Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis

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CRD summary
This review concluded that outpatient hysteroscopy may be associated with an improved outcome after in vitro fertilisation (IVF) in infertile women when performed in the cycle immediately prior to IVF. Overall, despite the variable quality of the evidence, the authors’ cautious conclusions and recommendations for further research are likely to be reliable.

Authors' objectives
To assess the effect of outpatient hysteroscopy on the outcome of the subsequent in vitro fertilisation (IVF) cycle.

Searching
MEDLINE, EMBASE, The Cochrane Library and National Research Register were searched up to July 2007. Search terms were reported. ISI Conference Proceedings after 1990 and ISRCTN Register and meta Register of Controlled Trials were searched. Reference lists of known primary and review articles were scanned for additional studies. No language restrictions were applied. Only published studies were included in the review.

Study selection
Randomised and non-randomised controlled studies that assessed the pregnancy rate achieved in infertile women who underwent IVF (with or without intracytoplasmic sperm injection) after receiving outpatient hysteroscopy in the preceding cycle were eligible for inclusion in the review. Eligible secondary outcomes included procedure-related complications and miscarriage rate.

Included studies mainly compared office 5mm hysteroscopy with no hysteroscopy carried out in the follicular phase in women with primary or unreported infertility. The most commonly used distension medium was saline. Most women had at least two previously failed cycles of IVF or were undergoing their first or subsequent IVF cycle. Most of the women had previously had a hysterosalpingogram (HSG). Abnormal findings were found in 25% to 56% of the included women.

Two reviewers independently assessed studies for inclusion. Any disagreements were resolved through consensus and consultation with other reviewers.

Assessment of study quality
Study validity was assessed according to guidance from the Centre for Reviews and Dissemination. Criteria included the method of randomisation, allocation concealment, blinding, intention-to-treat (ITT) analysis, baseline comparability of study groups and follow-up rates.

The authors did not state how the validity assessment was performed.

Data extraction
The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction. Study authors were contacted to provide further information where study methods or data were unclear or missing. Primary outcome data were extracted and used to calculate relative risks (RRs) with 95% confidence intervals (CIs).

Methods of synthesis
Studies were grouped by design and relative risks were pooled with 95% CIs using a fixed-effect model. Heterogeneity was assessed using forest plots and statistical heterogeneity using the $\chi^2$ test. Differences in population, intervention and
study quality were used to explore any evidence of heterogeneity. Further analyses used a random-effects model that grouped all studies regardless of design and examined the effects of excluding patients with abnormal outpatient hysteroscopy findings. Publication bias was assessed using funnel plots and the Egger test.

**Results of the review**

Five studies reported in the review included two randomised controlled trials (RCT) (n=941) and three non-randomised controlled studies (n=750). Study quality was described as variable. All of the studies included comparable study groups, followed up over 95% of participants and used an intention-to-treat analysis. Allocation concealment was reported in only one of the two RCTs, as was study blinding. Sample size ranged from 56 to 600. Two of the non-randomised studies assessed fewer than 100 participants.

Outpatient hysteroscopy was associated with a statistically significant increase in the pregnancy rate in RCTs (RR 1.57, 95% CI 1.29 to 1.92), non-randomised studies (RR 2.01, 95% CI 1.60 to 2.52) and overall (RR 1.75, 95% CI 1.51 to 2.03). There was no evidence of significant statistical heterogeneity in any of the analyses. The significant difference in favour of outpatient hysteroscopy remained after patients with abnormal outpatient hysteroscopy findings were excluded from the analysis (RR 1.63, 95% CI 1.35 to 1.98; two RCTs and two non-randomised controlled trials).

No evidence of publication bias was found.

**Authors' conclusions**

Evidence suggested that outpatient hysteroscopy may be associated with an improved outcome after IVF when performed immediately before commencement of an IVF cycle. Further research was required to confirm this finding.

**CRD commentary**

This review answered a well-defined research question with clear inclusion criteria. A number of databases and other sources were searched for studies. No language restrictions were applied, but it appeared that only published studies were included in the review. Assessments of publication bias suggested that there was no risk of bias. Some precautions were taken to reduce the risk of reviewer error and bias when selecting studies for inclusion, but it was unclear whether similar procedures were in place for data extraction and for assessment of study quality. Criteria used to assess the quality of the studies were based on published guidance. The authors reported that the overall quality of the included evidence was variable. Most studies were not randomised and had relatively few participants. Despite these problems, the studies were clinically quite similar (with the exception of study design) and no evidence of statistical heterogeneity was evident. However, statistical tests for both heterogeneity and publication bias were unlikely to be reliable given the small number of included studies. A number of different analyses were performed to assess the robustness of the findings given the differences in study design and population. Overall, despite the variable quality of the evidence, the authors’ cautious conclusions and recommendations for further research are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that high-quality RCTs were required to confirm the effectiveness of standard (5mm) outpatient hysteroscopy in different populations of infertile women. Research was also needed to compare the effects of newer less invasive techniques, including mini-hysteroscopy and hysterocontrast sonography, to no intervention.

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