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Endometrial scratching by pipelle biopsy in IVF (the PIP study): A pragmatic randomised controlled trial

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Study question:

Does endometrial scratching delivered by an endometrial pipelle biopsy, increase the probability of live-birth in women undergoing IVF/embryo transfer?

Summary answer:

Endometrial scratching was not associated with any improvement in live birth rate.

What is known already:

Endometrial scratching has been suggested to improve the probability of embryo implantation, and therefore pregnancy, in women undergoing IVF. It is proposed that the mechanical disruption to the endometrium results in a favourable inflammatory response, increasing the endometrial receptivity. Pooled results from randomised trials suggest benefit from endometrial scratching prior to an IVF cycle, especially in women with previous implantation failure. However, many of the studies had a high risk of bias secondary to study design, such as exposure of controls to endometrial disruption and lack of allocation concealment. Therefore, there is uncertainty about the validity of a beneficial effect.

Study design, size, duration:

A pragmatic, multi-centre, open-label, randomised trial was conducted between June 2014 and June 2017 in 13 centres across five countries. Women were randomised 1:1 to either endometrial scratching or no procedure, using an online trial-specific database which ensured allocation concealment. Sample-size was calculated separately in women with recurrent implantation failure (≥2 unsuccessful embryo transfers, 15% increase live-birth rate anticipated) and without (8% increase). At 80% power and a 5% significance level, 1300 women were required.

Participants/materials, setting, methods:

Eligible women were undergoing embryo transfer (fresh or frozen) using their own oocytes, with no recent exposure to disruptive intrauterine instrumentation. Women in the endometrial scratching arm underwent a pipelle biopsy between day 3 of the preceding cycle and day 3 of the IVF/embryo transfer cycle. The primary outcome was live-birth using an intention-to-treat approach. Risk ratio and 95% confidence intervals were calculated, and logistic regression was used to test for subgroup differences.

Main results and the role of chance:

A total of 1364 women were randomised: 690 to endometrial scratching and 674 to control. Baseline and cycle characteristics were similar between the two groups. Endometrial scratching was not associated with any improvement in live birth rate 26.1% (180/690) vs 26.1% (176/674), odds ratio =1.00 (0.78 to 1.27). The effect remained similar after adjusting for protocol deviations and the observation that fewer women in the control arm underwent an embryo transfer. There was no difference in the rate of biochemical pregnancy, ectopic pregnancy, ongoing pregnancy, clinical pregnancy or multiple pregnancy between the two groups. Subgroup analysis did not identify any subpopulations that may benefit from endometrial scratching; there was no evidence of a benefit in women: with recurrent implantation failure, undergoing fresh or frozen cycles, or depending on the timing of the scratch in relation to the embryo transfer. The median pain score from endometrial scratching was 3.5/10 (IQR 1.9-6.0). There were 14 adverse events related to endometrial scratching: 7 vasovagal reactions, 2 excessive bleeding and 5 excessive pain.

Limitations, reasons for caution:

Although a higher proportion of women in the endometrial scratching arm underwent embryo transfer, this did not impact the results. The definition of recurrent implantation failure was two or more previous unsuccessful embryo transfers, with no consideration for the stage or quality of the previously transferred embryos.

Wider implications of the findings:

This was a large trial and the pragmatic design increases the generalisability of the results. As the beneficial effects reported previously were not confirmed by this trial, and the procedure caused a moderate amount of pain and bleeding, the current use of endometrial scratching in fertility clinics should be abandoned.

Trial registration number:

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