

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

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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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