

Letter: role of probiotics in the COVID-19 pandemic—authors' reply

EDITORS,

We read with great interest the review of our article by Dr Aguila and colleagues.¹ We are grateful for their comments. Probiotics have been a hot and controversial topic in recent years. We agree that probiotics may be potentially helpful in the treatment of patients with severe COVID-19, but there is a lack of evidence to demonstrate the effect of probiotics directly inhibiting SARS-CoV-2 infection.

In the early days of the outbreak, antibiotics were commonly used empirically to prevent secondary bacterial infection. A review of 18 articles showed that although only 8% (62/806) of COVID-19 patients experienced bacterial/fungal co-infection, 72% (1450/2010) received antimicrobial therapy.² Besides co-infection, patients possibly suffered from the loss of helpful symbionts and from gut dysbiosis since most were severely or critically ill. Zuo *et al* reported differences in faecal microbiomes in 15 patients with moderate or severe COVID-19,³ supporting the use of probiotics as a potential treatment for COVID-19. However, the presence of altered gut microbiota in mild or asymptomatic patients needs to be verified.

Many studies have demonstrated the pathogenic links between microbiota and the gut-lung axis, which is a dynamic immune balance between these two mucosal sites. A respiratory pathogen may cause gut and lung dysbiosis as well as altered leucocyte level and activation disorders.⁴ Reintroduction of probiotics promotes the release of short chain fatty acids from microbiota⁵ or cytokines and chemokines from the lungs or gut of the host,⁶ thereby facilitating the recovery of a healthy microbiota composition as well as leucocyte homeostasis and activation. This helps prevent infection and immunopathogenesis. Therefore, probiotics may be more effective in treating patients with severe COVID-19 with a high level of inflammatory factors or those with a high risk of co-infection due to mechanical ventilation.

As suggested in the guideline drafted by China's National Health Commission,⁷ patients with a long hospital stay, more complications, poor immunity status or a rapidly progressive disease course may benefit more from probiotics. Probiotics were capable of reducing infections, systemic inflammatory response syndrome,



sepsis, days under mechanical ventilation, and mortality in critical illness.⁸ However, there is little evidence to support a direct effect of preventing SARS-CoV-2 infection. Although *Lactobacillus* and *Bifidobacterium* decreased in some patients with COVID-19,⁹ the choice and effect of probiotics require further study. We do not recommend probiotics for routine treatment of COVID-19 as most patients were mild and asymptomatic and dysbiosis of the intestinal flora was self-limiting in most cases. We do believe that it would be worthwhile to evaluate probiotics in critically ill COVID-19 patients.

ACKNOWLEDGEMENT

The authors' declarations of personal and financial interests are unchanged from those in the original article.¹⁰

LINKED CONTENT

This article is linked to Tian *et al* and Aguila *et al* papers. To view these articles, visit <https://doi.org/10.1111/apt.15731> and <https://doi.org/10.1111/apt.15898>

Yuan Tian 
Long Rong 

Department of Endoscopy Center, Peking University First Hospital, Beijing, China
Email: drronglong@foxmail.com

ORCID

Yuan Tian  <https://orcid.org/0000-0003-0192-3037>

Long Rong  <https://orcid.org/0000-0001-5450-0535>

REFERENCES

1. Aguila EJT, Lontok MADC, Aguila EJT. Letter: role of probiotics in the COVID-19 pandemic. *Aliment Pharmacol Ther.* 2020;52:931-932.
2. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* 2020.
3. Zuo T, Zhang F, Lui GCY, et al. Alterations in gut microbiota of patients With COVID-19 during time of hospitalization. *Gastroenterology.* 2020. <https://doi.org/10.1053/j.gastro.2020.05.048>
4. Budden KF, Gellatly SL, Wood DLA, et al. Emerging pathogenic links between microbiota and the gut-lung axis. *Nat Rev Microbiol.* 2017;15:55-63.
5. Samuelson DR, Welsh DA, Shellito JE. Regulation of lung immunity and host defense by the intestinal microbiota. *Front Microbiol.* 2015;6:1085.

AP&T correspondence columns are restricted to letters discussing papers that have been published in the journal. A letter must have a maximum of 500 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via <http://mc.manuscriptcentral.com/apt>.

6. Schuijt TJ, Lankelma JM, Scicluna BP, et al. The gut microbiota plays a protective role in the host defence against pneumococcal pneumonia. *Gut*. 2016;65:575-583.
7. National Health Commission of the People's Republic of China. Guidance on coronavirus disease 2019 (COVID-19), China (version 7). publish online Mar 3. http://www.gov.cn/zhengce/zhengceku/2020-03/04/content_5486705.htm
8. Manzanares W, Lemieux M, Langlois PL, Wischmeyer PE. Probiotic and synbiotic therapy in critical illness: a systematic review and meta-analysis. *Crit Care*. 2016;19:262.
9. Xu K, Cai H, Shen Y, et al. Management of corona virus disease-19 (COVID- 19): the Zhejiang experience. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2020;49(1). (in Chinese).
10. Tian Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Aliment Pharmacol Ther*. 2020;51:843-851.