

## **Fertile Battle on Endometrial Scratching at preceding an IVF cycle: stop offering it YES**

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*Should we stop offering endometrial scratching and why?*

One in seven couples experience difficulty in conceiving. Many of them require in-vitro fertilisation (IVF) as a treatment for prolonged unresolved infertility. Amidst the huge amounts invested into improving IVF, endometrial receptivity remains an important rate-limiting step affecting the success of IVF as the delivery rates are 36.3% per transfer in the United States in 2016 (<https://www.cdc.gov/art/reports/2016>). Even with replacement of euploid embryos following preimplantation genetic testing for aneuploidy using comprehensive chromosome screening, successful implantation cannot be guaranteed. It is obviously that the endometrium carries an important role in achieving implantation.

Different interventions have been tried in order to improve endometrial receptivity and implantation especially in those with repeated implantation failure (RIF). Endometrial scratching is an intentional local mechanical injury of the endometrial lining with the aim to improve endometrial receptivity. It is commonly performed using a pipelle biopsy in an outpatient setting. The issue of whether to scratch or not to scratch has been widely debated.

An updated Cochrane review (1) of 14 trials including 1063 women in the intervention groups and 1065 women in the control groups indicates that endometrial scratching performed between day 7 of the previous cycle and day 7 of the embryo transfer cycle is associated with an improvement in live birth and clinical pregnancy rates in women with more than two previous embryo transfers. However, eight of the 14 included studies were considered to be at

high risk of bias in at least one domain. Many RCTs are of small size and were published in journals with no or very low impact factor.

My group (2) conducted a randomized controlled study of 300 unselected infertile women undergoing IVF and found no difference in the on-going pregnancy and miscarriage rates between the endometrial scratching and non-intervention groups. In the subgroup analysis of women undergoing repeated IVF cycles, the ongoing pregnancy rate was even significantly lower in the endometrial scratching group than in the non-intervention group. A decrease in pregnancy rate after endometrial scratching in women undergoing a first or second IVF was supported by another RCT (3). A recent large multicentre RCT of endometrial scratching before IVF also demonstrated that endometrial scratching did not result in a higher live-birth rate than no endometrial scratching, including those who had failed at least once (4). Although these RCTs did not study women with RIF only, improvement in the ongoing pregnancy or live-birth rates is anticipated after endometrial scratching in unselected infertile women undergoing IVF.

In short, these high quality studies did not support any benefit in the IVF outcomes following endometrial scratching, which should not be offered to patients before IVF with an intention to improve the IVF success.

*Are there any circumstances where you would continue to offer it?*

Historical observations made in the guinea pig provided the first evidence that injury to the progesterational endometrium resulted in decidualisation and subsequent improved uterine receptivity (5). It has been postulated that endometrial scratching induces secretions of cytokines and growth factors that enhance decidualisation and facilitate implantation and up-

regulates the gene expressions related to endometrial receptivity and development. In stimulated cycles, local injury to the proliferative endometrium has been postulated to delay endometrial development thereby inducing synchronicity between endometrium and embryo stage and facilitate implantation. However, Simon and Bellver (6) concluded there is no evidence to demonstrate that endometrial scratching in the previous cycle modulates molecular/cellular phenotype induced by ovarian stimulation.

Endometrial scratching should not be offered to infertile patients including RIF before IVF because of the lack of biological plausibility and absence of clinical benefit shown by high quality RCTs.

*Is it ethical to continue to offer it?*

Proponents of endometrial scratching would argue that compared with the high costs of IVF, it is a simple and low cost intervention that could possibly improve implantation rates, so why not? However, there is great danger in widely adopting intervention that has no proven benefit, or may even cause potential harm such as pain and pelvic infection associated with endometrial scratching. It is, therefore, not ethical to offer it to infertile patients outside the context of research.

## **References**

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