Does progesterone prophylaxis to prevent preterm labour improve outcome? A randomised double-blind placebo-controlled trial (OPPTIMUM)

Jane E Norman,[1]* Neil Marlow,[2] Claudia-Martina Messow,[3] Andrew Shennan,[4] Philip R Bennett,[5] Steven Thornton,[6] Stephen C Robson,[7] Alex McConnachie,[3] Stavros Petrou,[8] Neil J Sebire,[2] Tina Lavender,[9] Sonia Whyte[1] and John Norrie[10] for the OPPTIMUM study group

[1]Tommy's Centre for Maternal and Fetal Health, MRC Centre for Maternal and Fetal Health, University of Edinburgh, Edinburgh, UK
[2]Institute of Women's Health, University College London, London, UK
[3]Robertson Centre for Biostatistics, Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK
[4]Women's Health Academic Centre, King's College London, London, UK
[5]Obstetrics and Gynaecology, Department of Surgery and Cancer, Imperial College London, London, UK
[6]Obstetrics and Gynaecology (Barts), Queen Mary University of London, London, UK
[7]The Medical School, University of Newcastle, Newcastle, UK
[8]Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK
[9]School of Nursing, University of Manchester, Manchester, UK
[10]Centre for Healthcare Randomised Trials, Health Services Research Unit, University of Aberdeen, Aberdeen, UK

*Corresponding author jane.norman@ed.ac.uk

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Scientific summary

The OPPTIMUM RCT

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Scientific summary

Background

Progesterone prophylaxis is widely used to prevent preterm birth, but does not have licensing approval, and there is little information on long-term outcome.

Objective

To determine the effect of progesterone prophylaxis in women at high risk of preterm birth on obstetric, neonatal and childhood outcomes.

Design

Double-blind, randomised placebo-controlled trial.

Setting

Obstetric units in the UK and Europe.

Participants

Women with a singleton pregnancy who were at a high risk of preterm birth.

Interventions

Fibronectin test at 18^{+0} to 23^{+0} weeks of pregnancy to determine the risk of preterm birth. Women with a positive fibronectin test and selected women with a negative fibronectin test were randomised to 200 mg of progesterone or placebo taken vaginally from 22^{+0} to 24^{+0} weeks' until 34^{+0} weeks' gestation.

Main outcome measures

There were three primary outcomes, as follows: (1) obstetric – fetal death or delivery before 34^{+0} weeks' gestation; (2) neonatal – a composite of death, brain injury on ultrasound scan (according to specific criteria in the protocol) and bronchopulmonary dysplasia; and (3) childhood – the Bayley-III cognitive composite score at 22–26 months of age.

Results

In total, 96 out of 600 (16%) women in the progesterone group and 108 out of 597 (18%) women in the placebo group experienced the primary obstetric outcome [odds ratio (OR) 0.86, 95% confidence interval (CI) 0.61 to 1.22]. Forty-six out of 589 (8%) babies of women in the progesterone group and 62 out of 587 (11%) babies of women in the placebo group experienced the primary neonatal outcome [OR 0.72,

95% CI 0.44 to 1.17]. The Bayley-III cognitive composite score at age 2 years for the child was 97.3 points [standard deviation (SD) 17.9 points] in the progesterone group and 97.7 points (SD 17.5 points) in the placebo group (difference in means –0.48, 95% CI –2.77 to 1.81).

Limitations

Overall compliance with the intervention was 69%.

Conclusions

In this study, progesterone had no significant beneficial or harmful effects on the primary obstetric, neonatal or childhood outcome.

Future work

We hope to participate in a comprehensive individual patient-level data meta-analysis examining women with a singleton pregnancy and with a variety of risk factors for preterm birth.

Trial registration

This trial is registered as ISRCTN14568373.

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