Trattamento della COVID-19 nelle persone che vivono con HIV: una doppia sfida.

Treatment of COVID-19 in People Living with HIV: a double challenge.

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Riassunto

La Malattie da Coronavirus 2019 (COVID-19) ha causato migliaia di morti nel mondo. Il virus SARS-COV-2 infetta primariamente le cellule alveolari causando polmonite e sindrome da distress respiratorio acuta (ARDS).

Diversi approcci terapeutici sono stati fin qui proposti e numerosi trials sono in corso. Tuttavia, il corretto approccio al trattamento del COVID-19 nelle persone con HIV deve essere ancora determinato così come al sicurezza della co-somministrazione dei farmaci anti SARS-CoV-2 e anti HIV. Lo specialista in Malattie Infettive dovrebbe essere sempre consultato prima di iniziare un trattamento anti COVID-19 in persone con HIV.

Abstract

Coronavirus disease 2019 (COVID-19) has caused thousands of deaths around the world. SARS-CoV-2 infects primarily the lung alveolar epithelial cells causing pneumonia and Acute Respiratory Distress Syndrome (ARDS). Different treatment approaches have been proposed, and several trials are ongoing. However, the correct approach to COVID-19 treatment in people living with HIV (PLWH) is still to be determined as well as the safety of the concurrent administration of anti SARS-CoV-2 drugs and antiretroviral therapy. Therefore, the infectious disease specialist should be consulted before starting anti COVID-19 treatment in PLWH.

Since December 2019, when the first case of SARS-CoV-2 infection was described, Coronavirus disease 2019 (COVID-19) has caused thousands of deaths around the world. SARS-CoV-2 infects primarily the lung alveolar epithelial cells causing pneumonia and Acute Respiratory Distress Syndrome (ARDS) (1). Different treatment approaches have been proposed, and several trials are ongoing. Among HIV boosted protease inhibitors (PI), lopinavir/ritonavir has been evaluated in a randomized clinical trial for the treatment of severe COVID-19, showing no benefit in time to clinical improvement overall. However, an advantage in terms of shorter intensive Care Unit (ICU) stays and shorter time to clinical improvement were observed, and reduced mortality if started early (2).

Recently, the study by Rosemberg et al. (3) reported on the use of hydroxychloroquine and azithromycin in real life, in a cohort of almost 2400 patients with COVID-19. In particular, the secondary outcome, regarding the increased risk of cardiac arrest when the two drugs were given in combination, draws our attention. Hydroxychloroquine and azithromycin could be administrated at home in different types of subjects, including people living with HIV (PLWH) with COVID-19. However, PLWH have a significant burden of cardiovascular disease (CVD) associated with the virus itself, with combination antiretroviral treatment (cART), and with their lifestyle, that frequently requires pharmacological treatment. In a recent study, Härter et al. (4) described a case series of 33 HIV infected patients with COVID-19, treated with different antiretroviral regimens. However, no data were reported on COVID-19 treatment and possibly related side effects.

Remdesivir (GS-5734) is a nucleoside analogue prodrug displaying in vitro inhibitory effects on pathogenic animal and human coronaviruses, including SARS-CoV-2 (5). The first trial showed that Remdesivir was superior to placebo in shortening the time to recovery, but did not impact significantly on mortality (6). In a later retrospective cohort study, comparing 312 patients with severe COVID-19 who received remdesivir with 818 matched patients, remdesivir was associated with significantly greater recovery and 62% reduced risk of death versus standard-of-care treatment (7). A randomized, open-label, phase 3 trial involving hospitalized

patients with confirmed SARS-CoV-2 infection (ClinicalTrials.gov number, NCT04292899) did not show a significant difference between a 5-day course and a 10-day course of remdesivir. By day 14, a clinical improvement of 2 points or more on the ordinal scale occurred in 64% of patients in the 5-day group and in 54% in the 10-day group, in patients who did not need mechanical ventilation (8).

Remdesivir is currently indicated for the treatment of COVID-19 in patients with radiologically proven pneumonia requiring oxygen therapy. No specific indication is given for the treatment of PLWH receiving ART. However, a possible increased risk of lactic acidosis due to additive mitochondrial toxicity should be carefully considered and lactate levels should be closely monitored.

Besides, azithromycin and hydroxychloroquine have drug-drug interactions (DDI) with antiretrovirals that could increase the risk of adverse events. Lopinavir/ritonavir may prolong QTc interval and, as other boosted PIs, increase both azithromycin and hydroxychloroquine concentration. Furthermore, among non-nucleoside reverse transcriptase inhibitors, rilpivirine has demonstrated a tendency to increase QTc during treatment, with a possible cumulative effect in multiple drug administration (9). When considering all these aspects, the treatment of COVID-19 in PLWH may result in a real challenge, and, in our opinion, some urging issues remain open.

First of all, although data on the efficacy on SARS-CoV-2 are scarce, if a cART switch from other anchor drugs to lopinavir/ritonavir is considered, the risk of QTc prolongation and DDI should be carefully considered. Secondly, the risk-benefit ratio of cART modification in order to avoid DDI and additive toxicity should be carefully considered, given the risk of HIV viral failure.

A recent position paper from the Italian society of Infetious Diseases has reviewed the existing literature on COVID-19 and gave some clinical indications about treatment approaches (10).

In conclusion, the efficacy and safety of therapies for COVID-19 in PLWH should be carefully considered, and the consultation of an Infectious Diseases specialist is recommended before administration.

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