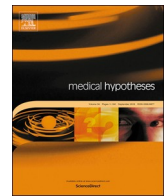




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Old medication for a novel disease?



Laboratory confirmed cases of COVID-19 are millions of people worldwide with hundreds of thousands fatalities (Johns Hopkins University). Most of these fatalities are induced by acute respiratory syndrome (ARDS) and those who survive, might suffer from long term complications of severe pulmonary inflammation. The purpose of this letter is to propose that aldosterone antagonists might improve the outcome of ARDS.

It has been proved by multiple studies on cell lines, animal model, and also human subjects that aldosterone induces collagen synthesis in different tissues [1,2], and that aldosterone antagonists (e.g. spironolactone) can inhibit collagen synthesis in different tissues including heart, muscle, kidney, and lung [3–5]. There has been a few studies done on ARDS and it has been shown that spironolactone improves the outcome in this condition as well [6].

Studies have shown that expression of ACE2 might facilitate infection by SARS-CoV-2, but it was demonstrated that aldosterone antagonists (which increase expression of ACE2) can protect against ARDS in animal models [7].

Based on the previous evidence and also pathophysiology of ARDS it seems reasonable to consider spironolactone for improvement of ARDS outcome if started early in the course of the disease. Now that we have a surge in ARDS cases caused by COVID-19 and since there is not effective treatment or vaccine available yet, we need to decrease mortality and morbidity it seems that early initiation of aldosterone antagonist early in the course of COVID-19 might improve the outcome by decreasing fibrosis in lung tissue.

Sources of support in the form of grants

We had no source of funding and no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.109830>.

References

- [1] Nagai Y, Miyata K, Sun GP, Rahman M, Kimura S, Miyatake A, et al. Aldosterone stimulates collagen gene expression and synthesis via activation of ERK1/2 in rat renal fibroblasts. *Hypertension* 2005;46(4):1039–45.
- [2] Lavall D, Selzer C, Schuster P, Lenski M, Adam O, Schäfers HJ, et al. The mineralocorticoid receptor promotes fibrotic remodeling in atrial fibrillation. *J Biol Chem* 2014;289(10):6656–68.
- [3] Zannad F, Alla F, Dousset B, Perez A, Pitt B. Limitation of excessive extracellular matrix turnover may contribute to survival benefit of spironolactone therapy in patients with congestive heart failure: insights from the Randomized Aldactone Evaluation Study (RALES). *Circulation* 2000;102(22):2700–6.
- [4] Guney I, Selcuk NY, Altintepe L, Atalay H, Başarali MK, Büyükbay S. Antifibrotic effects of aldosterone receptor blocker (spironolactone) in patients with chronic kidney disease. *Renal Failure* 2009;31(9):779–84.
- [5] Ferreira JP, Rossignol P, Pizard A, Machu JL, Collier T, Girerd N, et al. Potential spironolactone effects on collagen metabolism biomarkers in patients with uncontrolled blood pressure. *Heart* 2019;105(4):307–14.
- [6] Naldan ME, Atalay C, Coskun A, Karaca M, Aydin Y, Dorman E. The efficacy of spironolactone and surfactant treatment on HMGB1, CRP, IL-1b and TNF-a levels in acute lung injury. *Türk Gogus Kalp Dama* 2015;23:538–43.
- [7] Li Y, Zeng Z, Cao Y, Liu Y, Ping F, Liang M, et al. Angiotensin-converting enzyme 2 prevents lipopolysaccharide-induced rat acute lung injury via suppressing the ERK1/2 and NF-κB signaling pathways. *Sci Rep* 2016;6(1):27911.

Dariush Jahandideh^{a,*}, Andisheh Taheri^b

^a Yale University Affiliated Griffin Hospital, Internal Medicine Department, United States

^b Shiraz University, Iran

E-mail address: djahandideh@griffinhealth.org (D. Jahandideh).

* Corresponding author at: 130 Division St, 130 Division St, Derby, CT 06418. Griffin Hospital, Yale University affiliated hospital, Medical Education, Internal Medicine, United States.

<https://doi.org/10.1016/j.mehy.2020.109830>

Received 12 April 2020; Accepted 8 May 2020

0306-9877/© 2020 Elsevier Ltd. All rights reserved.