

Thrombocytopenia in Epileptic Patients on Valproic Acid

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ABSTRACT

Aim: To see the frequency of thrombocytopenia in epileptic patients, receiving valproic acid

Methods: This descriptive study was conducted at WAPDA Teaching Hospital Complex, Lahore. All the epileptic patients on valproic acid were included in the study, excluding patients already having thrombocytopenia or some disease or treatment with the potential of causing thrombocytopenia. Platelet count below $150 \times 10^9/L$ was taken as thrombocytopenia. *Hospital information system* was used to note the demographic information and relevant data on the disease, laboratory investigations and treatment of the patients.

Results: Out of total 122 patients 63(51.64%) were male and 59(48.36%) were female. Mean age was 49.79 ± 19.97 years (range 10–79 years). Out of 122 patients, 23(18.85%) developed thrombocytopenia. Four thrombocytopenic patients were below 20 years, 5 were between 21 and 60 years and 14 were above 60 years of age. Average dose of valproic acid in patients with thrombocytopenia was 1315 ± 478 mg/ day as compared to 868 ± 415 mg/day in patients without thrombocytopenia.

Conclusion: Thrombocytopenia is a common adverse effect of valproic acid. Its chances are increased in old age and increased dosage.

Keywords: Valproic acid, Thrombocytopenia, Platelets, Epilepsy

INTRODUCTION

Epilepsy is a common disorder. It remains undertreated because of false beliefs and stigma associated with it. Mainstay of treatment is anticonvulsant drugs which are chosen according to seizure types¹. Valproic acid is a potent and broad spectrum anticonvulsant. It is the first line drug in majority of seizures types and is widely used. However there are some serious adverse effects which limit its use^{2,3}.

Thrombocytopenia is a serious adverse effect of valproic acid. It may be responsible for dose reduction and even discontinuation of this important drug. However this important adverse effect is sometimes ignored. Firstly, many laboratories do not include platelet count in the routine blood examination. This leads to missing of thrombocytopenia by busy physicians, unless specially looked for and ordered. Secondly, other common side effects especially those related to women with epilepsy and hepatotoxicity etc. gain more attention of the physicians⁴.

In WAPDA Teaching Hospital Complex, Lahore, we have computerized record of all the patients. Because of free medical facility, follow up of the patients is very good. On the other hand there is lack of Pakistani data on the frequency of thrombocytopenia in patients receiving valproic acid. Therefore this study was planned to have insight into the local scenario of this important issue. Aim of the study was to investigate the frequency of thrombocytopenia in epileptic patients on valproic acid.

MATERIALS AND METHODS

This descriptive study was conducted at WAPDA Teaching Hospital Complex, Lahore. All the epileptic patients receiving valproic acid during the period from 01.01.2012 to 31.12.2013 were included in the study. Following patients were excluded from the study.

1. Patients already having thrombocytopenia
2. Patient with any disease having potential for thrombocytopenia e.g. dengue fever, hepatitis c etc.
3. Patients receiving any other medicine with the potential of thrombocytopenia e.g. interferone.

Total 122 patients met these criteria. Platelet count below $150 \times 10^9 / L$ was taken as thrombocytopenia. Hospital information system was used to note the demographic information and relevant data on the disease, laboratory

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investigations and treatment of the patients. Statistical analysis was done using SPSS version 14. Descriptive statistics was used for the analysis of different variables. Mean and standard deviation were calculated for numeric variables like age of patient and dose of valproic acid. Percentages were calculated for categorical variables like gender of patient and frequency of thrombocytopenia.

RESULTS

Out of total 122 patients 63(51.64%) were male and 59(48.36%) were female. Mean age was 49.79±19.97 years (range 10–79 years). Out of 122 patients, 23(18.85%) developed thrombocytopenia. Thirteen (56.52%) out of these 23 were males and 10(43.48%) were female. Table 1 shows distribution of patients with thrombocytopenia in different age groups. Average dose of valproic acid in patients with thrombocytopenia was 1315±478mg/day as compared to 868±415mg/day in patients without thrombocytopenia. Overall average dose in total 122 patients was 952±460 mg/ day.

Table 1: Distribution of patients with Thrombocytopenia in different age groups (n=100)

Age group	n	%age
<20	4	17.39
21- 60	5	21.74
> 60	14	60.87

DISCUSSION

Relationship between thrombocytopenia and patients receiving valproic acid has been studied in different settings and patient populations in different studies. Examples include indoor patients, paediatric population, psychiatric patients and epileptic patients. Mixed results have been seen in all these studies.

The aim of our study was to see the frequency of thrombocytopenia in epileptic patients who were receiving valproic acid, at a tertiary care hospital.

Out of total 122 patients, 23(18.85%) developed thrombocytopenia. The study conducted by Nasreddine and Beydoun, on epileptic patients receiving valproic acid, showed thrombocytopenia in 17.7%⁵. Another study conducted by Ko CH. et al on 96 neurologically impaired children showed same figure (17.7%)⁶. Allarakhia IN et al in their study on paediatric population have shown thrombocytopenia in 21.6 % patients⁷. Our result is consistent with the results of these studies.

In our study there was no sex predilection for thrombocytopenia however age of the patients had some relationships with thrombocytopenia. Table 1 shows that chances of thrombocytopenia are

increased in old age. Conley EL et al have shown same finding in their study⁸.

Dose of valproic acid was also found to be associated with the chances of thrombocytopenia. In our study average dose of valproic acid in patients with thrombocytopenia was 1315mg/day as compared to 868mg/day in patients without thrombocytopenia. Most of the studies have also shown the same result^{5,6,7,8}.

Although mechanism of thrombocytopenia in patients receiving valproic acid is not fully understood, immune mediated peripheral destruction of platelets has been attributed to it⁹. High doses of valproic acid have also been associated with thrombocytopenia through bone marrow suppression¹⁰. This can explain increased tendency of thrombocytopenia with higher doses of valproic acid.

CONCLUSIONS

Thrombocytopenia is a common adverse effect of valproic acid. Its chances are increased in old age and with increased dosage. Frequent monitoring of platelet count is recommended in epileptic patients receiving this drug.

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