

incidence of bacterial superinfections in patients with COVID-19, by the severity of the clinical status of many patients without improvement despite the antiviral therapy, by the possibility that patients were immunocompromised because of immunomodulatory therapy, and by the fact that half of tracheal aspirates was obtained during antibiotic therapy, increasing the diagnostic difficulty.

Our preliminary data suggest that in mechanically ventilated COVID-19 patients undergoing immunomodulatory therapy, tracheal aspirates should be obtained as soon as possible and antibiotic therapy potentially withheld until microbiology results become available, because of the low rate of positive tracheal aspirates. Based on our local conditions, use of empirical broad-spectrum antibacterial drugs was inappropriate in a substantial number of cases, and narrow-spectrum antibiotics would be preferred. For use of broad-spectrum antibiotics, we can infer that de-escalation based on the results of susceptibility tests or negative tracheal aspirates should be applied as early as possible.

Absence of a specific cure, evidence that intensive care surge capabilities were rapidly overwhelmed, clinical suspicion of nosocomial infections, and wide use of immunomodulatory therapy modified our practice and led us to misuse or overuse antibacterial drugs, failing de-escalation irrespective of the culture results. Evidence from our small cohort of patients call for an urgent and comprehensive analysis of pulmonary co-infections in COVID-19 patients admitted to the ICU. In line with these goals, the COVID-19 Critical Care Consortium is currently collaborating with more than 400 ICUs worldwide to characterise secondary bacterial infections associated with SARS-CoV-2 and provide urgent recommendations on appropriate empiric therapies.

Declarations of interest

The authors declare that they have no conflicts of interest.

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Opioids and the COVID-19 pandemic: does chronic opioid use or misuse increase clinical vulnerability?

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Editor—Opioids have predictable analgesic actions and are widely used in many clinical settings, but they also produce unwanted side-effects including respiratory depression, tolerance and are misused. Misuse and poor opioid stewardship in the therapeutic arena are generally accepted as the underlying cause of what we describe as the ‘opioid

epidemic’ or ‘opioid crisis’.¹ According to a UK Office for National Statistics report in 2019,² there were 139 845 people in contact with drug services during the 2018–19 period; some of these will be opioid dependent, but for many this will not be a single substance misuse. Moreover, a Public Health England (PHE) report suggests 540 000 patients

(retrospective) were continuously prescribed opioids for 3 yr,³ and some of these may be opioid dependent. It is possible that some patients in the PHE report may have also made contact with drug services. Patients presenting to substance misuse services are likely to be using multiple substances so purist ascription of effect to opioid alone is problematic.

The current coronavirus disease 2019 (COVID-19) pandemic and 'opioid epidemic' or dare I say pandemic have clearly intersected. There is an excellent, thought-provoking opinion piece on this by Becker and Fiellin.⁴ The thrust of several papers on opioids and COVID-19 and the main narrative revolves around opioid prescribing, access to opioids, and sociological considerations (e.g. Dubey and colleagues⁵ and Khatri and Perrone⁶). What about the side-effects of opioids in COVID infection? Is the opioid epidemic fuelling the COVID-19 pandemic?

As we know, opioids depress respiratory drive⁷ and long-term use is immunosuppressive,⁸ although direct clinical trial evidence for the latter is lacking.⁹ That said, some of the seminal early work showing opioid immunosuppression is based on data showing increased infections in addicts.¹⁰ COVID infection is more likely to produce adverse outcomes in immunosuppressed patients, and this is part of the scientific evidence for shielding in this patient group. The respiratory effects of COVID-19 infection are known only too well to anaesthetists and intensivists, and ventilation of acutely unwell patients has been the mainstay of treatment and of ICU workload. Opioids may be required for pain management in COVID-19 patients,¹¹ and paradoxically opioids have been suggested in COVID-19 palliative care for patients experiencing the sensation of suffocation.¹²

In those using opioids chronically or misusing opioids, where immune depression and a propensity to respiratory depression is likely, COVID-19 infection may be all the more deadly. At the time of writing I am not aware of any published clinical data to support this prediction, although Shanthanna and colleagues¹³ suggest that patients with chronic pain taking opioids might be more susceptible to COVID-19. Individuals who are opioid dependent also present with a range of additional co-morbidities, social deprivation, and homelessness. Whilst not suggesting these are a direct consequence of opioid misuse, they may be linked and combining to a major public health issue. With respect to COVID-19 protection, the UK Government defines a category of clinically vulnerable people where those with 'mild to moderate respiratory disease' and those with a 'weakened immune system as the result of certain conditions or medicines they are taking' are advised to take extra care.¹⁴ Surely those using chronic opioids therapeutically or those misusing opioids should be included in the clinically vulnerable group?

Declarations of interest

DGL is chair of the board of the *British Journal of Anaesthesia*. DGL is also a non-executive director of Cellomatics, a small- or medium-sized enterprise contract research organisation.

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