

Efficacy doubts over pre-IVF hysteroscopy

June 30 2014

A large multicentre trial seems finally to have resolved one of IVF's long-running controversies - whether the outlook for women with a poor IVF record can be improved by routine hysteroscopy performed before further IVF treatment.(1) For the TROPHY study, whose results are reported today at the 30th Annual Meeting of ESHRE in Munich by Dr Tarek El-Toukhy from Guy's and St Thomas's Hospital, London, has now found no significant difference in IVF success rates between those who had outpatient hysteroscopy performed before their IVF and those who didn't. "Based on these findings, outpatient hysteroscopy before IVF doesn't significantly improve IVF results and cannot be considered essential for women with recurrent IVF failure," said Dr El-Toukhy.

Only around one-third of IVF cycles achieve a pregnancy, and unsuccessful attempts (implantation failure) can usually be explained by embryonic or uterine factors. As a result, outpatient hysteroscopy is performed routinely in many fertility clinics before further attempts, first diagnostically to visualise the surface of the uterus and check for any abnormal growths, and then operatively during the same procedure to remove these growths. Several studies have suggested that this can be beneficial prior to further IVF.

However, the TROPHY study has now found such benefit to be less than previously suggested.

This was a large randomised trial performed in eight IVF centres in Europe between 2010 and 2013. More than 700 women were randomised to IVF with hysteroscopy (in the preceding cycle), or IVF

without; all were under the age of 38, without known uterine pathology, and had history of unsuccessful IVF (two to four failed cycles).

First, results showed that some abnormality of the uterine cavity was found in 11% of the patients having hysteroscopy.

Second, outcome results following IVF showed no significant difference between the two groups - a live birth rate per patient of 31% in the hysteroscopy group and 29% in the control group.

"The results indicate that routine outpatient hysteroscopy prior to IVF in women who have experienced two to four failed IVF attempts do not significantly improve the subsequent IVF outcome," said Dr El-Toukhy. However, he acknowledged that other studies had indicated that hysteroscopy may well be beneficial before IVF. For example, a meta-analysis performed by Dr El-Toukhy himself in 2008 had provided some evidence that outpatient hysteroscopy might improve IVF results.(2)

However, if the gold standard of a randomised trial has now failed to show any significant benefit of outpatient hysteroscopy before IVF, where might the source of any benefit lie? "It is possible that endometrial scratching rather than routine outpatient hysteroscopy could be responsible for the previously reported improvements," said Dr El-Toukhy, referring to a procedure which too has raised controversy in recent years. Several studies - and study reviews - have shown that "injury" to the surface of the uterus (endometrium), which includes scratching, biopsy or even hysteroscopy, may improve implantation following embryo transfer in IVF.

One recent review of endometrial scratching described endometrial receptivity as one of the key factors regulating embryo implantation and proposed "that mechanical trauma to the endometrium alters gene expression, enhances secretion of growth factors and makes it more

receptive for implantation".(3) Results of the review suggested that endometrial scratching is 70% more likely to result in pregnancy than no treatment. A more recent review - but examining the same studies - concluded that "hysteroscopy and/or endometrial scratching in the cycle preceding ovarian stimulation should become a standard for patients with [recurrent implantation failure]. The optimal timing and number of scratches remains to be determined in randomized controlled trials".(4)

Commenting on the impact of hysteroscopy in women with recurrent implantation failure in IVF, Dr El-Toukhy explained that in this study it was mainly applied diagnostically - although "when an abnormality was found and deemed treatable by the surgeon, it was treated either at the same hysteroscopy or at a latter date under anaesthetic". In view of the neutral results of the study it seems possible that some of the abnormalities found "had little clinical significance" - although the study was not designed to test this.

Meanwhile, infertile women with recurrent IVF failure in IVF remain a challenging treatment group, with still little consensus on how they might best be treated.

More information: Abstract O-066: A multi-centre randomised study of pre-IVF outpatient hysteroscopy in women with recurrent IVF-ET failure: The TROPHY Trial

Notes

1. Outpatient hysteroscopy is one of the common investigations proposed after recurrent IVF failure. It is a well-tolerated minimally-invasive procedure, which allows visual assessment of the cervical canal and uterine cavity and provides the opportunity to perform therapy at the same time. Intrauterine pathologies, such as polyps, have been shown to be present in up to 25% of infertile patients, and can be a valid reason

for implantation failure. Thus, routine hysteroscopy prior to IVF has been suggested by a number of investigators to ensure normality of the uterine cavity before embryo transfer.

2. El-Toukhy T, Sunkara SK, Coomarasamy A, et al. Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis *Reprod Biomed Online* 2008; 16: 712-719.

3. Potdar N, Gelbaya T, Nardo LG. Endometrial injury to overcome recurrent embryo implantation failure: a systematic review and meta-analysis. *Reprod Biomed Online* 2012; 25: 561-571.

4. Implantation in assisted reproduction: a look at endometrial receptivity. *Reprod Biomed Online* 2013; 27: 530-538.

Provided by European Society of Human Reproduction and Embryology

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