Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

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The Carotid Atherosclerosis: MEtformin for insulin ResistAnce (CAMERA) study

Researchers
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Aim
To determine whether metformin, a drug commonly used to treat type 2 diabetes (T2DM), is able to reduce markers of heart attack risk in patients with heart disease but without T2DM, namely:

1. Carotid artery thickness (called carotid intima-media thickness or cIMT)
2. Presence of carotid plaque
3. Other markers such as glucose levels, weight, waist circumference, cholesterol

Project Outline/Methodology
Metformin, the most commonly used drug for T2DM, has been shown to reduce the risk of suffering a heart attack in T2DM. However, it is unknown what effect is has in individuals without T2DM. CAMERA was a double-blinded randomised trial in which we compared treatment with metformin to treatment with placebo in 173 participants (average age 63) over 18 months to determine whether any risk factors for heart attack improved. Participants all had ischaemic heart disease, elevated waist sizes and were already on statin therapy but none were allowed to have T2DM. Most participants were identified from GP surgeries in/near Glasgow. They attended seven visits at the Glasgow Clinical Research Facility where various measurements were conducted, including ultrasound scans of the carotid arteries (large blood vessels in the neck) which were conducted at three visits to measure cIMT and assess the presence of cholesterol-containing plaques.

Key Results
During CAMERA, we observed no difference in the change of thickness of the carotid arteries in participants receiving metformin and participants receiving placebo over the 18 months. Similarly, metformin had no effect on the presence of plaque. Metformin also had no effect on total cholesterol levels, LDL-cholesterol ('bad' cholesterol) levels or HDL-cholesterol ('good' cholesterol levels. As expected, the drug improved various measurements related to the control of blood sugar and risk of developing T2DM. Notably, those treated with metformin lost a substantial amount of weight compared to placebo (>3kg), the majority of which was body fat. This reduction in weight was progressive throughout the study. No safety concerns were noted during CAMERA. However, those on metformin did experience more nausea and more diarrhoea, both known side-effects.

Conclusions
Metformin failed to reduce markers of heart attack risk, namely cIMT, the presence of carotid plaques and cholesterol over 18 months in the CAMERA study. However, metformin did reduce markers of T2DM risk, most notably weight.

What does this study add to the field?
Drugs which can reduce risk of heart attacks and strokes in patients with and without T2DM are much sought after. Metformin is inexpensive and has an excellent safety record. For this reason, if research is also able to demonstrate benefit for metformin in patients without T2DM, it would be a very cost-effective treatment both in the UK and internationally. Metformin was studied in this novel trial based on findings of reduced heart attacks in patients with T2DM treated with metformin. While our trial was relatively small, it demonstrated that meformin did not reduce markers of heart attack risk in patients with known heart disease but no T2DM.

Implications for Practice or Policy
CAMERA findings are not definitive due to the fact that we analysed indicators of heart attack risk, rather than counting heart attacks themselves. For the timebeing, policy and practice should not change.

Where to next?
A large clinical trial is the next step to determine what place metformin has in the treatment of non-diabetic individuals at high risk of heart attack. A pilot study is currently underway in the UK.

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