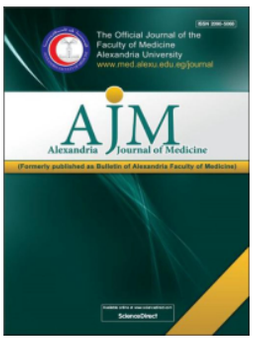

Alexandria Journal of Medicine

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/tajm20

Is fenofibrate the missing piece in COVID-19 management?

Ehab Mudher Mikhael

To cite this article: Ehab Mudher Mikhael (2020) Is fenofibrate the missing piece in COVID-19 management?, Alexandria Journal of Medicine, 56:1, 132-133, DOI: 10.1080/20905068.2020.1785144

To link to this article: https://doi.org/10.1080/20905068.2020.1785144

Published online: 05 Aug 2020.

ALEXANDRIA JOURNAL OF MEDICINE
2020, VOL. 56, NO. 1, 132–133
https://doi.org/10.1080/20905068.2020.1785144

Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

Is fenofibrate the missing piece in COVID-19 management?

Dear editor,

The world nowadays is facing a pandemic of coronavirus disease-19 (COVID-19) [1]. The overall mortality rate of COVID-19 is approaching 1% [2], and it may exceed 60% in those suffering from severe COVID-19 [3]. The mortality rate is higher among elderly and especially those with diabetes mellitus and cardiovascular diseases [4]. The main cause of COVID-19 mortality is the virus infectivity to lungs leading to pulmonary inflammation and pneumonia; in this regard, the virus stimulates the induction of T-cells over-activation, which in turn leads to excessive release of inflammatory mediators like tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), IL-8, IL-10, and vascular endothelial growth factor. All these mediators are associated with increasing risk of pulmonary edema, alveolar damage, acute respiratory distress syndrome (ARDS), and eventually death [5]. In addition to that, some COVID-19 patients may die due to a cytokine storm which characterized by lymphopenia and high levels of IL-6 and fibrinogen [6]. Furthermore, death can occur due to systemic viral sepsis that provokes a systemic inflammatory response and multi-organ damage [5]. Unfortunately, till now, there is no specific treatment for COVID-19. Most of the currently used therapies are aimed to prevent virus entry to the cell and/or viral replication [7]. Anti-inflammatory therapies are usually used for patients with severe disease [8] such as Anakinra (IL-1 receptor antagonist) and Tocilizumab (IL-6 inhibitor) which are undergoing multiple trials and some results are encouraging. Similarly, use of anti-inflammatory cytokines like IL-37 and IL-38 is hypothesized to be useful and is under research [9].

Fenofibrate is an antidyslipidemic agent that acts as peroxisome proliferator-activated receptor-α agonist. Besides its ability to lower triglyceride level, it has pleiotropic effects such as anti-inflammatory, antioxidant, and anti-angiogenesis. In this regard, fenofibrate can lower nuclear factor-KB, TNF-α, IL6, vascular adhesion molecule, cyclooxygenase-2, matrix metalloproteinase, vascular endothelial growth factor-1 signaling, and oxidative stress [10,11]. All these effects seem to be meaningful for reversing the harmful effects of coronavirus on human body organs; besides that fenofibrate is effective to lower fibrinogen, so this means that fenofibrate maybe a highly valuable therapy for patients with severe COVID-19 and especially those suffering from cytokine storm [12].

One drawback for fenofibrate is its ability to increase the expression of angiotensin-converting enzyme-2 (ACE2) [13] which increases the risk of viral entry to cells. This problem can be counteracted by the addition of chloroquine/hydroxychloroquine (approved by food and drug administration (FDA)), at which such medication is shown to be effective in mild-moderate cases of COVID-19 [14] by stopping the glycosylation of ACE2 and thus hinders the binding of viral spike protein to ACE2 and prevent viral cell entrance [15]. Meanwhile, scientists found that ARDS severity is inversely related to ACE2 level [16], this can be a further encouragement for fenofibrate usage in COVID-19 management.

The expected benefits of fenofibrate can be confirmed by scientific suggestions about the benefits of statins to reduce mortality for patients infected with corona virus [17,18]. Meanwhile, fenofibrate has at least comparable systemic anti-inflammatory effect [19,20] and even better than statin among elderly people [21]. Furthermore, fenofibrate maybe superior than statins in reducing mortality due to lung damage by COVID-19 since it increases ApoA1 more than statins [22] and it is well known that ApoA1 plays a protective role against lung damage [23].

To confirm the above claims, clinical trials using fenofibrate as add-on therapy to chloroquine/hydroxychloroquine are highly advocated to elderly people with moderate–severe COVID-19 and without end organ damage..

Disclosure statement

No potential conflict of interest was reported by the author.

References

[1] El ZME, Järhult JD. From SARS to COVID-19: A previously unknown SARS-CoV-2 virus of pandemic potential infecting humans – call for a one health approach. One Health. 2020;9:100124.
[2] Rajgor DD, Lee MH, Archuleta S, et al. The many estimates of the COVID-19 case fatality rate. Lancet Infect Dis. 2020 Published Online 2020 Mar 27. DOI:10.1016/S1473-3099(20)30244-9
[3] Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet. 2020;395 (10229):1014–1015.
[4] Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ. 2020;368:m1198.
[5] Jin Y, Yang H, Ji W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. Viruses. 2020;12(372):1–17.
[6] Zheng C, Wang J, Guo H, et al. Risk-adapted treatment strategy for COVID-19 patients. Int J Infect Dis. 2020 Mar 27;S1201-9712(20):30179–X. Epub ahead of print.

[7] Zhang L, Liu Y. Potential interventions for novel coronavirus in China: A systematic review. J Med Virol. 2020;92(5):479–490.
[8] Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033–1034.. Epub 2020 Mar 16.
[9] Salvi R, Patankar P. Emerging pharmacotherapies for COVID-19. Biomed Pharmacother. 2020;128:110267.
[10] Noonan JE, Jenkins AJ, Ma JX, et al. An update on the molecular actions of fenofibrate and its clinical effects on diabetic retinopathy and other microvascular end points in patients with diabetes. Diabetes. 2013;62(12):3968–3975.
[11] Prasad GS, Govardhan P, Deepika G, et al. Anti-inflammatory activity of anti-hyperlipidemic drug, fenofibrate, and its phase-I metabolite fenofibric acid: in silico, in vitro, and in vivo studies. Inflammopharmacology. 2018;26(4):973–981.
[12] Chan NN, Chow FC. Effects of fenofibrate and gemfibrozil on plasma homocysteine. Lancet. 2001;358(9295):1811.
[13] Ibarra-Lara L, Hong E, Soria-Castro E, et al. Clofibrate PPARα activation reduces oxidative stress and improves ultrastructure and ventricular hemodynamics in no-flow myocardial ischemia. J Cardiovasc Pharmacol. 2012;60(4):323–334.
[14] Pastick KA, Okafor EC, Lofgren SM, et al. Review: hydroxychloroquine and chloroquine for treatment of SARS-CoV-2 (COVID-19). Open Forum Infect Dis. 2020;7(4):ofaa130.
[15] Vincent MJ, Bergeron E, Benjannet S, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005 Aug 22;2: 69.
[16] Wösten-van Asperen RM, Bos AP, Bem RA, et al. Imbalance between pulmonary angiotensin-converting enzyme and angiotensin-converting enzyme 2 activity in acute respiratory distress syndrome. Pediatr Crit Care Med. 2013;14(9):e438–41.
[17] Yuan S. Statins may decrease the fatality rate of middle east respiratory syndrome infection. mBio. 2015;6(4):e01120.
[18] Fedson DS, Opal SM, Rordam OM. Hiding in plain sight: an approach to treating patients with severe COVID-19 infection. mBio. 2020;11:e00398–e00420.
[19] Krysiak R, Gdula-Dymek A, Okopien B. Effect of simvastatin and fenofibrate on cytokine release and systemic inflammation in type 2 diabetes mellitus with mixed dyslipidemia. Am J Cardiol. 2011;107(7):1010–1018.e1.
[20] Goto M. A comparative study of anti-inflammatory and antidyslipidemic effects of fenofibrate and statins on rheumatoid arthritis. Mod Rheumatol. 2010;20 (3):238–243.
[21] Krysiak R, Gdula-Dymek A, Marek B, et al. The effect of hypolipidaemic treatment on monocyte release of proinflammatory cytokines in different age groups of patients with type 2 diabetes and atherogenic dyslipidaemia. Endokrynol Pol. 2016;67(2):190–196.
[22] Sharma R, Mahajan M, Singh B, et al. Apolipoprotein modifying effects of statins and fibrate in various age groups of coronary artery disease patients. J Indian Med Assoc. 2006;104(9):492–494.
[23] Gordon EM, Figueroa DM, Barochia AV, et al. High-density lipoproteins and apolipoprotein A-I: potential new players in the prevention and treatment of lung disease. Front Pharmacol. 2016;7:323.

Ehab Mudher Mikhael
Department of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia
Department of Clinical Pharmacy, College of Pharmacy, University of Baghdad, Baghdad, Iraq
ehab_pharma84@yahoo.com