Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Sedation in mechanically ventilated patients with COVID-19


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Delirium in critical illness represents a considerable burden for individual patients, their family members, health-care services, and society. In the past decade, a number of initiatives have been launched with some success in the UK and internationally, with the aim of educating and challenging clinicians to improve sedation practice.[1,2] Less sedation results in lower delirium prevalence, and lower prevalence of delirium is associated with better patient outcomes.[3,4] The Pan American and Iberian Federation of Critical Medicine and Intensive Therapy, German, and US sedation guidelines all recommend mechanically ventilated patients are kept awake or easily aroused, with effective pain control.

Sedation of critically ill patients requiring mechanical ventilation is a complex health-care intervention and patient distress is an understandable concern for clinicians. Progress has been made regarding recognition of the importance of sedation assessment, routine delirium screening, and improving sedation practice. However, in a 2019 sedation reduction trial, only 52–57% of all patients were lightly sedated (defined as at least briefly awoken by voice) in the first 48 h after intensive care unit (ICU) admission.[5] In the context of a research trial, it is difficult to achieve the correct level of sedation, thus, how much more difficult is it to achieve in day-to-day clinical practice? Difficulty in achieving optimum levels of sedation combined with the challenges and clinical course of COVID-19 infection creates a difficult scenario for clinicians.[6]

The cohort study in *The Lancet Respiratory Medicine* by Brenda Pun and colleagues[7] is unique and large in size and breadth.[7] A diverse group of clinicians were able to mobilise in a short period of time to do the study, which bodes well for the future of ICU delirium management and research. The authors aimed to identify the risk factors for delirium in patients admitted to the ICU with COVID-19, and to investigate the provision of an evidence-based standard of care bundle. The risk factors identified are similar to those reported in previous studies. An important finding was that patient interaction with family, even if delivered virtually, which has become standard practice during the COVID-19 pandemic, lowered the risk of development of delirium (odds ratio 0·73 [95% CI 0·63–0·84], p<0·0001).

Another key finding was that ICU patients with COVID-19 were kept in a coma for prolonged periods—a median of 10 days (IQR 6–15) compared with 1 day (IQR 1–2) reported for patients without COVID-19.[8] The authors identified factors that were likely to have contributed to the use of deep sedation. The study raises many questions and process evaluation is needed to understand the reasons for the rapid changes in sedation practice adopted after the onset of the COVID-19 pandemic. For example, what was the extent of proning patients or use of muscle relaxants, both of which require deep sedation? What was the impact of a reduction in trained staff? 30% of ICUs had a shortage of personal protective equipment for care providers, which alone might have influenced the decision not to reduce a patient's sedation.

This study also provides evidence to explain why over-sedation was commonly observed, since the prevalence of more agitated delirium was high in patients with COVID-19. Before the COVID-19 pandemic, the reported incidence of new agitated delirium was up to 13%, with an overall prevalence of up to 20%, in adults with critical illness.[9] In this cohort study, more than 50% of patients had hyperactive delirium. Similarly, Helms and colleagues reviewed 58 consecutive ICU patients with COVID-19, of whom 40 (69%) became agitated following cessation of muscle relaxation and sedation.[10] Agitation on emergence from sedation combined with a shortage of resources might partly explain the shift in practice observed from minimal sedation to maintenance of deep sedation. These results also suggest that encephalopathy resulting from COVID-19 infection, when it manifests as delirium, is different because it results in symptoms of hyperactive rather than hypoactive delirium.

Perhaps it is unrealistic to expect that clinicians will be able to safely maintain light sedation in at least half of patients in the prolonged acute stage of COVID-19. The optimal approach to sedation in COVID-19 remains uncertain, although available evidence-based practice outside the context of COVID-19 should form the basis of the approach to delirium management. As the severity of COVID-19 illness is modified with reduced viral load, reduction in risk factors, and earlier presentation, and more is understood about

encephalopathy caused by COVID-19, clinicians might be able to safely manage the majority of these patients without the use of deep sedation.

I declare no competing interests.

Valerie Page
valerie.page2@nhs.net

Intensive Care Unit, Watford General Hospital, Watford WD18 0HB, UK

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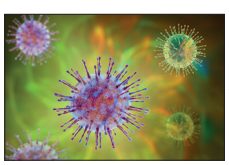
COVID-19 is not influenza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COVID-19 is often compared to influenza. In the middle of a pandemic with a new coronavirus transmitted from the respiratory tract, it is obvious to look at previous influenza pandemics and seasonal influenza for comparison. Yet it is important to understand that COVID-19 is not influenza. During the COVID-19 pandemic, several countries have struggled with overburdened intensive care unit capacity, whereas during the H1N1 pandemic in 2009, intensive care unit capacity was sufficient. For example, influenza never exceeded 4·5% of the total national intensive care unit (ICU) bed capacity in Denmark.[1] In the spring of 2020, mortality for COVID-19 in Lombardia, Italy, reached 159 per 100 000 population.[2] By contrast, a study of influenza deaths during the 2009 pandemic estimated the all-age mortality in the USA to be 4·1 per 100 000.[3]

In *The Lancet Respiratory Medicine*, Piroth and colleagues[4] report results of a retrospective study using data from the French national administrative database (PMSI), which includes discharge summaries for all public and private hospital admissions in France. The study compared 89 530 patients with COVID-19 admitted to hospital in March or April, 2020, with 45 819 patients with influenza admitted during the seasonal influenza outbreak between December, 2018, and February, 2019. The large sample size is an important strength of the study and it is assumed that the indication for hospital admission in the two periods was the same and thus does not bias the results.

The results of the study by Piroth and colleagues clearly show that COVID-19 is more serious than seasonal influenza. In-hospital mortality was 16·9% (15 104 of 89 530) for patients with COVID-19 and 5·8% (2640 of 45 819) for patients with influenza and thus the relative risk of death for COVID-19 was 2·9 (95% CI 2·8–3·0).

Hospitalised patients with COVID-19 were more likely to develop respiratory distress, pulmonary embolism, and septic shock, but were less likely to develop myocardial infarction or atrial fibrillation.[4] Only haemorrhagic strokes (and not other types of stroke) were more frequent among patients with COVID-19. The median length of stay in the ICU for COVID-19 was twice as long as for influenza (15 days [SD 14] *vs* 8 days [9]; p<0·0001).[4]

Patients with COVID-19 were more often obese or overweight, diabetic, hypertensive, and dyslipidaemic, whereas patients with influenza more often had chronic heart failure, peripheral vascular disease, chronic respiratory disease, cirrhosis, and deficiency anaemia. By contrast, people living with HIV were not over-represented or under-represented in the COVID-19 group. These results are consistent with a study from New York including 393 patients with COVID-19 reported in April, 2020,[5] and a study including 10 021 patients with COVID-19 from Germany.[6]

The studies by Piroth and colleagues[4] and others[5,6] clearly show that the risk groups are those with