Could heart medications increase COVID-19 risk?

26 April 2021

Credit: Pixabay/CC0 Public Domain

During infection, SARS-CoV-2 binds to a cellular receptor known as angiotensin converting enzyme 2 (ACE2) before entering a cell and replicating. Because it is not well established whether common blood pressure medications can increase the levels of ACE2, there has been some concern that patients taking these medications might be more susceptible to COVID-19.

In a new study, researchers led by Hans Ackerman, MD, DPhil, in the Laboratory of Malaria and Vector Research (LMVR) at the National Institute of Allergy and Infectious Diseases, found that mice treated with an ACE inhibitor blood pressure medication showed increased levels of ACE2. However, mice that received both an ACE inhibitor and a different blood pressure medicine known as an angiotensin receptor blocker (ARB) did not exhibit the increase.

"Based on these findings, we recommend that researchers analyze existing and ongoing clinical studies to determine whether people on ACE inhibitor-ARB combination therapy show different COVID-19 susceptibility, complications and outcomes than patients taking only an ACE inhibitor or ARB medication," said Steven Brooks, Ph.D., a post-doctoral research fellow in the Ackerman laboratory.

Aline da Silva Moreira, Ph.D., a post-doctoral research fellow in the Ackerman laboratory, will present the new research at the American Society for Pharmacology and Experimental Therapeutics annual meeting during the virtual Experimental Biology (EB) 2021 meeting, to be held April 27-30.

In the new study, the researchers treated healthy mice with either the ACE inhibitor lisinopril or the ARB losartan alone, in combination, or a placebo. After three weeks, they measured levels of ACE2 in the lung, small intestine, brain and kidney. While the lung and small intestine are most likely to encounter the virus, they also examined the brain and kidney because people with COVID-19 often develop complications in these organs.

Their analysis showed that the abundance of ACE2 molecules varied significantly depending on the tissue type. For mice that received the placebo, the levels of ACE2 in the small intestine was ten times higher than in the kidney and 100 times higher than in the brain or lung.

After three weeks of receiving treatment, lisinopril broadly raised the level of ACE2 molecules across all four tissues while losartan raised ACE2 only in the small intestine. Mice treated with both lisinopril and losartan did not show increased levels of ACE2 in any tissue. Three weeks after treatment stopped, the levels of ACE2 no longer differed among the groups of mice, indicating that discontinuing either blood pressure medication returns ACE2 levels to the those found in placebo-treated mice.

"These results provide a controlled, tissue-specific analysis of the effects of ACE inhibitors, ARB and combination therapy on the levels of ACE2 in healthy mice," said Ackerman. "Our findings that

ACE inhibitor treatment increases tissue expression of ACE2 are in agreement with a previous study in rats that showed ACE2 increased in heart tissue, and a separate study in rats that showed ACE2 increased in lung tissue, following treatment with ACE inhibitors."

The researchers caution that whether heart medications—including ACE inhibitors and ARBs—change disease risk and severity for COVID-19 has been an intense ongoing area of debate during the COVID-19 pandemic. "Thus far, clinical studies have not identified an increase in COVID-19 risk or severity among in people taking these drugs," said Ackerman. "We recommend that patients taking heart medications work with their healthcare providers to manage their medications."

More information: Aline da Silva Moreira will present the findings in poster R4584 (abstract).

Provided by Experimental Biology