Title: COVID-19 and Treatment: Old Friends for a New Enemy?

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Dear Editor - While we wait for the "best good news" of a vaccine that allows us to control the SARS-CoV-2 virus that causes COVID-19, we have to try to find a solution to lessen the adverse effects on people's health. The situation is not comfortable, according to the World Health Organization -WHO- 4,278,180 people have been infected, of whom 292,376 have died (May 13, 2020), many in a productive age who surely were out of the economic upheavals due to the measures adopted to anticipating the pandemic will also have a negative impact on the world economy.

The global effort to develop a vaccine for the COVID-19 pandemic is unprecedented in humanity, and it is postulated that with this speed, we are going to get good news in one or two years. To date, there are more than 100 efforts for possible vaccines, of which more than half are in active process (1). However, due to the complexity and the time that this development can take, it is necessary the finding of a successful treatment, even if it is temporary, that allows reducing the adverse effects of the infection on humanity.

Searching in PubMed since 1970 using the following terms (SARS-CoV-2 or SARS-CoV-1 or COVID-19 or SARS or MERS or coronavirus and pharmacology), 31,178 articles were obtained (May 13, 2020), of which 38% are published in 2020 (11,900 articles), in just 5 months (Figure 1). Besides, the results show that the articles increased dramatically in 2003 when SARS appeared.
Several strategies for COVID-19 treatment were proposed. Natural products with known activity against different species of CoV are now potential candidates. Most of them are herbs from Traditional Chinese Medicine, and some examples are *Lycoris radiata*, *Rheum officinale* and *Polygonum multiflorum* which exerted a strong effect against SARS-CoV-2 (2).

The antiviral effect in vitro of several agents was demonstrated, but due to the rush to find pharmacological treatments, several clinical studies with standard treatments approved for other medical conditions have been conducted: chloroquine and hydoxychloroquin, treatment of malaria and chronic inflammatory diseases; the lopinavir/ritonavir combination, antiretroviral therapy for HIV; the antiviral umifenovir, currently approved for treatment of influenza; the monoclonal antibody IL-6 receptor agonist, used in rheumatoid arthritis treatment, and also the combination of interferon-β with the antiviral therapies (3-7). The investigational drugs remdesivir and favipiravir, used for Ebola and influenza virus respectively are also studied (8).

A recent review from Sanders. *et al.* concluded that despite the high volume of published literature about pharmacological treatments for COVID-19, any medical therapy has been definitely shown to improve the outcome, and powered randomized trials are needed (8). However, remdesivir and favipiravir, are described as the most promising treatments (8-9).

In this line, the WHO started a streamlined global clinical trial to collect robust scientific data during the pandemic called SOLIDARITY, that will randomize confirmed cases into the potential treatments remdesivir, chloroquine or hydroxychloroquine, lopinavir/ritonavir and this combination plus interferon-β (10).

The physiopathological mechanism of novel coronavirus was recently described using bioinformatics and revealed that some viral proteins attack 1-beta chain of hemoglobin, and others bind to porphyrin, leading to a restrained carry of oxygen (11). In addition, this study showed that chloroquine could prevent these bindings and potentially relieve the symptoms of respiratory distress. Recently, a study demonstrates that both chloroquine and its less toxic derived hydroxychloroquine, inhibits SARS-CoV-2 in vitro, instead suggesting that the antiviral activity of hydroxychloroquine seems to be less potent than chloroquine, both drugs effectively
blocked the transport from endosomes to endolysosomes (12). At the end of March, around 20 studies with chloroquine and hydroxychloroquine were conducted in China, but according to the WHO, no data has been shared (10). A French team conducted two small trials using hydroxychloroquine in combination with azithromycin, and showed a significant reduction on the viral load and also a clinical improvement (3-4). Recently, the same team revealed promissory data from a larger study conducted in a cohort of 1061 COVID-19 patients. The combination of hydroxychloroquine and azithromycin revealed a good clinical outcome of 91.7% within 10 days, and also a very low mortality rate (0.47 %) (13). Since no cardiac toxicity was found, the authors present this combination as a safe and efficient treatment.

The epidemic continues spreading, but in the same way the scientific community is working and the research findings are increasing. More randomized clinical trials are conducted right now, and the evidence is growing, leading to make better choices about the treatments: maybe the repurposed medications are the answer or maybe will help to complete the studies for the promissory ones. All these efforts are exactly that we need to face this challenge and effectively combat the pandemic.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

REFERENCES