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CASE REPORT

Synergistic neurotoxicity of ciprofloxacin and nimesulide in unmasking a hidden catalyst for seizures: A case report

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Abstract

Background: Fluoroquinolones are widely prescribed broad-spectrum antibiotics with favourable pharmacokinetics but are associated with neurotoxicity in 1–2% of users. Reported manifestations include seizures, encephalopathy, psychosis, myoclonus, and dyskinesia. Ciprofloxacin, a commonly used agent, disrupts central nervous system homeostasis by inhibiting γ–aminobutyric acid-A (GABA-A) receptors and enhancing N-methyl-D-aspartate (NMDA) receptor activity, creating an excitatory milieu that heightens seizure risk, especially in predisposed individuals.

Case description and management: A 54-year-old man with type 2 diabetes mellitus presented with diarrhoea, fever, and abdominal discomfort. He was empirically started on ciprofloxacin, nimesulide, and paracetamol; stool analysis later confirmed polymicrobial gastroenteritis. Two hours after his second ciprofloxacin dose, he developed a generalized tonic–clonic seizure (GTCS) despite no prior seizure history. Comprehensive metabolic, infectious, and neuroimaging evaluations were unremarkable. The Naranjo score was 7, indicating a probable adverse drug reaction. Ciprofloxacin was discontinued and seizures were controlled with levetiracetam and lacosamide. His antimicrobial therapy was switched to amoxicillin–clavulanic acid, resulting in full neurological recovery and no further seizures.

Conclusion: Ciprofloxacin-induced seizures likely stem from GABA inhibition and NMDA overactivation, potentiated by concomitant NSAID use. Prompt drug withdrawal and appropriate seizure management are essential. Prudent fluoroquinolone prescribing is critical to minimize CNS adverse effects and ensure patient safety.

Key messages

Ciprofloxacin, though widely prescribed for its efficacy, can precipitate seizures via GABA-A antagonism, especially when combined with NSAIDs such as nimesulide. This case report highlights the critical need for clinicians to be aware of ciprofloxacin-induced neurotoxicity in vulnerable patients. Early recognition, drug discontinuation, and targeted anticonvulsant therapy are essential to prevent life-threatening complications and ensure optimal neurologic recovery in affected individuals.

Introduction

Ciprofloxacin, a second-generation fluoroquinolone introduced in 1986, is widely used to treat various bacterial infections because of its potent bactericidal activity [1]. It targets DNA gyrase and topoisomerase IV, disrupting DNA replication and transcription in both Gram-positive and Gram-negative bacteria. Its favourable pharmacokinetics, including high oral bioavailability and excellent tissue penetration, make it a preferred choice for urinary, respiratory, gastrointestinal, and soft tissue infections [2]. However, central nervous system (CNS) adverse drug reactions (ADRs), although rare, have gained increasing recognition.

Neurotoxicity from fluoroquinolones includes a range of effects, from mild anxiety and insomnia to hallucinations, psychosis, and seizures. The U.S. FDA has issued warnings about fluoroquinolone-induced neuropsychiatric effects. The proposed mechanism involves antagonism of γ−aminobutyric acid type A (GABA-A) receptors, leading to reduced inhibitory neurotransmission and increased neuronal excitability. When co-administered with nonsteroidal anti-inflammatory drugs (NSAIDs), these effects may be exacerbated due to synergistic inhibition of GABA-A [3]. Recognising these rare but serious events is essential for clinical safety.

Case description and management

A 54-year-old male with type 2 diabetes mellitus (on metformin 500 mg once daily) presented with a 7-day history of watery diarrhoea, fever, and abdominal pain. Two days before admission, he was empirically started on ciprofloxacin (500 mg twice daily) along with nimesulide (100 mg) and paracetamol (325 mg) for fever. Stool multiplex PCR identified Campylobacter jejuni, Salmonella enterica, and Escherichia coli as the causative organisms.

On hospital admission, he was hydrated and continued on ciprofloxacin. After the second dose, the patient experienced a generalised tonic-clonic seizure lasting two minutes, followed by postictal confusion. He had no prior history of seizures, head trauma, or neurological illness. Neurological examination was unremarkable before the episode. Laboratory investigations revealed serum calcium of 9.0 mg/dL (reference range: 8.5–10.5 mg/dL) and serum magnesium of 2.0 mg/dL (reference range: 1.7–2.3 mg/dL), both within normal limits, excluding electrolyte imbalance as a precipitating factor. Blood cultures taken before antibiotics were started remained sterile after 72 hours of incubation, and serum procalcitonin was 0.23 ng/mL (reference <0.5 ng/mL), thereby ruling out sepsis as the cause. Quantitative estimation of serum ciprofloxacin levels was not performed, as therapeutic drug monitoring for fluoroquinolones is not routinely available at the institution. Other laboratory parameters, including electrolytes, blood glucose, renal and hepatic profiles, and arterial blood gases, were within normal limits. A non-contrast computed tomography (CT) scan of the brain showed no intracranial abnormalities.

A clinical pharmacist's review implicated ciprofloxacin as the probable cause. The seizure was attributed to ciprofloxacin's GABA-A antagonism, potentially worsened by concurrent NSAID use. The Naranjo algorithm yielded a score of 7, suggesting a "probable" adverse drug reaction [4]. Ciprofloxacin and nimesulide were discontinued. The patient was treated with intravenous levetiracetam (1 g) and a loading dose of lacosamide (100 mg). Antibacterial therapy was switched to intravenous amoxicillin-clavulanate. He remained seizure-free, neurologically stable, and was discharged after 72 hours with outpatient neurology follow-up.

Discussion

Fluoroquinolone-induced seizures are rare but serious. Ciprofloxacin is known to lower the seizure threshold through GABA-A receptor inhibition and possible NMDA receptor modulation [5]. In this patient, several contributing factors likely increased susceptibility: diabetes-associated subclinical renal impairment, systemic inflammation from polymicrobial gastroenteritis, and co-administration of nimesulide—an NSAID known to potentiate fluoroquinolone neurotoxicity [3].

Although there is no obvious renal dysfunction, impaired clearance of ciprofloxacin cannot be discounted. NSAIDs may decrease renal perfusion, leading to increased systemic drug levels. Additionally, inflammatory cytokines from infection might disrupt neurotransmitter balance, sensitising neurons to excitotoxic injury. These combined effects likely triggered the seizure.

The patient's rapid recovery after stopping the medication, lack of structural CNS pathology, and typical presentation strongly suggest ciprofloxacin as the cause. Treatment with levetiracetam, known for its minimal interactions and wide-ranging anti-epileptic effectiveness, was successful [6]. The Naranjo score further confirmed the drug-event association [4]. This case underscores the importance of clinical vigilance when prescribing fluoro-

Table 1 Fluoroquinolone-associated neurotoxicity cases with co-therapy, symptoms, and management

Ref.	Age Sex	Medication	Dosage (mg)	Route/ Frequency	Co-therapy	Symptom onset	Motor dysfunction	Symptom duration	Intervention
4	49 Woman	Ciprofloxacin	200 mg	Intravenous 12 hourly	Paracetamol	Day 2	Involuntary facial myokymia	Not reported	Clonazepam[a]
7	84 Man	Ciprofloxacin	500 mg	Per oral 6 hourly	Acetylsalicylic acid	Day 3	Dysarthria with involuntary oromandibular dyskinesia	48 hours	Sodium valproate 200 mg per oral 8 hourly[b]
8	67 Man	Levofloxacin	300 mg	Per oral daily	Mefenamic acid derivative	Day 4	Choreiform tremors, gait ataxia, visual perceptual disturbances	7 days	No pharmacologic intervention
10	68 Man	Ciprofloxacin	500 mg	Per oral 12 hourly	Paracetamol	Day 5	Orofacial dyskinesia with buccolingual stereotypies	8 hours	Biperiden 2 mg[c]

[a]Specific details on dose, frequency, and duration not provided; [b]Medication was discontinued upon hospital discharge; [c]Number of doses administered was not documented

quinolones, especially in patients with chronic illness, concurrent NSAID use, or systemic infections. Ciprofloxacin's favourable pharmacokinetics must be weighed against its neurotoxic potential, particularly in vulnerable populations.

Relevant studies on fluoroquinolone-associated neurotoxicity with concurrent pharmacotherapy in Table1. These cases demonstrate a range of neurological symptoms, including dyskinesias, choreiform tremors, and orofacial stereotypies, occurring at different dosages and routes of adminis-tration. The variety of symptoms and the influence of concomitant medications, such as NSAIDs and paracetamol, further emphasise the multifactorial nature of fluoroquinolone-induced CNS toxicity. This comparison reinforces the idea that fluoroquinolone-related neurotoxicity is not solely determined by drug dose or route but involves an interaction between pharmacodynamic effects and patient-specific susceptibilities.

Conclusion

Ciprofloxacin can precipitate seizures even in individuals without a prior seizure history, particularly when metabolic stress, systemic infection, or interacting medications are present. In this case, the temporal association with ciprofloxacin and the patient's rapid recovery after discontinuation suggest a probable drug-related event, with nimesulide serving as a possible contributory factor rather than an independent cause. Although paracetamol exposure and infection-related meta-bolic disturbances cannot be entirely excluded, the overall clinical pattern favours ciprofloxacin-induced neurotoxicity. Clinicians should remain vigilant when prescribing fluoroquinolones—especially in patients with underlying comorbidities or concurrent agents such as nimesulide—and promptly withdraw the suspected drug when neurological symptoms emerge.

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Author contributions

Manuscript drafting and revising it critically: VRG, ANJ, SD. *Approval of the final version of the manuscript:* VRG, AKG, SD, ANJ. *Guarantor accuracy and integrity of the work*: ANJ.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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