



Monitoring of biochemical parameters and coagulation tests in children with epilepsy treated with levetiracetam monotherapy

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Dear Editor:

Levetiracetam (LEV)-associated hyponatremia, hypokalemia, and hypomagnesemia and increase in serum albumin have been described in adult patients [2, 5, 7]. Furthermore, in well-controlled studies of add-on levetiracetam therapy for epilepsy, the incidence of coagulation and bleeding disorders was slightly higher in the LEV group than that in the placebo group (2.8% vs 1.7%) [3]. Whether young age may have a protective role in the prevention of the above LEV-associated disorders has not been studied. The objective of this study was to prospectively investigate the long-term effect of LEV monotherapy in all the above parameters in children with epilepsy.

The study population consisted of 28 ambulatory children (16 females, mean age 6.5 ± 4.4 years, range 1–15 years) that were treated for new-onset epilepsy with LEV monotherapy. Twenty-three children suffered from focal epilepsy and 5 from generalized epilepsy. An informed parental consent was obtained and the study was approved by the Institutional Review Board of “Attikon” University Hospital.

Serum sodium, potassium, magnesium, albumin, globulin, international normalized ratio, prothrombin time, and activated partial thromboplastin time were measured before and at 12 months of LEV treatment. Measurements were

performed, using a fasting morning (between 8:00 and 10:00 a.m.) sample, at the Department of Clinical Biochemistry of “Attikon” University Hospital according to the usual standard methods.

Data were analyzed using the Statistical Package for Social Sciences (SPSS version 23.0, IBM Corp., Armonk, NY, USA). The Wilcoxon signed-rank test was used to assess the statistical significance of changes in the parameters between baseline and after treatment with LEV. Correlation between parameters and LEV dose was assessed by using Spearman’s correlation coefficient. A p value < 0.05 was considered statistically significant.

There were no significant alterations in serum sodium, potassium, magnesium, albumin, globulin, international normalized ratio, prothrombin time, and activated partial thromboplastin time evaluated during the study (Table 1). All parameters evaluated were within normal limits. The mean value of drug dose (mg/kg) was 21.2 ± 9.9 at 12 months of treatment.

Our study showed no significant effect of long-term LEV monotherapy on sodium, potassium, magnesium, albumin, globulin, international normalized ratio, prothrombin time, and activated partial thromboplastin time in children with epilepsy.

Hyponatremia or hypokalemia and hypomagnesemia have been reported in adults during LEV treatment, attributed to inappropriate antidiuretic hormone secretion (SIADH) [2, 6, 7]. Authors have suggested advanced age or female gender as possible predisposing factors. Young age of our study group may have played a protective role in the prevention of the above LEV-associated disorders.

Significant elevation of the serum albumin has been reported during treatment with new antiepileptic drugs, including LEV. This elevation has been inversely associated with the plasma cortisol levels [5]. The present study showed no effect of LEV monotherapy on serum albumin

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Table 1 Serum biochemical parameters and coagulation tests (mean \pm SD) in 28 epileptic children before and at 12 months of levetiracetam monotherapy

Parameters	Pretreatment	12 months	<i>p</i>
Sodium (mmol/L)	140.31 \pm 2.65	140.83 \pm 2.05	0.416
Potassium (mmol/L)	4.58 \pm 0.33	4.45 \pm 0.28	0.279
Magnesium (mg/dL)	2.17 \pm 0.15	2.12 \pm 0.16	0.158
Albumin (g/dL)	4.64 \pm 0.29	4.65 \pm 0.24	0.281
Globulin (g/dL)	2.22 \pm 0.41	2.45 \pm 0.51	0.348
International normalized ratio (INR)	1.02 \pm 0.06	1.04 \pm 0.07	0.279
Prothrombin time (PT, s)	12.07 \pm 0.72	12.15 \pm 0.87	0.469
Activated partial thromboplastin time (aPTT, s)	30.76 \pm 4.89	32.69 \pm 4.09	0.394

P indicates statistical differences between pre-treatment and post-treatment levels

or globulin levels; however, further prospective studies including larger number of patients are needed to definitely clarify this issue.

LEV does not appear to cause clinically significant effect on coagulation parameters in healthy male volunteers [3]. However, cases of bleeding complications in patients receiving levetiracetam at the time of epilepsy surgery or following addition of levetiracetam to long-term carbamazepine therapy have been described [1, 4]. Our study showed no significant effect of long-term LEV monotherapy on international normalized ratio, prothrombin time, and activated partial thromboplastin time.

The present study has limitations: the number of children studied was small and multiple measurements were not done with LEV monotherapy. The strengths of the present report are the homogeneity of the study group and the prospective design up to 1 year.

In conclusion, long-term LEV monotherapy does not cause significant disturbances in serum electrolytes such as sodium, potassium and magnesium, albumin, globulin, and coagulation tests in children with epilepsy and, thus, long-term monitoring of these parameters may not be needed.

Compliance with ethical standards An informed parental consent was obtained and the study was approved by the Institutional Review Board of “Attikon” University Hospital.

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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