Immunotherapy for recurrent miscarriage

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Key Findings

For women with recurrent miscarriage thought to have an immunological basis (such as failure to develop protective maternal antibodies) the chance of a live birth was not significantly improved with the following interventions:

- Immunization with paternal cells
- Immunization with third party donor leukocytes
- Immunization with trophoblast membrane infusion
- Intravenous immunoglobulin

Evidence included in this review

Twenty randomized trials involving 1137 women were included.

Quality assessment

Included trials were of high quality.

Clinical implications

Recurrent miscarriage is a uniquely distressing experience for couples. Extensive counseling and reassurance are essential, and may even be therapeutic. Possible underlying causes such as infections (e.g. syphilis), endocrine disorders including diabetes, thrombophilias and parental chromosome anomalies must be actively sought and treated. For many couples, no cause is found. Unfortunately, early hopes that outcomes could be improved with immunotherapy have not been supported by randomized trial evidence. For these couples, the mainstay of management remains supportive counseling.

Further research

The fact that pregnancy constitutes a partial allograft with maternal exposure to paternally derived foreign antigens, suggests that the maternal immune response may be important for pregnancy survival. Because of biological and epidemiological evidence suggesting an immune basis for some cases of recurrent miscarriage, further research on methods to manipulate the maternal immune response to pregnancy are justified, particularly simplified methods which could be widely implemented.
Abstract

Because immunological aberrations might be the cause of miscarriage in some women, several immunotherapies have been used to treat women with otherwise unexplained recurrent pregnancy loss.

The objective of this review was to assess the effects of any immunotherapy, including paternal leukocyte immunization and intravenous immunoglobulin on the live birth rate in women with previous unexplained recurrent miscarriages.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (11 February 2014) and reference lists of retrieved studies.

Randomized trials of immunotherapies used to treat women with three or more prior miscarriages and no more than one live birth after, in whom all recognized non-immunologic causes of recurrent miscarriage had been ruled out and no simultaneous treatment was given.

The review author and the two co-authors independently extracted data and assessed study quality for all studies considered for this review.

Twenty trials of high quality were included. The various forms of immunotherapy did not show significant differences between treatment and control groups in terms of subsequent live births: paternal cell immunization (12 trials, 641 women), Peto odds ratio (Peto OR) 1.23, 95% confidence interval (CI) 0.89 to 1.70; third-party donor cell immunization (three trials, 156 women), Peto OR 1.39, 95% CI 0.68 to 2.82; trophoblast membrane infusion (one trial, 37 women), Peto OR 0.40, 95% CI 0.11 to 1.45; or intravenous immunoglobulin, (eight trials, 303 women), Peto OR 0.98, 95% CI 0.61 to 1.58.

Paternal cell immunization, third-party donor leukocytes, trophoblast membranes, and intravenous immunoglobulin provide no significant beneficial effect over placebo in improving the live birth rate.

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