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SHORT COMMUNICATION

Short-term effect of levetiracetam monotherapy on haematological parameters in children with epilepsy: A prospective study



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KEYWORDS

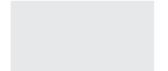
Haematological parameters; Levetiracetam; Lymphocytes; Epilepsy; Children Summary Studies evaluating the effect of levetiracetam (LEV) on haematological parameters in patients with epilepsy are very limited. Clinical trials have also reported an unexplained increased incidence of pharyngitis and rhinitis in LEV-treated patients. The objective of this study was to evaluate prospectively the changes in haematological parameters in children treated with LEV monotherapy. White blood cell, neutrophils, lymphocytes, monocytes, haemoglobin, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin concentration and platelets were measured in 22 children (13 females, mean age 6.70 ± 4.23 years) with epilepsy, before and after 2 and 6 months of LEV monotherapy. Lymphocyte count was significantly decreased at 6 months (p=0.019) of treatment and this effect was not dose dependent. One child (4.5%) at 2 months and four children (18%) at 6 months of treatment had lymphocyte count below 10th percentile for age. There were no significant alterations in the other parameters evaluated during the study. LEV monotherapy may significantly decrease lymphocyte count at six months of treatment in children with epilepsy. Further

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prospective studies are needed to investigate the effect of LEV on haematological parameters and the possible association with the higher incidence of infections reported in children receiving LFV

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Introduction

Levetiracetam (LEV) is a relative new, broad-spectrum antiepileptic drug whose efficacy and tolerability in epilepsy treatment is well recognized (Verrotti et al., 2010; Vigevano, 2005). Studies evaluating the effect of LEV on haematological parameters in patients with epilepsy are very limited. Furthermore, several clinical trials have reported an unexplained increased incidence of infections such as pharyngitis and rhinitis in patients treated with LEV (Ben-Menachem and Falter, 2000; Betts et al., 2000; Cereghino et al., 2000; French et al., 2001; Harden, 2001; Piña-Garza et al., 2010; Shorvon et al., 2000).

The objective of this study was to prospectively investigate changes in haematological parameters in children treated with LEV monotherapy. White blood cell (WBC), neutrophils (NEUT), lymphocytes (LYMPH), monocytes (MONO), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and platelets were measured in 22 children with epilepsy, before and at 2 and 6 months of LEV monotherapy. This is the first pediatric study evaluating the effect of LEV on haematological parameters in a prospective manner.

Material and methods

The study population consisted of 22 children (13 females, 9) males, mean age 6.70 ± 4.23 years, range 2-15 years) that were treated for new-onset epilepsy with LEV monotherapy. Sixteen children suffered from a localization related epilepsy and 6 from a generalized epilepsy. LEV was prescribed at a dose of 10-45 mg/kg/day. Apart from epilepsy, all patients were judged to be in good health with nutritionally adequate diets, normal liver and renal function and absence of any other medication. An informed parental consent was obtained and the study was approved by the Institutional Review Board of "Attikon" University Hospital. A fasting blood sample was obtained in the morning, between 8.00 and 10.00 a.m. into EDTA-containing 5 ml sterile tubes. All the blood samples were obtained during a period at least 4 weeks far from infection. All haematological parameters were analyzed using the Sysmex XE-2100 automated haematology analyzer (Roche Diagnostics), according to the manufacturers' instructions.

Data were expressed as mean \pm SD values and were analyzed using the statistical package for social sciences (SPSS 13.0, Chicago IL). The Wilcoxon Signed Ranks Test was used to assess the significance of changes of haematological parameters at base and after treatment with LEV. Correlations between all parameters were assessed by using the Spearman's correlation coefficient. A p value <0.05 was considered as statistically significant.

Results

During the 6 month period 12 patients had an absolute response to the treatment with 10 of them requiring a minimal dose titration (up to 18 mg/kg) and 2 of them a significant dose titration up to 35 mg/kg. The rest 10 patients had a partial control of epilepsy despite a dose titration up to 45 mg/kg and after 6 months LEV was substituted or another antiepileptic was added to the regiment.

Lymphocyte count was significantly decreased at 6 months (p = 0.019) of LEV treatment (Table 1). The absolute peripheral blood lymphocyte count (ALC) in the study group before and during LEV monotherapy is shown in Table 2. All children had ALC above 10th percentile for age before initiation of LEV treatment, while one child (4.5%) at 2 months and four children (18%) at 6 months of treatment had ALC below 10th percentile for age according to normative data in healthy children (Shearer et al., 2003). There were no significant alterations in the other parameters evaluated during the study (Table 1).

Mean value of drug dosage (mg/kg) was 17.05 ± 3.31 at 2 months and 23.50 ± 10.90 at 6 months of treatment. No association was found between lymphocyte count and LEV dosage (mg/kg) at 6 months of treatment.

Discussion

Our study showed a significant effect of LEV monotherapy on lymphocyte count in children with epilepsy. The absolute peripheral blood lymphocyte number was significantly decreased at 6 months of LEV treatment. No significant alterations in the other haematological parameters were found at 2 and at 6 months of LEV treatment.

So far, the effect of LEV monotherapy on haematological parameters has not been investigated in large cross-sectional or prospective studies. In clinical trials, small but statistically significant decreases between LEV and placebo groups were seen for HGB and HCT (French et al., 2001). A recent cross-sectional study (Bachmann et al., 2011), reported significantly lower platelet counts in 52 adult patients treated with LEV for at least 6 months compared with controls, with no difference in HGB or WBC. Our study showed no significant effect of LEV monotherapy on WBC, NEUT, MONO, HGB, HCT, MCV, MCH, MCHC and platelet counts in children with epilepsy treated for a period up to 6 months. However, this is the first pediatric study evaluating the effect of LEV on haematological parameters in a prospective manner and a longer term follow-up is needed for more accurate conclusions.

Interestingly, the present study demonstrated a significant decrease in peripheral blood lymphocyte count at 6 months of LEV treatment, compared with the pre-treatment level. Furthermore, one child (4.5%) at 2 months and four

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