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COMMENTARY

Repurposing therapeutic agents and herbal medicines to defeat viral nemesis

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The coronavirus (CoV) pandemic has boosted the research for treatments of this unmet medical emergency. A recent commentary appeared in this journal has pointed out that a rapid way to develop new therapies could be the repurposing of Angiotensin type 1 receptor blockers (Gurwitz, 2020), commonly referred to as sartans and previously suggested by Sun, Yang, Sun, and Su (2020). After a deep analysis and exhaustive illustration of both the rationale behind this tentative approach and related safety concern, Gurwitz suggested that data mining of clinical patient records survived to COVID-19 epidemic might be useful to assess the feasibility of sartans' repurposing as therapeutic treatment to decrease acute respiratory distress syndrome (ARDS) and reduce the aggressiveness from severe acute respiratory syndrome CoV-2 (SARS-CoV-2) infections.

An emerging experiment based on a 2019-novel CoV (2019-nCoV)-related pangolin CoV GX_P2V/pangolin/2017/Guangxi also suggests the putative role of angiotensin-converting enzyme 2 (ACE2) as a host receptor for viral attachment and the feasibility of its targeting by inhibitors such as selamectin and mefloquine (Fan et al., 2020). The structural basis of ACE2 binding with 2019-nCoV is currently under intense study (Yan et al., 2020).

Obviously, repurposing old drugs for COVID-19 may start from therapeutic agents with proven efficacy against other lethal viral infections. One therapeutic agent of great interest is remdesivir that showed efficacy against Middle East respiratory syndrome CoV (MERS-CoV) in a transgenic humanized mouse model. The potential application of this drug along with HIV-1 protease inhibitors and interferon-β in COVD-19 was suggested (Ko et al., 2020; Martinez, 2020). In fact, remdesivir has been the standard reference drug in human trials of antibodies and other therapeutic agents against the Ebola virus (Inungu, Iheduru-Anderson, & Odio, 2019; Mulangu et al., 2019). Interestingly, the Gurwitz's approach was previously proposed during the 2014–2016 Ebola outbreak (Lentini & Habtemariam, 2015), with an emphasis on cardiovascular medicines circumstantially used by surviving Ebola patients. An overview of the literature (Rojek, Horby, & Dunning, 2017; Sweiti, Ekwunife, Jaschinski, & Lhachimi, 2017) does not allow to say if this approach against Ebola epidemic has been pursued or not. However, a retrospective study of Ebola patient outcome data showed significantly lower mortality (50.7%) for artesunate–amodiaquine group compared with artemether–lumefantrine group (64.4%) (Gignoux et al., 2016). This outcome was serendipitously reported since Ebola patients received the antimalarial combination artesunate–amodiaquine in lieu of the first-line antimalarial treatment (artemether–lumefantrine), which was incidentally lacking because of supply failure. Thus, the retrospective clinical analysis suggested the possible repurposing of certain antimalarials against Ebola virus (Garbern et al., 2019). Interestingly, the antimalarial, amodiaquine analog chloroquine has been recently proposed (Gao et al., 2020) and debated (Touret & de Lamballerie, 2020) as an option in the treatment of SARS-CoV-2. On the other hand, the use of traditional Chinese remedies as a therapeutic approach for combating SARS-CoV has been well publicized (World Health Organization [WHO], 2003) and it was recently proposed for prevention of COVID-19 (Luo et al., 2020). Despite some warring aspects (Editorial, 2019), WHO has recently recognized traditional Chinese medicine in its influential global medical compendium (Cyranoski, 2018). Recording which plant(s) was(were) used by Chinese survivors in the last few months could thus offer a golden opportunity to identify a possible source of new antiviral lead compounds (Habtemariam & Lentini, 2015). Of course, two aspects, among others, would deserve mandatory attention: herbal extract quality control and clinical trials performed according to the current standards.

While the therapeutic potential of anti-inflammatory drugs for COVID-19 is yet to be established, there is no doubt that exaggerated inflammatory response is involved in the pathology of the lethal human corona viruses (SARS-CoV, MERS-CoV, and SARS-CoV-2). Citing the association of severe pneumonia with the high mortality rate

in COVID-19 patients, speculative argument on anti-inflammatory therapeutic approach has been presented (Sun et al., 2020). This is an evolving area, however, and some evidences already showed that corticosteroid treatment does not ameliorate lung injury under COVID-19 (Russell, Millar, & Baillie, 2020). The efficacy of these drugs also depends on the severity and stage of the disease: the earlier viral replication phase that may be targeted by antiviral approach or the late inflammatory/pneumonia stage that may respond to immunotherapy. The large volume of synthetic and natural products already proven to show anti-inflammatory effects in chronic lung diseases remains to be explored. A further approach is of course testing natural products with multiple or polypharmacology effects that combine antiviral, anti-inflammatory, and organoprotective activities. Whatever sources of drugs (natural, synthetic, or repurposed) are suggested to be used for COVID-19, their efficacy should be proven through a valid clinical trial.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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