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Recombinant Human Granulocyte - Colony Stimulating Factor (rhG-CSF) in women with unexplained Recurrent Pregnancy Losses (RESPONSE Study): randomised, double-blind, multicentre, placebo controlled trial

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Study question:

Does administration of recombinant human granulocyte - colony stimulating factor in the first trimester of pregnancy improve outcomes in women with a history of unexplained recurrent pregnancy losses?

Summary answer:

There is no evidence that administration of rhG-CSF in the first trimester of pregnancy improves outcomes, among women with history of unexplained recurrent pregnancy losses

What is known already:

rhG-CSF is shown to improve pregnancy outcomes by immunomodulation. The evidence prior to this study is only one RCT which was a smaller single centre study and another 4 observational study which suggested statistically significant increase in pregnancy rates and live birth rates

Study design, size, duration:

Women between the age of 18 to 37 years with a BMI of 19-35 (at the time of consent) and actively trying to conceive naturally after being diagnosed with a history of unexplained recurrent pregnancy losses were eligible. 340 women were screened into the study of which 150 were randsomised between June 2014 and June 2016. This was a double bind, placebo controlled randomised trial.

Participants/materials, setting, methods:

The participants were recruited from 21 hospitals with established recurrent pregnancy loss clinics from across the United Kingdom. Eligible participants were randomised to receive rhG-CSF 130 mcg or placebo in a 1:1 ratio. Stratified permuted block randomisation was used with number of prior miscarriages (3, >3), and age (<35, 35-37 years)as the stratification factors. An online computerised system was used for randomisation. The primary outcome was ongoing clinical pregnancy at 20 weeks of gestation.

Main results and the role of chance:

A total of 340 participants were screened for eligibility, of whom 150 women were randomised. 76 were randomised to rhG-CSF and 74 were randomised to placebo. All women were followed-up to primary outcome, and beyond to live birth. The clinical pregnancy rate at 20 weeks, as well as the live birth rate, was 59.2% (45/76) in the rhG-CSF group, and 64.9% (48/74) in the placebo group,

giving a relative risk of 0.9 (95% CI: 0.7 to 1.2; p=0.48). There was no evidence of a significant difference between the groups for any of the secondary outcomes.

Limitations, reasons for caution:

The limitation of this study was that participants were not screened prior to inclusion to demonstrate immune dysfunction as the reason for their pregnancy losses. This is because there is no accepted test(s) for immune dysfunction in reproductive immunology. This trial was therefore exclusively for women with unexplained recurrent miscarriages.

Wider implications of the findings:

G-CSF is widely used in reproductive medicine to treat recurrent miscarriages. Observational studies suggested statistically significant improvements in clinical pregnancy rates after administration of G-CSF. However, we now have high quality evidence suggesting that G-CSF is not an effective treatment for patients with unexplained recurrent miscarriages

Trial registration number:

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Yes
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