



# Ciprofloxacin-induced paroxysmal atrial fibrillation

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## Abstract

### Introduction

Ciprofloxacin is a second generation fluoroquinolone with a broad spectrum of antibacterial activity. It has good bioavailability after oral administration, good to excellent tissue penetration and is relatively safe. Generally well tolerated, Ciprofloxacin remains one of the safest among antibiotics with remarkably few reactions. Ciprofloxacin however, can induce cardiotoxicity that is associated with increased QT and QTC interval, action potential prolongation, tachyarrhythmias and torsade de pointes. This report aims to highlight possible cardiac toxicity caused by one of the most widely used drugs which are fluoroquinolones, especially in patients over 60 and thus improve our knowledge of these phenomena.

### Case report

This case report describes a patient with an episode of paroxysmal atrial fibrillation induced by Ciprofloxacin treatment for urinary tract infection.

### Conclusion

This paper has shown that Ciprofloxacin has cardiotoxic potential. Patients' cardiac function status should be considered before initiating Ciprofloxacin clinical use.

### Introduction

Most commonly used drugs, as fluoroquinolones are for non-cardiac conditions can have unexpected and serious cardiac side effects.

Fluoroquinolones have demonstrated from the beginning of usage, high safety profiles.

In particular, Ciprofloxacin and Levofloxacin both remain the safest and better tolerated fluoroquinolones. The most common rare adverse effects related to these drugs involve the gastrointestinal tract and the central nervous system, plus tendinopathy especially in patients under 30 years old<sup>1</sup>.

An underlying cardiac abnormality can be a predisposing factor. The cardiovascular system can be involved due to possible occurrence of arrhythmias in patients with underlying heart disease, and for this reason the question of cardiac safety in newer fluoroquinolones<sup>2</sup> has been raised.

In patients taking Ciprofloxacin, atrial fibrillation was reported most often within 42 days of administration, with no change in event rate over that time. Syncope and tachycardia were also reported with Ciprofloxacin and Ofloxacin<sup>3</sup>.

Cardiovascular adverse reactions such as palpitations, tachycardia, and phlebitis have very rarely been reported in the data sheet of the drug. We report here a curious case report of paroxysmal atrial fibrillation following administration of Ciprofloxacin for a lower urinary infection in a 61-year-old male.

### Case report

The authors report a case of paroxysmal atrial fibrillation presumably caused by Ciprofloxacin administered for lower urinary tract infection in a 61 year-old healthy male, being treated for mild hypertension and well compensated type 2 diabetes mellitus for several years with ACE inhibitors (Enalapril

20 mg die) and oral hypoglycaemic agents (Metformin 500 mg, twice daily). After 3-4 days of Ciprofloxacin taken orally (500 mg, twice daily) assumption for a febrile non-gonococcal urethritis appeared malaise, with dizziness and profuse sweating. The patient was also in a confusional state with detection of arterial hypotension in absence of palpitations or tachycardia.

When the patient came to our rooms physical examination revealed an irregular heartbeat with asynchronous pulse and resting ECG (Figure 1A) showed atrial fibrillation at high average ventricular response without haemodynamic consequences.

The patient was sent to the emergency department where intravenous bolus beta-blocker was infused to reduce the ventricular rate (Figure 1B) and subsequently administered orally to control the heart rate, together with anticoagulant therapy to prevent cardioembolic risks. Ciprofloxacin was immediately interrupted. An electrocardiogram, recorded two days later, showed early recovery of the sinus rhythm (Figure 2) and transthoracic mono and bidimensional echocardiography showed no structural abnormalities or valvular disease and, indicated, normal size of the heart chambers, in particular left atrium volume, with good left ventricular systolic and diastolic function.

The patient remained in sinus rhythm without signs of recurrence of asymptomatic atrial fibrillation as documented by 72-hour Holter monitoring, and in ECG control that followed for many days.

### Discussion

The onset of arrhythmias related to the assumption of Ciprofloxacin cannot be excluded beforehand. In fact, compared to other quinolones there are numerous reports concerning cardiovascular

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events such as arrhythmia induced by Ciprofloxacin occurring within 42 days of administration. Recently, Siepman and Kirch have reported the first case of tachycardia presumably associated with intake of Moxifloxacin<sup>4</sup>.

Ciprofloxacin is generally safe and well-tolerated. The most common adverse reactions include gastro-intestinal tract, central nervous system and haematological system. Recently, increasing cases of Ciprofloxacin-associated toxicity have been reported.

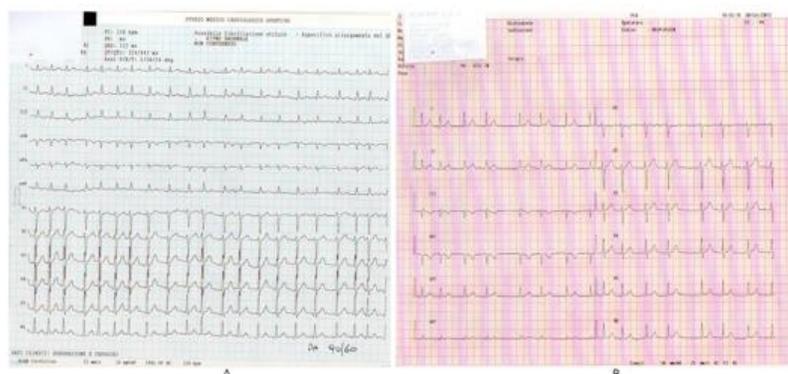
The mechanism of Ciprofloxacin cardio-toxicity has not been fully understood yet, but clinical experience shows that Ciprofloxacin can induce cardiotoxicity marked by increased QT and QTC interval, consequently prolongation of action potential duration. This modification increases the risk of the onset of malignant arrhythmias such as torsade de pointes<sup>5</sup>.

As reported by Adikwu and Bramaifa Ciprofloxacin induced cardiotoxic effect could be associated with blocking cardiac voltage-gated potassium channels particularly the rapid component (IKr) of the delayed rectifier potassium current<sup>6</sup>; eHealthMe study from FDA reports (Figure 3) says that 4.793 people have reported side effects when taking Ciprofloxacin. Among them, 170 people had atrial fibrillation, with 80% of them aged over 60.

The authors believe that in this case it is very likely due to the induction of AF by Ciprofloxacin, although it is known that this event can happen in any older patients suffering from hypertension or diabetes. Most reports of atrial fibrillation (AF) induced by non-cardiovascular drugs are case reports<sup>8</sup>, and because AF is so common, it is difficult to determine if the association is causal or incidental.

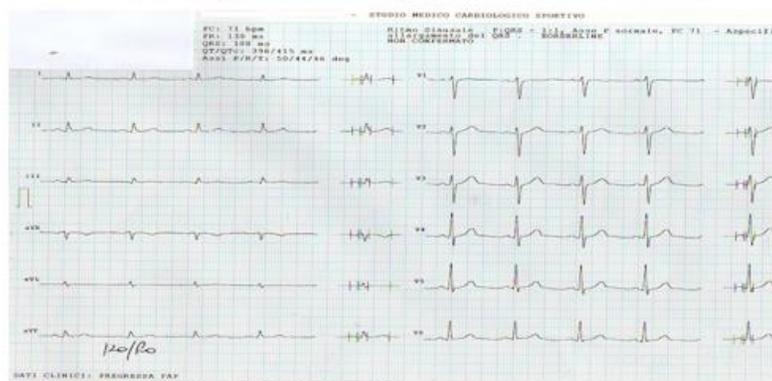
However, despite the in-ability to reproduce AF with drug re-challenges that would support causality, the presence of neurological adverse

### Lone atrial fibrillation



**Figure 1:** Panel A Resting Ecg shows atrial fibrillation with high ventricular response; Panel B: Resting ECG shows atrial fibrillation with normal ventricular rate.

### Resting ECG after ciprofloxacin withdrawal



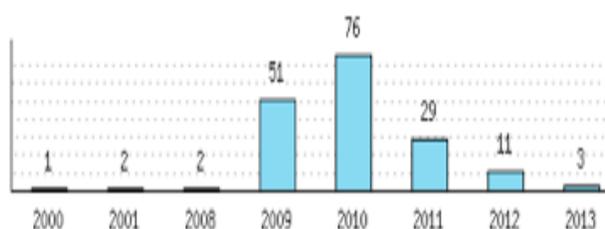
**Figure 2:** Resting ECG shows normal sinus rhythm.

events during initiation of therapy with Ciprofloxacin as well as the subsequent onset of atrial fibrillation plus the rapid disappearance of the arrhythmia a few days after discontinuation of antibiotic therapy, strengthens the suspicion of the cause and effect relationship between drug intake and the occurrence of the arrhythmia.

Further confirmation of this

observation is the absence of structural cardiac abnormalities and the presence of normal sized heart chambers not subject to valvular disease after echocardiography examination causes the authors to hold that this case falls within the field of cardiotoxicity due to fluoroquinolones. This report aims at highlighting possible cardiac toxicity especially in patients aged over 60 brought on by fluoroquinolones, one of the most widely used drugs

### Trend of "Atrial fibrillation in Cipro" reports



**Figure 3:** The eHealthMe study from FDA report.

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administered to patients, and thus to improve our knowledge of these phenomena.

Furthermore, this report intends to explain the difficulty in pro-arrhythmia risk management of these drugs in the context of polypharmacy and feasible interaction amongst various drugs in patients with multiple comorbidities and risk factors concerning arrhythmias. One should take into consideration that fluoroquinolones are drugs that interact with the hepatic cytochrome P450 system, thus any CYP450 modification could lead to higher drug serum concentrations with possible proarrhythmic effects. Currently, awareness of the proarrhythmic potential of non-cardiac drugs combined with logical, clinical reasoning would help mitigate the risk-factor and help avoid incorrect decisions<sup>7</sup>.

### Conclusion

In conclusion this paper has shown that Ciprofloxacin has cardiotoxic potential. Patients' cardiac function status should be considered before initiating Ciprofloxacin clinical use. Idiopathic paroxysmal atrial fibrillation can be attributed to the adverse effects of cardiotoxic drugs, amongst which we must also consider quinolones such as Ciprofloxacin.

### Consent

The authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial Office/Chief Editor/Editorial Board members of this journal.

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