Serum Homocysteine Level in Chronic Epileptic Patients

Thesis

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بسم الله الرحمن الرحيم

﴿وما يستوي الأعمى والبصير ۞ ولا الظلمات ولا النور﴾

(فاطر: ١٩، ٢٠)

﴿الله ولي الذين آمنوا يخرجهم من الظلمات إلى النور﴾

(البقرة: ٢٥٧)

﴿وقل رب زدني علماً﴾

(طه: ١١٤)

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A, but also to the risks associated with hyperhomocysteinemia.

Abbreviations

AAN	American Academy of Neurology
AD	Alzheimer's disease
AEDs	Anti epileptic drugs
A_β	beta-Amyloid
CBZ	Carbamazepine
CK	Creatinine Kinase
CSF	Cerebrospinal fluid
CSF-SAM	Cerebrospinal fluid-S-adenosyl methionine
CSF-tHcy	Cerebrospinal fluid-total homocysteine
DALY	Disability Adjusted Life Years
DTT	Dithiothreitol
EDTA	Ethylene-Diamine-Tetra-Acetate
EEG	Electroencephalogram
ESR	Eryrthocyte Sedimentation Rate
GGT	Gamma-Glutamyl Transferase

GTC	Generalized Tonic-Clonic
ILAE	International League Against Epilepsy
MBP	Myelin Basic Protein
MRI	Magnetic Resonance Imaging
MS	Multiple sclerosis
MTHFR	Methylene tetrahydrofolate reductase
NIDDM	Non-Insulin Dependant Diabetes Mellitus
NMDA	N-Methyl D-Aspartate
PD	Parkinson's Disease
PHT	Phenytoin
SAH	S-Adenosyl Homocysteine
SAM	S-Adenosyl Methionine
SD	Standard Deviation
SGPT	Serum Glutamic Pyruvic Transaminase
tHcy	Total homocysteine

ABSTRACT

Epilepsy is a common chronic neurological disorder, which warrants prolonged, and often lifetime, treatment with AEDs. It is commonly associated with hyperhomocysteinemia, a known risk factor for vascular diseases, and which is also related to several other neurological diseases. Homocysteine is an experimental epileptogenic, and nearly 20% of patients with homocystinuria suffer from fits. Hyperhomocysteinemia in epileptic patients is probably related to administration of AEDs.

The aim of our present study is to assess the relationship between treatment with classic anti-epileptic drugs and serum homocysteine level, and to outline the impact of this relationship on patient control and management.

Accordingly we studied 40 patients with the diagnosis of idiopathic epilepsy, who were classified into 3 subgroups; group A which included 10 epileptic patients with newly diagnosed epilepsy or patients on no treatment for at least 6 weeks as a control group, group B which included 15 epileptic patients with controlled seizures and group C which included 15 epileptic patients with uncontrolled seizures. Subjects recruited in the study were subjected to the following: Thorough history taking and neurological examination. Routine laboratory investigations. AEDs serum level determination for patients receiving AEDs. Homocysteine serum level determination. Seizure severity scale estimation. Electroencephalography. Further research: Long term effects of AEDs with or without folate supplementation with respect to seizure control, cardiovascular disease, cognitive performance and mood. Effect of newer AEDs on homocysteine to evaluate their relative safety in cases of feared hyperhomocysteinemia. A prospective study of patients initiating AEDs monotherapy can provide information from intra-patient measurement of homocysteine which can outline the individual AEDs effect on homocysteine.

Keywords:

Serum homocysteine
Chronic epileptic
Hyperhomocysteinemia

Introduction

Introduction:

Elevated concentration of total homocysteine (Hcy) in plasma (> 12 micromol/l) is a risk factor for several diseases of the central nervous system. Epidemiological studies have shown a dose-dependent relationship between concentrations of homocysteine and the risk for neurodegenerative diseases. Homocysteine is a marker for B-vitamin deficiency (folate, B12 and B6). Hyperhomocysteinemia causes hypomethylation which is an important mechanism that links homocysteine to dementia. ***(Herrmann et al., 2007)***

The position of epilepsy is more sophisticated, since major anti-epileptic drugs have direct and powerful effects on homocysteine levels, and so the need for follow up of homocysteine levels and the suspicion of its causation in dyscontrol of patients is more justified. ***(Apeland et al., 2001)***

Homocysteine is regarded as a neuroexcitatory substance, which is therefore used as an epileptogenic agent in experimental epileptology. Experiments "in vivo" as well as "in vitro" revealed its relation to N-Methyl D-Aspartate (NMDA) glutamate receptors, and its potential neurotoxicity. ***(Kolínová et al., 2006)***

AEDs increase serum homocysteine by lowering blood folate levels. Multiple studies have therefore concluded that folic acid supplementation is mandatory in epileptic patients on long term anti-epileptic drugs therapy, with greater stress on children. ***(Elliott et al., 2007)***

Hyperhomocysteinemia is present in 15.5% of children receiving long-term AED treatment. Multidrug treatment and long duration of therapy enhance the risk for hyperhomocysteinemia. ***(Huemer et al., 2005)***

From the clinical aspect, hyperhomocysteinemia, mostly as a marker of the risk factor in the vascular damage, was often studied in patients treated with antiepileptic drugs. However, the neuroexcitatory influence of mild hyperhomocysteinemia was rarely discussed. ***(Kolínová et al., 2006)***

Aim of the work:

The aim of this study is to assess:

- The relation between treatment with classic anti-epileptic drugs and serum homocysteine level.
- Its impact on patient control and management.