Use of antiviral drugs to reduce COVID-19 transmission

As the coronavirus disease 2019 (COVID-19) spreads, efforts are being made to reduce transmission via standard public health interventions based on isolation of cases and tracing of contacts. In their modelling study, Joel Hellewell and colleagues[1] predict that such a strategy could contribute to reducing the overall size of an outbreak, but will still be insufficient to achieve outbreak control of COVID-19 when the basic reproduction number (R_0) is higher than 1·5 or the proportion of contacts traced is lower than 80%.

One of the main assumptions of the model by Hellewell and colleagues is that all individuals with symptomatic infection with severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) are eventually tested and reported. However, under the guidelines of most countries with low-grade transmission, clinicians will test suspected patients only if they have travelled to an epidemic region since the outbreak began. A second assumption of the model is that isolation of cases is 100% effective in stopping transmission. Yet home confinement of infected individuals and contacts is challenging, efficacy is variable, and the rigorous tracking involved requires a considerable amount of public health resources.

The current COVID-19 emergency warrants the urgent development of potential strategies to protect people at high risk of infection—particularly close contacts and health-care workers, among others—even if more robust data on antiviral therapies is yet to come. A key reason for such an approach is the high estimates for the secondary attack rates of SARS-CoV-2 in households (~15%) and among close contacts (~10%).[2] Pre-exposure prophylaxis and postexposure prophylaxis (PEP) with antimicrobial drugs are effective in preventing illness before potential exposure or after documented exposure to a variety of microbial pathogens, and in reducing the risk of secondary spread of infection. Based on experiences with PEP for other infections, we recommend starting PEP as soon as possible after a recent possible exposure to SARS-CoV-2. For example, PEP with rifampicin is given to people exposed to index cases of invasive meningococcal infection, and oseltamivir has been recommended by WHO for people at high risk of infection before or after exposure to pandemic influenza.[3]

Antiviral drugs administered shortly after symptom onset can reduce infectiousness to others by reducing viral shedding in the respiratory secretions of patients (SARS-CoV-2 viral load in sputum peaks at around 5–6 days after symptom onset and lasts up to 14 days), and targeted prophylactic treatment of contacts could reduce their risk of becoming infected.[3]

The implementation of antiviral treatment and prophylaxis has several requirements. The stockpile of drugs must be adequate, the safety of treatment must be very high, and costs should ideally be low. The antimalarial drug, hydroxychloroquine, is licensed for the chemoprophylaxis and treatment of malaria and as a disease-modifying antirheumatic drug. It has a history of being safe and well tolerated at typical doses. Notably, the drug shows antiviral activity in vitro against coronaviruses, and specifically, SARS-CoV-2.[4] Pharmacological modelling based on observed drug concentrations and in vitro drug testing suggest that prophylaxis with hydroxychloroquine at approved doses could prevent SARS-CoV-2 infection and ameliorate viral shedding.[5] Clinical trials of hydroxychloroquine treatment for COVID-19 pneumonia are underway in China (NCT04261517 and NCT04307693). We are reviewing the results from China as they emerge. The first study (NCT04261517) has showed positive preliminary outcomes (albeit not conclusive because of the small sample size) in terms of clinical management, with published data expected soon.

We are planning a multicentre randomised controlled trial (NCT04304053) to evaluate the efficacy of antiviral treatment in anyone found to be infected, and the efficacy of prophylactic hydroxychloroquine in preventing secondary SARS-CoV-2 infections and disease symptoms among all contacts. Our objective is to evaluate the reduction in transmissibility of SARS-CoV-2 and in disease progression among the contacts of an index case. The design intervention is based on the design used during the Ebola ça Suffit vaccination trial for Ebola in 2015.[6] A person newly diagnosed with the disease becomes the index case, around whom an epidemiologically defined ring of contacts is formed. This ring is then randomised to either intervention or control in a 1:1 ratio on an open-label basis. The study will be done over the course of the COVID-19 outbreak in the Catalonia region of Spain, with initial results expected in May, 2020. Identifying a treatment for the prevention of COVID-19 would change the course of the outbreak entirely.

We declare no competing interests.

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