Original Article

Serum aminotransferase activity in patients of epilepsy and mania taking sodium valproate

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Keywords: *Aminotransferase, Epilepsy, Mania, Sodium Valproate*

Abstract

Background: Our aim is to study the serum aminotransferase activity in patients of epilepsy and mania taking sodium valproate. Sodium valproate is a common drug to be prescribed to the patients of epilepsy and mania. Aminotransferase, both AST (Aspartate amino transferase) and ALT (Alanine amino transferase) is an accepted marker for any liver injury.

Methods: Serum sample of fifty patients of known cases of epilepsy and mania, who were on sodium valproate since at least 3 month and fifty normal subjects were taken. Serum aminotransferase level (both AST & ALT) were estimated by colorimetric method in fully automated Erba XL-640 Analyser.

Results: The level of aminotransferase enzymes were increased in patients of epilepsy and mania after administration of sodium valproate and elevation was highly significant as compared to the normal subjects (p value <0.05).

Conclusion: From our study it is concluded that there is a need for monitoring serum aminotransferase level in patients receiving sodium valproate.

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Date of Submission: May 21, 2014 **Date of Acceptance:** June 18, 2014 **Date of Publishing:** July 20, 2014

How to cite this paper:
Khubchandani A, Parmar V, Jadav J, Sidhu G, Solanki V, Gangwani S, Solanki M. Serum aminotransferase activity in patients of epilepsy and mania taking sodium valproate. Annals of Pathology and Laboratory Medicine. 2014;1(1):20-23.

1. Introduction

Epilepsy is a syndrome of different cerebral disorders of the Central Nervous System (CNS) which is characterized by excessive discharges of large numbers of neurons.[1] It is very disabling condition, rendered especially disturbing because of its unpredictability and its being a common neurological disorder worldwide.[2] The liver is the primary organ for drug metabolism and elimination for many antiepileptic drugs (AEDs) and thus is subjected to drug-induced toxicity. There is a wide range of hepatotoxic reactions, from mild and transient elevations of hepatic enzymes to fatal hepatic failure.[3]

Liver enzymes can serve as markers of hepatocellular injury e.g. aspartate aminotransferase (AST), alanine aminotransferase (ALT) or of an obstruction in the bile flow cholestasis e.g. alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT). Although these enzymes are elevated in liver disease, the elevation can also be secondary to enzyme induction without hepatic pathology.[4] In particular, antiepileptic drugs have many serious reactions, as seen with sodium valproic acid (VPA). Though relatively rare, when compared with other consistently known hepatotoxic drugs, the hepatotoxicity induced by antiepileptic drug can lead to death or an acute liver failure which could imperatively require liver transplantation. The hepatotoxicity induced by antiepileptic drug occurs either because of production of reactive toxic metabolites or because of induction of immune-allergic reactions.[5] Such antiepileptic drugs (AED) are associated with mild elevations of liver enzymes, which may occur in up to 50% of patients. These elevations are usually transitory or dose-related.

Usually, hepatotoxicity is associated with other clinical manifestations of drug allergy (fever, rash and eosinophilia). Another idiosyncratic hepatotoxic reaction comes from hepatotoxic metabolites because of aberrant metabolism. This reaction has been observed with VPA.[3]

A more than two to threefold increase in liver enzymes during AED therapy should caution the physician of a potential of coexistent liver disease. If subsequent follow-up reveals a progressive increase in the values of the enzymes, investigations for coexistent liver disease are warranted and may require a switch to an alternative AED.[4]

Our aim is to study the serum aminotransferase activity in patients of epilepsy and mania taking sodium valproate.

2. Materials and Methods

The cross sectional study was conducted in Civil Hospital, Ahmedabad during June 2013 to October 2013. We have taken institutional approval for conducting this study. Fifty patients of confirmed diagnosis of epilepsy and mania who were on sodium valproate for (daily dose ranging from 200 to 800mg) at least since 3 month were taken (n=50). Their age range was between 25-65 years, 37 male and 13 female patients participated in this study. Fifty normal healthy persons (n=50) aged 25-65 years (34 male and 16 female) were used as control. The study included epileptic and manic patients receiving sodium valproate for at least since 3 month. The study excluded epileptic and manic patients who had concomitant liver diseases, using other drugs causing elevation of liver enzymes (e.g. antibiotics, anti-rheumatic drugs, statins and non-steroidal anti-inflammatory drugs) or those who were alcohol drinkers.

Venous blood samples were collected from epileptic patients and also from controls. About five milliliters of venous blood was drawn by utilizing disposable plastic syringes and transferred into sterile test tube. The blood was allowed to clot and centrifuged at 5000 rpm for 5 minute. Sera were separated and stored at -4ºC until analysis. The supernatant blood serum was used for the analysis of aminotransferase level (ALT & AST) by colorimetric method in Erba XL-640 fully auto analyzer with Modified IFCC method.[6,7,8] And results were analyzed with Graphpad Instat software by using student's t-test for statistical significance of 0.05.

3. Result

The mean age of patients was found to be 41.48 years. The mean age of control was found to be 36.86 years. Table 1 shows and compares the results of serum amino transferase level between case and control group. The results are expressed as mean ± standard deviation.

Table 1: Serum level of AST and ALT in cases and controls.

Level of serum aminotransferase	Cases (mean ±SD)	Controls (mean ±SD)	p value
AST(U/L)	63 ± 31	21 ± 9	< 0.05
ALT(U/L)	58 ± 22	23 ± 10	< 0.05

Serum AST and ALT level of epilepsy and mania patients were significantly higher ($p<0.05$) than the level in normal subjects.
Normal range of serum AST: 12 to 38 U/L.
Normal range of serum ALT: 7 to 41 U/L.

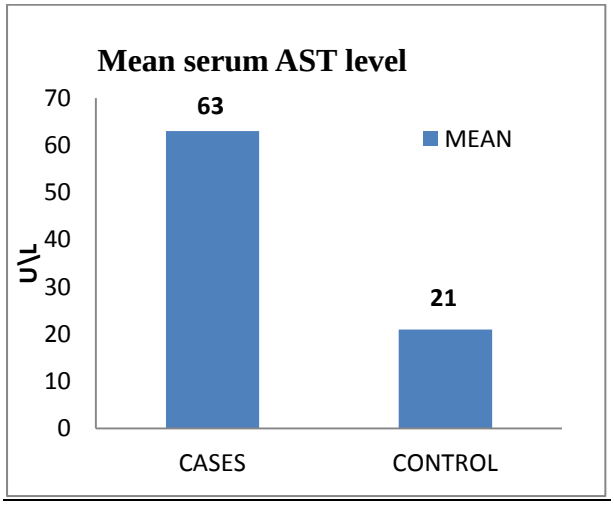

Figure 1: Mean serum AST level in Control & Cases.

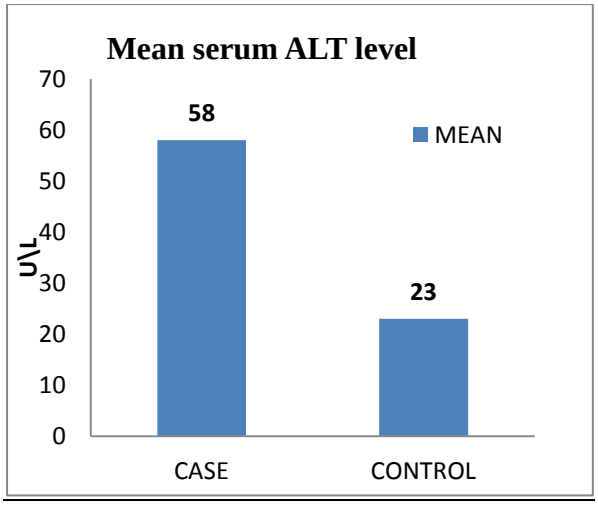

Figure 2: Mean serum ALT level in Control & Cases.

4. Discussion

In our study, we found that there is a significant increase in serum transaminase level in epilepsy and mania patients as compared with normal subjects. In agreement with our study, Verma and Haidukewych showed a statistically significant correlation between the dose of valproic acid and AST.[9] Moreover, Spiller et al reported that valproic acid mediated hepatic injury is associated with dose dependent rise in serum liver enzymes.[10] Contrary to our results, Sussman noted that valproic acid-associated hepatotoxicity is distinct from the form of dose-related liver enzyme elevation that appears to be reversible with a reduction in dosage or discontinuation of the drug.[11] Felker et al and Willmore et al demonstrated through retrospective studies a transient elevation of liver ALT and AST in epileptic patients on valproic acid.[12,13] Further more study with larger sample size and long term follow-up of patients is required for more satisfactory result.

Boelsterli and Lim have recently proposed a hypothesis that involves underlying genetic or acquired mitochondrial abnormalities as a major determinant of susceptibility to hepatotoxicity induced by valproic acid.[14]

5. Conclusion

To conclude, serum aminotransferase levels are increased in epilepsy and manic patients on sodium valproate therapy, which is hepatotoxic drug. So, routine screening of hepatic enzymes level during the chronic use of antiepileptic drugs is recommended. The need for obtaining baseline liver function tests is essential before starting antiepileptic therapy and regular monitoring of serum aminotransferase values is recommended. Precautions should be taken when using antiepileptic drugs in epileptic patients with pre-existing hepatic disorders, in patients using other potentially hepatotoxic drugs or if signs or symptoms of hepatic impairment appear. Also we recommended, controlled studies in larger samples should be carried out to reveal the frequency and the risk factors of serious hepatotoxicity.

Acknowledgements

Thanks and gratitude to my associate professor and my colleagues in Clinical Biochemistry Department for their help in conducting this study. And thanks to my wife for helping in paper writing and giving her moral support to me.

Funding

None.

Competing Interests

None declared.

References

1. Nikalje A, Ghodke M, Girbane A. GABA modulating agents: a brief review. Asian Journal of Biological Sciences 2011; 4: 201-20.

2. Ahmad M. Epilepsy: stigma and management. Current Research in Neuroscience 2011;201:1-14.
3. Arroyo S, de la Morena A. Life-threatening adverse events of antiepileptic drugs. Epilepsy Research 2001;47:155-74
4. Ahmed SN, Siddiqi ZA. Antiepileptic drugs and liver disease. Seizure 2006; 15: 156-64.
5. Lee WM. Drug-induced hepatotoxicity. New England Journal of Medicine 2003; 349:474-85.
6. Bergmeyer HU, Horder M, Rej R. Clin. Chem. Clin. Biochem. 1986;24:481-95.
7. Henry RJ, Cannon DC, Winkerman JW. Clinical Chemistry Principle and Techniques, 2nd. Edn. Hagerstown MD., harper and Raw. 1974
8. Teitz NW. Clinical Guide to Laboratory tests. 3rd ed, W.B. Saunders. Philadelphia USA, 1995.
9. Verma NP, Haidukewych D. Differential but infrequent alterations of hepatic enzyme levels and thyroid hormone levels by anticonvulsant drugs. Archives of Neurology 1994;51:381-4.
10. Spiller HA, Spiller H, Krenzelok EP, Klein-Schwartz W, Winter ML, Weber JA, et al. Multicenter case series of valproic acid ingestion: serum concentrations and toxicity. Clinical Toxicology 2000; 38: 755-60.
11. Sussman NM. Hepatotoxicity of valproic acid. Neurology 1979;29:601.
12. Felker BL, Sloan KL, Dominitz JA, Barnes RF. The safety of valproic acid use for patients with hepatitis c infection. American Journal of Psychatry 2003;160:174-8.
13. Willmore LJ, Wilder BJ, Bruni J, Villarreal HJ. Effect of valproic acid on hepatic function. Neurology 1978;28: 961-4.
14. Boelsterli UA, Lim PLK. Mitochondrial abnormalities: a link to idiosyncratic drug hepatotoxicity. Toxicology. 2007; 220: 92 -107.

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