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.

Archives of Medical Research 51 (2020) 345–346

Archives of Medical Research

OPINION

Is the ACE2 Overexpression a Risk Factor for COVID-19 Infection?

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Received for publication March 21, 2020; accepted March 30, 2020 (ARCMED_2020_327).

In the recent coronavirus disease (COVID-19) outbreak, a higher proportion of patients with severe disease were found in older persons with comorbidities. This observation has been related to the use of drugs that can increase the cellular expression of angiotensin-converting enzyme 2 (ACE2) that has been recognized as target to which the virus bind to cells. Although this hypothesis is possible, it may also have other explanations which are discussed.

Key Words: Coronavirus infections, Coronavirus, Hypertension, Diabetes mellitus.

In the report of 72 314 patients infected with the novel coronavirus disease (COVID-19) in China, a higher proportion of patients with severe disease were found in older persons with comorbidities such as cardiovascular disease, diabetes mellitus, or hypertension (1). Therefore, Lei Fang and colleagues have speculated that this could be related to the use of drugs such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II type I receptor blockers (ARBs), thiazolidinediones, or ibuprofen, which cause an increase in the cellular expression of angiotensin-converting enzyme 2 (ACE2), that has been recognized as the target to which the virus bind to cells, and suggest a treatment adjustment to modulate ACE2 expression, using the antihypertensive calcium channel blockers as alternative (2).

Although this hypothesis is possible, the association between such comorbidities and the development of severe and fatal COVID-19 may have other explanations. The prevalence of hypertension in the Chinese adult population ≥18 years of age based on the 2017 American College of Cardiology/American Heart Association guideline is 46.4%, and increased in relation to age, reaching 78.7% in the population ≥75 years (3). China is the country with the highest number of patients with diabetes (116.4 million reported in 2019) (4), with and overall prevalence estimated in 11.6%, and a progressive increase by age group to a maximum of 23.5% in people ≥70 years (5). China has the highest burden of cardiovascular disease (6). Therefore, the high prevalence of comorbid conditions elderly patients with COVID-19 may be explained in part by the high prevalence of diabetes and hypertension in the Chinese population.

There are no data regarding the treatment received by patients with COVID-19 for the management of their comorbidities, but there is no certainty about the use ACE inhibitors, ARBs or thiazolidinediones. According to a study that analyzed the antihypertensive treatment in the Chinese population, the ACE inhibitors and ARBs are used in 24.5 and 4.1%, respectively (7). In relation to pharmacological treatment for diabetes in China, thiazolidinediones are used only in 17.2% (8).

Ibuprofen, similarly to others nonsteroidal anti-inflammatory drugs (NSAIDs), is a commonly prescribed drug among the elderly population. Patients over the age of 65 years have altered metabolism and pharmacodynamics that increase their susceptibility to adverse side effects (renal dysfunction, heart failure, gastrointestinal toxicity and cardiovascular disease) (9). Inappropriate prescription of NSAIDs in elderly patients with COVID-19 may increase such adverse effects and worsen the evolution of infection.

As final observation, the presence of concomitant disease (cardiovascular disease, hypertension, diabetes mellitus) are factors for development of severe disease in cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection, however, unlike COVID-19, to enter host cells, this virus uses the dipeptydil peptidase 4 as receptor (10,11). Thus, it is possible that these risk factors are independent of the pathogenesis.

In conclusion, the current evidence does not support any modification of treatment for patients receiving

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0188-4409/$ - see front matter.
https://doi.org/10.1016/j.arcmed.2020.03.011

ACE inhibitors, ARBs or thiazolidinediones for the management of their underlying diseases. Furthermore, such modifications may place their health status at stake. In relation to the use of ibuprofen or others NSAIDs, the risks and benefits should be balanced carefully in individual patients to optimize overall outcomes, especially in the elderly.

References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. JAMA, 2020. https://doi.org/10.1001/jama.2020.2648.
2. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8:e21.
3. Wang Z, Chen Z, Zhang L, et al. Status of Hypertension in China: Results From the China Hypertension Survey, 2012−2015. Circulation 2018;137:2344−2356.
4. International Diabetes Federation. IDF Diabetes Atlas. 9th ed. Brussels, Belgium: International Diabetes Federation; 2019. https://www.diabetesatlas.org/en/. Accessed March 16, 2020.
5. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. JAMA 2013;310:948−959.
6. Du X, Patel A, Anderson CS, et al. Epidemiology of Cardiovascular Disease in China and Opportunities for Improvement: JACC International. J Am Coll Cardiol 2019;73:3135−3147.
7. Wang Z, Wang X, Chen Z, et al. Hypertension control in community health centers across China: analysis of antihypertensive drug treatment patterns. Am J Hypertens 2014;27:252−259.
8. Ji L, Lu J, Weng J, et al. China type 2 diabetes treatment status survey of treatment pattern of oral drugs users. J Diabetes 2015;7:166−173.
9. Wongrakpanich S, Wongrakpanich A, Melhado K, et al. A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drug Use in The Elderly. Aging Dis 2018;9:143−150.
10. Park JE, Jung S, Kim A, et al. MERS transmission and risk factors: a systematic review. BMC Public Health 2018;18:574.
11. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. Lancet 2015;386:995−1007.