Endometrial scratching before in vitro fertilisation does not increase live birth rate

Endometrial scratching can be offered to women undergoing in vitro fertilisation to increase the probability of pregnancy. Previous research has indicated that it may increase live birth rates in some women; however, the evidence is conflicting and of moderate quality. This large randomised trial addresses this lack of clear evidence.

Annette Plüddemann, Igbo J. Onakpoya

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Endometrial scratching is a procedure that may be offered to women undergoing *in vitro* fertilisation (IVF) to improve endometrial receptivity and increase the probability of pregnancy. The most common technique is endometrial biopsy, where the endometrium is disrupted using a flexible plastic tube, called a pipelle catheter [1]. The biological process as to why this procedure might improve the probability of pregnancy is unclear; one hypothesis is that the inflammatory response in the endometrium helps with implantation of the embryo [2]. A 2016 review highlighted the lack of evidence for fertility interventions offered to patients in the UK [3]. Although it identified some evidence showing that endometrial scratching potentially increased live birth rate, the benefit was only observed in women with more than two previous embryo transfers. In a recently published RCT [4], the authors assessed the effects of endometrial scratching before IVF on live birth rates.

What did they do? This multicentre, open-label, randomised controlled trial included 1364 women undergoing IVF. Women were randomly assigned to receive either endometrial scratching using a pipelle according to usual clinical practice (690 women) or no intervention (674 women). The primary outcome was a live birth. Several secondary outcomes were measured including ongoing pregnancy, biochemical pregnancy, miscarriage, and pain and bleeding due to the procedure.

What did they find? The frequency of live birth was 26.1% (180 of 690) women in the endometrial-scratch group and 26.1% (176 of 674 women) in the control group (adjusted odds

ratio, 1.00; 95% confidence interval, 0.78 to 1.27). No significant differences were recorded for any of the secondary outcomes. Subgroup analyses also did not identify any populations of women who might benefit.

How secure is the evidence? This was a large trial, with 80% power to detect a between-group difference in live-birth rates of 7 percentage points. The trial protocol was published and randomisation and allocation concealment procedures were conducted well, therefore minimising selection and reporting bias [5]. The study reported the most relevant primary outcome – live birth rate, using an intention to treat analysis. It included women undergoing their first IVF treatment, as well as women who had previously had multiple failed cycles of IVF (25% of the participants had undergone two or more previous unsuccessful embryo transfers), therefore making the results applicable to both these populations. The study was not blinded, which may have resulted in more women in the intervention group undergoing embryo transfer as they may have perceived benefits of this treatment. However, results from the study were not substantially changed in the per protocol analysis.

A recent systematic review assessing endometrial scratching for women undergoing a first embryo transfer concluded that the current evidence does not show any benefit in terms of live birth rate or ongoing pregnancy [6]. Using the random-effect model of the Review Manager (RevMan) software, we combined the results from the RCT with those of that review. The combined results show that endometrial scratching has no statistically significant beneficial effects on live birth rates: Risk difference (RD) 0.05, 95% CI -0.02 to 0.13, P=0.17 (Figure 1).

The results from this RCT contrast to those of a 2018 systematic review which concluded that endometrial scratching had significant benefits on live birth rates in women with 2 or more previous failed embryo transfers [7]. The combined results of the RCT with those of the 2018 review showed no significant difference in the pooled live birth rates between endometrial scratching and controls (Figure 2; raw data obtained from the corresponding author).

Given the data presented in this trial, combined with the data from recent systematic reviews, current evidence does not support endometrial scratching as an intervention for improving live birth rates; this has previously been noted by other commentators [8]. The traffic light system recently published by the UK Human Fertilisation and Embryology Authority (HFEA) [9] should be updated for endometrial scratching to reflect this evidence and help patients make informed decisions about this treatment.

EBM Verdict: Endometrial scratching before *in vitro* fertilisation does not result in higher live birth rates in women undergoing a first embryo transfer, nor in women with one or more previous failed embryo transfers.

Declaration of interests

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FIGURES

Footnotes

(1) NCT01882842. ClinicalTrials.gov; 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT01882842>.

Figure 1: Effect of endometrial scratch injury (ESI) on ongoing pregnancy/live birth rates. (Lensen et al 2019 data added to previously published systematic review).

Figure 2: Effect of endometrial scratch injury (ESI) on live birth rates in women with at least 2 previous failed embryo transfers. (Lensen et al 2019 data added to previously published systematic review. Raw data obtained from corresponding author).