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.

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Hypoxaemia does not necessitate tracheal intubation in COVID-19 patients. Comment on *Br J Anaesth* 2021; 126: 44-7

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Editor—We read with interest the editorial, 'The "third wave": impending cognitive and functional decline in COVID-19 survivors', by Baker and colleagues.[1] The authors provide a timely and succinct account of cognitive complications experienced by patients recovering from coronavirus disease 2019 (COVID-19) and put forward an interesting scheme of potential mechanisms of brain disturbances.

Baker and colleagues claim that the hypoxaemia experienced by critically ill patients in COVID-19 'has largely necessitated tracheal intubation'. We agree that large numbers of patients with COVID-19 were intubated with rates exceeding 80% in some ICUs. However, we disagree that hypoxaemia 'necessitates' intubation. The most common reason for intubation (and mechanical ventilation) in ICU patients is an increase in work of breathing, and hypoxaemia is usually managed with less invasive strategies.[2]

Hypoxaemia in critically ill patients with COVID-19 is caused by an amalgam of ventilation–perfusion mismatch and shunt. When ventilation–perfusion mismatch prevails, arterial oxygen tension (Pa_{O_2}) increases substantially in response to supplemental oxygen; a satisfactory level of arterial oxygenation can be sustained in these patients without recourse to intubation (and mechanical ventilation).[3] When intrapulmonary shunt is dominant, the increase in Pa_{O_2} with supplemental oxygen is modest or absent. Some of these patients may progress to invasive ventilator assistance.

Commenting on patients managed in their New York hospital in March–April of 2020, Baker and colleagues reflect that 'Patients were intubated early in their disease progression'. Mechanical ventilation is life-saving in appropriate circumstances. Decades of research, however, document that intubation and mechanical ventilation is associated with numerous life-threatening complications.[2] Emerging data in several countries reveal a decrease in rates of intubation between February–March and April–May.[4] Concurrent with the lower intubation rate is a decrease in mortality over time.[4]

Observations obtained in patients with COVID-19 who do not complain of dyspnoea despite severe hypoxaemia yield substantial physiological insights.[5] Patients with silent or

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happy hypoxaemia can exhibit pulse oximetry saturations of 60–70% and Pa_{O_2} values of 4 kPa (30.0 mm Hg) to 5 kPa (37.5 mm Hg), be cognitively intact and be free of dyspnoea because of concurrent factors that influence the respiratory control system.[5] Hypoxaemia in this situation commonly responds to supplemental oxygen and noninvasive strategies short of tracheal intubation (also termed endotracheal intubation).

Hypoxaemia can be dangerous, and physicians are frequently fearful of oxygen levels that do not endanger life. Bickler and colleagues[6] commented that 'we are struck by the widespread lack of knowledge concerning the tolerability of acute, profound hypoxaemia in humans … many clinicians believe that even momentary saturations in the 70s can cause brain damage'. Tourists on drives to the top of Mount Evans, Clear Creek County, CO, USA (14 271 ft; 4350 m) can experience oxygen saturations of 65% for prolonged periods without problems. Detailed neuropsychological testing in elite breath-hold divers exposed to 20 yr of repeated hypoxaemia (sufficient to induce transient neurological symptoms) revealed no long-term cognitive changes.[7]

Failure of cardiovascular compensation is the critical factor that determines whether severe hypoxaemia causes brain injury. When cats were exposed to 25 min of marked hypoxaemia (decrease in Pa_{O_2} from 14.1 kPa [106 mm Hg] to 2.3 kPa [17 mm Hg]), none developed brain injury if mean arterial pressure (MAP) was maintained above 65 mm Hg.[8] The same Pa_{O_2} accompanied by severe hypotension (MAP <45 mm Hg for 4 min) produced severe brain injury.

Baker and colleagues claim that 'Cognitive impairment is frequently seen in patients with chronic hypoxaemia, including chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea'. Research into the cognitive impairment in these disorders has been conducted for more than 40 yr. The cognitive impairment in patients with sleep apnoea is at least as likely to be the result of sleep fragmentation as hypoxaemia.[9] Baker and colleagues cite a study by Yerlikaya and colleagues[10] in support of their arguments. Yerlikaya and colleagues measured event-related potentials (ERPs) and observed no difference in P300 amplitudes between patients with sleep apnoea who had severe hypoxaemia *vs* those with mild hypoxaemia.

With regard to COPD, patients free of hypoxaemia also exhibit cognitive impairment, casting doubt on the role of hypoxaemia as a causative factor.[11] Correlation between Pa_{O_2} and cognitive function in COPD is weak (r=~0.2), and oxygen levels account for only 5% of predicted variance in cognitive performance[11] Although cognition in sleep apnoea and COPD is an area of ongoing research, a convincing link between hypoxaemia and cognitive impairment has not been documented by rigorous investigation.

In conclusion, hypoxaemia is common in COVID-19 patients. It is tempting for a physician to feel that inserting a tracheal tube is acting on the side of safety. Intubation, however, is not an unalloyed good and it exposes patients to a host of life-threatening complications. The level of hypoxaemia required to produce brain damage is considerably lower than what many physicians suspect. The hypoxaemia observed in COVID-19 usually responds to measures short of tracheal intubation, which itself is associated with the high mortality observed in the early weeks of the pandemic. Hypoxaemia is not in itself justification for intubation in COVID-19 patients.

Declarations of interest

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