disorder
Oxidative stress
Total oxidative status
Total antioxidative status
Oxidative stress index

ABSTRACT

Various psychological, social, genetic and biochemical factors are thought to be involved in etiology of obsessive–compulsive disorder (OCD). To the best of our knowledge there are no studies investigating the effects of free radicals in children and adolescents with OCD. This study evaluated total oxidant and antioxidant status, oxidative stress index, and arylesterase and paraoxonase activity in children and adolescents with OCD. The study included 28 patients diagnosed with OCD and 36 healthy children as an age- and sex-matched control group. Their serum total oxidant status (TOS) and total antioxidant status (TAS) were measured and the oxidative stress index (OSI) was calculated. Although serum TOS and OSI values in the OCD patients were significantly higher than those in the control group ($p = 0.008$, $p < 0.001$, respectively), TAS and paraxonase activity were significantly lower ($p < 0.001$ for both). However, no statistically significant difference in arylesterase activity was found ($p > 0.05$). The increase in oxidative status and decrease in antioxidants in patients with OCD demonstrate that oxidative stress may have an important role in the pathophysiology of the disease. It has been suggested that drugs that contain antioxidants should be added to conventional pharmacotherapy during follow-up.

1. Introduction

Obsessive–compulsive disorder (OCD) is classified as an anxiety disorder in DSM-IV-TR (APA, 2000). OCD may be chronic or have a periodic course and significantly affects social and daily functions of patients. Although it was thought to be mostly seen in adulthood, studies in children and adolescents have shown a prevalence of OCD of 1–4% (Douglass et al., 1995; Flament et al., 1998).

Publications reporting onset of OCD before age 6 years and treatment notifications are available (Coskun and Zoroglu, 2009; Garcia et al., 2009). The coexistence of OCD and other psychiatric disorders is high. OCD is mostly associated with depression, tic disorder, and other anxiety disorders. More than 80% of patients diagnosed with OCD report that related symptoms began before the age of 18 years (Pauls et al., 1995).

In terms of symptoms, OCD is heterogenous in its clinical appearance (Leckman et al., 2009). Phenotypic differences suggest that genetic, environmental, psychological, social and biochemical factors are involved in the etiology (Grisham et al., 2011; Iervolino et al., 2011; Hollander and Simeon, 2004). Recent work has emphasized that disturbances in free radicals and the antioxidant defense system have a pathogenic impact on human neural tissues and therefore could be important factors in the development of various brain disorders (Dubinia et al., 2007; Kuloglu et al., 2002; Mahadik and Mukharjee, 1996; Bilici et al., 2001; Akyol et al., 2004; Atmaca et al., 2004; Attari et al., 2002; Tezcan et al., 2003; Ersoy et al., 2008).

Free radicals are produced during normal cell metabolism by many different biochemical reactions such as destruction of bacteria and other microorganisms taken up by phagocytosis, activation of the general immune system, lipid peroxidation, electron transport system, and ischemia. However, free radicals can also be produced by exposure to radiation, tobacco and other environmental pollutants, or excessive exercise, hypoxia, and trauma. An excessive concentration of free radicals in cells may lead to cell damage and death. This damage can be prevented or relieved by the presence of antioxidant molecules (Cheeseman and Slater, 1993; Gutteridge, 1995).

Paraoxonase (PON) and arylesterase (ARE) are enzymes in the esterase group encoded by the same gene, and their active sites are

* Corresponding author.
E-mail address: kandemirhsn@yahoo.com (H. Kandemir).

0022-3956/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jpsychires.2013.08.010

similar. A well-known common feature of PON1 and ARE is the ability to hydrolyze organophosphates and aryl and alkyl halides. PON1 also has an antioxidant function due to the protective activity of LDL against oxidation and the capacity to neutralize other radicals, including hydrogen peroxide. ARE is accepted as the indicator of the actual protein levels and is not affected by changes in PON1 (Li et al., 1993).

Recent studies have investigated the association of OCD and affective disorders with biology. As far as we know, no study has investigated the relationship of childhood OCD with oxidative damage and PON1 activity. We aimed to evaluate whether a relationship exists between OCD and oxidative damage and PON1 activity.

2. Materials and methods

Between August 2011 and August 2012, 28 children (17 boys, 11 girls; [8–17 years]) were brought to the Harran University School of Medicine and Children's Mental Health Outpatient Clinic by their parents and diagnosed with OCD according to DSM-IV criteria. We also recruited 36 healthy children and adolescents (21 boys, 15 girls) aged 8–17 years matched for age and sex who attended a pediatric outpatient clinic for vaccination and other reasons. The Ethics Committee of Harran University School of Medicine approved the study. All of the participants were informed about the study and gave their voluntary signed consent.

All of the participants were evaluated for psychiatric disorders according to DSM-IV criteria using the Schedule for Affective Disorders and Schizophrenia for School Age Children–Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). K-SADS-PL is a semi-structured interview form used to assess psychopathology in children and adolescents. The validity and reliability of the Turkish version of K-SADS-PL were established by Gokler et al. (2004). An interview was conducted with children who met the diagnostic criteria for OCD and their families according to the Children's Yale–Brown Obsessive–Compulsive Scale (CY-BOCS) (Scahill et al., 1997). The reliability and validity of the Turkish version of this scale were established by Yücelen et al. (2006).

Patients with a history of chronic systemic disease such as epilepsy, diabetes mellitus and who had comorbid psychiatric disorders, mental retardation were excluded. Patients who had used psychotropic drugs in the previous six months and who received any antioxidant agents (e.g. vitamin E and C) were also excluded.

Venous blood samples from left forearm vein were collected into 5 ml vacutainer tubes at 8–9 a.m. after overnight fasting once. The blood samples were centrifuged at 3500 rpm for 10 min then the formed elements were discarded with the tube and the serum samples were stored at −80 °C. The biochemical analysis were made after all the blood samples were collected. The Total Antioxidant Status (TAS) and Total Oxidant Status (TOS) paraoxonase and arylesterase activities were measured on the study day colormetrically by auto-analyser (Abbott Aeroset, Abbott Diagnostics, Abbott Park, IL, USA).

TOS of plasma was determined using a novel automated measurement method, developed by Erel (2005). Oxidants present in the sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. The oxidation reaction is enhanced by glycerol molecules, which are abundantly present in the reaction medium. The ferric ion makes a colored complex with xylenol orange in an acidic medium. The color intensity, which can be measured spectrophotometrically, is related to the total amount of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide and the results were expressed in terms of micromolar hydrogen peroxide equivalent per liter (μmol H_2O_2 Eq/L).

AS of plasma was determined using a novel automated measurement method, developed by Erel (2004). In this method, the most potent biological radical, hydroxyl radical, is produced. In the assay, ferrous ion solution, which is present in reagent 1 [o-dianisidine (10 mM), ferrous ion (45 AM) in the Clark and Lubs solution (75 mM, pH 1.8) is mixed with hydrogen peroxide, which is present in reagent 2 [H_2O_2 (7.5 mM) in the Clark and Lubs solution]. The sequentially produced radicals such as brown colored dianisidinyl radical cation, produced by the hydroxyl radical, are also potent radicals. Using this method, the antioxidative effect of the sample against the potent free radical reactions that is initiated by the produced hydroxyl radical, is measured. The assay has excellent precision values of lower than 3%. The results were expressed as mmol Trolox Equiv/L.

The Oxidative Stress Index (OSI) was defined as percentage rate of TAS values to TOS values. Before the calculation the TAS test mmol unit value was translated to micromol units as in the TOS test. The results were expressed as Arbitrary units, calculated by the following formula: OSI (arbitrary unit) = TOS (μmol H_2O_2 equivalent/L)/TAS (mmol Trolox equivalent/L) × 10 (Kosecik et al., 2005).

Paraoxonase and arylesterase activities were measured using paraoxon and phenylacetate substrates. The rate of paraoxonhydrolysis (diethyl-p-nitrophenylphosphate) was measured by monitoring the increase of absorbance at 412 nm at 37 °C. The amount of generated p-nitrophenol was calculated from the molar absorptivity coefficient at pH 8, which was 17,000 M^{-1} cm−1. Paraoxonase activity was expressed as U/L serum. Phenylacetate was used as a substrate to measure the arylesterase activity. Enzymatic activity was calculated from the molar absorptivity coefficient of the produced phenol, 1310 M^{-1} cm−1. One unit of arylesterase activity was defined as 1 μmol phenol generated/min under the above conditions and expressed as U/L serum. Paraoxonase phenotype distribution was determined by a double substrate method that measures the ratio of paraoxonase activity (with 1 M NaCl in the ass assay) to arylesterase activity, using phenylacetate (Eckerson et al., 1983; Haagen and Brock, 1992).

SPSS for Windows version 11.5 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. The distribution of parameters was determined with a one-sample Kolmogorov–Smirnov test, and the distribution was evaluated as normal. The results were expressed as mean ± standard deviation (SD). For comparison of the parameters between patients and controls, independent samples *t*-tests and χ^2 tests were used. Values of $p < 0.05$ were considered statistically significant.

3. Results

The mean age of the 28 OCD patients was 12.32 ± 3.09 (8–17) years compared with 12.55 ± 2.57 (8–17) years in the control group. There was no significant difference in age and sex between the two groups ($p > 0.05$) (Table 1). In the OCD group, the mean CY-BOCS scores for obsession and compulsion were 10.67 ± 1.90 and 10.17 ± 2.27, respectively. The mean TOS and OSI values in the OCD group were significantly higher ($t = 2.762$, $p = 0.008$, $t = 5.002$, $p < 0.001$, respectively) than those in the control group. The mean values of TAS and PON activity were significantly lower ($t = -6.096$, $p < 0.001$, $t = -4.534$, $p < 0.001$) in the OCD group compared with the control group. There were no significant difference in mean ARE activities ($t = -1.801$, $p = 0.076$) (Table 2).

Table 1
Sociodemographic and clinical characteristic of patients.

	OCD ($n = 28$)	Control ($n = 36$)	Comparison
Sex: male/female (n)	17/11	21/15	$P = 0.847$ ($x^2 = 0.037$)
Age:mean ± SD (year)	12.32 ± 3.09	12.55 ± 2.57	$P = 0.742$ ($t = -0.330$)
Age range (year)	8–17	8–17	