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Case Report

Pharmacology Section

A Rare Instance of Levofloxacin Induced Myoclonus

SUSHIL KIRAN KUNDER[1], A. AVINASH[2], VEENA NAYAK[3], AMOD TILAK[4]

ABSTRACT

Levofloxacin is a widely used fluoroquinolone, mainly as a respiratory antimicrobial agent. It is employed as a second line therapeutic modality in pulmonary tuberculosis as well. The drug has been in use for ages, and is known to be both efficacious and safe. However, it is not free of adverse effects. The most dangerous ones are those involving the Central Nervous System (CNS). Although rare, levofloxacin can cause involuntary movements like chorea and myoclonus. Here by, we present a case of an elderly male patient who developed reversible myoclonus/chorea after a course of levofloxacin (which was initiated as part of his anti-tubercular therapy) following the development of peripheral neuropathy secondary to isoniazid.

Keywords: Chorea, Fluoroquinolones, Involuntary movements

CASE REPORT

An elderly man, 78-year-old (informed consent obtained from the patient), was admitted to the hospital, with complaints of difficulty in walking and brief shock like movements of all four limbs. The patient was a chronic smoker and alcoholic (for more than 40 years), with no prior comorbidities like diabetes mellitus, hypertension, renal issues or CNS disorders. Past history revealed that he had consulted doctors at other hospitals with complaints of cough with haemoptysis for which he was diagnosed to be a case of pulmonary tuberculosis and was initiated on 300 mg of isoniazid, 450 mg of rifampicin and 800 mg of ethambutol. Also, he was advised to continue this multidrug treatment for the next six months. However, after about a month, he developed numbness and tingling sensation, which was diagnosed to be peripheral neuropathy. As this peripheral neuropathy was suspected to be due to isoniazid, the drug was stopped and the patient was started on 500 mg of levofloxacin daily. Four days from the start of levofloxacin therapy, the patient had involuntary movements and on and off altered behaviour (clapping, hitting himself and altered speech). There was no history of loss of consciousness, urinary incontinence or burning sensation in the lower limbs. There was also no history of trauma, difficulty in swallowing or muscular pain.

On admission, a thorough workup was done. On CNS examination, the patient was alert and well oriented. The patient had involuntary movements, which were brief shock like and non rhythmic. He had a wide based gait. Laboratory investigations were done to rule out metabolic derangements as the cause. Routine blood counts (Hb: 9.3 g/dl, MCV: 88 fl), liver function tests (ALT: 46 IU/L, AST: 243 IU/L, ALP: 74 U/L), renal function tests (blood urea and serum creatinine within the normal range), blood sugars (Random blood sugar: 111 mg/dl) and serum electrolytes (Sodium: 141 mmol/L, Potassium: 4.8 mmol/l) were performed. No gross abnormalities were detected. The neurologist's opinion was obtained. He suspected this as a case of levofloxacin induced myoclonus/chorea. Levofloxacin was stopped immediately. The Fixed Dose Combination (FDC) of rifampicin and isoniazid was restarted, and ethambutol was continued. The patient was also started on oral diazepam 2 mg/day and oral pyridoxine 40 mg/day. Within three days of stopping the drug, and initiating the above mentioned intervention, there was significant reduction in the involuntary activity. A rechallenge test was not performed. The adverse event was reported through VigiFlow network to the pharmacovigilance programme. The patient was discharged, and there were no further episodes during his next follow up visit at one month following discharge.

DISCUSSION

Myoclonus is a sudden onset, brief episode of involuntary shock like movement caused due to muscle contractions. It can be due to metabolic derangements, neurodegeneration, infections of the central nervous system or due to drugs. Myoclonus can be reversible or irreversible. The most common cause for curable or reversible myoclonus is drug induced myoclonus. The common culprits among the drugs are cyclic antidepressants, bismuth salts, levodopa and serotonin reuptake inhibitors [1].

Fluoroquinolones are known to cause CNS adverse effects like delusions, hallucinations, dizziness, seizures etc., especially in the elderly, those with renal compromise or patients on concurrent non steroidal anti-inflammatory drugs or theophylline [2]. Levofloxacin has an oral bioavailability of almost 100%, which makes its oral dosage same as the intravenous dosage. It is chiefly excreted unchanged by the kidneys. It does not significantly affect the levels of theophylline, warfarin, cyclosporine or zidovudine, as does ciprofloxacin [3].

The patient in present case report had involuntary movements and behavioural abnormalities shortly after starting levofloxacin, which subsided on discontinuing the drug and starting the treatment with diazepam. In addition, the patient had no metabolic derangements or concomitant diseases. Also, the timing of the onset of chorea and myoclonus (a few days after starting the offending drug) strongly favours a temporal association.

Myoclonus and chorea due to treatment with levofloxacin have been cited previously. In the case report by Yasuda H et al., consisting of two cases, the patients were elderly (65 and 85 years) and one of them developed chorea/myoclonus on the 4th day after starting therapy with levofloxacin (as in our case). In addition, both of them improved when the offending drug was stopped, which is similar to the scenario in the present case report [4]. In a study done by Kalita J et al., rifampicin and levofloxacin were compared in terms

of efficacy and safety in patients with tuberculous meningitis. Three out of 60 patients developed myoclonus in the levofloxacin group, compared to none in the rifampicin group. However, it was not clear whether the myoclonus was due to levofloxacin or due to meningitis [5]. Lizarraga KJ et al., reported a case of levofloxacin induced reversible craniofacial dystonia in an elderly man aged 62 years, with end stage renal disease [6]. A common factor in the reports of Yasuda H et al., Lizarraga KJ et al., and our case report is that the movement disorders were seen in elderly patients. In addition, in our case, the patient had already developed peripheral neuropathy (secondary to the usage of isoniazid), which could probably denote the patient's susceptibility to neurological adverse effects [4,5].

The mechanisms to explain this adverse event are speculative. Levofloxacin induced CNS side effects are probably the result of excitation of NMDA receptors and inhibition of GABA-A receptors [7]. An alternative explanation would be triggering of the myoclonic generator [8]. Since our patient improved on treatment with diazepam, the most likely explanation is that levofloxacin caused GABA-A receptor inhibition, which improved on stopping the drug and starting therapy with diazepam, which is a positive allosteric modulator of GABA-A receptor.

CONCLUSION

In the clinical setup, levofloxacin is one of the most commonly used antibiotic, mainly for respiratory illnesses and enteric fever. Due to the drug's notoriety to cause CNS adverse effects like seizures, chorea and myoclonus, it is imperative for the clinician to have a watchful eye over any patient who is started on levofloxacin, particularly in the elderly population or those with a decline in renal function. Also, it is preferable not to coadminister drugs like NSAIDs and theophylline in such patients.

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PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.
2. Postgraduate, Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.
3. Associate Professor, Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.
4. Postgraduate, Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Veena Nayak,
Associate Professor, Department of Pharmacology, Kasturba Medical College,
Manipal University, Manipal-576104, Karnataka, India.
E-mail: veena.nayak@manipal.edu

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