Giving some pregnant women progesterone could prevent 8,450 miscarriages a year: experts

January 31 2020

Credit: CC0 Public Domain

Researchers at the University of Birmingham and Tommy's National Centre for Miscarriage Research say giving progesterone to women with

early pregnancy bleeding and a history of miscarriage could lead to 8,450 more babies being born each year.

The team have published two new studies evidencing both the scientific and economic advantages of giving a course of self-administered twice daily progesterone pessaries to women from when they first present with early pregnancy bleeding up until 16 weeks of pregnancy to prevent miscarriage.

Progesterone is a hormone that is naturally secreted by the ovaries and placenta in early pregnancy and is vital to the attainment and maintenance of healthy pregnancies.

Now the experts are calling for progesterone to be offered as standard in the NHS for women with early pregnancy bleeding and a history of miscarriage after their growing body of research has found it is both cost-effective and can increase women's chances of having a baby.

The first of the new studies, published today (31 Jan) in the *American Journal of Obstetrics and Gynecology* examines the findings of two major clinical trials—PROMISE and PRISM - led by the University of Birmingham and Tommy's National Centre for Miscarriage Research and funded by the National Institute for Health Research (NIHR).

PROMISE studied 836 women with unexplained recurrent miscarriages at 45 hospitals in the UK and the Netherlands, and found a 3% higher live birth rate with progesterone, but with substantial statistical uncertainty. PRISM studied 4,153 women with early pregnancy bleeding at 48 hospitals in the UK and found there was a 5% increase in the number of babies born to those who were given progesterone who had previously had one or more miscarriages compared to those given a placebo. The benefit was even greater for the women who had previous 'recurrent miscarriages' (i.e., three or more miscarriages) - with a 15%

increase in the live birth rate in the progesterone group compared to the placebo group.

The second of the new studies, published today (31 Jan) in *BJOG: an international Journal of Obstetrics & Gynaecology*, evaluates the economics of the PRISM trial and, importantly, concludes that progesterone is cost-effective, costing on average £204 per pregnancy.

Meanwhile, an unpublished survey by the University of Birmingham of 130 healthcare practitioners in the UK found that prior to the results of the PRISM study just 13% offered women at threat of miscarriage progesterone, while post publication of the results in the *New England Journal of Medicine* in May 2019, 75% now offer the treatment.

Dr. Adam Devall, Senior Clinical Trial Fellow at the University of Birmingham and Manager of Tommy's National Centre for Miscarriage Research, said: "Between 20 and 25 per cent of pregnancies end in a miscarriage, which has a major clinical and psychological impact on women and their families.

"The role of first trimester progesterone supplementation in the treatment of pregnancies at high risk of miscarriage is a long standing research question that has been debated in the medical literature for over 60 years.

"Thus far, policy makers have been unable to make evidence-based recommendations on the use of progesterone supplementation to improve outcomes.

"The PRISM and PROMISE Trials found a small but positive treatment effect, dependent on the number of previous miscarriages.

"We believe that the dual risk factors of early pregnancy bleeding and a

history of one or more previous miscarriages identify high risk women in whom progesterone is of benefit. The question is, how should this affect clinical practice?"

Arri Coomarasamy, Professor of Gynaecology at the University of Birmingham and Director of Tommy's National Centre for Miscarriage Research, said: "Our suggestion is to consider offering to women with early pregnancy bleeding and a history of one or more previous miscarriages a course of treatment of progesterone 400mg twice daily, started at the time of presentation with vaginal bleeding and continued to 16 completed weeks of gestation.

"In the United Kingdom, we estimate that implementing this treatment strategy would result in an additional 8,450 live births per year.

"We believe that women at high risk of having a miscarriage may not need absolute scientific certainty to choose to have a treatment. We recommend that they are informed about the uncertainty around treatment effects, so they can then decide for themselves the right course of action.

"We now urge policy makers and guideline developers to consider the evidence carefully to make a balanced recommendation."

Tracy Roberts, Professor of Economics at the University of Birmingham, said: "Miscarriage is a significant economic burden, costing the UK's NHS around £350 million per year for the management of miscarriage and complications.

"Given the distress to women and families associated with miscarriage, and the subsequent resources that might be associated with counselling and close antenatal attention in the subsequent pregnancies of women who experience miscarriage, progesterone is likely to be considered

good value for money in preventing miscarriage."

Faye Smith took part in the PRISM trial. The 40-year-old fundraiser lives in Solihull, UK, with her partner Dean and children Noah and Leila.

She said: "I experienced three miscarriages prior to participating in the PRISM trial. We were devastated and lost. The trial helped us to feel we were doing something positive and gave us hope that the outcome could be different. One of my miscarriages required additional hospital intervention due to complications and all of these experiences also led to anxiety for which I've received NHS treatment through cognitive behavioural therapy.

"The personal impact of miscarriage can be long term and far-reaching. It's clear that providing progesterone to those at risk would not only have significant benefits for women and their families, but also for the NHS."

Jane Brewin, Tommy's Chief Executive said: "Tommy's continues to hear from women who are being denied treatment and clinicians who seem unsure about the evidence. These thorough studies now provide women and their clinicians with an effective treatment option which women should be routinely offered. I'd like to call on NICE to amend the guidelines with this new information and for NHSE to encourage take up of this treatment across the country, preventing avoidable deaths."

Dr. Pat O'Brien, Consultant and Vice President of The Royal College of Obstetricians and Gynaecologists, said: "Miscarriage can be a devastating loss for women, their partners and families. We, therefore, welcome the findings from this well-researched trial which supports the use of progesterone among women with early pregnancy bleeding and a history of miscarriage.

"This treatment offers an increased chance of a successful birth and appears to be cost effective for the NHS, so we hope NICE will consider this important research in their next update of the guidance.

"For women with no prior history of miscarriage, there does not appear to be any benefit of the treatment, and women with concerns about their pregnancy should contact their midwife or early pregnancy unit for care and support. Reassuringly, most women who have had a miscarriage will have a successful pregnancy and birth in the future."

More information: Arri Coomarasamy et al. Micronized vaginal progesterone to prevent miscarriage: a critical evaluation of randomized evidence, *American Journal of Obstetrics and Gynecology* (2020). DOI: 10.1016/j.ajog.2019.12.006

Arri Coomarasamy et al. A Randomized Trial of Progesterone in Women with Recurrent Miscarriages, *New England Journal of Medicine* (2015). DOI: 10.1056/NEJMoa1504927

Arri Coomarasamy et al. A Randomized Trial of Progesterone in Women with Bleeding in Early Pregnancy, *New England Journal of Medicine* (2019). DOI: 10.1056/NEJMoa1813730

CB Okeke Ogwulu et al. The cost-effectiveness of progesterone in preventing miscarriages in women with early pregnancy bleeding: an economic evaluation based on the PRISM Trial, *BJOG: An International Journal of Obstetrics & Gynaecology* (2020). DOI: 10.1111/1471-0528.16068

Provided by University of Birmingham