

Peer Review

Review of: "A Randomized, Double-Blind, Placebo-Controlled Crossover Pilot Study of the Effect of Metformin on Airway Glucose in COPD: The Metformin and Airway Glucose in COPD (MAGIC) Trial"

Martin Lavin¹

1. University of Queensland, Australia

Previous data have shown that hyperglycaemia leads to increased respiratory infection with *S. aureus*. Thus, it might be expected that reducing airway glucose could prevent infection. Indeed, it has been shown that metformin is capable of limiting infection by altering glucose flux in an in vitro airway epithelia-bacteria co-culture model. Since patients with COPD have higher levels of airway glucose, the expectation here was that metformin would reduce airway glucose and ameliorate the condition. This was tested in a randomised crossover pilot study. Unfortunately, metformin treatment over two 3-month periods with metformin or placebo, followed by alternate treatments, did not reduce airway glucose significantly. As the authors point out, this was due to low participant numbers completing the trial. The goal was to recruit 40 patients, but due to interference by COVID, this was reduced to 14, and of these, several withdrawals occurred, further reducing the efficacy of the trial. Trial design was sound, and the methodology to measure glucose levels and airway function was well described. However, while the results do not support an effect of metformin on airway glucose levels, they are compromised by very low numbers. I cannot see how additional analysis of data would strengthen the study.

Not sure what advice to give since the authors have described the limitations of this trial. It is obvious that a new trial is required with larger numbers. Have they thought of carrying out a multi-centre trial led by their group? It is evident that "larger interventional studies," as they suggest, are indeed

required. However, it is appreciated that these require considerable input and effort and are costly. Reference is made to mechanism; perhaps this should be addressed using human airway epithelial air-liquid interface cultures established from patients.

Declarations

Potential competing interests: No potential competing interests to declare.