Effects of long-term antiepileptic drug monotherapy on the serum levels of Homocysteine and Folic Acid: a retrospective chart review in patients with focal seizures

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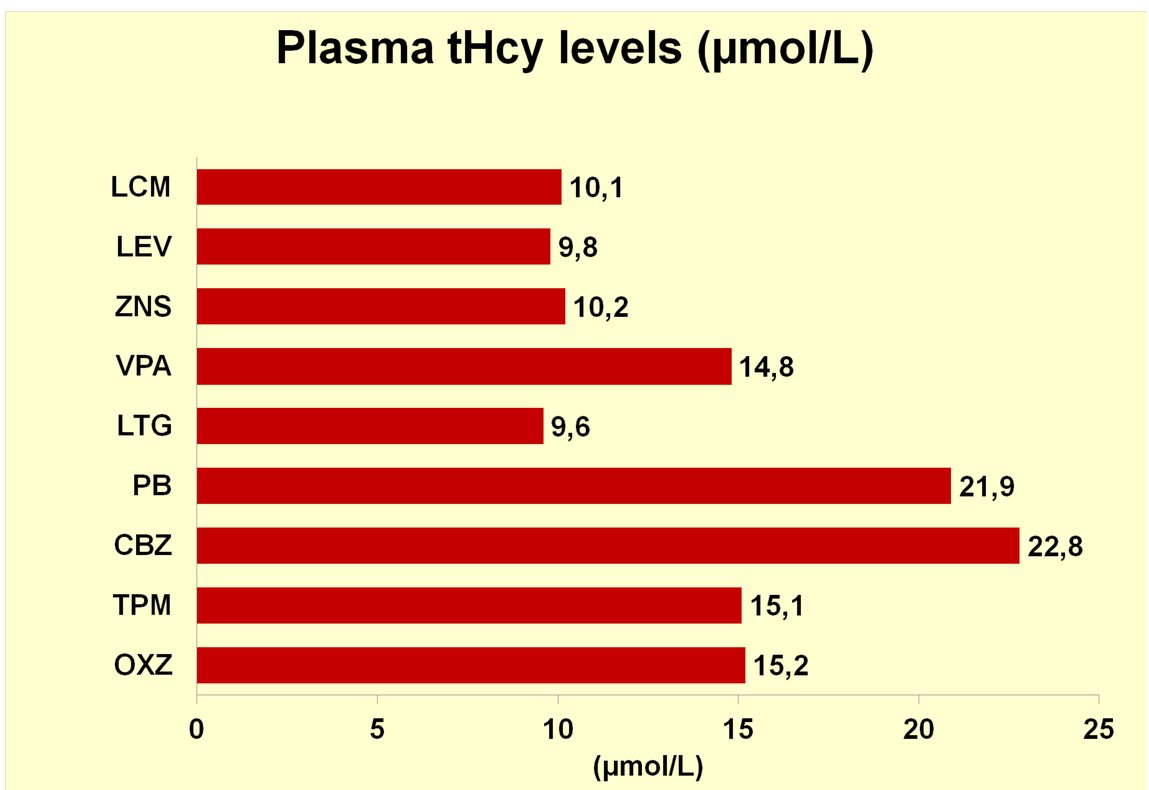
Background: Homocysteine (Hcy) is a thyol amino acid resulting from de-methylation of ethionine, an essential amino acid derived from dietary proteins. Several drugs may interfere with metabolic pathways of Hcy, leading to an alteration of plasma Hcy levels. The aim of the study was to evaluate the impact of antiepileptic drugs (AEDs) on plasma tHcy levels in subjects with epilepsy.

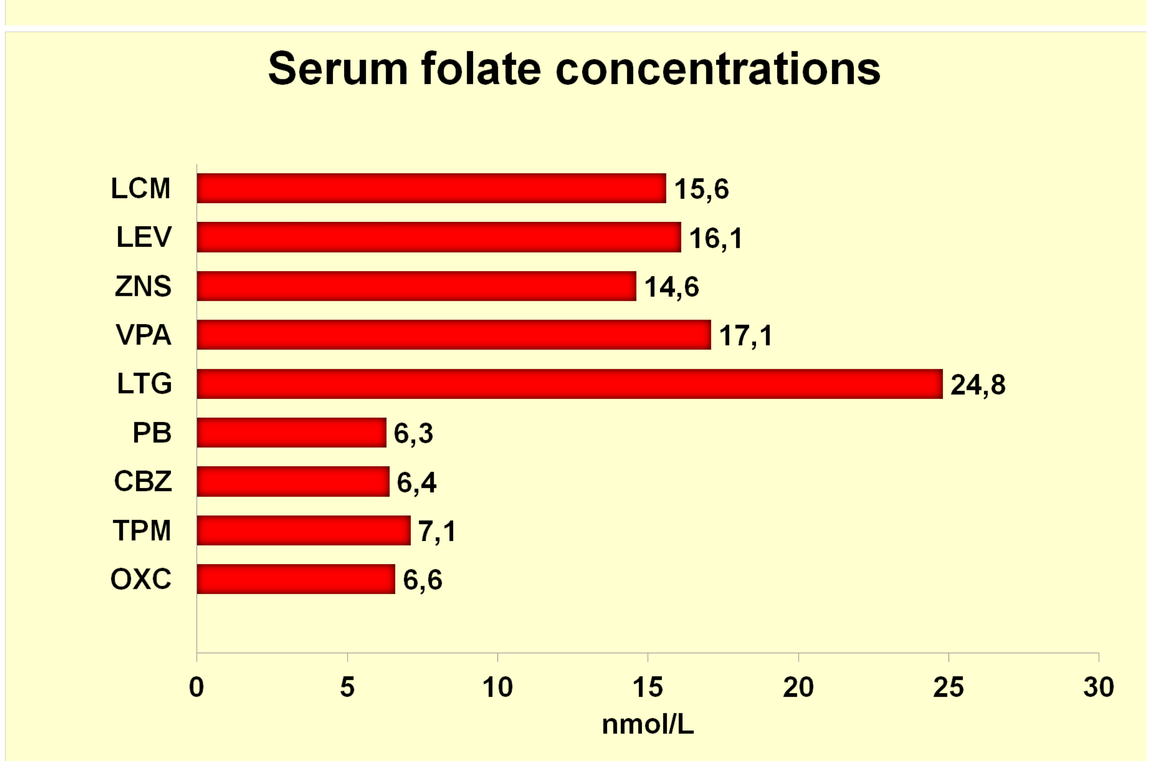
Methods: we retrospectively analysed data of consecutive patients suffering from focal seizures receiving stable, individually adjusted AED monotherapy, with no other possible cause of hyper-tHcy, referred to our Centre from 2012 to 2016. Informations on socio-demographic characteristics, neurologic examination, etiology, seizure type, EEG, neuroimaging, treatment and clinical course of epilepsy were obtained by review of their medical records.Concentrations of tHcy and folate were measured in plasma using standard methods.

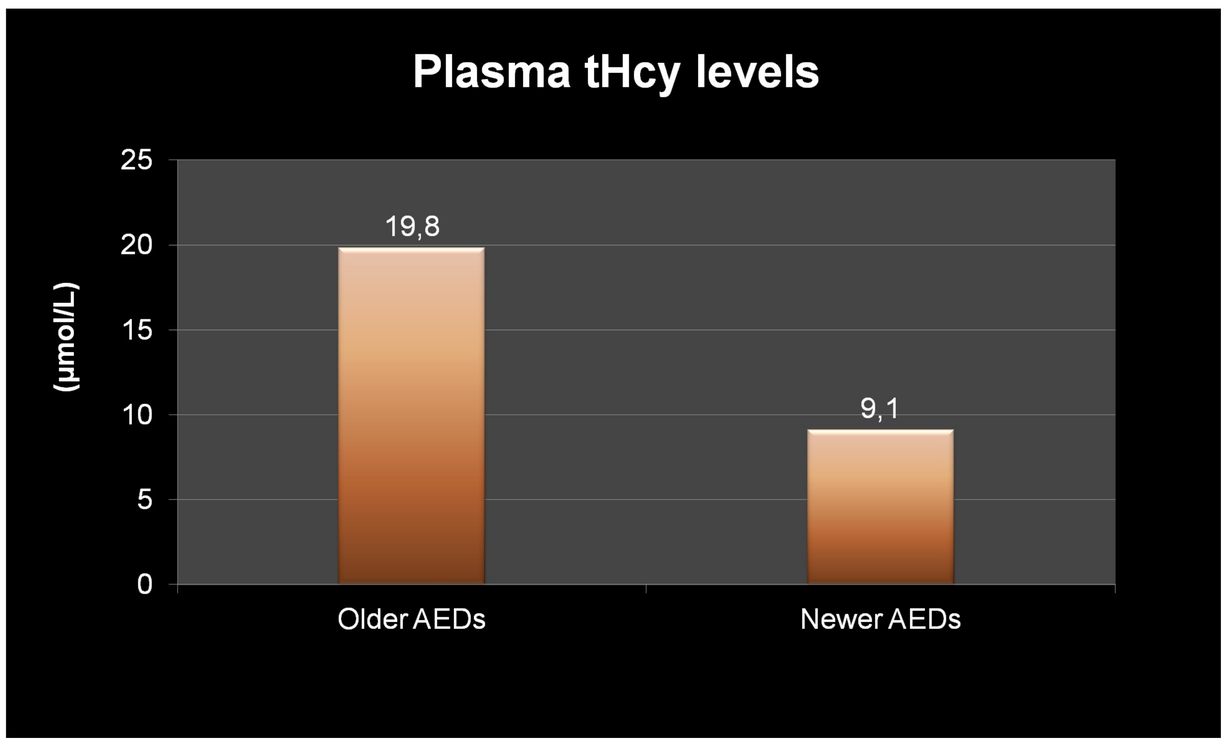
Results: 135 (82 on newer, 53 on older AEDs) of 242 patients were eligible for the study. 82 (60.7%) were female and 53 (39.3%) male. Mean age was 62.9±8.26 years. Mean duration of AEDs therapy was 12±1.4 years. Plasma tHcy levels were significantly higher (19.8 ± 2.8 vs 9.1 ±1.2 µmol/L; physiological range: 5-15 µmol/L) in patients treated with older AEDs as compared to newer ($p<0.05$). The serum folate concentration (normal range 3-17 ng/ml) was lower in patients treated with older AEDs (9.9 ±1.1 ng/ml) compared to newer AEDs (15.6 ±0.8 ng/ml) ($p<0.05$). Patients treated with oxcarbazepine, topiramate, carbamazepine and phenobarbital exhibited mean plasma tHcy levels above the physiological range (mean values 15.2, 15.1, 22.8 and 21.9 µmol/L respectively). Conversely, normal tHcy concentrations were observed in the lamotrigine, valproic acid, zonisamide, levetiracetam and lacosamide groups (9.6, 14.8, 10.2, 9.8 and 10.1 µmol/L respectively). The serum folate concentration was lower in patients treated with phenobarbital (6.3), carbamazepine (6.4) and oxcarbazepine (6.6); conversely was higher in lamotrigine (24.8), valproic acid (17.1). Finally normal serum folate concentrations was observed in topiramate (7.1), levetiracetam (16.1), zonisamide (14.6) and lacosamide (15.6) groups.

Discussion: These results, according to previous literature data, support that epileptic patients on prolonged AED treatment are more prone than the general population to develop hyper-tHcy and low folate levels. The consequences of this metabolic disturbance may be of clinical importance (risk factor for systemic vascular events including stroke).

Conclusions: Our results confirm that common anti-epileptic drugs, and especially older, has disadvantageous effects on homocysteine status.







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