Progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT): a randomised, double-blind, placebo-controlled study and meta-analysis

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Summary

Background
Women with twin pregnancy are at high risk for spontaneous preterm delivery. Progesterone seems to be effective in reducing preterm birth in selected high-risk singleton pregnancies, albeit with no significant reduction in perinatal mortality and little evidence of neonatal benefit. We investigated the use of progesterone for prevention of preterm birth in twin pregnancy.

Methods
In this double-blind, placebo-controlled trial, 500 women with twin pregnancy were recruited from nine UK National Health Service clinics specialising in the management of twin pregnancy. Women were randomised, by permuted blocks of randomly mixed sizes, either to daily vaginal progesterone gel 90 mg (n=250) or to placebo gel (n=250) for 10 weeks from 24 weeks’ gestation. All study personnel and participants were masked to treatment assignment for the duration of the study. The primary outcome was delivery or intrauterine death before 34 weeks’ gestation. Analysis was by intention to treat. Additionally we undertook a meta-analysis of published and unpublished data to establish the efficacy of progesterone in prevention of early (<34 weeks’ gestation) preterm birth or intrauterine death in women with twin pregnancy. This study is registered, number ISRCTN35782581.

Findings
Three participants in each group were lost to follow-up, leaving 247 analysed per group. The combined proportion of intrauterine death or delivery before 34 weeks of pregnancy was 24.7% (61/247) in the progesterone group and 19.4% (48/247) in the placebo group (odds ratio [OR] 1.36, 95% CI 0.89–2.09; p=0.16). The rate of adverse events did not differ between the two groups. The meta-analysis confirmed that progesterone does not prevent early preterm birth in women with twin pregnancy (pooled OR 1.16, 95% CI 0.89–1.51).

Interpretation
Progesterone, administered vaginally, does not prevent preterm birth in women with twin pregnancy.

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