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# Comment on 'Comparison of losartan and amlodipine effects on the outcomes of patient with COVID-19 and primary hypertension: A randomised clinical trial'

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## To the editor

We read with great interest the publication by Masoud Nouri-Vaskeh and colleagues 'Comparison of losartan and amlodipine effects on the outcomes of patient with COVID-19 and primary hypertension: a randomised clinical trial' published as format epub ahead of print in the Int J Clin Pract.<sup>1</sup> We would like to present several limitations of their work.

1 The aim of their study was to compare, using a randomised clinical trial in hospitalised patients with COVID-19 and primary hypertension, the effects of losartan and amlodipine using two primary outcomes: 30-day mortality and length of hospital stay. In the design of such study, the calculation of the number of subjects required is mandatory, and it has not been reported in the methods section. Taking into account the mortality rate of COVID-19 in inpatients in Iran with hypertension (10%-14%<sup>1, 2</sup> mean 12%), the expected difference, if one of the drugs was associated with lower mortality, could be 50%. With an alpha coefficient of 5%, a beta power of 90%, an expected difference of 50% (6% versus 12%) and a bilateral test (no a priori hypothesis of superiority of amlodipine or losartan), the number of subjects in each group must be of at least 465 (163 for an expected difference of 75%, 3% versus 12%). The same comment can be done for the second primary outcome. Hence, the study should be considered as underpowered to answer the research question.

2 One risk factor of mortality in COVID-19 patients is the age,<sup>2</sup> and in this study, a stratified randomisation of age has not been done, the mean age of the groups was 67.3 years and 60.1 years, respectively.

3 The authors reported the results of a recent retrospective<sup>3</sup> study that found significant improvement in mortality in COVID-19 patients with hypertension receiving either nifedipine or amlodipine comparatively with patients receiving other or no hypertensive treatment. Moreover, two other retrospective studies<sup>4, 5</sup> found significantly reduced mortality in COVID-19 patients treated by amlodipine than patients treated by other medications. Contrary to the study by Masoud Nouri-Vaskeh et al, the three cited studies were performed in patients who were chronically treated by amlodipine. This point is important as studies<sup>5</sup> have suggested that a chronic administration of amlodipine allowing to reach the steady state (ie at least 9 to 18 days given the elimination half-life of amlodipine: 30 to 60 hours<sup>6</sup>) could be necessary to achieve the inhibition of acid

sphingomyelinase explaining the protective effect in COVID-19 infection. Moreover, the fact that losartan and its carboxylic active metabolite have much shorter elimination half-lives (about 2 hours and 6-9 hours, respectively) compared with amlodipine may constitute a bias that may favour losartan for which steady state is achieved more rapidly.

In conclusion, considering the above remarks, the conclusion of the study by Masoud Nouri-Vaskeh et al deserve to be considered with caution.

## Disclosures

The authors declared no conflict of interest.

## References

- 1 - Nouri-Vaskeh M, Kalami N, Zand R, et al. Comparison of losartan and amlodipine effects on the outcomes of patient with COVID-19 and primary hypertension: a randomised clinical trial. *Int J Clin Pract.* 2021; 1:e14124. doi:10.1111/ijcp.14124
- 2 - Salari A, Mahdavi-Roshan M, Ghorbani Z, et al. An investigation of risk factors of in-hospital death due to COVID-19: a case-control study in Rasht. Iran. *Ir J Med Sci.* 2021; 9: 1- 13. doi:10.1007/s11845-020-02455-5
- 3 - Solaimanzadeh I. Nifedipine and amlodipine are associated with improved mortality and decreased risk for intubation and mechanical ventilation in elderly patients hospitalized for COVID-19. *Cureus.* 2020; 12:e8069. doi:10.7759/cureus.8069
- 4- Zhang LK, Sun Y, Zeng H, et al. Calcium channel blocker amlodipine besylate therapy is associated with reduced case fatality rate of COVID-19 patients with hypertension. *Cell Discov.* 2020; 6: 96. doi:10.1038/s41421-020-00235-0
- 5 - Darquennes G, Le Corre P, Le Moine O, Loas G. Association between functional inhibitors of acid sphingomyelinase (FIASMs) and reduced risk of death in COVID-19 patients: a retrospective cohort study. *Pharmaceuticals.* 2021; 14: 226. doi:10.3390/ph14030226
- 6 - Micromedex Drug-Reax system (Truven Health Analytics, Greenwood Village, CO, USA).  
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