Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Safe use of hydroxychloroquine and its combination with azithromycin in the context of Sars-CoV-2 outbreak: Clinical experience in a Belgian tertiary center

Dear Editor,

Based on studies showing in vitro antiviral activity of chloroquine (CQ) and hydroxychloroquine (HCQ) on SARS-CoV-2 [1], Belgian COVID interim guidelines rapidly (March 13th, 2020) recommended treating hospitalized patients suffering from severe COVID-19 with HCQ, 400 mg bid the first day followed by 200 mg bid for 4 additional days (for GFR > 30 ml/min).

Despite some encouraging preliminary clinical data [2,3], major concerns have been raised about the use of HCQ to treat COVID-19 [4], particularly regarding potential cardiac toxicity (i.e. QTc increase and risk of *torsade de pointe*). Because HCQ has been safely used for many years for various indications (e.a. connective tissue diseases) [5], we decided to follow interim Belgian guidance for all eligible patients hospitalized in our COVID-19 wards. Moreover, we decided to add azithromycin (AZM), 500 mg Id for 3 days, for selected patients, based on our knowledge of its antibiotic, immunomodulatory and possible antiviral actions [3].

Between March 8 and April 15, 2020, a total of 114 patients with confirmed COVID-19 pneumonia were hospitalized in our dedicated units. Patient characteristics are summarized in Table 1. The mean age was 63 years and men represented 55.3%. A vast majority (n = 104) presented with severe disease and half (n = 59) had cardiovascular disease history. Other comorbidities are listed in Table 1. HCQ was administered to 107 patients after QTc evaluation by electrocardiogram (ECG). HCQ was avoided in patients under palliative care (n = 4), if QTc was over 500 msec (n = 1), and if patients had received prior treatment with CQ (n = 2). Mean initial QTc was 429 msec (Bazett formula used for correction). Biochemistry was followed on a regular basis, and ionic disturbances (hypokalemia, hypomagnesemia) were treated by supplementation if present. Repeat ECG was not systematically performed during HCQ treatment, except in case of drug-drug interaction which could potentially increase QTc (see footnote of Table 1). The main drug-drug interaction was driven by addition of AZM (n = 28). In this group, QTc was controlled at day 2 of combination therapy (n = 24). We observed a significant increase in mean QTc, from 418 to 433 msec ($p < 0,01$ with paired *t*-test), but none of the patients showed a QTc over 500 msec.

Furthermore, in our entire cohort there were no sudden deaths nor syncope requiring resuscitation or ICU admission. All ICU admissions (n = 13) were linked to respiratory failure resulting from COVID-19 pneumonia. One patient on HCQ presented AV nodal reentry tachycardia in parallel with respiratory failure, and was successfully treated with adenosine. All deaths in our cohort (n = 12) were attributed to COVID-19 infection.

In conclusion, based on our clinical experience, no safety issues were encountered with the use of HCQ for the treatment of COVID-19. In coherence with recent data published here [6], its association with AZM also seems to be safe, despite a significant increase of QTc that should be carefully monitored. The efficacy of HCQ and its combination with azithromycin on COVID-19 infection needs, of course, to be strengthened with further evidence from large randomized clinical trials. However, at this point of the COVID-19 pandemic, we find it relevant to share our clinical experience with this well-known, readily available compound (HCQ) which has limited contraindications and may help in the fight against this outbreak.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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Table 1
Characteristics of patients.

No. Patients	114
Age, mean [range], years	63 [19–95]
Sex	63 (55.3)
Male (%)	51 (44.7)
Female (%)	
Patients with comorbidities (%)	29 (25,4%)
None	59 (51,8%)
Cardiovascular disease	56 (49,1%)
Hypertension	17 (14,9%)
COPD	25 (21,9%)
Diabetes	17 (14,9%)
Immunosuppression	
O^2 sat. on admission. while breathing ambient air, mean [range], %	90,1 [55–99]
Clinical presentation[a] (%)	0 (0%)
Mild disease	10 (8,8%)
Moderate disease	104 (91,2%)
Severe disease	
HCQ (%)	107 (93.8)
ECG pretreatment (% of HCQ)	100 (93.4)
QTc initial, mean [range] msec	429 [342–493]
Drug-drug interaction (% of HCQ)	34 (31.8)
Azithromycin	28 (26.2)
Other[b]	6 (5.6)
ECG CTRL at day 2 (% of patient w. drug-drug interaction)	27 (79.4)
Azithromycin	24 (70.5)
Other	3 (8.8)

[a] "Mild disease" was define as symptoms of upper respiratory infection (fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing) or digestive symptoms (nausea, vomiting, abdominal pain, diarrhea); "moderate" as clinical (fever and cough) and radiological pneumonia (infiltrates) without hypoxemia; "severe" as clinical and radiological pneumonia with hypoxemia (O^2 saturation < 93%).

[b] Other consisted in escitalopram, citalopram, fluconazole, valproate, mirtazapine and olanzapine.

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