

VALPROIC ACID-INDUCED THROMBOCYTOPENIA: A LONGITUDINAL STUDYManoj Kumar Sahu¹, Surbhi Dubey²¹Associate Professor & HOD, Department of Psychiatry, Pt. JNM Medical College, Raipur.²Assistant Professor, Department of Psychiatry, Pt. JNM Medical College, Raipur.**ABSTRACT****BACKGROUND**

Valproate shows the most promising efficiency in treating mood as well as anxiety disorders; however, thrombocytopenia is one of the most common side effects associated with it. The perceived novelty and under recognition of the platelet lowering effects of valproate is illustrated by various case reports of thrombocytopenia associated with valproate in psychiatric populations.

AIMS

Present study aims is to investigate the relationship between platelet count & VPA therapy, age, and duration of medication.

SETTINGS AND DESIGN

It was a longitudinal observational study conducted at Department of Psychiatry, Pt. JNM Medical College, Raipur.

METHODS AND MATERIAL

The sample consisted of patients of either sex, aged between 18 to 65 years who were prescribed valproate therapy by the treating doctor. Patients were evaluated at baseline, at every month up to three months and at six months. The platelet counts were determined using an automatic haematology analyser.

STATISTICAL ANALYSIS

Correlation statistics were used to analyse the collected data.

CONCLUSION

Most of the time thrombocytopenia is mild and transient which resolves spontaneously. Regular monitoring of platelet level is required in the high risk groups.

KEYWORDS

Valproic Acid, Thrombocytopenia, Psychiatric Disorders.

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INTRODUCTION: Valproic Acid (VPA) has been used with increasing frequency for the treatment of many psychiatric conditions like: - depression, anxiety and psychotic disorder,⁽¹⁾ including those in elderly patients.⁽²⁾ Valproate shows the most promising efficiency in treating mood as well as anxiety disorders, with possible efficiency in the treatment of agitation and impulsive aggression and less convincing therapeutic response in treating psychosis, alcohol withdrawal or dependence.⁽³⁾ Thrombocytopenia is one of the most common side effects associated with VPA therapy, with incidence ranging from 1% to 30%.^(4, 5) It is mild to transient in most cases which usually resolves spontaneously on dosage reduction or withdrawal of the drug.^(6, 7)

There have been wide ranging reports of thrombocytopenia and other forms of platelet dysfunction as

side effects of valproate therapy but exact incidence is not known.⁽⁸⁾ Thrombocytopenia has been reported in 6%-33% of adult patients with epilepsy taking valproate but a lowering of platelet count was seen in almost all patients which appeared to be dose related.⁽⁹⁾ Thrombocytopenia associated with valproate therapy has been reported to resolve without interruption of valproate treatment⁽¹⁰⁾ and has also been reported to endure over time or to have an erratic course.⁽⁵⁾ Reports on the use of valproate with psychiatric patients have described a drop in platelet count without thrombocytopenia or with a minimal incidence of thrombocytopenia^(11,12) without any associated adverse clinical events related to these findings.⁽¹³⁾ The perceived novelty and under recognition of the platelet lowering effects of valproate is illustrated by various case reports of thrombocytopenia associated with valproate in psychiatric populations.⁽¹⁴⁾ Thrombocytopenia is one of the most common side effects associated with VPA therapy, with incidence ranging from 1% to 30%.^(4,5) It is mild to transient in most cases which usually resolves spontaneously on dosage reduction or withdrawal of the drug.^(6,7) The aim of the present study is to investigate the relationship between

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platelet count & VPA therapy, age, and duration of medication.

METHODOLOGY: It was a longitudinal observational study conducted from February 2012 to July 2013. The study was approved by the Institutional Ethical Committee [EC, Pt. JNM MC] and carried over in the Department of Psychiatry. The sample consisted of patients of either sex, aged between 18 to 65 years who were prescribed valproate therapy by the treating doctor. Those patients with comorbid medical illness or patients treated with other drugs were excluded. Patients already taking valproate were also excluded. Total 100 consecutive patients fulfilling inclusion and exclusion criteria were enrolled in the study. Detailed clinical history, medication history and other relevant information were directly obtained from the patient and the accompanying family persons. Informed consent was taken from the patient as well as guardian. Patients were evaluated at baseline, at every month up to three months and at six months. Blood sample was performed on a single peripheral

vein drawn from the antecubital vein without vein occlusion and transferred into glass container containing 3.8% trisodium citrate and were stored at 37°C and tests were performed randomly. The platelet counts were determined using an automatic haematology analyser. For the present study, Thrombocytopenia was defined as mild (1.01 lakh - 1.5 lakh/mm³), Moderate (0.4 lakh -1 lakh/mm³), Severe (<0.4 lakh/mm³).

RESULTS: Out of total 100 patients, 72 patients (51 male and 21 female) completed the study and were included for the final analysis. Majority were males (71%) and within the age group of 21 to 30 years (37.5%). Nine patients (12.5%) developed thrombocytopenia. Of these, five were male (9.8%) and four were female (19.04%). Patients in 51 to 60 years age group had the highest percentage of thrombocytopenia (55.5%) whereas 18 to 30 years age group had the lowest rate of thrombocytopenia (2.7%). All patients had mild thrombocytopenia. No case of moderate or severe thrombocytopenia was found in our study.

Sl. No.	Platelet in Lakhs	Total No. of Patient (N=72)						
		Baseline	1 month	2 months	3 months	4 months	5 months	6 months
1	1-1.5	0	0	0	1	4	4	3
2	1.51-2	9	9	13	13	12	11	11
3	2.1-2.5	26	24	22	21	27	24	29
4	2.51-3	21	26	26	31	23	27	25
5	3.1-3.5	8	8	8	5	5	3	3
6	3.51-4	7	3	2	1	1	2	1
7	4.1-4.5	1	2	1	0	0	1	0

Table 1: Frequency Distribution of Platelet Count in Patients on VPA Treatment up to 6 months

Table indicates that there is thrombocytopenia in varying degrees during specific month and some patients have recovered also. It appears that thrombocytopenia is a transient phenomenon and resolves spontaneously.

DISCUSSION: The percentage of thrombocytopenia in the present study was found to be 12.5%. In previous studies, the frequency of VPA-induced thrombocytopenia has varied greatly ranging from 0-32%.⁽¹⁵⁻²⁵⁾ One of the reasons for this wide variability in reported frequencies is the definition of thrombocytopenia. Contrary to the reports of VPA-induced thrombocytopenia being dose related, we did not find any correlation between thrombocytopenia and VPA dose.

Consistent with earlier studies, incidence of thrombocytopenia was higher in elderly patients with 55.5% patients in the age group of 51-60 years developing thrombocytopenia. Contrary to the finding of women being more likely to develop thrombocytopenia, we did not find any gender difference in our study.

One of the important finding of our study was the correlation between thrombocytopenia and the duration of VPA treatment. The decrease in mean platelet count was significantly correlated with duration of therapy.

CONCLUSION: Our findings underline the importance of monitoring platelet counts on patients treated with VPA, as advised in the product label, before the onset and during the therapy. This monitoring should be continued regularly. More vigilant monitoring of platelet level is required in the higher age group and in females. However, the discontinuation of the drug is not necessary in majority of cases. Most of the time thrombocytopenia is mild and transient which resolves spontaneously.

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