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[Intervention Review]

Follicular flushing during oocyte retrieval in assisted reproductive techniques

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ABSTRACT

Background

Follicular aspiration under transvaginal ultrasound guidance is routinely performed as part of assisted reproductive technology (ART) to retrieve oocytes for in vitro fertilisation (IVF). However, controversy as to whether follicular flushing following aspiration yields a larger number of oocytes and hence is associated with greater potential for pregnancy than aspiration only is ongoing.

Objectives

To assess the safety and efficacy of follicular flushing as compared with aspiration only performed in women undergoing ART.

Search methods

We searched the following electronic databases up to 18 July 2017: Cochrane Gynaecology and Fertility Group (CGF) Specialised Register of Controlled Trials, the CENTRAL Register of Studies Online (CRSO), MEDLINE, Embase, PsycINFO, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). We also searched the trial registries ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform to identify ongoing and registered trials up to 4 July 2017. We reviewed the reference lists of reviews and retrieved studies to identify further potentially relevant studies.

Selection criteria

We included randomised controlled trials (RCTs) that compared follicular aspiration and flushing with aspiration alone in women undergoing ART using their own gametes. Primary outcomes were live birth rate and miscarriage rate per woman randomised.

Data collection and analysis

Two independent review authors assessed studies against the inclusion criteria, extracted data, and assessed risk of bias. A third review author was consulted if required. We contacted study authors as required. We analysed dichotomous outcomes using Mantel-Haenszel odds ratios (ORs), 95% confidence intervals (CIs), and a fixed-effect model, and we analysed continuous outcomes using mean differences (MDs) between groups presented with 95% CIs. We examined the heterogeneity of studies via the I^2 statistic. We assessed the quality of evidence by using GRADE (Grades of Recommendation, Assessment, Development and Evaluation) criteria.

Main results

We included ten studies, with a total of 928 women. All included studies reported outcomes per woman randomised. We assessed no studies as being at low risk of bias across all domains and found that the main limitation was lack of blinding. Using the GRADE method, we determined that the quality of the evidence ranged from moderate to very low, and we identified issues arising from risk of bias, imprecision, and inconsistency.

Comparing follicular flushing to aspiration alone revealed probably little or no difference in the live birth rate (OR 0.95, 95% CI 0.58 to 1.56; three RCTs; $n = 303$; $I^2 = 30\%$; moderate-quality evidence). This suggests that with a live birth rate of approximately 41% with aspiration alone, the equivalent live birth rate with follicular flushing is likely to lie between 29% and 52%. None of the included studies reported on the primary outcome of miscarriage rate.

Data show probably little or no difference in oocyte yield (MD -0.28 oocytes, 95% CI -0.64 to 0.09; six RCTs; $n = 708$; $I^2 = 0\%$; moderate-quality evidence). Very low-quality evidence suggests that the duration of oocyte retrieval was longer in the follicular flushing group than in the aspiration only group (MD 166.01 seconds, 95% CI 141.96 to 190.06; six RCTs; $n = 714$; $I^2 = 88\%$). We found no evidence of a difference in the total number of embryos per woman randomised (MD -0.10 embryos, 95% CI -0.34 to 0.15; two RCTs; $n = 160$; $I^2 = 58\%$; low-quality evidence) and no evidence of a difference in the number of embryos cryopreserved (meta-analysis not possible). Data show probably little or no difference in the clinical pregnancy rate (OR 1.07, 95% CI 0.78 to 1.46; five RCTs; $n = 704$; $I^2 = 49\%$; moderate-quality evidence). Only two studies reported on adverse outcomes: One reported no differences in patient-reported adverse outcomes (depression, anxiety, and stress), and the other reported no differences in needle blockage, vomiting, and hypotension. No studies reported on safety.

Authors' conclusions

This review suggests that follicular flushing probably has little or no effect on live birth rates compared with aspiration alone. None of the included trials reported on effects of follicular aspiration and flushing on the miscarriage rate. Data suggest little or no difference between follicular flushing and aspiration alone with respect to oocyte yield, total embryo number, or number of cryopreserved embryos. In addition, follicular flushing probably makes little or no difference in the clinical pregnancy rate. Evidence was insufficient to allow any firm conclusions with respect to adverse events or safety.

PLAIN LANGUAGE SUMMARY

Follicular flushing during oocyte retrieval in assisted reproductive technology

Review question

Cochrane authors sought to assess the safety and efficacy of flushing follicles as part of egg collection in women undergoing interventions to help them get pregnant, termed assisted reproductive technology (ART).

Background

Couples who have difficulty becoming pregnant naturally may choose to have interventions to help them get pregnant. These interventions are known as assisted reproductive technology (ART). One of these interventions is in vitro fertilisation (IVF), or a variant of IVF, called intracytoplasmic sperm injection (ICSI). During IVF, controlled ovarian stimulation uses hormones to stimulate multiple eggs to develop in the ovaries. After ovarian stimulation, a needle guided by ultrasound is used to collect these eggs that are inside follicles. Instead of using only suction to obtain the contents of follicles (aspiration), it has been proposed that flushing the follicles after aspiration may lead to collection of more eggs and higher chances of becoming pregnant and having a baby. This technique is called follicular flushing.

Study characteristics

This review included ten research studies that randomly assigned a total of 928 women to follicular aspiration alone or follicular flushing after aspiration. To see if there was a difference between the two techniques, we wanted to look at the main results of live birth rate (number of babies born per 1000 women) and miscarriage rate (number of miscarriages per 1000 women). We carried out a comprehensive search to identify all relevant research in this field available in July 2017.

Key results

Three studies reported on the main result of live birth rate and noted that follicular flushing probably has little or no effect on live birth rate compared with aspiration alone (moderate-quality evidence). This suggests that if a live birth rate of approximately 41% is seen with aspiration alone, the equivalent live birth rate with follicular flushing is likely to lie between 29% and 52%. None of the included studies reported on the miscarriage rate.

Studies also found that follicular flushing probably makes little or no difference in the number of eggs retrieved, the number of embryos, or the clinical pregnancy rate compared with aspiration alone. Although the quality of evidence was very low, it appears that follicular flushing takes much longer to perform than aspiration alone. Evidence was insufficient to permit any firm conclusions with respect to adverse events or safety.

More research is needed to find out whether any specific patient groups would benefit from follicular flushing.

Quality of the evidence

The quality of evidence for the main outcome of live birth rate was moderate. The quality of evidence for the other outcomes ranged from very low to moderate. The main limitations of included studies were lack of blinding (the process whereby women participating in the trial as well research staff are not aware of the intervention used), inconsistency (differences between different studies), and imprecision (insufficient data).