

Recurrent miscarriage: Diabetes drug could lead to new treatment

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A drug designed to tackle diabetes could also be repurposed as the first treatment to prevent miscarriage by targeting the lining of the womb itself, according to a clinical trial led by the University of Warwick.

The treatment works by increasing the amount of [stem cells](#) in the lining of the womb, improving conditions in the womb to support [pregnancy](#).

The research by Warwick Medical School is reported today (9 January) in the journal *EBioMedicine* from research conducted with University Hospitals Coventry and Warwickshire and supported by the NIHR Coventry and Warwickshire Clinical Research Facility. The research was funded by and took place at Tommy's National Miscarriage Research Centre.

Recurrent [miscarriage](#) is defined as the loss of two or more consecutive pregnancies, with additional miscarriages decreasing the likelihood of a successful pregnancy. Previous research by the Warwick team revealed that a lack of stem [cells](#) in the womb lining is causing thousands of women to suffer from recurrent miscarriages. The team also demonstrated that stem cells protect specialised cells, called decidual cells, from excessive stress and inflammation. Decidual cells surround the implanting embryo and excessive stress can cause breakdown of the womb lining in pregnancy.

A new class of diabetes drugs called gliptins targets an enzyme involved in the recruitment of circulating stem cells to the womb. The researchers investigated whether inhibiting this enzyme, called DPP4, using a particular drug, sitagliptin, would improve conditions in the womb for pregnancy.

In a pilot clinical trial, thirty-eight women aged 18 to 42 who had experienced a large number of recurrent miscarriages (average five) were given either an oral course of sitagliptin or a placebo for three menstrual cycles. Biopsies of the womb were taken at the start of the course of treatment and afterwards to determine the number of stem cells present before and after the course.

They found an average increase in stem cell count of 68% in those women who took the full course of sitagliptin. This compares to no significant increase in those in the control group receiving an identical placebo pill. They also saw a 50% decrease in the number of 'stressed' cells present in the lining of the womb. There were minimal side effects for the participants.

The researchers now hope to take the treatment to clinical trial and, if successful, it would be the first targeted specifically at the lining of the womb to prevent miscarriage.

Professor Jan Brosens, of Warwick Medical School and Consultant in Reproductive Health at University Hospitals Coventry and Warwickshire NHS Trust, said: "There are currently very few effective treatments for miscarriage and this is the first that aims at normalising the womb before pregnancy. Although miscarriages can be caused by genetic errors in the embryo, an abnormal womb lining causes the loss of chromosomal normal pregnancies. We hope that this new treatment will prevent such losses and reduce both the physical and psychological burden of recurrent miscarriage."

Professor Siobhan Quenby from Warwick Clinical Trials Unit and an Honorary Consultant at University Hospital Coventry and Warwickshire NHS Trust, said: "We have improved the environment that an embryo develops in and in doing so we hope to improve the chances of a successful pregnancy. Although this research was specifically designed to test whether we could increase the presence of stem cells in the womb, follow-up of participants found that there were no further losses of normal pregnancies in those who took sitagliptin. These are very early results and the treatment now needs to be further tested in a large-scale clinical trial."

Jane Brewin, Chief Executive at Tommy's said: "For far too long it has

often been said by many health professionals that miscarriage is not preventable, and parents have been left with little hope given the paucity of treatment options available. This situation prompted Tommy's to invest in the Tommy's National Centre for Miscarriage Research and this breakthrough research by the world leading team at Warwick shows great promise for an effective treatment which will reduce miscarriage and possibly later pregnancy loss too. A large-scale trial is needed to verify the findings and we hope that this will get underway quickly."

Stem cells play a key role in creating the decidual cells in the womb lining which support the placenta throughout pregnancy. Insufficient stem cells in the womb lining leads to an excess of stressed and inflammatory decidual cells, which in turn may cause placental bleeding and miscarriage. Sitagliptin was effective not only in increasing stem cells in the [womb](#) lining but also decreasing the abundance of stressed decidual cells.

More information: 'Impact of sitagliptin on endometrial mesenchymal stem-like progenitor cells: A randomised, double-blind placebo-controlled feasibility trial' is published in *EBioMedicine*, [DOI: 10.1016/j.ebiom.2019.102597](#)

Provided by University of Warwick

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