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Letter to the Editor

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Letter to the Editor From Abobaker and Darrat: "Circulating Levels of Calcitonin Gene-Related Peptide Are Lower in COVID-19 Patients"

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Abbreviations: ARDS, adult/acute respiratory distress syndrome; CGRP, calcitonin gene–related peptide.

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We read with great interest the research article of Ochea-Callejero et al, who detected low circulatory levels of calcitonin gene-related peptide (CGRP) in patients with COVID-19 regardless of disease severity [1]. CGRP is a peptide molecule which has a role in some aspects of pulmonary physiology, such as pulmonary vasoregulation and tissue repair [1]. Ochea-Callejero et al suggested that restoration of normal CGRP circulatory levels can be considered as a potential therapeutic option in COVID-19 [1]. They supported their argument with the fact that low levels of CGRP could have a negative impact on lung physiology as it increases risk of vasoconstriction, which could lead to pulmonary hypertension, and it negatively affects angiogenesis and epithelial repair [1, 2]. In addition, Ochea-Callejero et al found an increased expression of CGRP receptors in proliferating type II pneumocytes of 3 patients who died of COVID-19 as compared with non-COVID-19 patients [1]. This might indicate that CGRP has an important role in lung epithelial repair process following viral induced acute lung injury. Despite the findings of this study, we think that restoring the normal circulatory levels of CGRP in patients with COVID-19 could potentially cause harmful effects. There are multiple reports providing evidence in the literature suggest that during acute infectious or inflammatory stage, CGRP could increase the chance of development of acute lung injury which subsequently leads to adult respiratory distress syndrome (ARDS). In fact, CGRP induces release of inflammatory cytokines, including interleukin-6, which could trigger the development of a massive host inflammatory response, known as cytokine storm [2, 3]. Cytokine storm is considered as a major cause of development of ARDS [4]. Furthermore, CGRP contributes to smoke inhalation lung injury as it increases airways hyperemia and capillary permeability, which leads to transvascular fluid leakage, due to its potent vasodilatory effect [5]. Pretreatment of animal models with CGRP receptors antagonist provided a protective effect against lung damage induced by smoke inhalation [5]. Another animal study showed that disruption of CGRP gene was protective against acid-induced acute lung injury [6]. Therefore, treatment with a CGRP receptor antagonist is perhaps a safer and more effective option in management of COVID-19 as compared with CGRP analogue or restoration of normal circulatory levels of CGRP. However, CGRP receptor antagonist should be used on a short-term basis during the management of COVID-19, as long-term use could abolish the protective effect of CGRP on pulmonary vasoregulation, which in turn increases the risk of development of pulmonary hypertension. The Food and Drug Administration has recently approved the use

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of CGRP receptor antagonist in a phase 2 clinical trial as a treatment option that might reduce lung inflammation in COVID-19 [2]. Once the results of this clinical trial are available, we might have a better idea about whether CGRP receptor antagonists are an effective and safe treatment option in COVID-19.

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Additional Information

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