

Case Report

An Adverse Drug Interaction of Haloperidol with Levodopa

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ABSTRACT

Drug interactions are known to play a significant role in the incidence of adverse drug reactions (ADRs) both in the community and in hospitals. Both the newer atypical antipsychotics and their more traditional counterparts are subject to drug — drug interactions amongst themselves, with other psychotropics, and with the agents used in the treatment of various physical ailments. The most common interactions encountered in clinical practice are pharmacodynamic in nature. It is well established that antipsychotic drugs reduce the efficacy of levodopa in parkinson's disease by blockade of dopamine receptors in the corpus striatum. The case reported here illustrates a common pharmacodynamic drug interaction of haloperidol with levodopa in a 60-year-old female patient.

Key words: Adverse drug interaction, haloperidol, levodopa, parkinsonism

INTRODUCTION

The vast increase in the number of new psychopharmacologic agents has made more therapeutic options available, but has also complicated patient treatment. Combination therapy used in psychiatric practice makes drug interactions more likely and increases the risk of adverse outcomes to the patients.^[1] There are numerous known interactions involving psychotropic drugs. Many interactions have minor clinical significance; however, there are many potentially hazardous interactions that should always be considered.^[2] The significance of a drug interaction can also vary between individuals, depending on

factors such as co-morbidities, gender, and age.^[3] According to a recently published study, psychiatric medications can account for up to 50% of the adverse drug reactions (ADRs) for hospitalized patients with mental illness, many of which can be attributed to drug — drug interactions.^[4] ADRs resulting from drug — drug interactions leading to hospitalization are often preventable.^[5] It has been estimated that 26% of ADRs requiring hospital admissions may be due to drug — drug interactions.^[5] Haloperidol is a psychotropic drug of the butyrophenone family and is used for both chronic and short-term therapy.^[6] Parkinsonism is one of the most common Extrapyramidal side effects (EPS) of haloperidol. There are reports on drug — drug interactions of haloperidol with neuroleptics, drugs known to prolong the QT interval, and drugs known to cause electrolyte imbalance, and the interactions are pharmacodynamic in nature.^[2,6] It is well established that haloperidol may impair the antiparkinsonian effect of levodopa.^[2,6] We are reporting a case of drug interaction of haloperidol with levodopa in a parkinsonism patient.

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CASE REPORT

A 60-year-old female weighing 52 kg was admitted to the hospital with the complaints of excessive drooling, involuntary movements of upper and lower limbs, slurring of speech, and difficulty in walking with stiffness in arms and legs since 12 weeks. Ten years back, she was diagnosed to have parkinsonism disease and initiated on antiparkinsonian drugs. She was on tablet syndopa 110 mg TID and tablet trihexyphenidyl (THP) 1 mg TID for past 3 years. There was no past history of illicit substance or alcohol abuse. There was no family history of movement disorders.

Four months ago, she had consulted a local doctor for decreased sleep and headache and was prescribed tablet haloperidol 5 mg TID. After 4 weeks of initiation of haloperidol, her condition worsened. She increased the dose of syndopa and THP, but the symptoms persisted. Patient was receiving no other medication including over-the-counter medications. A month later, she visited our hospital and was admitted to the inpatient psychiatric unit with an additional diagnosis of neuroleptic-induced parkinsonism. On physical examination, she was found to have bradykinesia, lip smacking, flexed posture, and cogwheel rigidity. Findings from her routine blood work including complete blood cell count with differential and comprehensive metabolic profile were within normal limits. Based on literature search and detailed review of the patient medical history, haloperidol was suspected to be the causative agent for current episode in this patient and was replaced with tablet risperidone 1 mg BD. However, she continued to receive syndopa (110 BD) and THP (2 mg in the morning) during the remaining 11 days of her hospital stay.

Eight days after the withdrawal of haloperidol, her symptoms improved significantly. Three days later, she was discharged with tablet syndopa 110 BD, tablet THP 2 mg one in the morning and one in the noon, and tablet clonazepam 0.5 mg HS, and advice for review after 2 weeks.

DISCUSSION

A drug interaction occurs when the toxicity or effectiveness of a drug is altered by the concurrent administration of another drug. Drug interactions can be pharmacokinetic or pharmacodynamic in nature. A pharmacokinetic drug interaction occurs when a drug alters the absorption, distribution, metabolism, or excretion of another drug.^[7] Pharmacodynamic interactions occur when two drugs act on interrelated receptor sites, resulting in either additive or antagonistic effect.^[2,7] The prevalence of drug interactions is

largely unknown. Drug interactions have been documented to occur with many agents commonly used in conjunction with antipsychotics such as anticholinergics, anticonvulsants, antidepressants, anxiolytics, and lithium.^[2] It is widely recognized that neuroleptic drugs can induce a state of parkinsonism, a major adverse reaction attributed to antagonism at striatal dopamine receptors.^[8]

The temporal relationship between starting of haloperidol and progression of the patient's parkinsonian signs confirms that this clinical observation is very likely to be due to haloperidol. One explanation of our finding is the possibility of drug — drug interaction of haloperidol and levodopa. Haloperidol reduces the efficacy of levodopa in parkinson's disease by blockade of dopamine receptors in the corpus striatum.^[2,6] The result may be worsening motor function, a relapse of psychosis, or a combination of both. It usually occurs rapidly and is moderate in severity.

Another possibility is the mechanism by which haloperidol causes parkinsonism. Positron emission tomography (PET) studies have indicated that the therapeutic effects of antipsychotics are achieved at a blockade of 60-70% of dopamine receptors, and antipsychotic-induced parkinsonism (AIP) was observed at D2 occupancy of 34-80%.^[9-11] A greater affinity of conventional antipsychotics for dopamine D2 receptors may account for their increased risk of AIP. Several studies have reported that between 26% and 67% of patients using conventional antipsychotics develop AIP.^[10-14] The interval between initiation of antipsychotics and onset of AIP is highly variable, ranging from a few days to several months.^[11] In our case, onset was observed within 13 weeks of initiation of haloperidol. Although no rechallenge was attempted, the symptoms were improved after 11 days of cessation of haloperidol, which is suggestive of possible association between haloperidol and the current episode of patient condition.

Besides that, elderly people are more prone to develop adverse drug interactions because of their age-related changes in the pharmacokinetic and pharmacodynamic parameters.^[11,12] It is well documented that younger people tend to metabolize the drug faster than older people, and men faster than women.^[12] According to different studies, about 40% of elderly treated with conventional agents develop AIP.^[13,14]

In our patient, most likely, a combination of these factors, i.e. dopamine blocking, drug interaction, age, high dose of the drug, and gender, may have given rise to this episode of parkinsonism. The probability of a causal relationship between a potential drug interaction

and the event was “possible,” as assessed by Drug Interaction Probability Scale (DIPS). In practice, only a few of the possible drug interactions may be clinically relevant; the practitioner must still consider the critical factors associated with drug — drug interactions. Such factors include the potency and concentration of the drugs involved, the therapeutic index balanced between efficacy and toxicity, the presence of active metabolites, and the extent of the metabolism of the substrate drug.

CONCLUSION

It is imperative that all healthcare professionals working with older adult population should take a comprehensive medication history and do careful monitoring for identification, management, and prevention of negative clinical consequences. The influence of AIP on the quality of life of elderly patients should be evaluated. With the increase in the number and types of medications being prescribed for or used by patients, it is important to look at all medications, including over-the-counter ones.

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