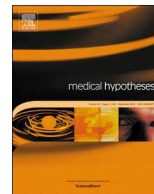




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Letter to Editors

Dapsone, colchicine and olanzapine as treatment adjuncts to prevent COVID-19 associated adult respiratory distress syndrome (ARDS)



A novel coronavirus (COVID-19) has caused a global pandemic. There is currently no vaccine or antiviral treatment. The most serious complication from COVID-19 is death often from acute respiratory distress syndrome (ARDS) [1].

Neutrophils are chemotactic to many signaling gradients, interleukin-8 (IL-8) being one. ARDS patients have elevated IL-8 in bronchoalveolar lavage fluid and other neutrophil chemoattractants are present and act in synergy with that IL-8 [2].

Evidence points to the ability of dapsone to inhibit neutrophil chemotaxis to both N-formylmethionyl-leucyl-phenylalanine and to IL-8 via interference with neutrophils' adherence functions [3,4].

To work in concert and synergy with with Dapsone, we note that colchicine [5]—a drug that has been used for millennia—is also a potent neutrophil inhibitor working by inhibiting microtubule polymerization.

One risk factor for mortality identified in patients hospitalized with COVID-19 infection is elevated IL-6 levels [1]. Histamine acting through the H1 receptor is a strong positive regulator of IL-6 [6]. Atypical antipsychotic medications such as olanzapine and quetiapine are particular potent H1 antagonists [7,8] and thus we think thus could be most useful in lowering IL-6 levels.

A trial of dapsone 100 mg every 12 h, colchicine 0.4 mg daily and olanzapine 10 mg daily in hospitalized but not yet ventilated patients may be warranted.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.109774>.

References

- [1] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020 Mar 11. pii: S0140-6736(20)30566-3. doi: 10.1016/S0140-6736(20)30566-3.
- [2] Stapleton RD, Suratt BT, Neff MJ, et al. Bronchoalveolar fluid and plasma inflammatory biomarkers in contemporary ARDS patients. *Biomarkers* 2019;24(4):352–9.
- [3] Booth SA, Moody CE, Dahl MV, Herron MJ, Nelson RD. Dapsone suppresses integrin-mediated neutrophil adherence function. *J Invest Dermatol*. 1992;98(2):135–40.
- [4] Molinelli E, Paolinelli M, Campanati A, et al. Metabolic, pharmacokinetic, and toxicological issues surrounding dapsone. *Expert Opin Drug Metab Toxicol* 2019;15:367–79.
- [5] Slobodnick A, Shah B, Krasnokutsky S, Pillinger MH. Update on colchicine, 2017. *Rheumatology (Oxford)*. 2018 Jan 1;57(suppl_1):i4–i11.
- [6] Triggiani M, Gentile M, Secondo A, et al. Histamine induces exocytosis and IL-6 production from human lung macrophages through interaction with H1 receptors. *J Immunol* 2001;166:4083–91.
- [7] Richelson E, Souder T. Binding of antipsychotic drugs to human brain receptors focus on newer generation compounds. *Life Sci* 2000;68:29–39.
- [8] Altschuler EL, Kast RE. Using histamine (H1) antagonists, in particular atypical antipsychotics, to treat anemia of chronic disease via interleukin-6 suppression. *Med Hypotheses* 2005;65:65–7.

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