



International Journal of Medicine and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijmpr



CASE REPORT

A Case Report on Sodium Valproate Induced Tremors

Neelam Swathi*, M. Swetha, Y. Himabindu, Ramesh Dhani

Ratnam Institute of Pharmacy, Pidathapolur, Muthukur, Nellore, Andhra Pradesh, India.

ABSTRACT

Mood stabilizers are agents that act by balancing certain brain chemicals that control emotional states and behavior. Valproic acid, also known as sodium valproate, is often prescribed as a stabilizing medication for patients who do not tolerate lithium therapy well. Valproate is a mood stabilizer which is approved for use in acute and maintenance mania. It is the first-line drug for bipolar patients with presence of rapid cycling, irritable mania, bipolar disorder with comorbid substance use disorders, severe mania with psychosis, mixed mania and secondary mania. Sodium valproate takes a shorter period of time to work than lithium. It exerts its effects by enhancement of brain gamma aminobutyric acid (GABA) levels. Diagnosis of tremors after sodium valproate administration is clinically based and straightforward. Several drugs that cause tremors include asthma medicines (theophylline), seizure medicines (valproic acid), cancer medicines (thalidomide), mood stabilizers (lithium carbonate), antivirals (acyclovir), stimulants (caffeine and amphetamine). Tremors are the most common adverse effect reported with sodium valproate administration because it may be due to abnormalities of dopamine and norepinephrine. Management of tremors is done by withdrawal or stoppage of the drug that is responsible for tremors (sodium valproate) or addition of drugs like beta-blockers (propranolol) for treating tremors. Various drugs are given for the treatment of sodium valproate-induced tremors, including propranolol, amantadine, diphenhydramine, benzotropine, cyproheptadine. Propranolol was clearly the most therapeutic, and hence beta-blockers are often used as a first-line pharmacologic intervention for valproate tremor.

Keywords: Sodium valproate, mood stabilizer, tremors.

ARTICLE INFO

*Corresponding Author

Neelam Swathi
Ratnam Institute of Pharmacy,
Pidathapolur, Muthukur, Nellore,
Andhra Pradesh, India.
MS-ID: IJMPR3571



PAPER QR-CODE

ARTICLE HISTORY: Received 21 December 2017, Accepted 29 January 2018, Available Online 10 February 2018

Copyright © 2018 Neelam Swathi, et al. Production and hosting by Pharma Research Library. All rights reserved.

Citation: Neelam Swathi, et al. A Case Report on Sodium Valproate Induced Tremors. *Int. J. Med. Pharm. Res.*, 2018, 6(1): 26-28.

CONTENTS

1. Introduction	31
2. Case Report	31
3. Treatment Outcome	31
4. ADR Assessment	31
5. Conclusion	32
6. References	32

1. Introduction

Mood stabilizers are agents acts by balancing certain brain chemicals that control emotional states and behavior¹. valproic acid also known as sodium valproate is often prescribed as a stabilizing medication for patients who do not tolerate lithium therapy well⁶. Valproate is a mood stabilizer which is approved for use in acute and maintainance mania. It is the first line drug for bipolar patients with presence rapid cycling, irritable mania, bipolar disorder with comorbid substance use disorders, severe mania with psychosis, mixed mania and secondary mania. sodium valproate takes shorter period of time to work than lithium⁷. It exerts its effects by enhancement of brain gamma aminobutyric acid (GABA) levels^{11,12}. Diagnosis of tremors after sodium valproate administration is clinically based and straight forward. Several drugs that causes tremors includes asthma medicines (theophylline), seizure medicines (valproic acid), cancer medicines (thalidomide), mood stabilizer (lithium carbonate) antivirals (acyclovir), stimulants (caffeine and amphetamine). Tremor of hands is a common side effect of lithium and valproate treatment. Incidence of tremors by sodium valproate administration mainly due to abnormalities of dopamine and norepinephrine^{15,16}. The patient complaints of tremors after one year of treatment with sodium valproate (within 1 year). Incidence of valproate induced tremors is thought to occur in 6-45% of patients³. Approximately 25% of patients taking valproate are found to develop a tremor within 3-12 months of initiating therapy².



Figure 1

Table 1: Drugs Commonly Causing Tremors

S.No	DRUGS
1.	Valproic acid
2.	Carbamazepine
3.	Verapamil
4.	Cyclosporine
5.	Epinephrine
6.	flunarizine

2. Case Report

A 60 years male patient was consulted the physician in the psychiatric department ward with the chief complaints of shaking hands and low mood since 2 weeks. He is the known case of bipolar affective disorder (BPAD) since 1 year. From 1year he was kept on treatment with olanzapine, sodium valproate, escitapram based on her complaints .

After treatment with sodium valproate about 1 year the patient complaints of tremors. For which the sodium valproate is prescribed along with beta blocker (propranolol) from that day itself¹⁴. Sodium valproate acts by balancing certain brain chemicals that control emotional states states and behavior (dopamine & epinephrine). The patient complaints of tremors after prolonged use of drug for more than 11 months.

3. Treatment Outcome

For tremors the physician prescribed propranolol (beta blocker) which acts excellently in controlling tremors with minimal sedation. The sodium valproate is prescribed as a mood stabilizer and it is well tolerated by patient in minimizing the symptoms of bipolar affective disorder (BPAD) since one year. patient freshly complaints of shaking of hands (tremors) since 2 weeks .The sodium valproate acts very effectively in reducing the symptoms or improving the patient condition and hence the valproate is not stopped or withdrawn .The same therapy was continued with the addition of other drug that acts by subsiding the adverse effect like tremors. After administration of propranolol (20mg) twice daily the tremor activity is subsided. The patient is recovered from tremors early after treating with propranolol



Figure 2



Figure 3

4. ADR Assessment

After collection of all the subjective and objective data it was suspected that the current treatment with the sodium valproate since 1 year is responsible for the occurrence of tremors. After checking all the ADR profiles of prescribed drugs it was confirmed that sodium valproate has a most probable relation in causing this reaction. ADR assessment is done by using scales like narinjo scale and WHO-UMC

scales and those scales conforms this reaction is a probable type as shown in table 1.

Discussion

Tremor is an unintentional, rhythmic muscle movement involving to-and-fro movements (oscillations) of one or more parts of the body. it is most common of all involuntary movements that affect the hands, arms, head, face, voice, trunk, and legs. Most tremors occurs in the hands. Tremor is a symptom of a neurological disorder or appears as a side effect of certain drugs like theophylline, lithium, acyclovir, thalidomide etc. Various drugs are given for the treatment of sodium valproate induced tremors which include propranolol, amantidine, diphenhydramine,

benztropine, cyproheptadine¹⁴. Among them Amantidine was moderately effective, but cyproheptadine, diphenhydramine, and benztropine gave little or no relief¹⁴. Propranolol was clearly the most therapeutic and hence the beta blockers are often used as a first-line pharmacologic intervention for valproate tremor. propranolol 20mg twice daily seemed to be provide excellent control of the valproate induced tremor with little sedation^{10,12}. Propranolol acts by blockade of both peripheral and central beta adrenergic receptors .it is possible that an increase in circulating epinephrine or other catecholamines is important in the development of tremors due to effectiveness of propranolol, there will be reduction of valproate tremors^{4,5}.

Table 2A: Causality assessment of suspected ADR

S.No	Suspected drug	ADR	Narinjo scale	WHO
1.	Sodium valproate	Tremor	Probable	Probable

Table 2B: Causality assessment of suspected ADR

ADR	Suspected drug	Severity	Predictability	Preventability
Sodium valproate induced tremors	Sodium valproate	Moderate	Predictable	Probably Preventable

5. Conclusion

Even there in a lower increase in possibility of causing tremors by using the mood stabilizer like sodium valproate it is a role of health care providers be aware of this complication which can occur only after the long term use of drug and should be vigilant on recognizing tremors and provide prompt treatment accordingly.

6. References

[1] Jacquelyn E. Canning, Stephanie Burton, and Beth Hall. Lithium and valproate-induced tremors. *Mental Health Clinician*: January 2012, 1(7): 174-176.

[2] Arbaizar B, Gómez-Acebo I, Llorca J. Postural induced-tremor in psychiatry. *Psychiatry Clin Neurosci*. 2008, 62(6): 638-45.

[3] Rinnerthaler M, Luef G, Mueller J, Seppi K, Wissel J, Trinka E. Computerized tremor analysis of valproate-induced tremor: a comparative study of controlled-release versus conventional valproate. *Epilepsia*. 2005, 46(2): 320-3.

[4] Karas BJ, Wilder BJ, Hammond EJ, Bauman AW. Treatment of valproate tremors. *Neurology*. 1983; 33(10):1380-2.

[5] Karas BJ, Wilder BJ, Hammond EJ, Bauman AW. Valproate tremors. *Neurology*. 1982, 32(4): 428-32.

[6] Ayano G (2016) Bipolar Disorders and Valproate: Pharmacokinetics, Pharmacodynamics and Therapeutic Effects and Indications of Valproate: Review of Articles. *Bipolar Disord* 2:109.

[7] Depakene, Stavzor (valproic acid) (2014) dosing, indications, interactions, adverse effects and more. Medscape Reference. WebMD.

[8] Shiah IS, Yatham LN, Baker GB (2000) Divalproex sodium increases plasma GABA levels in healthy volunteers. *Int Clin Psychopharmacol* 15: 221.

[9] Chang P, Walker MC, Williams RS (2014) Seizure-induced reduction in PIP3 levels contributes to seizure-activity and is rescued by valproic acid. *Neurobiol Dis* 62: 296-306.

[10] Kostrouchová M, Kostrouch Z, Kostrouchová M. Valproic acid, a molecular lead to multiple regulatory pathways (PDF). *Folia Biol (Praha)*, 2007, 53: 37-49.

[11] Chiu CT, Wang Z, Hunsberger JG, Chuang DM. Therapeutic potential of mood stabilizers lithium and valproic acid: beyond bipolar disorder. *Pharmacol Rev*, 2013, 65: 105-142.

[12] Death AK, McGrath KC, Handelsman DJ. Valproate is an anti-androgen and anti-progestin. *Steroids*. 2005, 70: 946-953.

[13] B.J. Karas, B. J. Wilder, E.J. Hammond, A. W. Bauman *Neurology*. 1983, 33 (10): 1380.

[14] Sherifa Ahmed Hamed. The effect of antiepileptic drugs on the kidney function and structure. *Expert Review of Clinical Pharmacology* 2017, 10(9): 993-1006.

[15] Hyman NM, Dennis PD, Sinclair KG. Tremor due to sodium valproate. *Neurology*. 1979, 29(8): 1177-80.

[16] Van der Zwan A Jr. Transient Parkinson syndrome and tremor caused by the use of sodium valproate. *Ned Tijdschr Geneesk*. 1989, 133(24): 1230-2.

[17] Poolsup N, Li Wan Po A, de Oliveira IR. Systematic overview of lithium treatment in acute mania. *J Clin Pharm Ther*. 2000, 25(2): 139-56.