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An evaluation of serum paraoxonase together with arylesterase activities and oxidative stress in children with intractable epilepsy: A cross-sectional study

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Summary Epilepsy is the most common chronic neurological illness in childhood and adolescence. The aim of this study was to investigate paraoxonase and arylesterase activities along with oxidative status parameters in children with intractable epilepsy. The study comprised 42 subjects with intractable epilepsy and a control group of 35 healthy subjects. Serum paraoxonase and arylesterase activities, and lipid hydroperoxide levels were determined. All paraoxonase and arylesterase activities were significantly lower in the intractable epilepsy subjects than in the controls ($P < 0.001$), whereas lipid hydroperoxide levels were significantly higher ($P < 0.05$).

In conclusion, paraoxonase and arylesterase activities were decreased and the lipid hydroperoxide level was increased in patients with intractable epilepsy. These results showed that intractable epilepsy subjects may be more prone to the development of atherosclerosis.

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Introduction

Epilepsy is the most common chronic neurological illness in childhood and adolescence. Children with epilepsy may respond well to pharmacological therapy, although around 10% to 23% continue to have refractory seizures despite multiple anticonvulsant medications (Arts et al., 2004; Berg and Kelly, 2006).

These children typically have significant morbidity, deteriorated quality of life, and multiple side effects of the anticonvulsant medication related to the metabolic, hematological, endocrinological, and vascular systems (Greenwood, 2000; Kayani and Sirsi, 2012; Calik et al., 2014). In some experimental and clinical trials, epilepsy has been shown to be associated with increased oxidative stress and atherosclerosis risk (Hamed et al., 2007; Jakubus et al., 2009). In recent years, increasing evidence has suggested that the oxidative modification of low-density lipoprotein cholesterol (LDL-C) is an important factor responsible for atherosclerosis related to vascular complications in epileptic children who are treated with antiepileptic drugs (Varoglu et al., 2010; Yildiz et al., 2010).

Serum paraoxonase-1 (PON1), an antioxidant enzyme with paraoxonase, arylesterase, and dyazoxonase activities, is a 45-kDa glycoprotein that is expressed in the liver and has been found to be associated with high-density lipoprotein (HDL) particles in the blood (Durrington et al., 2001). Previous reports have demonstrated that PON1 deficiency is related to increased susceptibility to LDL-C oxidation and the development of atherosclerosis (Witztum, 1994; Watson et al., 1995).

The objective of this study was to investigate serum paraoxonase and arylesterase activities, and oxidative status in patients with intractable epilepsy.

Methods

Subjects

This cross-sectional study was conducted at the Department of Pediatrics, Neurology, Pharmacology, and Clinical Biochemistry of Harran University School of Medicine between June 2011 and December 2013. The study groups consisted of 42 patients with intractable epilepsy and a control group of 35 healthy individuals. All patients were diagnosed as having intractable epilepsy, based on the findings of clinical seizure semiology and interictal and ictal electroencephalography (EEG) obtained during video-EEG monitoring as well as on the results of high-resolution magnetic resonance imaging (MRI). Intractable epilepsy is a traditionally defined as a failure to respond to at least 2 anticonvulsant drugs tried at reasonable doses for several weeks (Berg et al., 2006). Informed consent for participation in this study was obtained from all the legal guardians of the children. The study protocol conforms to the principles of the Helsinki Declaration and was approved by the Medical Ethics Committee of Harran University.

Exclusion criteria

Exclusion criteria of the epileptic patients included usage of supplementary vitamins, the presence of hyperlipidemia, acute-chronic liver diseases or renal dysfunction. The control group consisted of 35 healthy subjects (without a history of chronic or recurrent disease). The subjects in the control group were asymptomatic with an unremarkable medical history and a normal physical examination. None of the control subjects were receiving treatment of antibiotics or antioxidant vitamin supplements including vitamins C and E.

Blood sample collection

After 12 h of fasting, blood samples were drawn from the cubital vein. The serum was then separated from the cells by centrifugation at 3000 rpm for 10 min, and the blood samples were stored at −80 °C until analysis.

Biochemical analysis

Paraoxonase and arylesterase activities were measured using paraoxon and phenyl acetate substrates, respectively (Eckerson et al., 1983). Paraoxonase activity is expressed as U/L of serum. One unit of arylesterase activity is defined as mmol of phenol generated/min and is expressed as kU/L of serum (Haagen and Brock, 1992). The phenotype distribution of PON1 was determined in the presence of 1 mol/L NaCl (salt-stimulated paraoxonase). The ratio of the salt-stimulated paraoxonase activity to the arylesterase activity was used to assign individual subjects to one of the three phenotypes (Eckerson et al., 1983). Serum lipid hydroperoxide (LOOH) levels were measured with the ferrous ion oxidation–xylenol orange assay as previously described (Nourooz-Zadeh, 1999). The levels of triglycerides (TG), total cholesterol (TC), HDL-C, LDL-C, glucose, urea, creatinine, sodium and other serum electrolyte levels were determined using commercially available assay kits (Abbott®) with an autoanalyzer (Aeroset®, Abbott®).

Statistical analysis

All statistical analyses were made using the Statistical Package for Social Sciences (SPSS 11.5, SPSS Inc., Chicago, IL). All data were expressed as mean ± standard deviation (SD). Qualitative variables were assessed with the *Chi-square test* and the comparisons of parameters were made using *Student's t test*. One-way ANOVA with the Tukey-HSD multiple comparison tests were used with normally distributed continuous data. A value of $P < 0.05$ was accepted as statistically significant.

Results

The demographic and clinical data of the study population are shown in Table 1. The study comprised a total of 42 patients; 27 males and 15 females. The control group was formed of 35 healthy individuals; 22 males and 13 females. The mean age was 8.85 ± 0.49 years in the patient group and 8.65 ± 0.48 years in the control group. No statistically