# Levocetirizine Withdrawal anxiety: A Case Report

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***Abstract***

Levocetirizine, an antihistamine, is commonly prescribed for allergic conditions. The drug is often sold on an over the counter basis without any consideration of potential side effects or susceptibility to abuse. Here we present one such case who had withdrawal anxiety features after taking levocetirizine for a prolonged period which resolved after gradual tapering of levocetirizine under clonazepam coverage. Though second generation antihistamines do not cross the blood brain barrier and are believed to have no neurological effects, this case highlights the possibility that this may not be entirely true.

**Keywords**

Levocetirizine, antihistamine, anxiety, withdrawal

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## INTRODUCTION

Levocetirizine is the R-enantiomer of cetirizine and has similar pharmacokinetic and pharmacodynamic properties such as rapid onset of action, high bioavailability, high affinity for H1-receptor, limited distribution, minimal hepatic metabolism and minimal untoward effects.[1] As it does not cross the blood brain barrier and has no significant affinity for H3 receptors present in the central nervous system (CNS), levocetirizine is believed to have minimal neurological effects.[2] Contrary to this belief, a 10 year period of pharmacovigilance database of Food and Drug Administration (FDA) reports that almost 25% of the adverse drug reactions reported in pediatric population were psychiatric complaints. These included complaints such as psychomotor agitation, insomnia, hypersomnia, nightmares, depression and suicidal ideation.[3] All of these complaints were related to drug intake for few days. No such data was found for the adult population. Owing to its modest sedative effect, the therapeutic role of first generation antihistamines in insomnia has been explored. However the current guidelines do not recommend its use for insomnia due to very weak evidence and concerns about possible tolerance. No specific recommendation has been made for second generation antihistamines such as levocetirizine.[4] Here we present a case who after taking levocetirizine for a prolonged period started having anxiety features on trying to stop the medicine. An informed consent was obtained from the patient for publication of this report.

## CASE

A 41 years married, housewife presented to our outpatient services with complain of palpitation, restlessness and not able to sleep for 2 years. 10 years prior to presentation she had developed sore throat and runny nose. As the symptom didn't resolve after around a week she went to a local pharmacy and was given levocetirizine 5 mg which she continued taking since then. Around 4 years prior to presentation she developed palpitation, restlessness and decreased sleep and went to the same pharmacy where levocetirizine was increased to 10 mg. She did not seek any specialist consultation during this period. She was then maintaining well till around 2 years back when she was told by a friend that taking medicines for long term can damage vital organs. Since then she had been trying to stop levocetirizine repeatedly but was unsuccessful in these attempts. Each time she would start having palpitation, itching, apprehension and decreased sleep on the 2nd/3rd day of stopping medicine. However patient denied having other symptoms such as pruritus. These symptoms would resolve after restarting levocetirizine. There was no significant past or family history. Premorbid personality was well adjusted. Physical and mental state examination did not reveal any abnormality. Investigations including complete blood count, thyroid function test, blood sugar and vitamin D levels were within normal limits. Patient was then

diagnosed as levocetirizine withdrawal anxiety with a differential of independent anxiety disorder. Levocetirizine was reduced to 5 mg which was stopped in 14 days along with clonazepam 0.5 mg for 10 days then tapered to 0.25 mg and stopped in another 10 days. At a 2 week follow up patient had improved significantly with no complains. She has been maintaining well since then with two more follow ups each after 1 month of becoming premorbid. As the symptoms had a temporal relationship with reduction of levocetirizine dose and patient did not have a recurrence during drug free period a final diagnosis of levocetirizine withdrawal anxiety was made.

## DISCUSSION

Antihistamines work by blocking histamine receptors, which are G protein–coupled receptors. Four main receptor subtypes are known: H1, H2, H3, and H4, although additional non-H1 to H4 receptors have recently been described, with unclear functions. Among these, H3 receptors are found mainly in the central nervous system, especially in the basal ganglia, hippocampus, and cortical regions. Through presynaptic H3 receptors, histamine can regulate its own release via negative feedback and also suppress the release of other neurotransmitters, including dopamine, serotonin, and acetylcholine.[5] Elevated histamine levels have been linked to anxiety.[6] In the dorsal and ventral striatum, most H3 receptors are postsynaptic and closely associated with dopamine receptors. Their location and interaction with dopamine signaling suggest that histamine may contribute to the development and persistence of addictive behaviors.[7]

There have been case reports of abuse with first generation antihistamines such as diphenhydramine with an apparent link to antipsychotic use where patients claimed to have abused diphenhydramine for "feeling good" and stopping the tremors.[8,9] We did not come across any report on abuse of second generation antihistamine though there are reports of itching on sudden stoppage after prolonged use.[10] Since second generation antihistamines do not cross blood brain barrier, theoretically they have minimal neurological effects. However the FDA pharmacovigilance database says otherwise. Though those reported by FDA are ADRs related to short term drug intake, these do indicate that the commonly held belief of second generation antihistamines not having neurological effects may not be the truth. These three findings – levocetirizine having some neurological effects, presence of H3 receptors in CNS at sites commonly implicated in addictive disorder; and the complex interaction of histamine with dopamine – indicate that the propensity of antihistamines to cause dependence and withdrawal should not be neglected.

## CONCLUSION

Levocetirizine is a drug commonly used for allergic conditions, often without a prescription. There is limited information available about its neurological effects despite FDA making a call to be alert about such effects. Large scale prospective studies are required to properly understand such effects of levocetirizine.

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