



COVID-19 and Diarrhoea: the Therapeutic Role OF LMWH

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Dear Editor,

We read with great interest the paper by Ghimire S et al. [1] demonstrating that diarrhoea in COVID-19 is related to a worse prognosis. Furthermore, the authors confirmed that it is the most common gastrointestinal symptom related to SARS-COV-2 infection.

How to treat diarrhoea is not still clear; however, the therapeutic role of low molecular weight heparin (LMWH) should be underlined because it is based on pathophysiological principles.

On one hand, an association between diarrhoea in COVID-19 and increased level of serotonin (5-HT) has been recently demonstrated [2], and it is widely known that 5-HT stimulates platelet aggregation [3] and consequently increases the risk of micro and macro-thrombosis, worsening the prognosis of the disease.

On the other hand, diarrhoea in COVID-19 seems to be related to both direct and indirect mucosal damage: the direct damage may be due to the disruption of the tight-junctions by SARS-COV-2 itself [4], and the indirect effect can be caused by the systemic inflammatory response and the ischemic damage of enterocytes [4]. This mucosal damage may increase the bacterial translocation through the intestinal wall.

That contributes to the persistence of diarrhoea and can cause a bacterial systemic superinfection: IL-6, a fundamental pathogenetic cytokine for COVID-19 severity but also a biomarker of inflammation associated with endotoxemia and sepsis [5], achieved high levels in patients with diarrhoea [2].

Furthermore, the associated damage of enterochromaffin cells and intrinsic enteric neurons can increase the release of circulating 5-HT, establishing a vicious circle [3].

LMWH acts on these pathogenetic mechanisms.

On one side, it decreases systemic and local platelet aggregation interfering with the hypercoagulable state induced by 5-HT [3]; on the other side, it improves intestinal microcirculation able to decrease enterocytic damage and therefore bacterial translocation [5].

For these reasons, LMWH represents the proper therapy for diarrhoea in COVID-19 patients and, so on, contributes to improve the prognosis.

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Declarations

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This article is part of the Topical Collection on *COVID-19*

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References

1. Ghimire S, Sharma S, Patel A, Budhathoki R, Chakinala R, Khan H, et al. Diarrhoea is associated with increased severity of disease in COVID-19: systemic review and metaanalysis. *SN Compr Clin Med*. 2021:1–8. <https://doi.org/10.1007/s42399-020-00662-w>.
2. Ha S, Jin B, Clemmensen B, Park P, Mahboob S, Gladwill V, et al. Serotonin is elevated in COVID-19-associated diarrhoea. *Gut*. 2021: gutjnl-2020-323542. <https://doi.org/10.1136/gutjnl-2020-323542>.

3. De Clerck F. The role of serotonin in thrombogenesis. *Clin Physiol Biochem.* 1990;8(Suppl 3):40–9.
4. Lin L, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. *Gut.* 2020;69(6):997–1001. <https://doi.org/10.1136/gutjnl-2020-321013>.
5. Villa E, Cammà C, Marietta M, Luongo M, Critelli R, Colopi S, et al. Enoxaparin prevents portal vein thrombosis and liver decompensation in patients with advanced cirrhosis. *Gastroenterology.* 2012;143(5):1253–1260.e4. <https://doi.org/10.1053/j.gastro.2012.07.018>.

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