



PHENYTOIN INDUCED PARKINSONISM: A RARE CASE REPORT

Shaik Kareemulla¹, Chandana T.*², A. V. Kavyasree³ and M. Prashanth⁴

¹Assistant Professor, Department of Pharmacy Practice, P. Rami Reddy Memorial College of Pharmacy (PRRMCP), Kadapa.

^{2,3,4}Pharm.D Interns, P. Rami Reddy Memorial College of Pharmacy (PRRMCP).

*Corresponding Author: Chandana T.

Pharm.D Interns, P. Rami Reddy Memorial College of Pharmacy (PRRMCP).

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ABSTRACT

Anti-epileptic drugs cause diverse adverse effects of cognitive impairment, skin reactions and teratogenic effects of offspring in pregnant population and metabolic alterations due to enzyme induction. Majority of these reactions are being reported and extensively monitored for better patient compliance. In contrast the motor adverse effects of AEDs' have not become recognised as a serious adverse event of AEDs'. Drug Induced Parkinsonism is one among the motor disorders that are caused by chronic usage of AEDs'. An elaborated literature search had disclosed that very few reports of phenytoin induced Parkinsonism were published and in this scarcity, we report a case of 26 year old male patient who developed Parkinsonism after chronic treatment with phenytoin. After discontinuation of the culprit drug the symptoms were improved and another AED was added to the regimen.

KEYWORDS: AED, DIP, Movement Disorders, Parkinson Disorder (PD).

INTRODUCTION

Anti-Epileptic Drugs are used in the management of different forms of epilepsies. Phenytoin, first identified to have anti-seizure activity and is the oldest non-sedating drug used in the treatment of epilepsy. It is prescribed for the prevention of focal seizures and generalized tonic-clonic seizures and for the acute treatment of status epilepticus.^[1] Phenytoin limits the repetitive firing of action potentials evoked by a sustained depolarization. This effect is mediated by a slowing of the rate of recovery of voltage-activated Na⁺ channels from inactivation. At therapeutic concentrations, the effects on Na⁺ channels are selective, without changes in spontaneous activity or in responses to GABA or glutamate.^[2] In spite of its widest indications this drug causes many adverse reactions of major organ systems including hepatic system, nervous system and metabolic alterations of essential elements in the body.^[3] Phenytoin can also causes movement motor disorders like dyskinesia, bradykinesia, Drug Induced Parkinsonism and tardive dyskinesia. The *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-V), defines DIP as the presence of resting tremor, muscular rigidity, akinesia, or bradykinesia, developing within a few weeks of starting or raising the dosage of a medication (typically a neuroleptic) or after reducing the dosage of an antiparkinsonian agent.^[4]

CASE REPORT

A 26 year old male patient was admitted in the psychiatry inpatient department with complaints of stiffening of fingers, jerk like movements of upper and lower limbs and slowness of his movements. While focusing on his past medical history he was a known case of Epileptic disorder from the age of 10 years, for which he was being prescribed with Tablet Phenytoin 100mg as prophylactic therapy. He did not have family history of any neurological disabilities.

On Physical examination, dystonic posturing of the trunk to the right side while standing was observed, excess drooling was noticed and the patient was unable to stand. Other systems examination was done and nothing remarkable found. His laboratory findings of complete blood picture, liver profile, renal profile, urinalysis and electrocardiogram were in the normal limits. Patient care taker interview was taken as patient was not able to talk fluently, and it revealed since two years gradually all these symptoms were exposed and even deteriorated to DIP.

Currently he was diagnosed as Drug Induced Parkinsonism and following the deranged report and past medical history, and the tablet phenytoin was replaced with another AED Divalproex 750mg. Along with the anti-epileptic therapy, fluid therapy and vitamines supplementation were added to the regimen. The length

of hospital stay was two weeks and keen follow-up was done for six months.

DISCUSSION

DIP is the second most cause of Parkinson's Disorder^[5] as the primary PD is idiopathic in mechanism and at the beginning the well-known and widely accepted culprit of DIP is neuroleptic drug. But subsequently DIP is considered as complication of a number of other compounds including antiemetics, cholinomimetics, antidepressants, anti-vertigo medications, calcium channel antagonists, antiarrhythmics, and antiepileptic drugs.^[6] The prevalence of DIP cannot be exactly determined because most of them were indistinguishable from PD since the clinical manifestations of DIP are very similar to those of Parkinson's disease (PD), patients with DIP are frequently misdiagnosed as having PD, and it leads to false prevalence of DIP.^[7-9]

The hidden mechanism behind this phenytoin induced Parkinsonism is uncertain. However, the most widely accepted theory is that phenytoin blocks sodium channels, which can decrease the repetitive high-frequency firing of action potentials that is associated with epilepsy.^[10] They further hypothesized that phenytoin accumulate in the brain with extended administration and at supratherapeutic concentrations can decrease calcium influx and thus decrease neurotransmitter release from neurons; decrease calcium and calmodulin, thus impacting protein phosphorylation and second messenger pathways; prevent cyclic adenosine monophosphate increases; and increase GABA concentrations.^[10] Recent evidence suggests that at serum concentrations and in clinical practice, phenytoin does not modify GABA (both presynaptic and postsynaptic).^[11] Another suggestion is that it is due to oxidative stress and mitochondrial dysfunction.^[12] Phenytoin is also associated with a decrease in acetylcholinesterase activity.^[13] Evidence suggests that phenytoin may affect dopamine signalling because patients with Parkinson disease who have previously received phenytoin have a decreased response to LDOPA.^[14]

Risk factors for developing DIP are older age, female sex, previous brain injury or dementia, early extrapyramidal symptoms, and African and African American race and Coexistence of tardive dyskinesia.^[15] Clues that might suggest DIP includes Sub acute bilateral onset and progression of symptoms time-locked with medication intake, Early presence of postural tremor.^[16] DIP is generally treated by cessation of the offending drugs. Patients who cannot stop taking antipsychotic drugs because of their psychiatric diseases, such as those with schizophrenia or major depressive disorders, may be switched to atypical antipsychotics that have a lower risk of EPS.^[17] There are many reports of phenytoin induced movement disorders for instance orofacial dyskinesia, Parkinsonism and tics. All other anti-

epileptic drugs are also associated with these motor adverse effects.

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