CASE REPORT

A case report on sodium valproate induced young onset hypertension in a case of mania

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ABSTRACT

This case report examines the association between sodium valproate, an FDA-approved medication for bipolar disorder and epilepsy, and the onset of hypertension in a young patient presenting with manic symptoms. Conducted at Saveetha Medical College Hospital, this retrospective study focuses on an 18-year-old male, highlighting the importance of monitoring blood pressure in patients receiving sodium valproate. A clear temporal relationship was observed between the initiation of sodium valproate and the development of hypertension, which resolved after medication adjustment without the need for antihypertensive drugs. This case underscores the necessity for clinicians to remain vigilant regarding the cardiovascular side effects of sodium valproate and advocates for further research to enhance patient safety and optimize treatment practices.

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INTRODUCTION

Valproate, a simple branched-chain fatty acid approved by the FDA, is a cornerstone treatment for bipolar disorder and various forms of epilepsy. While its exact mechanism of action remains incompletely understood, it is known to block voltage-sensitive sodium channels and elevate gamma-aminobutyric acid (GABA) levels in the brain. Despite its efficacy, valproate is associated with a range of adverse effects, including thrombocytopenia and hepatotoxicity. Cardiovascular side effects, though less common, have been reported in approximately 1–5% of patients on valproate therapy, presenting as hypertension, tachycardia, and palpitations [1].

The global burden of disease, particularly in relation to cardiovascular and neurological disorders, underscores the importance of understanding the broad implications of commonly prescribed medications like valproate [2]. Additionally, research into the nephroprotective effects of compounds highlights the complexity of managing drug-induced side effects in clinical practice [3].

The global burden of causes of death and the impact of interventions like Wharton's jelly mesenchymal stem cells for COVID-19 treatment highlight the need for comprehensive approaches in understanding the multifaceted effects of treatments like sodium valproate in psychiatric care [4, 5]. In the dynamic sphere of psychiatric medicine, the sophisticated interaction between psychotropic drugs and unexpected physiological outcomes has emerged as a critical area of study [1]. This case report aims to delve into the fascinating intersection of sodium valproate usage and the manifestation of hypertension in a young patient with manic symptoms [1]. Although the efficacy of sodium valproate in treating bipolar disorder and epilepsy is well-documented, its association with hypertension, especially among younger patients, is sparsely investigated and understood [1]. Significant contributions from Indian research have shed light on the cardiovascular implications of sodium valproate [4].

CASE REPORT

An 18-year-old high school student was brought to medical attention by his parents due to exhibiting sleep disturbances, irritability, heightened self-esteem, behavioral changes, and nonsensical speech for the past five days. These symptoms emerged following an altercation with peers at school, which also resulted in a nasal injury. The patient had no notable personal or familial psychiatric history. Initial mental status evaluation highlighted an irritable mood and confused affect, with his thought content characterized by grandiose beliefs and exaggerated self-perception. Assessment of higher mental functions revealed compromised personal and social judgment, alongside a minimal level of insight (Grade 1). Based on these findings, he was provisionally diagnosed with an acute manic episode and subsequently admitted to the psychiatric ward for further management. Following his admission and considering the assault-induced head injury, both CT and MRI scans (Figure 1) of the brain were performed, effectively ruling out any organic etiologies.

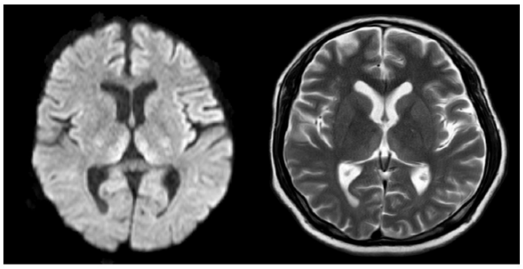

Figure 1:This MRI scan of the brain was performed to rule out any organic etiologies contributing to the patient's psychiatric symptoms. The scan shows normal findings, with no evidence of structural abnormalities such as lesions, hemorrhages, or space-occupying masses.

Subsequent to routine laboratory evaluations, including liver function tests (LFTs), thyroid function tests (TFTs), and an electrocardiogram (ECG), a pharmacological regimen was initiated. This included Olanzapine 5mg, Lorazepam 2mg, Chlorpromazine 100mg, and Trihexyphenidyl 2mg, tailored to address his psychiatric symptoms. Due to the persistence of symptoms, the patient's medication dosages were adjusted after one week.(Figure 2 and 3) The dosage of Olanzapine was increased from 5mg to 10mg, and Trihexyphenidyl remained at 2mg. Additionally, Sodium valproate 500mg and Haloperidol 10mg were introduced to his treatment regimen. Subsequent to these adjustments, an elevation in blood pressure was observed, necessitating close monitoring at four-hour intervals, which revealed a gradual increase in BP levels. In response to ongoing symptoms and the observed increase in blood pressure, the treatment plan was further modified. Quetiapine was initiated at a dose of 50 mg, and Risperidone was started at 4 mg, later increased to 6 mg. The dose of Sodium valproate was also gradually escalated to 2000 mg. Given the persistent elevation in blood pressure, a consultation with the internal medicine department was sought, resulting in the initiation of antihypertensive medications, Telmisartan 40 mg and Amlodipine 5 mg. Comprehensive evaluations, including an ultrasound of the abdomen and kidneys, ureters, and bladder (KUB), renal artery Doppler, and a 24-hour urinary metanephrine test, were conducted to investigate potential medical causes of hypertension. These investigations yielded negative results, effectively ruling out medical etiologies for the hypertension. As the patient's manic symptoms showed significant improvement, reaching a state akin to his premorbid level, the decision was made to gradually taper the dosage of Sodium valproate from 2000mg to 500mg. Concurrent with this medication adjustment, a gradual decline in blood pressure was observed through meticulous monitoring via a four-hourly blood pressure chart. Remarkably, this decrease in BP occurred even in the absence of antihypertensive medications, leading to the discontinuation of such treatments. The patient continued to tolerate his psychiatric medications well, without experiencing any significant adverse effects.

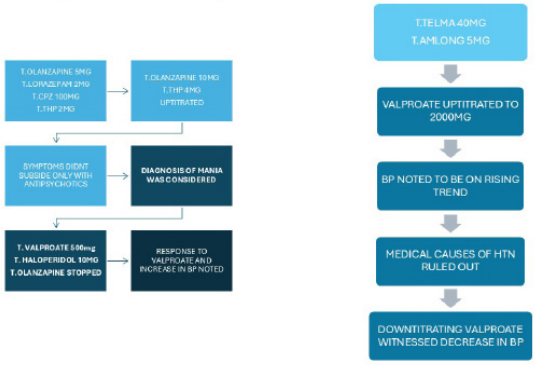

Figure 2: Timeline of Medication Adjustments and Blood Pressure Changes with Sodium Valproate Dosage

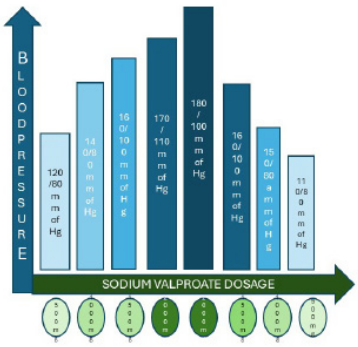

Figure 3: Blood Pressure Changes with Varying Sodium Valproate Dosages

This case report highlights the potential for sodium valproate to contribute to elevated blood pressure levels, echoing a small number of previous case reports that have suggested a link between valproate use and induced hypertension. It underscores the necessity for clinicians to vigilantly monitor blood pressure in patients initiated on sodium valproate therapy. Further research is imperative to solidify the understanding of the relationship between sodium valproate administration and hypertension, particularly in individuals treated

for mood disorders. This could lead to more informed clinical practices and potentially adjust monitoring protocols for patients on valproate therapy.

Following admission, the patient experienced an acute exacerbation of bronchial asthma, for which the pulmonology team prescribed oral steroids alongside nebulization therapy. Initially, the psychiatric treatment regimen included Escitalopram 10mg, Lorazepam 2mg, and Sodium Valproate 500mg. However, within a span of 10 days, the patient transitioned to a hypomanic state characterized by increased verbal output, heightened phone usage, overfamiliarity with ward occupants, and a notable increase in appetite, with specific food preferences and interests emerging. Given the patient's swift transition into hypomania, the administration of steroids was halted, and her asthma management was adjusted to rely solely on nebulization treatments. Subsequent evaluations of her liver function tests (LFTs), thyroid function tests (TFTs), and electrocardiogram (ECG) preceded the initiation of Lithium at 400mg and an increase in Sodium Valproate dosage to 1200mg. Despite these adjustments, her elevated mood persisted, leading to an increase in Lithium dosage to 800mg, post verification of serum lithium levels. Tragically, within a fortnight, the patient's maternal uncle's suicide precipitated a depressive episode, necessitating grief therapy alongside an uptitration of Lithium to 800mg and an increase in Escitalopram to 20mg.

Managing the patient's condition proved particularly challenging due to her comorbid bronchial asthma, which flared up during the course of her psychiatric treatment. Adjusting the dosages of antidepressants, mood stabilizers, and oral steroids to achieve remission while contending with exacerbations of asthma highlighted the complexities of treating patients with concurrent psychiatric and medical conditions.

DISCUSSION

Our clinical scenario highlights a significant association between sodium valproate use and the onset of hypertension in younger patients. The most striking finding from our case report was the onset of hypertension within 2-3 days of initiating sodium valproate. BP levels were noticed to be on a rising trend, and after ruling out medical causes, the patient showed a positive response to the prescribed anti-manic medications. On tapering sodium valproate, a decrease in BP was observed on serial monitoring of BP values without the need for antihypertensives. This observation aligns with global data on disease burden, emphasizing the need for a comprehensive approach to managing psychiatric and physical health in patients . Further investigation into the nephroprotective effects of certain compounds could inform future research on minimizing adverse effects in psychiatric treatment [10].

The role of long-chain non-coding RNAs in the pathogenesis of diseases, including breast cancer, underscores the complexity of drug interactions and the potential for unforeseen physiological outcomes in psychiatric care. Similarly, understanding the immune modulation by parasites such as Blastocystis sp. may provide insights into managing immune responses in patients on psychotropic medications. It is important to note that this report is based on a single case, which inherently limits the generalizability of the findings. Larger, controlled studies are essential to better understand the relationship between sodium valproate and hypertension, particularly in younger populations [1].

Additionally, the absence of long-term follow-up data in this case limits our ability to assess the ongoing effects of sodium valproate after the resolution of hypertension. Future research should include longer monitoring periods to determine whether the hypertension induced by sodium valproate is a transient phenomenon or if there are persistent risks [1, 2]. The necessity of extended monitoring in clinical settings is also highlighted by the growing understanding of long-term side effects associated with various psychotropic medications [1, 2]. The importance of personalized medicine in psychiatry is also underscored by this case. Given the variability in individual responses to psychotropic medications, clinicians should consider genetic, metabolic, and environmental factors when prescribing sodium valproate. Pharmacogenetic testing, where available, might help identify patients at risk for adverse cardiovascular effects, allowing for more tailored treatment approaches. Similarly, there have been previous case reports indicating sodium valproate-induced hypertension in young patients [1]. Our findings from this case further reinforce the existing literature, suggesting a strong relationship between sodium valproate and elevated blood pressure in young individuals. However, these findings must be interpreted with caution, and further research is needed to clarify the mechanisms underlying this association and to develop guidelines for monitoring and managing blood pressure in patients treated with sodium valproate.

CONCLUSION

This case highlights the potential for sodium valproate to induce hypertension in young patients treated for manic symptoms. The rapid rise in blood pressure following valproate initiation and its normalization upon tapering the medication highlights the need for careful monitoring of blood pressure in these patients. This case report adds to the burgeoning evidence of the cardiovascular side effects of psychotropic drugs, particularly sodium valproate-induced hypertension. Our findings emphasize the importance of vigilance in managing the cardiovascular side effects of sodium valproate.

Ethical Considerations: The study was conducted with a commitment to upholding ethical principles, ensuring patient confidentiality and informed consent at all times. Approval was sought and obtained from the institutional review board (IRB) IEC-Reference number 028/12/2023/IEC/SMCH affirming compliance with the required ethical standards for conducting this research.

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REFERENCES

1. Abosi O, Lopes S, Schmitz S, Fiedorowicz JG. Cardiometabolic effects of psychotropic medications. Horm Mol Biol Clin Investig. 2018;36(1). Available from: https://www.degruyter.com/document/doi/10.1515/hmbci-2017-0065/html. doi: 10.1515/hmbci-2017-0065
2. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024;403(10440):2133-2161. doi: 10.1016/S0140-6736(24)00757-8.
3. Subramaniyan V, Shaik S, Bag A, Manavalan G, Chandiran S. Potential action of Rumex vesicarius (L.) against potassium dichromate and gentamicin induced nephrotoxicity in experimental rats. Pak J Pharm Sci. 2018;31(2):509-516.
4. GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):2100-2132. doi: 10.1016/S0140-6736(24)00367-2.
5. Gupta G, Hussain MS, Thapa R, Dahiya R, Mahapatra DK, Bhat AA, Singla N, Subramaniyan V, Rawat S, Jakhmola V, S R, Dua K. Hope on the horizon: Wharton's jelly mesenchymal stem cells in the fight against COVID-19. Regen Med. 2023;18(9):675-678. doi: 10.2217/rme-2023-0077.