Metformin use reduces risk of death for patients with COVID-19 and diabetes

14 January 2021, by Jeff Hansen and Savannah Koplon

Metformin 500mg tablets. Credit: public domain

Use of the diabetes drug metformin—before a diagnosis of COVID-19—is associated with a threefold decrease in mortality in COVID-19 patients with Type 2 diabetes, according to a racially diverse study at the University of Alabama at Birmingham. Diabetes is a significant comorbidity for COVID-19.

"This beneficial effect remained, even after correcting for age, sex, race, obesity, and hypertension or chronic kidney disease and heart failure," said Anath Shalev, M.D., director of UAB's Comprehensive Diabetes Center and leader of the study.

"Since similar results have now been obtained in different populations from around the world—including China, France and a UnitedHealthcare analysis—this suggests that the observed reduction in mortality risk associated with metformin use in subjects with Type 2 diabetes and COVID-19 might be generalizable," Shalev said.

How metformin improves prognosis in the context of COVID-19 is not known, Shalev says. The UAB findings suggest that the mechanisms may go beyond any expected improvement in glycemic control or obesity, since neither body mass index, blood glucose nor hemoglobin A1C were lower in the metformin users who survived as compared to those who died.

"The mechanisms may involve metformin's previously described anti-inflammatory and anti-thrombotic effects," Shalev said.

The study—first made available in MedRxiv and now published in the peer-reviewed journal *Frontiers in Endocrinology*—included 25,326 patients tested for COVID-19 at the tertiary care UAB Hospital between Feb. 25 and June 22 of last year. Of the 604 patients found to be COVID-19-positive, 311 were African Americans.

The primary outcome in the study was mortality in COVID-19-positive subjects, and the potential association with subject characteristics or comorbidities was analyzed.

Researchers found that Blacks, who are only 26 percent of Alabama's population, were 52 percent of those who tested positive for COVID-19, and only 30 percent of those who tested negative. In contrast, only 36 percent of the COVID-19-positive subjects were white, while whites made up 56 percent of those who tested negative, further underlining the racial disparity. Once COVID-19-positive though, no significant racial difference in mortality was observed.

"In our cohort," Shalev said, "being African American appeared to be primarily a risk factor for contracting COVID-19, rather than for mortality. This suggests that any racial disparity observed is

likely due to exposure risk and external socioeconomic factors, including access to proper health care."

Overall mortality for COVID-19-positive patients was 11 percent. The study found that 93 percent of deaths occurred in subjects over the age of 50, and being male or having high blood pressure was associated with a significantly elevated risk of death. Diabetes was associated with a dramatic increase in mortality, with an odds ratio of 3.62. Overall, 67 percent of deaths in the study occurred in subjects with diabetes.

The researchers looked at the effects of diabetes treatment on adverse COVID-19 outcomes, focusing on insulin and metformin as the two most common medications for Type 2 diabetes. They found that prior insulin use did not affect mortality risk.

However, prior metformin use was a different matter. Metformin use significantly reduced the odds of dying, and the 11 percent mortality for metformin users was not only comparable to that of the general COVID-19-positive population, it was dramatically lower than the 23 percent mortality for diabetes patients not on metformin.

After controlling for other covariates, age, sex and metformin use emerged as independent factors affecting COVID-19-related mortality. Interestingly, even after controlling for all these other covariates, death was significantly less likely—with an odds ratio of 0.33—for Type 2 diabetes subjects taking metformin, compared with those who did not take metformin.

"These results suggest that, while diabetes is an independent risk factor for COVID-19-related mortality," Shalev said, "this risk is dramatically reduced in subjects taking metformin—raising the possibility that metformin may provide a protective approach in this high-risk population."

The researchers say future studies will need to explore how metformin is protective, as well as assess the risks and benefits of metformin treatment and the indications for its use in the face of the ongoing COVID-19 pandemic.

More information: Andrew B. Crouse et al, Metformin Use Is Associated With Reduced Mortality in a Diverse Population With COVID-19 and Diabetes, *Frontiers in Endocrinology* (2021). DOI: 10.3389/fendo.2020.600439

Provided by University of Alabama at Birmingham