

ABSTRACT

Background

In a recent survey, most physicians worldwide considered that hydroxychloroquine (HCQ) and azithromycin (AZ) are the two most effective drugs among available molecules against COVID-19. Nevertheless, to date, one preliminary clinical trial only has demonstrated their efficacy on the viral load. Additionally, a clinical study including 80 patients was published, and in vitro efficiency of this association was demonstrated.

Methods

The study was performed at IHU Méditerranée Infection, Marseille, France. A cohort of 1061 COVID-19 patients, treated for at least 3 days with the HCQ-AZ combination and a follow-up of at least 9 days, was investigated. Endpoints were death, worsening and viral shedding persistence.

Findings

From March 3rd to April 9th, 2020, 59655 specimens from 38617 patients were tested for COVID-19 by PCR. Of the 3165 positive patients placed in the care of our institute, 1061 previously unpublished patients met our inclusion criteria. Their median age was 43.8 years old and 493 were male (46.4%). No cardiac toxicity was observed. Virological cure was obtained in 973 patients within 10 days (91.7%). Prolonged viral carriage at completion of treatment was observed in 47 patients (4.4%) and was associated to a higher viral load at diagnosis ($p < 10^{-2}$) but viral culture was negative at day 10 and all but one were PCR-cleared at day 15. A poor outcome was observed for 46 patients (4.3%), 10 were transferred to ICU, 5 patients died (0.47%) (74-95 years old) and 31 required 10 days of hospitalization or more. Among this group, 25 are now cured and 16 are still hospitalized (98% of patients cured so far). Poor clinical outcome was significantly associated to older age (OR 1.09), initial higher

severity (OR 13.46) and low hydroxychloroquine serum concentration. In addition, both poor clinical and virological outcomes were associated to the use of selective beta-blocking agents and angiotensin II receptor blockers ($p < 0.05$). Mortality was significantly lower in patients who had received ≥ 3 days of HCQ-AZ than in patients treated with other regimens both at IHU and in all of Marseille's public hospitals ($p < 10^{-2}$).

Interpretation

The HCQ-AZ combination, when started immediately after diagnosis, is a safe and efficient treatment for COVID-19, with a mortality rate of 0.5% in older patients. It avoids worsening and clears virus persistence and contagiousity in most cases.