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de Abajo FJ, Rodríguez-Martín S, Lerma V, et al.

Use of Renin-Angiotensin-Aldosterone System Inhibitors and Risk of COVID-19 Requiring Admission to Hospital: A Case-Population Study

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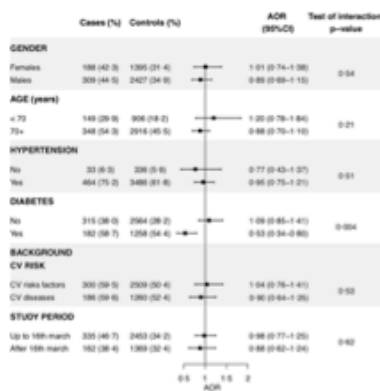
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USE OF RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM INHIBITORS AND RISK OF COVID-19 REQUIRING ADMISSION TO HOSPITAL: A CASE-POPULATION STUDY

Background: Concerns have been raised about the possibility that inhibitors of the renin-angiotensin-aldosterone system (RAAS) could predispose individuals to severe COVID-19; however, epidemiological evidence is lacking. We report the results of a case-population study done in Madrid, Spain, since the outbreak of COVID-19.

Methods: In this case-population study, we consecutively selected patients aged 18 years or older with a PCR-confirmed diagnosis of COVID-19 requiring admission to hospital from seven hospitals in Madrid, who had been admitted between March 1 and March 24, 2020. As a reference group, we randomly sampled ten patients per case, individually matched for age, sex, region (ie, Madrid), and date of admission to hospital (month and day; index date), from Base de datos para la Investigación Farmacoepidemiológica en Atención Primaria (BIFAP), a Spanish primary health-care database, in its last available year (2018). We extracted information on comorbidities and prescriptions up to the month before index date (ie, current use) from electronic clinical records of both cases and controls. The outcome of interest was admission to hospital of patients with COVID-19. To minimise confounding by indication, the main analysis focused on assessing the association between COVID-19 requiring admission to hospital and use of RAAS inhibitors compared with use of other antihypertensive drugs. We calculated odds ratios (ORs) and 95% CIs, adjusted for age, sex, and cardiovascular comorbidities and risk factors, using conditional logistic regression. The protocol of the study was registered in the EU electronic Register of Post-Authorisation Studies, EUPAS34437.

Findings: We collected data for 1139 cases and 11 390 population controls. Among cases, 444 (39.0%) were female and the mean age was 69.1 years (SD 15.4), and despite being matched on sex and age, a significantly higher proportion of cases had pre-existing cardiovascular disease (OR 1.98, 95% CI 1.62-2.41) and risk factors (1.46, 1.23-1.73) than did controls. Compared with users of other antihypertensive drugs, users of RAAS inhibitors had an adjusted OR for COVID-19 requiring admission to hospital of 0.94 (95% CI 0.77-1.15). No increased risk was observed with either angiotensin-converting enzyme inhibitors (adjusted OR 0.80, 0.64-1.00) or angiotensin-receptor blockers (1.10, 0.88-1.37). Sex, age, and background cardiovascular risk did not modify the adjusted OR between use of RAAS inhibitors and COVID-19 requiring admission to hospital, whereas a decreased risk of COVID-19 requiring admission to hospital



Risk of COVID-19 requiring hospital admission associated with RAAS inhibitors, stratified by different factors. Preprint figure

was found among patients with diabetes who were users of RAAS inhibitors (adjusted OR 0.53, 95% CI 0.34-0.80). The adjusted ORs were similar across severity degrees of COVID-19.

Interpretation: RAAS inhibitors do not increase the risk of COVID-19 requiring admission to hospital, including fatal cases and those admitted to intensive care units, and should not be discontinued to prevent a severe case of COVID-19.

Why do you highlight this publication?

In case-population study carried out in 7 hospitals from the Autonomous Community of Madrid, the researchers found no difference between RAAS inhibitors and other antihypertensive drugs with respect to the risk of COVID-19 requiring hospital admission, once fully adjusted for age, sex, and cardiovascular comorbidities and risk factors. Neither ACE inhibitors nor angiotensin-receptor blockers increased the risk. The lack of association between RAAS inhibitors and risk of COVID-19 requiring admission to hospital was observed in both the most severe (fatal cases and those needing admission to an intensive care unit) and less severe inpatients. An interesting finding is the protection the researchers found associated with the use of RAAS inhibitors among diabetic patients that should be further explored.

“RAAS inhibitors are not the villains some speculations suggested in the surge of COVID-19 pandemics and, in the next few weeks, they could be among the heroes. Our study shows that they are, at least, innocents.”. – Francisco J. de Abajo

Publication commented by:

Prof. Francisco J. De Abajo
Clinical Pharmacology Unit
University Hospital Principe de Asturias
Department of Biomedical Sciences (Pharmacology)
University of Alcalá
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