

COLCHICINE- A POSSIBLE ROLE IN THERAPY OF CORONAVIRUS COVID-19 DISEASE

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Recent developments in coronavirus COVID-19 with tocilizumab have identified cytokine storm as a therapeutic target (1, 2).

Some immunomodulation drugs like cortisone and hydrochloroquine have been tested, producing insignificant results. Cortisone has not been recommended in the therapy of COVID-19 disease (1, 2).

The mechanisms of the injury described for coronavirus COVID-19 (3), in rat coronavirus RCOV (4), and previously for influenza with lung injury (5), indicate that the injury is partly promoted by neutrophils and macrophages, and therefore could be responsive to treatment with colchicine.

It seems that patients with the most severe disease course have significantly more neutrophils than those with a more benign course. The threshold seems to be approximately $7 \times 10^9/l$ neutrophils (6).

As a result, the group of patients with neutrophilia ($> 7 \times 10^9/l$) could probably draw greatest benefits from immunomodulation with colchicine. At the same time, all symptomatic patients could possibly benefit from colchicine as well.

With colchicine being most efficient in the first twelve hours of other forms of acute tissue injury caused by local cytokine hypersecretion, such as gout arthritis (7), the optimal timing of its administration could be as early as neutrophilia is detected.

Thus, it would be necessary to urgently verify these hypotheses in animal models, like K18-hACE2 mice (8), and, if feasible, to start a randomized control trial of the drug starting with a low dose of colchicine 0.5-1 mg q.d.

To the best of author's knowledge, this is the first time that possible benefits of colchicine therapy for coronavirus COVID-19 disease are hypothesized.

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Bibliography:

- 1) Tim Smith, Tony Prosser; COVID-19 Drug Therapy — Potential Options Clinical Drug Information, Clinical Solutions, Elsevier , March 2020, https://www.elsevier.com/_data/assets/pdf_file/0007/988648/COVID-19-Drug-Therapy_Mar-2020.pdf
- 2) David J Cennimo, Michael Stuart Bronze, Coronavirus Disease 2019 (COVID-19) Treatment & Management; <https://emedicine.medscape.com/article/2500114-treatment>
- 3) Sufang Tian, Weidong Hu, Li Niu et. Al.; Pulmonary Pathology of Early-Phase 2019 Novel Coronavirus (COVID-19) Pneumonia in Two Patients With Lung Cancer; Journal of Thoracic Oncology (in press); <https://doi.org/10.1016/j.jtho.2020.02.010>
- 4) Anoria K. Haick, Joanna P. Rzepka, Elizabeth Brandon et al. Neutrophils are needed for an effective immune response against pulmonary rat coronavirus infection, but also contribute to pathology; Journal of General Virology (2014), 95, 578–590 DOI 10.1099/vir.0.061986-0
- 5) Qiang Liu, Yuan-hong Zhou, Zhan-qiu Yang; The cytokine storm of severe influenza and development of immunomodulatory therapy; Cellular & Molecular Immunology (2016) 13, 3–10
- 6) Qiao Shi , Kai-Liang Zhao , Jia Yu et al.; Clinical characteristics of 101 non-surviving hospitalized patients with COVID-19—A single center, retrospective study; medRxiv: <https://doi.org/10.1101/2020.03.04.20031039> medRxiv preprint doi
- 7) Anastasia Slobodnick, Binita Shah, Svetlana Krasnokutsky et al. ; Update on colchicine 2017, Rheumatology 2018;57:i4i11 doi:10.1093/rheumatology/kex453
- 8) Paul B. McCray, Jr, Lecia Pewe, Christine Wohlford-Lenane et al. Lethal Infection of K18-hACE2 Mice Infected with Severe Acute Respiratory Syndrome Coronavirus; Journal Of Virology, Jan. 2007, p. 813–821 Vol. 81, No. 2 ; doi:10.1128/JVI.02012-06

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