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Case Report on Seizure with Co administration of Levofloxacin and Theophyline

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ABSTRACT

Case Summary: An 84-year-old man was admitted to the hospital due to seizure episodes. One week before the patient was admitted to the same hospital with complaints of COPD exacerbation and was discharged with a prescription of levofloxacin, theophylline ceftriaxone, pantoprazole, montelukast, methylprednisolone, budesonide nebulization, ipratropium bromide nebulization, and syrup codylex. After receiving one dose of oral levofloxacin, the patient experienced a seizure. The patient was hyperglycaemic at the time of admission and had no history of a seizure disorder.

Discussion: Here the cause of seizure could be a drug-drug interaction (between theophylline and levofloxacin) with CYP1A2 substrates with no epileptogenic effects which could augment the concentration of levofloxacin and consequently results in seizures. In spite of that, it has to be kept in mind that the drug-drug interactions originate at various pharmacodynamic and pharmacokinetic levels and that drugs CYP affinities are rarely completely CYP-specific. Thus levofloxacin may have drug interactions at the level of CYPs other than CYP1A2.

Conclusion: the clinicians are advised to closely monitor the possibility of seizures in COPD patients who+ are taking both levofloxacin and theophylline. The physicians should also be encouraged to use the techniques of TDM to individualize the dose of narrow therapeutic drugs to avoid serious adverse effects.

Key words:
Levofloxacin ,
Theophyline ,
Seizure.

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INTRODUCTION

An adverse drug reaction (ADR) is an unwanted, undesirable effect of a medication that occurs during usual clinical use. About 80% ADR reported in the clinical setting is due to type A ADR. Type A reactions are also known as augmented type of ADR. It is mainly dose dependent, pharmacological effect of drug. The main predisposing factors for this type A ADR is the age (geriatric and paediatric patients), poly pharmacy, chronic diseases like renal and hepatic dysfunction etc. In all these physiologic conditions the drug concentration in the body changes. This change in the drug concentration can shift the drug levels in the body to its toxic range and produce undesirable side effects which are attributed as a toxicological action of the drug. Thus this type of ADR can be avoidable and preventable in patients. Avoiding the combination of drugs which has higher chance of drug interactions, use of therapeutic drug monitoring (TDM) to fix dose of drugs are some of such measures by which we can avoid this excess burden of type A ADR. Here, we present the case of a patient with a probable drug- drug interaction between theophyline and levofloxacin, who had developed seizures after initiating treatment with levofloxacin and had no any past history of convulsions.

CASE REPORT

An 84 year old male patient was admitted to the hospital due to seizure episodes. The patient had a history of COPD infective exacerbation, Sepsis and Hyponatremia and was admitted to the same hospital one week before and discharged with a prescription of ceftriaxone, pantoprazole, levofloxacin, montelukast, theophylline,methylprednisolone,budesonide nebulisation ,ipratropium bromide nebulisation and syrup codylex.The next day morning the patient experienced two seizure episodes which last for about ten minutes. His medications at the time were levofloxacin 500mg/day orally, Inj.Ceftriaxone 1.125gm BD,Pantoprazole 40mg BD, orally,Theophylline 150mg BD orally,Methylprednisolone 4mg BD and nebulisation Budesonide and ipratropium bromide.When reached the hospital the patient was transferred to the intensive care unit for workup of his seizures.Levofloxacin was discontinued and the patient was started on Inj.lorazepam stat,Inj.Fosphenytoin 150mg BD,T.Levipil 500mg BD for seizure control as well as Inj.cefepime +tazobactam 1.125gm BD for his infection. At the time of admission, the patient was hyperglycaemic with RBS level of 222 mg/dl.Complete blood count showed white blood cells of 11900 cells/cmm with 84% neutrophils, 15% lymphocytes 1%eosinophills, haemoglobin 11.1gm/dl, ESR 91mm/hr. Sodium,Potassium,Creatinine and Blood urea was within the normal range.SPO2 was 99%with O2.No further seizure activity was reported and he was discharged after 5 days in the hospital.

DISCUSSION AND CONCLUSION

From our literature survey, the convulsion reported by the patient could be due to the effect of theophyline and levofloxacin. Levofloxacin is one of the new fluoroquinolones which has been extensively prescribed based on its tolerability.

In a recent study, it was reported that levofloxacin is the safest among all other fuoroquinolones with an adverse drug reaction rate of 2%.Adverse effects involving the CNS are rare and includes insomnia, headache, agitation and dizziness. The most infrequent but a serious concern is the appearance of convulsions. A recent study stated that levofloxacin is the safest medication in its class with an adverse drug reaction rate of 2%.In fact,levofloxacin can readily crosses the blood brain barrier,thus its effects in the CNS can be rapidly observed. AlfredoBellon et al in their study stated that seizures appeared only 5hrs after the initial levofloxacin dose. In the similar way, the study done by Christie MJ et al reported levofloxacin induced seizures merely 7 hrs after the first dose.In contrast, the study done by Bird et al and Kushner et al reported convulsions some days after starting this antibiotic.The mechanism by which levofloxacin induce seizures remains poorly understood. It has been related to the ability of these antimicrobial to either antagonize the inhibitory effect of gamma-amino butyric acid(GABA) or to its capacity to activate the N-methyl-D-aspartate(NMDA) receptors. Mostlikely,the epileptogenic properties arise from a combination of both mechanisms. Previous reports have suggested that elderly and patients with decreased renal function are at higher risk.

theophyline can also be a suspected cause for inducing seizures. The epileptogenic property of theophyline could be attributed to the narrow therapeutic index of the drug. Patients with chronic pulmonary diseases tend to show raised levels of endorphin in their central nervous system. This raised level of endorphin renders the patients suspectable to the epileptogenic property of theophyline. While assessing this particular case it can be concluded that one although both drugs individually have epileptogenic property. The higher probability of the occurrence of the convulsion could be a manifestation of the drug- drug interaction occurred in the patient. Here the cause of seizure could be a drug –drug interaction (between theophyline and levofloxacin) with CYP1A2 substrates with no epileptogenic effects which could augment the concentration of levofloxacin and consequently results in seizures.Inspite of that it has to be kept in mind that the drug-drug interactions originate at various pharmacodynamic and pharmacokinetic levels and that drugs CYP affinities are rarely completely CYP-specific. Thuslevofloxacin may have drug interactions at the level of CYPs other than CYP1A2. To conclude the clinicians are advised to closely monitor the possibility of seizures in COPD patients who are taking both levofloxacin and theophyline. The physicians should also be encouraged to use the techniques of TDM to individualise the dose of narrow therapeutic drugs to avoid serious adverse effects

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CONFLICT OF INTEREST: Nil

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