

## Metformin and exercise combination less effective for glucose control

## August 19 2011

University of Alberta researchers looking at the effects of metformin and exercise in Type 2 diabetes patients found that a combination of these modalities didn't lower glucose control as much as hoped. Surprisingly, study participants showed better glucose control when sedentary. Researchers think that because metformin and exercise both act to lower glucose levels, the combination may have triggered a counter regulatory response by the body to prevent glucose levels dipping too much.

It's common enough for researchers to look at the impacts of prescribed drugs on the body. And if you're a <u>diabetes</u> researcher who believes that <u>exercise</u> has great benefits for those with <u>type 2 diabetes</u>, you're hoping your research will show that. But when Normand Boulé looked at the dual impacts of exercise and <u>metformin</u> – two of the most commonly-prescribed modalities for <u>glucose control</u> – on that very outcome, the hoped-for double whammy wasn't the result.

"The study had three objectives: we wanted to look at the effect of metformin on exercise in people with type 2 diabetes, examine the effect of exercise on metformin concentrations in the body, and finally to look at the effects of metformin and exercise on glucose control, which is essential for people with diabetes," says Boulé, whose study – a randomized, double-blind, crossover study - involved a multi-disciplinary team of researchers from five faculties at the University of Alberta.



Ten men and women between 30 and 65 with type 2diabetes, but not taking glucose-lowering medication or insulin for their condition were recruited into the study. Participants were randomly assigned to take metformin or a placebo for the first 28 days of the study, then crossed over so those taking the placebo received metformin and vice versa for a second 28 day period. On days 27 and 28, participants spent six hours in the exercise physiology lab and performed different tests, including approximately 40 minutes of exercise on day 28.

"Metformin reduces glucose in the blood and many believe it does so by activating exercise-like pathways," explains Boulé. "As expected, in our study metformin lowered the blood glucose concentrations measured during a two-hour period after lunch. But we found that on the non-exercise day metformin led to better glucose control after lunch than on the day our participants took metformin and exercised."

Boulé thinks that because both metformin and exercise act to lower glucose levels, the combination may have triggered a counter regulatory response by the body to prevent glucose levels dipping too much. "During exercise, glucagon concentrations increased in the blood (a hormone secreted by the pancreas that raises glucose levels) but when we combined exercise and metformin the glucagon levels were almost twice as elevated."

He also said that the combination of metformin and exercise is not always worse than metformin alone. The findings of their study was likely impacted by the timing of meals relative to the exercise session participants underwent and that the intensity of exercise may have had an impact as well, including the fact that these levels were measured after a single bout of exercise as opposed to regular daily exercise.

In terms of the other foci of the study Boulé says the data for the impacts of metformin on exercise were consistent with previous studies



looking at this: participants showed slightly increased lactate levels, and increased use of fats as an energy source during exercise. However, he believes his study was the first to document a significantly increased heart rate when performing aerobic exercise of various intensities with metformin (six beats per minute on average). "However, all participants were able to complete the exercise portion in both metformin and placebo conditions," he says.

"Also surprising is that throughout the day that they exercised, metformin concentrations were higher than on the day that they didn't," says Boulé. The reasons for this are not well understood.

Boulé says despite these findings, "exercise has hundreds of benefits" and should still be an important part of a healthy approach to glucose control for those with diabetes, including those taking metformin.

"What we've learned is that the relationship between exercise and metformin is complex, and this opens the door for more research to examine how different treatments work together, especially because exercise is widely prescribed for people with diabetes and metformin is often the first line drug of choice for treating type 2 diabetes."

## Provided by University of Alberta

Citation: Metformin and exercise combination less effective for glucose control (2011, August 19) retrieved 25 April 2024 from <a href="https://medicalxpress.com/news/2011-08-metformin-combination-effective-glucose.html">https://medicalxpress.com/news/2011-08-metformin-combination-effective-glucose.html</a>

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