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## Chloroquine and QTc interval

Sirs,

Chloroquine is a medication commonly used in rheumatology because it is cheap, easy to use and has a wide spectrum of therapeutic indications.

One of our patients using chloroquine and methotrexate for rheumatoid arthritis complained of an unspecific chest pain and underwent an electrocardiogram. A prolongation of QTc interval (0.45sec) was found to be reverted to normal when chloroquine was suspended. This can be explained by the fact that chloroquine belongs to the pharmacological group of quinidine (a Ia antiarrhythmic drug known to have a prolongation effect on QT interval (1)).

Prolongation of QT interval has already been described with chloroquine in healthy volunteers (2), *in vitro* with feline myocytes (3), and in cases of treatment for resistant malarial infection with halofantrine (4). On the other hand, Wosniaka *et al.* studied 28 lupus patients using chloroquine but did not find arrhythmias, conduction disturbances, nor alterations in QTc interval (5).

We decided to study the QTc interval on the electrocardiogram of 46 patients using antimalarials for rheumatoid arthritis (8 patients), systemic lupus (28 patients), erosive hand osteoarthritis (8 patients), Sjögren's syndrome (1 patient) and cutaneous lupus (1 patient). All included patients gave informed consent. These patients had been on antima-

**Table I.** QTc intervals in patients before and after stopping antimalarial.

PATIENT	Chloroquine dosing	Time of chloroquine use (months)	Concomitant drugs	QTc interval (in seconds)	
				With antimalarial	After stopping antimalarial
ALF, 77 years	120mg/day	4	Hydrochlorthiazide; paracetamol	0,463	0,431
IMV, 29 years	240mg/day	43	Paracetamol	0,448	0,381
OV, 30 years	240mg/day	50	Prednisone, azathioprine	0,472	0,395
TMN, 30 years	240 mg/day	26	Prednisone, methotrexate	0,452	0,407
EP, 44 years	240 mg/day	29	None	0,474	0,431
ESG, 62 years	240mg/day	32	Paracetamol	0,447	0,419
LV, 38 years	240 mg/day	6	None	0,446	0,406
EA, 30 years	240 mg/day	38	None	0,443	-

larials from 1 to 84 months (median = 27.24 months; SD  $\pm$  19.76). All but 2 patients were female; 42 were using chloroquine (Cloroquina<sup>®</sup>, Far-Manguinhos, RJ, Brazil) and 4 were using hydroxychloroquine (Reuquinol<sup>®</sup>-Apsen). We considered the maximal value for a normal QTc to be 0.440 sec (6).

We found a prolongation in the QTc interval in 8 patients (17.39%). All of them were female and had been using chloroquine from 4 to 50 months (mean  $28.5 \pm 16.42$ ). None of the four hydroxychloroquine users had a QTc prolongation. None of the patients with QTc prolongation previously had other heart conditions except for one with mild arterial hypertension. Concomitant medications used by this group of patients are shown in Table 1. We could not find a difference in the groups of patients using 240 mg/day or 120 mg/day of chloroquine (Fisher's test;  $p = 0.574$ ); nor a relationship with time of use (Fisher's test;  $p = 0.09$ ).

The 8 patients with prolongation of QTc interval were advised to stop the drug and seven of them agreed upon repeating the electrocardiogram within 2 weeks. In these patients, the QTc interval returned to normal (Table I).

Having observed the return to normal of QTc interval after withdrawal of medication and that there was no use of other drugs in these patients that could explain this prolongation, we think chloroquine may be implicated in causing this abnormality.

Although this is a small, uncontrolled study, we would like to call attention to the findings, because prolongation of QT interval can induce "torsade de points" ventricular tachycardia which may cause syncope and even sudden death.

We would like to advise taking an ECG in all patients using antimalarials. Studies with a larger number of patients and also specifically addressing the role of hydroxychloroquine are needed for a better understanding of QTc prolongation with these medications.

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