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LETTERS TO THE EDITOR

Clinical-scientific notes

COVID-19 and chronic obstructive pulmonary disease: therapeutic potential of blocking SARS-CoV2 adhesion factors

The ongoing pandemic of SARS-CoV2 poses unique challenges to the healthcare community to outsmart the virus and limit both initial infection and subsequent morbidity, especially in patients with pre-existing chronic obstructive pulmonary disease (COPD) and other pro-inflammatory chronic disease such as diabetes. Analysis of Chinese data revealed three times higher case fatality among those with COPD. Several potential therapies such as direct anti-virals and interferons, as well as (hydroxy)-chloroquine with a less obvious mechanism are under investigation,[1] although early study data suggest that effectiveness is limited.[2]

For many years we have been advocating for a non-antibiotic approach to common respiratory infections in COPD, such as *Haemophilus influenzae* and rhinovirus, by utilising what we now know about the general microbial requirement for (blockable) airway epithelial adhesion

before clinical infection can occur, for example using available platelet-activating factor-receptor (PAFr) blockers.[3] A similar promising therapeutic target with drugs already available could be blockade of host adhesion sites that SARS-CoV2 employs for epithelial adherence before invasion.[4] These could be used for prophylaxis or just deteriorating respiratory status.

There are now mainly non-peer-reviewed reports that show SARS-CoV2 may bind up to four different epithelial receptors in humans, namely cell-surface angiotensin-converting enzyme-2 (ACE-2), furin cleavage sites, glucose-regulated protein-78 and CD-147 spike protein. Some of these appear to be upregulated in smokers and especially COPD,[5] as we have found markedly for common respiratory pathogen adhesive proteins, such as PAFr and intercellular adhesion molecule-1 (ICAM1).

Further reliable verification of these SARS-CoV2 adhesion sites in smokers, COPD and in others with high-risk conditions, could be quickly achieved through access to well phenotyped lung tissues, unfortunately even if obtained at post-mortems. We also need urgent epidemiological data on relative COVID-19 incidence and outcomes for those already on potential blocking drugs such as ACE antagonists.

Responding to concerns that anti-ACE drugs may be harmful, a recent Australian/New Zealand consensus statement on managing cardiovascular disease (CVD) and COVID-19 recommends the continuation of angiotensin-converting enzyme-inhibitors (ACE-I/angiotensin receptor blocker (ARB)) in patients with hypertension, heart failure and CVD,[6] which is in line with the recommendation of American College of Cardiology.[7] Potentially, this could have the dual benefit of managing CVDs and also blocking SARS-2 viral adhesion to the host respiratory epithelium and indeed in multiple other organs, including intestine, kidney, heart and endothelia, thus mitigating the severity of COVID-19 in highly susceptible patients with cardiovascular comorbidity.

Several clinical studies assessing the therapeutic potential of ARB are now underway, albeit not in COPD patients (https://clinicaltrials.gov/ct2/results?cond=arb+covid&term=&cntry=&state=&city=&dist=). Thus, especially those COPD patients or smokers who do not respond to the available therapies could be treated with clinically safe anti-adhesion drugs such as ARB, or TMPRSS2 inhibitor or specific mono-/polyclonals. It should also be important to collect/analyse epidemiological data for individuals who currently are on ACE-I/ARB, and compare clinically significant infection rates and outcomes with those not taking such a drug. Any perceivable differences in the prevalence, severity, mortality or SARS-2 viral titres would help ascertain the role of ACE-2 in COVID-19, which may prove helpful for any further waves of this infection, or the next virulent COVID to emerge.

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