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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Letter to the Editor

Nutritional interventions to modulate haemoglobin-oxygen affinity in COVID-19 patients

Dear Editor,

We read with interest the study *Modulation of Hb-O_2 affinity to improve hypoxemia in COVID-19 patients*, by Woyke et al. [1]. The opinion paper discussed the potential impact of a nutritional intervention in patients with Coronavirus-19 (COVID-19), where supplementing 5-Hydroxymethylfurfural (5-HMF) could increase haemoglobin-oxygen (Hb-O_2) affinity. Typically, hypercapnia, acidosis and hyperthermia shift the oxygen dissociation curve (ODC) to the right, reducing Hb-O_2 affinity and worsening hypoxaemia. This scenario could justify the rationale for the conclusion that a nutritional intervention shifting the ODC to the left could improve oxygenation in hypoxaemic respiratory failure [2], such as in COVID-19 patients.

The scenario presented is physiologically sound and based on evidence available at the time of publication. However, a recent study showed that Hb-O_2 affinity was actually higher in mechanically ventilated COVID-19 patients [average(SD); p_{50} 23.4 (3.1) mmHg) compared to the normal value for p_{50} of 26.7 mmHg, as well as compared to a control group of critically ill patients [p_{50} 24.6 (5.4) mmHg] [3]. In addition, COVID-19 is characterised by shunt and dead space – across the severity of oxygenation - that differ from the typical acute respiratory distress syndrome [4,5]. This observed left-shift of the ODC may be a compensatory mechanism that, while facilitating oxygen uptake in the pulmonary circulation and arterial oxygenation, could reduce the rate of peripheral oxygen unloading, although the rate of oxygen unloading may be increased if/when peripheral carbon dioxide and temperature are elevated.

The proposed nutritional intervention remains a potentially effective approach, especially in the absence of significant side effects, pending some important considerations. An optimum degree of ODC left-shift needs to be identified in terms of balancing the benefits of more rapid pulmonary oxygen uptake and arterial oxygenation with the associated reduced rate of peripheral oxygen unloading – therefore the modulation of other factors such as pH may be relevant. The nutritional intervention modality and timing needs to be determined: it may be beneficial only to a subset of COVID-19 patients with a defined clinical phenotype [5] or perhaps earlier in the disease. Here lies the difficulty particularly if patients are asymptomatic or do not perceive hypoxaemia. Finally, the overall outcome of interest and the effect size need to be defined, particularly with reference to the efficacy in the reduction of p_{50}.

Despite the complexity of the proposed therapeutic nutritional intervention and the characterisation of the associated physiological responses, its implementation might be worth investigating.

Author contributions

FF, DV and LC conceived the study, interpreted the data and approved the final manuscript.

Conflict of interest

The authors declare no competing interests.

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