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The Hematology Profiles of Adults Affiliated with Epilepsy after Receiving Valproic Acid Therapy

Christiyan Naydenov*, Ivan Mindov

Department of Neurology and Psychiatry, Trakia University, Stara Zagora City, Bulgaria

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***Correspondence:** Christiyan Naydenov, Department of Neurology and Psychiatry, Trakia University, Stara Zagora City, Bulgaria.
E-mail: kristiyan.naydenov@trakia-uni.bg
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Abstract

AIM: Epilepsy is a socially significant neurological disease spread all over the world. Valproic acid (VPA) is one of the most used antiepileptic drug (AED) for treatment which has some side effects on hematology field. A nowadays update to the adult safety information is needed. The current aim is to conduct a cross-sectional study and to describe the hematology profile of adults with epilepsy treated by VPA.

MATERIALS AND METHODS: Data collection was done retrospectively and includes characteristics of the subjects such as age, gender, electroencephalography (EEG) finding, duration of VPA treatment, type of treatment, and hematology profile. We report 50 subjects treated by VPA at least 1 year.

RESULTS: The mean age is 46, 4 years, 50% male and 50% female. About 92% were generalized tonic-clonic seizure. Seven percent were partial complex epilepsy. Twenty-four EEG results were abnormal (48%). We found 4 cases (7%) of thrombocytopenia at therapeutic dose and 8 cases (16%) of mild anemia.

DISCUSSION: Gender differences were eliminated by having the same number of participants of each gender. The EEG findings were almost equally normal and abnormal. Reported drug reactions due to VPA were thrombocytopenia and anemia. Thrombocytopenia requires discontinuation of VPA.

Introduction

Epilepsy is a chronic paroxysmal disease characterized by a sudden quantitative and/or qualitative disturbance of consciousness, sensibility, motor activity, autonomic functions, and psyche. Seizures occur as a result of hypersynchronous bioelectrical discharges of neurons in the cerebral cortex. Depending on the localization of these changes and their distribution, individual clinical forms differ. Epilepsy is a socially significant neurological disease spread all over the world. Electroencephalography (EEG) is a way of graphically recording the electrical potentials of the brain, supporting the diagnose. It is performed with a special device - an electroencephalograph [1]. We determined and grouped the qualitative changes in the EEG, considering as abnormal only the focal or generalized epileptic graph elements such as sharps, spikes, and sharp-and-slow complexes or focuses of theta and delta rhythms. All other changes in the type of oscillations, phase amplitude coupling, phase-to-phase coupling, amplitude-to-amplitude coupling, cross-frequency phase coupling, and inter-hemisphere bands are defined as general non-specific changes. The normal EEG results are according to the reference values of the software analysis, reported by us earlier [1]. Many side effects of valproic acid (VPA) are related and occur according to the dosage [2]. VPA is one of the most used antiepileptic drugs (AEDs) for treatment as first line which has some known side effects on hematology field [3], [4]. A nowadays update to the adult safety information is needed as same as the children are already reported [5]. The aim of current study is to describe the hematology profile during treatment with VPA.

Materials and Methods

This is a cross-sectional study describing the hematology profile of epilepsy patients during treatment with VPA. Data collection was done retrospectively. The inclusion criteria are adults with epilepsy and use VPA as the AED at least 1 year. We excluded samples of patients with known other reasons for deviations of their hematological status. This study protocol was reviewed and approved by Local Ethics Committee of Trakia University - Stara Zagora city, Bulgaria. Ethical Approval Number: 14 from 02 October 2020.

All participants voluntarily signed an informed consent form before inclusion in the study. The current study includes characteristics of the subjects such as age, gender, EEG finding, duration of VPA treatment, type of treatment, and hematology profile. We report 50 subjects. The mean age is 46, 4 years, 50% male, and 50% female. About 92% were generalized tonic-clonic seizure. Seven percent were partial complex epilepsy. Twenty-four EEG results were abnormal (48%). We determined and grouped the qualitative changes in the EEG, considering as abnormal only the focal or generalized epileptic graph elements such as sharps, spikes, and sharp-and-slow complexes or focuses of theta and delta rhythms. All other changes in the type of oscillations, phase amplitude coupling, phase-to-phase coupling, amplitude-to-amplitude coupling, cross-frequency phase coupling, and inter-hemisphere bands are defined as general non-specific changes. The patient's laboratory results were recorded and statistically analyzed from electronic database. Our local laboratory lower range for hemoglobin is <120 g/L and for the platelets is <144 $\times 10^9$/L. Materials and methods are according to developed ones by Putri *et al*., 2019 [5].

Results

We report 50 subjects. The mean age is 46, 4 years (from 18 to 64), 50% (n = 25) male, and 50% (n = 25) female. About 92% (n = 46) were generalized tonic-clonic seizure. Seven percent (n = 4) were partial complex epilepsy. Twenty-four EEG results were abnormal (48%) and 26 were normal (52%). More than half of adults (n = 32) with epilepsy are satisfying controlled with uses of VPA as a monotherapy and the others were treated by combination (n = 14) or polytherapy (n = 4). All of the patients were treated at least 1 year with VPA. Regarding to the hematology profile, we found 4 cases (7%) of thrombocytopenia (all men) at therapeutic dose level (plasma concentration of VPA between 50 and 100 ug/mL) and 8 cases (16%) of mild anemia.

Discussion

This cross-sectional study has described the hematology profile of adults with epilepsy treated by VPA. Gender differences were eliminated by having the same number of participants of each gender. The EEG findings were almost equally normal and abnormal. As the first-line therapy, VPA is the most used AED in our practice according to the recommendations. The cases with combination were mostly with carbamazepine. Reported drug reactions due to VPA were thrombocytopenia and anemia. We also found 6 subjects with slightly increased AST but 5 subjects with doubled levels of their AST; 8 subjects with slightly increased ALT and 7 with doubled levels of their ALT. Many AEDs are associated with deviations from the hematological status, mostly thrombocytopenia, and anemia [6]. Thrombocytopenia requires discontinuation of VPA. Our results are supported also from children's data reported by Putri *et al*., 2019 [5].

Conclusion

VPA is not the most suitable for symptomatic epilepsy in adults with comorbidity because of the safety profile. It leads to deviations from the hematological status, mostly thrombocytopenia and anemia and also is not enough to control the seizure's frequency. It is recommended to do more precise choice for the first monotherapy and to follow-up possible side effects to eventual discontinuation of VPA.

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Scientific Responsibility Statement

The author declares that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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