

LEVOFLOXACIN INDUCED INSOMNIA**Mohammed Salim KT^{*a} and Nathaliya PM^a**^aPharm D Intern, Department of Pharmacy Practice, Al Shifa College of PharmacyArticle Received on
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Author****Mohammed Salim KT**Pharm D Intern,
Department of Pharmacy
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of Pharmacy**ABSTRACT**

Fluroquinolones can cause adverse neuropsychiatric side effect, which are more common in older age. We present three cases of levofloxacin which induced insomnia. In all cases immediate discontinuation lead to remission.

INTRODUCTION

Levofloxacin is a fluroquinolone which inhibit the enzyme DNA gyrase thereby interrupt the transcription or replication occurring with microbial infestation.^[1] Improved activity against Streptococcal pneumonia, essentially all H. influenzae and M. catarrhalis isolates (irrespective of penicillin susceptibility),^[1, 2] other gram positive and

gram negative bacteria when comparing with ofloxacin. 100% oral bioavailability as well as a single daily dose (500mg) sufficient enough to produced desired action, it is widely prescribed in General Medicine Department. Half-life is 8 hours. Community acquired pneumonia and exacerbations of chronic bronchitis are the main indication pertaining to the drug (87-96% cure rate). Sinusitis, pyelonephritis and skin/ soft tissue infection are also are benefited with the levofloxacin.

Levofloxacin has been considered to be safe, however side effects has been reported. CNS impairments such as headache, restlessness, anxiety, insomnia requires medical attention.^[1]

CASE REPORTS**CASE 1**

A 65 year old male patient was diagnosed with urinary tract infection. He was prescribed with levofloxacin 500 mg once daily at night. On the very first day he could not sleep throughout the night. He was feeling anxious for no reason and was in a highly irritable mood. The patient could not sleep on the next day morning also. Physician stopped

levofloxacin, once he was informed about the problems, after which the neuropsychiatric symptoms remitted. The same day night the patient had adequate and satisfactory sleep.

CASE 2

An 85 year old female patient was prescribed once daily dose of 500 mg levofloxacin after she was diagnosed with urinary tract infection. The patient did not fall asleep at night after the first dosing. She seemed to be irritated throughout the night. She could not sleep for the next day also. She consulted her physician the next day. He stopped levofloxacin, after which her neuropsychiatric symptoms remitted.

CASE 3

A 24 year old male patient who developed upper respiratory tract illness took levofloxacin 500 mg per day as per physician's advice. He did not get adequate sleep throughout the day and night for 2 days and had complaints of nocturnal awakening. He stopped levofloxacin after contacting his physician. There were no more complaints of sleeplessness or irritability after the stoppage of levofloxacin.

All the three patients were evaluated by the psychiatrist to rule out any primary psychiatric disorder. But no significant illness was found in past medical, family or social history. Moreover none of them took other medications along with levofloxacin.

DISCUSSION

Quinolones besides active against bacterial infection, it can produce ADRs that are related to Central Nervous System.^[3] Studies had shown cases of mania, insomnia, acute psychosis and delirium being reported by the patients. Apart from Levofloxacin, its congeners - Ciprofloxacin, Ofloxacin, and pefloxacin neurological and psychiatric adverse drug reactions according to literature.^[4] The side effects associated, has been found to prevail for a longer period.^[12]

In the brain, the affinity towards GABA (γ -amino butyric acid) receptors and its subsequent binding can relate CNS effects of quinolones. GABA is an inhibitory neurotransmitter of brain. Quinolones distort the normal binding of GABA with their receptors thereby increases CNS stimulation.^[5] The directly activating N-methyl-d-aspartate (NMDA) and adenosine receptors (excitatory pathways), associated with antagonism of inhibitory pathways (GABA), observable CNS symptoms are manifested. The above three case, their insomnia might be

associated with this mechanism.^[6,7] These mechanisms are even correlating with non-dopaminergic pathways of psychosis. It is even possible that the above-said cases might have progressed on to psychosis, if the full course of levofloxacin therapy was completed.^[8] The other interesting thing to be noted from above 3 cases is that, none of them had any CNS-related disorders. This is important because the previous literature available on fluoroquinolones suggest that neuropsychiatric adverse effects are frequently noted in people with CNS lesions.^[8, 10, 11]

In Case 1, levofloxacin had been withdrawn from the patient regimen which he consumed for a day. He was not provided with an alternative, taking into account the possibility of antibiotic resistance for a particular organism. Similarly, case 3 state that the patient distorted the course of the antibiotic after consuming them for two days. However, in case 2, the bactericidal / bacteriostatic activity produced by the drug to the spectrum of microorganism was compensated with cefoperazone and sulbactam.

CONCLUSION

Levofloxacin is prone to cause neuropsychiatric side effects. Some of the side effects like insomnia and anxiety go unnoticed many a times. So by presenting the above three cases, we like to emphasize on the following points.

1. Physicians and psychiatrists should be aware of neuropsychiatric side effects of levofloxacin. Although neuropsychiatric side effects of fluoroquinolones are more common in the elderly, they can also affect younger patients.
2. Stopping the drug in time may prevent the progress of nonspecific anxiety and insomnia to major psychiatric disorders like psychosis. Suddenly stopping a medicine refers to going from a full, regular dose one day to no dose of that medicine the next day. And not starting that medicine back up after that.
3. Although there are neuropsychiatric side effects mentioned as rare in the drug leaflet provided by the pharmaceutical companies, this case series and other reports from the literature indicate that neuropsychiatric side effects are relevant and require more systematic research on their prevalence.
4. The research should also look whether there is a dose relation between levofloxacin and side-effects.
5. There should also be a surveillance of the effect of combined prescriptions like NSAIDs, anti-histaminics, anti-tubercular drugs, etc with levofloxacin.

6. Cooperation of psychiatrists, pulmonologists, and general practitioners is required in further interdisciplinary research on neuropsychiatric side effects of levofloxacin and other fluoroquinolones.

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