Ulutas Med J 2018;4(1):53-63
DOI: 10.5455/umj.20180207122003

CASE REPORT / LITERATURE REVIEW OPEN ACCESS

Fluoroquinolone Induced Movement Disorders: Case Report and Literature Review

Duane Bates[1] ▪ Jenny Edwards[1] ▪ Justin Chow[2] ▪ Michael Fisher[3] ▪ Christine Morris[1] ▪ Aaron Switzer[4]

[1] Pharmacy Department, Peter Lougheed Center, Alberta Health Services, Calgary Alberta, Canada
[2] Internal Medicine Resident, University of Calgary, Calgary, Alberta, Canada
[3] Clinical Assistant Professor, University of Calgary, General Internal Medicine, Calgary Alberta, Canada
[4] Medical Student, University of Calgary, Calgary, Alberta, Canada

Background: Movement disorders are a very rare adverse effect of fluoroquinolones. The mechanism involves inhibition of GABA-A-receptors as well as activation of the excitatory NMDA receptors. This is thought to induce a hyper excitable neuronal state. A literature review suggests this is a class effect and occurs shortly after initiation and resolves within a few days of discontinuation.

Case Presentation: A 62-year-old man with Campylobacter jejuni was treated with levofloxacin. The patient had normal liver enzymes and serum creatinine. Two hours after the initial dose of levofloxacin it was noted that the patient's neck would shake and turn to the left and his right arm would abduct at the shoulder and flex at the elbow. The movements would occur every 1 to 2 minutes. There were muscle fasciculation's in the bicep and forearm of the right arm briefly after the neck movement. The patient was given diphenhydramine 25 mg IV x 1 dose and within 20 minutes there was a reduction in the abnormal movements. Within 24 hours the movement disorder had completely resolved.

Conclusion: The case presented and literature review summarizes the data on fluoroquinolone induced movement disorders.

Keywords: Fluoroquinolone, levofloxacin, movement disorder, motor dysfunction

Introduction

Fluoroquinolone antibiotics are commonly prescribed due to their broad spectrum of activity, excellent oral bioavailability and well tolerated side effect profile. However, a wide range of central nervous system (CNS) effects have been reported with an estimated incidence of 1-2% in patients taking fluoroquinolones (1-3). Neurotoxic manifestations have included psychosis, seizures, encephalopathy, myoclonus, ataxia, dysarthria, chorea and oral facial dyskinesia. We report a case of levofloxacin induced myoclonus and review the literature on fluoroquinolone induced movement disorders.

Corresponding Author: Duane Bates; Clinical Pharmacist Alberta Health Services, Peter Lougheed Center, 2500 26th Ave NE, Calgary, AB, Canada
E-mail: duane.bates@ahs.ca
Received: Jul 11, 2017 **Accepted**: Dec 17, 2017
Published: March 29, 2018

Case Presentation

A 62-year-old male presented to the emergency department with a 1 week history of poor oral intake, nausea, vomiting, bloody diarrhea and decreased urine output. The patient gave informed consent for publication of this case report. His past medical history included chronic obstructive pulmonary disease (COPD), hypertension, stroke, gastroesophageal reflux disease, constipation, chronic back pain, anxiety and remote stomach surgery twenty-five years prior to admission. He was an ex-smoker (56 pack/year) and drank approximately 8 beers per month. Medications prior to admission included: docusate 100 mg at the bedtime, candesartan 16 mg daily, pantoprazole 40 mg daily, tiotropium 18 mcg daily, budesonide 200 mcg/formoterol 6 mcg 2 puffs twice daily, lorazepam 0.5 mg twice daily and as needed, morphine sustained release 20 mg twice daily, morphine immediate release 5 mg twice daily as needed, salbutamol 100 mcg 2 puffs every 4 hours as needed, ipratropium 500 mcg/salbutamol 2.5 mg twice daily as needed, dimenhydrinate 50 mg daily as needed, ondansetron 8 mg every 8 hours as needed, and PEG 3350 2 tablespoons daily as needed. The patient denied any regular use of other over counter medications, herbal medications, natural health products or traditional medications. There were no medication changes in the last 3 months The allergy history was later confirmed to only include doxycycline which caused throat swelling. The patient had received numerous courses of levofloxacin in the past for acute exacerbations of COPD with no history of neurological adverse events.

Vitals on admission included: blood pressure 86/49 mmHg, heart rate 96 beats per minute, temperature 37.8°C, respiratory rate 20 breaths per minute and oxygen saturation 98% on 3 liters per minute of oxygen. On exam, the patient was drowsy, frail and cachectic with dry mucous membranes. A digital rectal exam revealed hemorrhoids and bright red blood. The remainder of the physical examination was unremarkable. Laboratory tests on admission included hemoglobin 117 (normal range 137-180 g/L), platelet count 292 × 109/L (normal range 150 × 109 /L-400 × 109/L), white blood cell count (WBC) 9.7 × 109/L (normal range 4 × 109/L-11 × 109/L), international normalized ratio (INR) 1 (normal range 0.9–1.1), serum potassium 5.6 mmol/L (normal range 3.3-5.1 mmol/L), serum magnesium 0.98 (normal range 0.65-1.05 mmol/L), serum creatinine 540 umol/L (normal range 50-120 umol/L), noting a serum creatinine of 56 umol/L 3 weeks prior to admission. Urea 44.4 (normal range 3-9 mmol/L), fractional excretion of sodium 0.05% (FENa <1% usually indicates a prerenal state such as dehydration or other forms of prerenal azotemia), corrected calcium 1.78 mmol/L (normal range 2.10-2.55 mmol/L), serum phosphate 2.66 mmol/L (normal range 0.8-1.5 mmol/L), and venous blood gas demonstrating a severe anion gap metabolic acidosis with a pH 7.05 (normal range 7.3-7.4), anion gap 23 mmol/L (normal range 4-16 mmol/L) and a normal lactate. The patients other investigations including liver enzymes, electrocardiogram, chest x-ray and abdominal plain film were largely unremarkable except for urinalysis which showed marked pyuria and hematuria in the absence of signs/symptoms of a urinary tract infection.

The patient was empirically treated with ceftriaxone 2 g IV daily for suspected sepsis as well as crystalloid for fluid resuscitation. He also received 100 mmol of IV sodium bicarbonate

8.4% and potassium was shifted with dextrose 50% and 10 units of regular insulin. Hypocalcemia has corrected with calcium gluconate 1 gram IV x 2 doses as he was symptomatic with clonus and myoclonic jerks. Candesartan, morphine, docusate, lorazepam, and PEG 3350 were held on admission.

On day 2, an ultrasound of the kidneys and bladder did not suggest hydronephrosis. Final report of the urine culture showed no growth. Calcium carbonate 800 mg elemental calcium twice daily and cholecalciferol 2000 units daily were started. Serum phosphate had decreased to 1.81 mmol/L. The patient received hydromorphone 1mg IV x 1 dose for pain.

On day 3, serum creatinine and phosphate had decreased to 91 umol/L and 0.88 mmol/L respectively. The ceftriaxone was discontinued as no infectious source was identified. Serum magnesium was 0.76 mmol/L and corrected calcium had increased to 2.53 mmol/L. The patient was complaining of chronic back pain, severe abdominal pain and nausea. The patient was prescribed hydromorphone 1 mg IV every 6 hours as needed (he was receiving 3-4 doses daily) & dimenhydrinate 50 mg IV every 4 hours and ondansetron 4-8 mg IV every 6 hours.

On day 4, ova and parasite, Clostridium difficile antigen test was negative but, stool culture was positive for Campylobacter jejuni. The patient has prescribed levofloxacin 500 mg orally daily x 3 doses as there was an allergy to clarithromycin with a reaction of throat swelling documented on the hospital chart. Two hours after the initial dose of levofloxacin it was noted that the patient's neck would shake and turn to the left and his right arm would abduct at the shoulder and flex at the elbow. The movements would occur every 1 to 2 minutes. There was muscle fasciculation's in the bicep and forearm of the right arm briefly after neck movement. A neurological exam was completed and revealed normal muscle tone in the upper and lower extremities, no promotor drift or tremor and no clonus in the ankles. The patient was given diphenhydramine 25 mg IV x 1 dose and within 20 minutes there was a reduction in the abnormal movements. The levofloxacin was discontinued and replaced with clindamycin 300 mg orally 4 times daily x 2 days. On day 5 the allergies were clarified with the patient's family doctor and community pharmacy and there was no allergy to clarithromycin. Regardless, the antibiotic was not changed and the patient completed the course of clindamycin. The movement disorder had completely resolved.

On day 8, the dimenhydrinate was stopped. The patient was still having diarrhea (up to 11 bowel movements daily). Day 9 patient was started back on his home dose of morphine. Computed tomography (CT) of the abdomen and pelvis was completed for ongoing abdominal and pelvic pain, nausea and vomiting, and perfuse watery diarrhea but, no abnormal pathology was identified. On day 10 the diarrhea and nausea had improved and ondansetron was discontinued. The patient was discharged and continued all previous home medications after discharge except for docusate, PEG 3350 and lorazepam.

Discussion

Hypocalcemia and morphine accumulation were the most likely causes of the initial presentation of myoclonus and myoclonic jerks. Calcium plays an important role in the propagation of neuromuscular activity but, the serum calcium was corrected prior to levofloxacin administration (4). Twenty to 40% or

oral morphine is absorbed with the majority of clearance by hepatic glucuronidation as morphine-3-glucuronide (50%) and morphine-6-glucuronide (M6G) (5 to 15%). Only M6G is active. Ninety percent of metabolites and free drug undergo renal excretion(5). Advanced age, high doses of opioids, rapid increases in opioid dose and renal failure are risk factors for morphine accumulation resulting in myoclonus (6). The only risk factor present in our patient was acute kidney injury with a 10 fold increase in serum creatinine from baseline. The patient had received 1 dose of hydromorphone and no morphine in the first 2 days and serum creatinine had returned to normal suggesting opioid accumulation was not a factor on the day of levofloxacin administration.

Campylobacter infection has been associated with neurological adverse effects. Guillain-Barre syndrome is an uncommon consequence of Campylobacter jejuni (estimated at 1case per 2000 infections) but usually occurs 2-3 weeks after diarrheal illness (7). Our patient did not have the classic symptoms of numbness or tingling in the fingers and toes and the development of muscle weakness in the legs and arms. All other potential causes of the movement disorder were ruled out in the case presented. The movement disorder was considered to be most likely an adverse drug reaction to levofloxacin as assessed by the Naranjo adverse reaction probability assessment tool (score of 6)(8).

A literature search of PubMed, Embase & Reactions Weekly from inception to October 2016 using the search terms, "ciprofloxacin", "gatifloxacin", "gemifloxacin", "grepafloxacin", "levofloxacin", "moxifloxacin", "norfloxacin", "ofloxacin", "trovafloxacin", "movement disorders" and "motor dysfunction" yielded 21 case reports (see table-1)(9-28). One case report was excluded from the analysis. The case involved a 40-year-old female who had a pseudomeningocele treated with a lumbar drain and developed Enterobacter cloacae meningitis. The patient had normal liver and kidney function. Ciprofloxacin was added to the antibiotic regimen and 4 days later the patient developed generalized tremulousness. The case was confounded by the patient's medication regimen which included; droperidol, meperidine, metoclopramide, oxycodone, amitriptyline and incomplete documentation of doses received (28).

There was a wide variation in the range of age from 25 to 87 years in the cases reviewed (see table-1). A history of neurological disease was present in 3 patients: transient ischemic attack (9), stroke (10), and Alzheimer dementia (11). Ciprofloxacin was implicated in 50% of the cases reported. The most frequently reported neurological manifestation was oral facial dyskinesia. No pathologic cause was identified on CT of the head (9-14) or magnetic resonance imaging of the brain in these cases (10,15-19). Three patients had a normal lumbar puncture (16,18,20) and 5 patients a normal electroencephalogram (EEG) (12,13,18-19,21). Two patients had abnormal electromyography (EMG). The case by Striano showed irregular, continuous, and multifocal myoclonus, more evident in the upper limbs and multifocal paroxysmal activity on EEG (22). The case by Post (19) noted increased muscle activity in the biceps brachii and paraspinal muscles with EMG bursts varying from 80 msec to 400 msec and symptoms lasted for 1 year. The authors proposed that ciprofloxacin triggered a spinal myoclonic generator that continued to be active even after discontinuation. In one case a

nerve conduction study suggested a demyelinating polyneuropathy (27). Review of the cases suggested the onset of symptoms generally ranged from hours after administration after the first dose up to day 5 of therapy with complete resolution of symptoms within 5 days in the majority of cases. Anticholinergics, neuroleptics, and benzodiazepines were the most common antidotes used. In all cases, the antibiotic was discontinued and the patient was not rechallenged. The literature review suggests renal (9,10,12,14,21,22,24) or hepatic dysfunction (17,18,25) are risk factors associated with fluoroquinolone induced movement disorders. In our case, the onset of symptoms occurred within 2 hours of administration which has been reported with both ciprofloxacin (14) and gatifloxacin (23). The ciprofloxacin case reported by MacLeod involved a 69-year-old woman with a history of metastatic cervical cancer, ischemic heart disease and diabetes mellitus (14). The patient presented to the emergency with anuria and fever. A uretic stent was replaced and following the procedure she was placed on cefazolin 1 gram IV every 6 hours and norfloxacin 400 mg PO daily (no other concomitant medications were reported).

Results of blood and urine cultures revealed Pseudomonas sensitive to ciprofloxacin. Norfloxacin was discontinued and the patient was started on ciprofloxacin 400 mg IV every 12 h with a serum creatinine of 271 umol/L. During the first infusion, the patient became unresponsive, demonstrating decorticate posturing with a rightward deviation of her gaze. A clinical diagnosis of the cerebral vascular accident was made and the results of a CT of her head was normal. Over the next 2 hours, she developed facial tics, consisting of grimacing and protruding of the tongue, an automatism of her right hand, echolalia and echopraxia. Ciprofloxacin was discontinued and her neurological symptoms resolved within several hours with supportive care. There were no residual effects and the patient was discharged 7 days later (14). In a case of Mohan, a 25-year-old patient received gatifloxacin for acute bronchitis but, was otherwise young and healthy and did not receive anyother concomitant medications (23). After receiving gatifloxacin he experienced an unsteady stance and gait but, the remainder of his neurological examination was normal. No further investigations were reported. The ataxia resolved within 6 hours of gatifloxacin discontinuation and the patient was discharged from the hospital(23). This parallels the patient's rapid resolution of symptoms in our case after the cessation of levofloxacin. The neuromuscular symptoms improved within 20 minutes of IV diphenhydramine and had completely resolved with 24 hours of levofloxacin discontinuation.

The mechanism by which fluoroquinolones cause neurotoxicity is not fully understood. Postulated mechanisms for fluoroquinolone-mediated CNS toxicity include inhibition of GABA-A-receptors as well as activation of the excitatory NMDA receptors (2). This is thought to induce a hyperexcitable neuronal state resulting in the development of a movement disorder (10,15,19,20,25). There is a similarity between the structure of certain substituents at position 7 of the fluoroquinolone nucleus and the neurotransmitter GABA (29). It is hypothesized that fluoroquinolones may compete with and displace GABA from its receptor sites in the CNS leading to stimulation of the CNS (29). Other mechanisms that have been suggested include the interaction of fluoroquinolones with opioid, dopamine and glutamate receptors (29).

Table 1. Summary of Fluoroquinolone Induced Movement Disorders

Ref	Age/Sex	Drug	Dosage	Route	F	Concurrent Medications	Onset	Movement Disorder	Duration	Treatment
9	72/M	Ciprofloxacin	500 mg	PO	Twice daily	Alfacalcidol Pregabalin ASA Atorvastatin Folic Acid Sevelamer Calcium Acetate Gliclazide Darbepoetin Esomeprazole	Day 3	Generalized Choreoathetosis Affecting Upper And Lower Limbs, Face, Tongue	6 days	Risperidone 0.5 Mg PO Twice Daily x 6 Days
20	43/F	Ciprofloxacin	NR	NR	NR	Cephalexin Amoxicillin Clavulanate	NR	Lip Smacking, Random Flowing Nonrepetitive Movements, Involuntary Tongue Protrusion, Dystonic Posturing Of Feet, Seizures	5 days	No Therapy
17	59/F	Ciprofloxacin	1000 mg & 400 mg	PO/IV	Daily	Lamivudine Spironolactone Furosemide Lactulose	Day 21	Random, Abnormal Non-Repetitive Movements Of The Left Extremities	6 days	Haloperidol 1 Mg IM Q8h[1]
14	69/F	Ciprofloxacin	400 mg	IV	Twice daily	Cefazolin	2 hours	Facial Tics Consisting Of Grimacing And Protrusion Of The Tongue, Automatism Of Right Hand, Echolia, Echopraxia	within several hours	Supportive Therapy
18	49/F	Ciprofloxacin	200 mg	IV	Twice daily	Acetaminophen	Day 2	Involuntary Facial Grimacing	nr	Clonazepam[2]

25	68/M	Ciprofloxacin	500 mg	PO	Twice daily	Acetaminophen	Day 5	Abnormal Involuntary Facial Movements Consisting Of Facial Grimacing And Distortions, Puckering And Pursing Of The Lips	8 hours	Biperiden 2 Mg[3]
19	55/M	Ciprofloxacin	1500-2250 mg	PO	Daily	NR	Day 9	Shock Like Flexion Of The Trunk And Hips	1 year	No Therapy
10	84/M	Ciprofloxacin	500 mg	PO	Four times Daily	ASA Furosemide Allopurinol Carvedilol Besartan	Day 3	Slurring Of Speech, Involuntary Movements Of The Mouth, Lower Part Of The Face	2 days	Sodium Valproate 200 Mg PO Q8h[4]
22	63/M	Ciprofloxacin	200 mg	IV	Daily	Thiazide Diuretic	Day 2	Multifocal Myoclonus	1 week	Lorazepam 1 Mg IV[3]
21	74/F	Ciprofloxacin	500 mg	PO	Twice daily	Metronidazole Isosorbide Dinitrate Sodium Bicarbonate Nitroglycerin Triazolam Nifedipine Atenolol Metolazone Insulin Aluminum Carbonate	Day 12	Generalized Body Jerk With Truncal Activity Spreading To The Arms And Legs	2 days	Clonazepam[5]
11	87/F	Gatifloxacin	400 mg	IV	Twice daily	Loratadine	12 hours	Myoclonus, Generalized Seizure	1 day	No Therapy
23	25/M	Gatifloxacin	200 mg	PO	NR	None	2 hours	Ataxia	6 hours	No Therapy
13	36/F	Gemifloxacin	320 mg	PO	Daily	NR	Day 3	Sustained Muscle Contractions Of The Hands, Forearm, Arm, Foot, Calf And Thigh	1 day	Promethazine 50 Mg IV x 1 Dose

24	77/F	Levofloxacin	500 mg	IV	Daily	Famotidine Furosemide Levothyroxine Paroxetine Warfarin Metronidazole	Day 5	Involuntary Rhythmic Facial Grimacing Cervical Muscular Contractures Uncontrolled Facial, Tongue Movements	1 day	Diphenhydramine 25 Mg IV x 1 Dose Lorazepam 0.5 Mg IV x 1 Dose
12	67/M	Levofloxacin	300 mg	PO	Daily	Fulfenamic Acid	Day 4	Hand Tremor Which Resembled Chorea Like Involuntary Movement, Gait Disturbance, Visual Hallucinations	7 days	No Therapy
14	85/M	Levofloxacin	200 mg	PO	Daily	None	Day 68 [6]	Gait Disturbance, Dysarthria, Chorea Like Involuntary Movements	14 days	No Therapy
15	58/F	Moxifloxacin	400 mg	PO	Daily	Multiple Vitamin	Day 3	Involuntary Choreic, Dystonic Movements Involving The Lips, Tongue, Jaw, Facial Muscles Dystonic Posturing Of The Neck, Shoulders	56 days	Clonidine 0.1 Mg PO Bid x 4 Weeks
16	71/M	Ofloxacin	200 mg	PO	Twice daily	Ticarcillin-Clavulanate Erythromycin B_2 Agonist	Day 1	Acute Disorientation, Echolalia, Echopraxia, Orofacial Grimacing, Limb Automatisms Coprolalia, Hypersalivation, Spitting	2 days	No Therapy
26	43/M	Ofloxacin	400 mg	NR	Daily	Venlafaxine	Day 3	Involuntary Facial Grimacing, Inability To Close The Jaws	NR	Biperiden 3.88 Mg IM x 1 Dose
27	50/M	Trovafloxacin	200 mg	PO	Daily	Felodipine Glipizide Doxazosin	Day 2	Profound Proximal Muscle Weakness	3 days	No Therapy

M: Male, **F**: Female, **PO**: Oral, **IV**: Intravenous, **IM:** Intramuscular, **NR**: Not Reported. [1] Duration Not Reported, [2] Dose, Frequency And Duration Not Reported, [3] Number Of Doses Not Reported, [4] Not Continued Upon Hospital Discharge Day5, [5] Dose And Frequency Not Reported But Was Tapered Over 7 Days, [6] Long Term Antibiotics For Chronic Bronchitis

Iigin et al studied the effects of ciprofloxacin on neurotransmitters (30). Rats were fed ciprofloxacin 20 mg/kg or 50 mg/kg day or saline solution as a placebo for 14 days. There were no significant alterations in the dopamine or noradrenaline levels measured in brain homogenates. Adrenaline levels were decreased and glutamate levels increased in both treatment groups. Ciprofloxacin 50 mg/kg significantly reduced serotonin and GABA.

Malondialdehyde, brain glutathione, superoxide dismutase, catalase were measured to determine the contribution of oxidative stress to ciprofloxacin neurotoxicity. In the rats fed ciprofloxacin decreased levels of brain glutathione and catalase activity were noted. There was no difference in superoxide dismutase activity. Brain malondialdehyde levels were higher in rats fed ciprofloxacin. The results suggest an enhanced oxidative stress/damage with a weakened oxidative defense system (30).

Penetration of drugs into the cerebral spinal fluid and brain tissue are dependent on meningeal inflammation, molecular size, lipophilicity, plasma protein binding, susceptibility to active transport systems & the degree of ionization of the medication (31). Most fluoroquinolones are moderately lipophilic with a molecular mass of approximately 300 daltons and low protein binding to plasma proteins (approximately 20-40%)(31). At physiologic pH, most of the agents are uncharged which favors their CNS penetration (31).

CNS reactions to fluoroquinolones are dose or concentration dependent but, neurotoxic reactions to fluoroquinolones are not strictly correlated with high plasma concentrations (1).

The AUCCSF/AUCserum for ciprofloxacin, levofloxacin, and moxifloxacin in uninflamed or mildly inflamed meninges ranges from 0.3-0.7 and with strong meningeal inflammation 0.7-0.9 (31). Due to their potential to cross the blood-brain barrier, it is logical that fluoroquinolones may be indicated in the treatment of certain CNS infections. They have not been extensively studied in the treatment of bacterial meningitis and are not part of standard therapy but may be used in patients with multiple severe drug allergies or in the treatment of highly resistant organisms (32, 33). In these instances, ciprofloxacin or moxifloxacin may be considered as an alternative therapy (32,33). Moxifloxacin or levofloxacin may also be used in the treatment of CNS tuberculosis (34). Low serum concentrations of norfloxacin are attained after oral administration of usual dosages. Use of norfloxacin is generally limited to genitourinary or gastrointestinal tract infections (35). Gatifloxacin (dysglycemia), gemifloxacin, grepafloxacin (QT prolongation), ofloxacin, trovafloxacin (hepatotoxicity) have been withdrawn from the market.

There is very little data on the concentrations of fluoroquinolones in brain tissue with only data on ciprofloxacin being reported. Five patients undergoing surgery for removal of brain tumor, aneurysms or other vascular malformations received ciprofloxacin 750 mg (route not specified) 3 to 5 hours prior to surgery. Three to 5 hours post administration the mean concentration of ciprofloxacin in serum was 2.82 mcg/mL (range 0.62-7.54 mcg/mL) and at 3 hours in brain tissue was 2.18 (0.69-5.05 mcg/mL). This study suggested ciprofloxacin brain tissue concentrations were approximately 25% lower than serum however, there was a wide variation in ciprofloxacin brain tissue concentrations (36). In another study, 14 patients undergoing brain tumor excision

received a single dose of ciprofloxacin 200 mg IV administered over 20 min. Blood samples were drawn 10 minutes after the infusion. Samples from subcutaneous fat, skull bone, dura mater and brain tissue were collected 60 min after ciprofloxacin administration. The concentrations showed considerable variability and were approximately 2-20 times higher than the corresponding concentrations in CSF (37). No clear relationship has been established between CNS penetration and adverse events for fluoroquinolones (2, 3).

Conclusion

Movement disorders are a rare adverse effect associated with fluoroquinolones. The proposed mechanism involves neuronal excitability through GABA inhibition and enhanced oxidative stress. The adverse reaction appears to be a class effect. Oral facial dyskinesia has been most commonly reported. Half of the cases reviewed occurred in patients with renal or hepatic dysfunction necessitating the need for appropriate dosing. The onset of symptoms is usually within 5 days after fluoroquinolone administration with complete resolution of symptoms within 7 days after fluoroquinolone discontinuation. The case presented and literature review summarizes the data on fluoro-quinolone induced movement disorders.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Reference

1. Stahlmann R, Lode. Safety considerations of fluoro quinolones in the elderly: an update. Drugs Aging, 27(3), 2010, 193-209.
2. Grill MF, Maganti RK. Neurotoxic effects associated with antibiotic use: management considerations. Br J Clin Pharmacol, 72(3), 2011, 381-93.
3. Lode H. Potential interactions of the extended-spectrum fluoroquinolones with CNS. Drug Saf, 21(2), 1999, 123-35.
4. Lau A, Chan LN. Electrolytes, other minerals and trace elements. In: Lee M. Basic skills in interpreting laboratory data. 5th edition. (Bethesda (MD): American Society Health-System Pharmacists. 2013) 119-149.
5. Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://micromedexsolutions.com(cited: Oct/ 24/2016).
6. Beaulieu I, Nadeau C. Myoclonus and convulsions. In: Neron A, editor. Care Beyond Cure: Management of Pain and Other Symptoms. 4th edition. (Montreal (QC): l'Association des pharmaciens des établissements de santé du Québec (A.P.É.S.) and the Canadian Society of Hospital Pharmacists (CSHP), 2009) 285-96.
7. Allos BM, Lovine NM, Blaser MJ. Campylobacter jejuni and related species. In: Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th edition. (Philadelphia, PA : Elsevier/Saunders, 2015) 2485-93.
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ. Clin Pharmacol Ther, 30(2), 1981, 239-45.
9. Addalla A, Ramly S, Boers P, Casserly L. Ciprofloxacin-associated choreoathetosis in a hemodialysis patient. BMJ Case Rep, 2013 Apr 18;2013.pii: bcr2013009293.
10. Cheung YF, Wong WWY, Tang KW, Chan JHM, Li PCK. Ciprofloxacin-induced palatal tremor. Mov Disord, 22(7), 2007, 1038-43.
11. Marinella MA. Myoclonus and generalized seizures associated with gatifloxacin treatment. Arch Intern Med, 161(18), 2001, 2261-62.
12. Yasuda H, Yoshida A, Masuda Y, Fukayama, Kita Y, Inamatsu T. Levofloxacin-induced neurological adverse effects such as convulsions, involuntary movement (tremor, myoclonus and chorea like). Visual hallucination in two elderly patients. Nihon Ronen Igakkai Zasshi, 36(3), 1999, 213-17.
13. Sharma DD, Aggarwal A, Sharma RC, Kumar R. A probable association of acute dystonia with gemifloxacin administration. Indian J Med Sci, 63(12), 2009, 557-60.
14. MacLeod W. Case report: severe neurological reaction to ciprofloxacin. Can Fam Physician. 2001 47(march), 2001, 553-55.
15. Mittal SO, Machado DG, Jabbari B. Orofacial dyskinesia after moxifloxacin treatment-case with normal hepato renal function and review of literature. Clin Neuropharmacol, 35(6), 2012, 292-4.
16. Thomas RJ, Reagan DR. Association of a Tourette-like syndrome with ofloxacin. Ann Pharmacother, 30(2), 1996, 138-41.
17. Kim SH, Jeong SH, Kim JW, Lee SH, Kim JM. A case of hemiballism as a rare side effect of ciprofloxacin in a patient with liver cirrhosis. Chemotherapy, 55(4), 2009, 207-10.
18. Lee CH, Cheung RTF, Chan TM. Ciprofloxacin-induced oral facial dyskinesia in a patient with normal liver and renal function. Hosp Med, 61(2), 2000, 142-43.
19. Post B, Koelman JHTM. Tijssen AJ. Prospinal myoclonus after treatment with ciprofloxacin. Mov Disord, 19(5), 2004, 595-97.
20. Azar S, Ramjiani A, Van Gerpen JA. Ciprofloxacin–induced chorea. Mov Disord, 20(4), 2005, 513-14.

21. Schwartz MT, Calveert JF. Potential neurological toxicity related to ciprofloxacin. DICP, 24(2), 1990, 138-40.
22. Striano P, Zara F, Coppola A, Ciampa C, Pezella M, Striano S. Epileptic myoclonus as ciprofloxacin associated adverse effect. Mov Disord, 22(11), 2007, 1675-76.
23. Mohan N, Menon K, Rao PG. Oral gatifloxacin-induced ataxia. Am J Health-Syst Pharm, 59(19), 2002, 1894.
24. Host BD, Sloan W. Orofacial dyskinesia associated with the use of levofloxacin. Ann Pharmacother, 48(1), 2014, 142-44.
25. Pastor P, Moitinho E, Elizalde I, Cirera I, Tolosa E. Reversible oral-facial dyskinesia in a patient receiving ciprofloxacin hydrochloride. J Neurol, 243(8), 1996, 616-17.
26. DeBleecker JL, Vervaet VL. Reversible orofacial dyskinesia after ofloxacin treatment. Mov Disord, 19(6), 2004, 731-32.
27. Murray CK, Wortmann GW. Trovafloxacin-induced weakness due to a demyelinating polyneuropathy. South Med J, 93(5), 2000, 514-5.
28. Farrington J, Stoudemire A, Tierney J. The role of ciprofloxacin in a patient with delirium due to multiple etiologies. Gen Hosp Psychiatry, 17(1), 1995, 47-53.
29. Sousa J, Alves G, Fortuna A, Falcao A. Third and forth generation fluoroquinolone antibacterials: a systematic review of safety and toxicity profiles. Curr Drug Saf, 9(2), 2014, 89-105.
30. Iigin S, Can OD, Atli O, Ucel UI, Sener E, Guven I, Ciprofloxacin-induced neurotoxicity: evaluation of possible underlying mechanisms. Toxicol Mech Methods, 25(5), 2015, 374-81.
31. Nau R, Sorgel F, Eiffert H. Penetration of drugs through the blood-cerebrospinal fluid/blood-brain barrier for treatment of central nervous system infections. Clin Microbiol Rev, 23(4), 2010, 858-83.
32. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis, 39(9), 2004, 1267-84.
33. Tunkel AR. Initial therapy and prognosis of bacterial meningitis in adults. UpToDate online [internet database]. Version 22.0. Waltham (MA): UpToDate Inc; [updated 2015 Oct 7; cited 2016 Oct 21]. Available from http.uptodate online.com. Subscription required to access content.
34. Leonard JM. Central nervous system tuberculosis. In: UpToDate online [internet database]. Version 22. Waltham (MA): UpToDate Inc; [updated 2015 Oct 7; cited 2016 Oct 21]. Available from http.uptodateonline.com. Subscription required to access content.
35. Lexicomp [database on the Internet]. Hudson (OH): Wolters Kluwer Clinical Drug Information; © 1978–2016 [updated daily; cited 2016 Oct 25]. Available from: http://online.lexi.com [subscription required to access content]
36. Davey PG, Charter M, Kelly S, Varma TRK, Jacobson I, Freeman A et al. Ciprofloxacin and sparfloxacin penetration into human brain tissue and their activity as antagonists of GABAA receptor of the rat vagus nerve. Antimicrob Agents Chemother, 38(6), 1994, 1356-62.
37. Leone M, Sampol-Manos E, Santelli D, Grabowski, Alliez B, Durand A et al. Brain tissue penetration of ciprofloxacin following the single intravenous dose. J Antimicrob Chemother, 50(4), 2002, 607-09.

How to cite?
Bates D, Edwards J, Chow J, Fisher M, Morris C, Switzer A. Fluoroquinolone Induced Movement Disorders: Case Report and Literature Review. Ulutas Med J. 2018;4(1):53-63

DOI: 10.5455/umj.20180207122003