Pharmacologic Therapy for COVID-19 Infection

Neil Nusbaum^{1,2,3}

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Abstract

The COVID-19 pandemic has focused attention on issues of epidemiology, public health, and vaccine design. I submit that attention to COVID-19 pharmacologic therapy needs similar emphasis, including identifying any existing medications that can be repurposed to treat COVID-19 patients.

Keywords COVID-19 · Case control studies · Antiviral therapy

Introduction

As this is written, there is a high level of concern and focus across the globe on how to best respond to the COVID-19 pandemic [1]. Almost all of the current attention has focused in the short term on the issues of understanding its epidemiology and how to contain it, and in the longer term on how to devise a vaccine against it. Much less attention has been directed to the therapy for those already infected.

Recent reports suggest that worldwide a large number of patients have already recently been infected with COVID-19, although that infection may only be identified on future testing [2]. Based on the likelihood that the pandemic cannot soon be contained and on the likelihood that an effective vaccine at best is many months away, I believe it is equally important to urgently investigate the best therapeutic strategies for this epidemic.

At present, the US Centers for Disease Control and Prevention (CDC) guidance on management of COVID-19 infection suggests on theoretical grounds to avoid corticosteroids, and notes some investigational drug therapy through clinical trials [3]. However, the CDC highlights that:

“No specific treatment for COVID-19 is currently available. Clinical management includes prompt implementation of recommended infection prevention and control measures

and supportive management of complications, including advanced organ support if indicated.” There has been great interest, but so far only anecdotal data, about potential therapeutics.

It is possible of course that novel therapeutic agents may be identified that are specific for the COVID-19 virus. Even if that were to happen, translation of such agents to broad clinical practice would likely take considerable time. Some delays in implementation would be required for establishing the safety and effectiveness of the new agents.

The epidemic itself has also already shown its ability to interrupt international manufacturing supply and distribution chains. Accordingly, one could expect that it might take a prolonged period for a ramp up of any novel agent’s supply sufficient to meet worldwide demand. In the short term, the only drugs that will be widely available to COVID-19 patients are those that have already been produced for other reasons.

In short, there appears to be strikingly little data available at present about potential therapeutic options for treating those now infected with the virus, including whether and how to use existing drugs. This is particularly true because of many of those with asymptomatic infection or mild disease have not even been identified as at risk for the disease. Many others of those who in fact have been affected by the disease to some degree have been advised to self-quarantine at home, where they are presumably treating their symptoms largely ad hoc with whatever happens to be available in the home medicine cabinet.

An important potential source for data on the observed course of the disease may be those cohorts of patients in the already identified disease clusters, notably those on cruise

✉ Neil Nusbaum
Nusbaum.Neil@gmail.com

¹ Central Texas Veterans Health Care System, Temple, USA

² University of Illinois College of Medicine At Rockford, Rockford, USA

³ 40 Quintana Drive, Galveston, TX 77554, USA

ships and in nursing homes. A higher case fatality rate is unfortunately expected among frail older individuals, many of whom are in these settings. From a statistical point of view this vulnerability would make it more apparent if a particular therapeutic measure was effective in reducing the case fatality rate among them. The higher case fatality rate means that a given relative risk reduction in that baseline rate represents a relatively large absolute risk reduction, and so a relatively low number needed to treat [NNT] in order to prevent a fatality.

An older population would already be anticipated at baseline to commonly be on multiple chronic medications (e.g. immune response modifiers, nonsteroidal anti-inflammatory drugs, vitamin supplements) for other reasons, and some of these medicines might potentially impact the course of incident COVID-19 infection. Further, it is likely that many of these patients upon undiagnosed COVID-19 illness onset had had additional agents that were added to treat presumptively for other pulmonary diagnoses, such as influenza or chronic obstructive pulmonary disease exacerbation.

As a result, there is likely to already be a large cohort of patients who received antipyretics, antibacterial drugs, antivirals intended for influenza treatment, and/or corticosteroids for what ultimately will be diagnosed as a recent episode of COVID-19 infection. As the pandemic progresses, the numbers of patients to populate case–control analyses will inevitably increase.

Case–control studies in fact would be useful to identify differences in COVID-19 mortality rates, in either direction, related to medications administered to treat other diagnoses in the days immediately preceding the correct diagnosis of COVID-19 in the patient. This data might give clues to medications to be tried for adjunctive treatment of COVID-19 as well as to medications that should be avoided. Promising candidates from case control data could then rapidly inform selection of agents [4] for randomized drug trials. Clues from case control analyses might complement therapeutic leads from mechanistic approaches.

It is reasonable to assume that individuals who suffer mortality on average would have more comorbidities than those who do not, and that those individuals with more comorbidities in general would be more likely to take a greater number of medications, and in turn be more likely to take any randomly chosen medication. A priori, one might well expect that even a medication that has no specific impact on COVID-19 biology to turn out to be more commonly used by individuals who suffer mortality during the pandemic than by those who do not suffer these consequences, so it would be of particular interest therefore to identify any medication that was less commonly used by those who suffer mortality than by those who do not. Such medication might potentially be of benefit for the prevention and/or treatment of COVID-19 infection.

Reference

1. Grasselli, G., Pesenti, A., & Cecconi, M. (2020). Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: Early experience and forecast during an emergency response. *JAMA*. <https://doi.org/10.1001/jama.2020.4031>.
2. Fink S, Baker M. ‘It’s Just Everywhere Already’: How delays in testing set back the U.S. Coronavirus Response. *The New York Times*. March 10, 2020. Retrieved from <https://www.nytimes.com/2020/03/10/us/coronavirus-testing-delays.html?action=click&module=Top%20Stories&pgtype=Homepage>.
3. Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). Retrieved from March 11, 2020 <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>.
4. University of Oxford, Chloroquine Prevention of Coronavirus Disease (COVID-19) in the Healthcare Setting (COPCOV). Retrieved March 11, 2020 <https://www.clinicaltrials.gov/ct2/show/NCT04303507>

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