

High Dose Ofloxacin-induced Bimodal Hallucinations in a 4 Years Old Child

Arnab Bhattacharya¹, Rajiv Sharan², Samir Kumar Praharaj³

Departments of ¹Psychiatry and ²Pediatrics, Tata Motors Hospital, Jamshedpur, ³Department of Psychiatry, Kasturba Medical College, Manipal, Udupi, India

Ofloxacin is a commonly used quinolone antibiotic both in adults as well as children. It is generally safe and well tolerated. Rarely, neurological and psychiatric adverse reactions are reported to occur with ofloxacin. We report a case of a child who developed delirium after ofloxacin treatment, that resolved after medication discontinuation and treatment with low dose olanzapine.

KEY WORDS: Ofloxacin; Hallucinations; Psychotic disorders; Delirium.

INTRODUCTION

Ofloxacin is a popular fluoroquinolone medication used in adults as well as children. Clinical trials with orally and intravenously administered ofloxacin have confirmed its potential for use for a wide variety of infections, where it has generally proved as effective as other standard treatments. The molecule acts by binding the topoisomerase of the bacteria and is generally well tolerated in comparison with other available fluoroquinolones is less likely to cause clinically relevant drug interactions.^{1,2} We report a case of a child who developed delirium after ofloxacin treatment, that resolved after medication discontinuation and treatment with antipsychotics.

CASE

A four-year-old girl weighing 24 kg presented with fever, vomiting and bouts of loose motion. She was admitted and treated for acute gastroenteritis with intravenous fluids, injection ofloxacin 70 mg twice daily and injection ondansetron 2 mg single dose. Blood investigations including serum electrolytes were normal. She was discharged on third day after clinical improvement with oral ofloxacin 400 mg, 1/4 tablet twice daily and asked to fol-

low up after two days.

A day later her parents brought her to the emergency department reporting that she had begun to see snakes in her room and felt ants crawling up her arms which she brushed off. She commented that her father had a helicopter in his hand and was putting it in a bag. She reported that strangers were standing in the room and looking at her. On clarification during psychiatry consultation, it was found that inadvertently she had been given full tablet of ofloxacin twice daily instead of the quarter tablet (thus she received 800 mg/day instead of the prescribed 200 mg/day). There was no past or family history of any psychiatric disorder or major medical illness.

Mental status examination showed a well kempt girl with ill sustained eye contact who clung to her mother, poor attention, occasional muttering and looking frequently at the ceiling of the examination room with an anxious affect. A diagnosis of ofloxacin-induced delirium was considered and the medication was stopped. She was started on olanzapine 2.5 mg per day. Her psychotic features subsided completely within the next 72 hours and the antipsychotic was tapered off in two weeks. She remains well with no recurrence two months later.

DISCUSSION

Our patient developed a bimodal hallucinatory psychosis (tactile and visual hallucinations) after ofloxacin therapy. The first mention of such side effects was in two patients developing psychosis after exposure to ofloxacin.³ Both were adult females (one was elderly), and both had

Received: April 18, 2016 / **Revised:** August 5, 2016

Accepted: October 10, 2016

Address for correspondence: Samir Kumar Praharaj, MBBS, MD, DPM

Department of Psychiatry, Kasturba Medical College, Manipal, Udupi, Karnataka 576104, India

Tel: +91-8971026304, Fax: +91-820-2571930

E-mail: samirpsyche@yahoo.co.in

© This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

thyroid disorder which can predispose to psychosis. Also, the elderly patient had a past history of mood disorder and urinary stones needing antispasmodics and analgesics; thus being vulnerable to develop psychiatric symptoms. Another report cites a 5 year old child developing visual hallucinations in response to ofloxacin.⁴⁾ She was suffering from organic cerebral disorder (epilepsy) and had taken ornidazole in addition to ofloxacin for diarrhoea, hence it may be difficult to ascertain as to which of the two medications had caused the psychosis. Similarly, in the report by Koul *et al.*,⁵⁾ the patient received a combination of ofloxacin and metronidazole. In our case, there was no underlying psychiatric or neurological disorder, and the child received ofloxacin monotherapy, making it likely that ofloxacin was the agent involved in producing such an adverse reaction. However, the poor attention span along with psychotic symptoms raises the possibility of delirium associated with ofloxacin toxicity. Delirium has been reported with ofloxacin use previously⁶⁾; which is clinically distinguishable from acute psychosis if 'attention impairment' or 'confusion' is present. A Naranjo algorithm score of 8 was obtained which implied a probable drug related causation of the phenomenon.⁷⁾ The psychotic symptoms resolved within 3 days with low dose of olanzapine treatment.

Psychosis is not only reported to occur with ofloxacin, but also with other fluoroquinolones such as ciprofloxacin, levofloxacin, norfloxacin and gatifloxacin,^{8,9)} which suggests a class effect, i.e. fluoroquinolone-induced psychosis. Similarly, delirium is also associated with fluoroquinolones other than ofloxacin, such as levofloxacin,^{10,11)} gatifloxacin¹²⁾ and ciprofloxacin.¹³⁾ Specifically, ciprofloxacin, ofloxacin and pefloxacin were the quinolones with more neurological and psychiatric adverse reactions reported in the literature.⁹⁾ In a systematic review by Mostafa and Miller,¹⁴⁾ fluoroquinolones, penicillins and trimethoprim-sulfamethoxazole were the three classes of antibiotics that were associated with acute psychosis. The mechanism of a fluoroquinolone-induced psychosis could involve the upregulation of glutamatergic transmission in the brain via NMDA receptor involvement.¹⁰⁾ There is also speculation that inhibition of GABA binding to the GABA-A receptors may result in stimulation of the central nervous system,¹⁵⁾ which has been found in electroencephalographic studies of volunteers taking ofloxacin.

Ofloxacin has a serum/plasma ratio of 47% to 87%, and at therapeutic doses the serum levels are inadequate to produce cerebrospinal fluid (CSF) concentrations needed for the adverse effects to occur.¹⁶⁾ In our case 800 mg of ofloxacin was suprathereapeutic for a 4 year old child and it is possible that sufficiently high CSF levels were attained leading to development of delirium. In conclusion, prescribers need to be aware of the possibility of the frequently used drug, ofloxacin to produce delirium or acute psychotic symptoms, specifically at higher doses in children, and the need for appropriate psychiatric intervention.

REFERENCES

1. Lipsky BA, Baker CA. *Fluoroquinolone toxicity profiles: a review focusing on newer agents. Clin Infect Dis* 1999;28:352-364.
2. Todd PA, Faulds D. *Ofloxacin. A reappraisal of its antimicrobial activity, pharmacology and therapeutic use. Drugs* 1991;42:825-876.
3. Zaudig M, von Bose M. *Ofloxacin-induced psychosis. Br J Psychiatry* 1987;151:563-564.
4. Chauhan U, Shanbag P, Kashid P. *Ofloxacin-induced hallucinations. Indian J Pharmacol* 2013;45:189-190.
5. Koul S, Bhan-Kotwal S, Jenkins HS, Carmaci CD. *Organic psychosis induced by ofloxacin and metronidazole. Br J Hosp Med (Lond)* 2009;70:236-237.
6. Fennig S, Mauas L. *Ofloxacin-induced delirium. J Clin Psychiatry* 1992;53:137-138.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* *A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther* 1981;30:239-245.
8. Ranjan A, Praharaj SK. *Ciprofloxacin-induced psychosis. J Neuropsychiatry Clin Neurosci* 2014;26:E36-E37.
9. Tomé AM, Filipe A. *Quinolones: review of psychiatric and neurological adverse reactions. Drug Saf* 2011;34:465-488.
10. Kiangkitiwan B, Doppalapudi A, Fonder M, Solberg K, Bohner B. *Levofloxacin-induced delirium with psychotic features. Gen Hosp Psychiatry* 2008;30:381-383.
11. Slobodin G, Elias N, Zaygraikin N, Sheikh-Ahmad M, Sabetay S, Weller B, *et al.* *Levofloxacin-induced delirium. Neurol Sci* 2009;30:159-161.
12. Jay GT, Fitzgerald JM. *Ciprofloxacin-induced delirium. Ann Pharmacother* 1997;31:252.
13. Sumner CL, Elliott RL. *Delirium associated with gatifloxacin. Psychosomatics* 2003;44:85-86.
14. Mostafa S, Miller BJ. *Antibiotic-associated psychosis during treatment of urinary tract infections: a systematic review. J Clin Psychopharmacol* 2014;34:483-490.
15. Domagala JM. *Structure-activity and structure-side-effect relationships for the quinolone antibacterials. J Antimicrob Chemother* 1994;33:685-706.
16. Unsel E, Ziegler G, Gemeinhardt A, Janssen U, Klotz U. *Possible interaction of fluoroquinolones with the benzodiazepine-GABA_A-receptor complex. Br J Clin Pharmacol* 1990;30:63-70.