A meta-analysis of outcomes of conventional IVF in women with polycystic ovary syndrome

CRD summary
The authors of this review concluded that pregnancy and live birth rates per in vitro fertilisation cycle were similar for women with and without polycystic ovary syndrome. Poor reporting of review methods, the lack of an assessment of validity, and the reliance upon retrospective studies that are subject to various potential biases mean that the reliability of the authors’ conclusions is unclear.

Authors’ objectives
To compare the outcomes for conventional in vitro fertilisation (IVF) in women with and without polycystic ovary syndrome (PCOS).

Searching
The authors reported the terms included in a search strategy, but did not report the sources searched. Human Reproduction (1991 to 2004) and Fertility Sterility (1988 to 2004) were handsearched, pharmaceutical companies (Ferring, Organon and Serono) were contacted for details of unpublished and ongoing studies, and the reference lists of identified studies were screened.

Study selection
Study designs of evaluations included in the review
Studies with a matched control group were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated IVF, used the same ovarian stimulation protocol in all patients, and did not use IVF or intra cytoplasmic sperm injection cycles in both study groups were eligible for inclusion. In most of the included studies, gonadotropin-releasing hormone agonists were used in combination with follicle-stimulating hormone and/or human menopausal gonadotropin (details of the treatment protocols were reported).

Participants included in the review
Studies that included women with and without PCOS (defined using the Rotterdam consensus criteria) were eligible for inclusion. Most of the included studies were in patients with a pure tubal factor; in one study there were no male factor patients. The mean age of the participants was 31.9 years for women with PCOS and 31.8 years for matched controls.

Outcomes assessed in the review
Studies that assessed the number of oocytes retrieved and pregnancy outcomes were eligible for inclusion. The primary review outcomes were the number of oocytes retrieved, number of oocytes fertilised, number of patients with ovarian hyperstimulation syndrome (OHSS) and the number of clinical pregnancies. Secondary outcomes included the number of cycles, cancellation cycles, oocyte retrieval and embryo transfer, the number of ampoules of gonadotropin used and the duration of stimulation.

How were decisions on the relevance of primary studies made?
Five of 129 articles excluded on the basis of irrelevant titles were read in full by one reviewer. One reviewer excluded studies based on the abstract. Seven of 60 remaining studies were screened by two reviewers. Two publications were included after the authors provided additional data.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study, the numbers of events of interest (or mean values plus standard errors for continuous data) were extracted for each group of patients and the odds ratio (OR) of events (or the difference between groups) was calculated.

Methods of synthesis
How were the studies combined?
Where at least 2 studies reported a similar outcome, pooled ORs for dichotomous data or weighted mean differences (WMDs) for continuous data were calculated with their respective 95% confidence intervals (CIs). Pooling was performed using the inverse of the variance as weight. Where there were at least 3 studies, random-effects estimates were calculated using likelihood methods.

How were differences between studies investigated?
Statistical heterogeneity was assessed but the methods used were not reported. Meta-analysis graphs were also presented.

Results of the review
Nine studies with a matched control group were included in the review (458 patients with PCOS undergoing 793 cycles and 694 matched control patients undergoing 1,116 cycles). Of these, one was a prospective matched study (84 patients with PCOS undergoing 104 cycles and 84 controls undergoing 116 cycles); the other studies were retrospective.

PCOS was associated with a significantly reduced chance of oocyte retrieval per started cycle (OR reported as 0.5 in the text, 95% CI: 0.2, 1.0; based on 4 studies, n=697), but there was no difference in the chance of embryo transfer per oocyte retrieved compared with patients without PCOS.

PCOS was associated with a significant increase in the number of oocytes per retrieval (random-effects WMD was reported as 3.4 in the text, 95% CI: 1.7, 5.1; based on 5 studies, n=1,020), but significant heterogeneity was found (p=0.005). There was no significant difference in the number of oocytes fertilised compared with patients without PCOS.

There was no significant difference in the clinical pregnancy rate (37.4% versus 32.3%; based on 8 studies, n=1,537).

The incidence of OHSS after oocyte retrieval was rarely clearly reported. One study reported a trend towards an increase in OHSS in patients with PCOS. One study reported that among patients with PCOS, 16.6% developed mild to moderate OHSS and 3.9% developed severe OHSS requiring hospitalisation. One study reported three cases of OHSS among patients with PCOS compared with one case among controls (sample size and reference were not reported so the relative proportions could not be calculated). There were no significant differences between women with or without PCOS in the clinical pregnancy rate per started cycle, the number of live births per cycle started, the clinical pregnancy rate per oocyte retrieved, or the number of miscarriages.

Authors' conclusions
Pregnancy and live birth rates per IVF cycle were similar for women with and without PCOS.

CRD commentary
The review question was clear in terms of the intervention, participants, study design and outcomes. The search strategy was incompletely reported but attempts were made to minimise publication bias. The potential for language bias could not be assessed. The methods used to select studies were incompletely described and those used to extract the data were not reported, thus the potential for reviewer error and bias cannot be ruled out. Since study validity was not assessed,
the results from these studies and any synthesis may not be reliable.

Statistical heterogeneity was assessed but the methods used were not reported. Where significant heterogeneity was found, potential reasons were not examined. There were slight discrepancies between the results reported in the text and graph. Incomplete reporting of review methods, the lack of an assessment of validity, and the reliance upon retrospective studies that are subject to various potential biases mean that the reliability of the authors’ conclusions is unclear.

Implications of the review for practice and research
Practice: The authors stated that IVF appears to be a reasonable option for women with PCOS but the risks, particularly the risk of OHSS, and costs need to be considered.

Research: The authors stated that further research is needed to determine the role of IVF and ovulation induction treatments for infertile women with anovulatory PCOS. Research to evaluate the effects of other treatments in women with PCOS, such as lifestyle changes, insulin sensitisers, aromatase inhibitors, laparoscopic electrocautery of the ovaries and IVF involving single embryo transfer, is also required.

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