Meta-analysis of recombinant versus urinary-derived FSH: an update

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CRD summary
The authors of this review analysed the results of studies comparing the use of recombinant follicle stimulating hormone (FSH) and urinary-derived FSH gonadotrophins in female fertility treatment. The authors concluded that there was no real difference between the two approaches in terms of increasing pregnancy rates. These conclusions follow appropriately from the evidence.

Authors’ objectives
To analyse the results of randomised controlled trials (RCTs) comparing recombinant follicle-stimulating hormone (FSH) and urinary-derived FSH gonadotrophins in an in vitro fertilisation (IVF)/intracytoplasmic sperm injection (ICSI) programme.

Searching
The authors searched MEDLINE, the Cochrane Menstrual Disorders and Subfertility Review Group's specialised register of controlled trials, as well as abstracts of meetings and conference proceedings (the European Society for Human Reproduction and Embryology, the American Society for Reproductive Medicine, and the International Federation of Fertility Sciences) from 1999 to 2002. The search terms were reported.

Study selection
Study designs of evaluations included in the review
RCTs were included in the review.

Specific interventions included in the review
Studies comparing recombinant FSH (rFSH) with urinary-derived FSH gonadotrophins for ovarian stimulation were included.

Participants included in the review
Studies of subfertile women undergoing IVF/ICSI in which pituitary down-regulation was achieved using the long protocol were included. The causes of infertility varied within the included studies.

Outcomes assessed in the review
The outcome evaluated in the meta-analysis was limited to the clinical pregnancy rate per cycle started.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity, although the level of concealment of treatment allocation for each study was given in the tables.

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, data were extracted on the clinical pregnancy rate per cycle started and expressed as odds ratios (ORs) with 95% confidence intervals (CIs).
Methods of synthesis

How were the studies combined?
The studies were combined in a meta-analysis using the Mantel-Haenszel method. A fixed-effect model was used where it was confirmed that statistically significant heterogeneity was not present.

A funnel plot was used to detect any publication bias.

How were differences between studies investigated?
Statistical heterogeneity was investigated using the Breslow-Day test (see Other Publications of Related Interest). Subgroup analyses were carried out according to the type of urinary gonadotrophin comparator, in order to test the robustness of the results. A subgroup analysis excluding studies sponsored by pharmaceutical companies was also conducted.

Results of the review

Twenty RCTs (4,610 cycles) were included in the review.

Pooled data from all studies showed no significant difference between rFSH and urinary-derived FSH gonadotrophins, in general, in the clinical pregnancy rate per cycle started (OR 1.07, 95% CI: 0.94, 1.22). Neither was the difference statistically significant between rFSH and human menopausal gonadotrophin, purified FSH, or highly purified FSH.

The studies were statistically homogeneous. The funnel plot indicated that publication bias was unlikely to have influenced the findings.

Authors' conclusions

There was no evidence of clinical superiority in clinical pregnancy rate for rFSH over different urinary-derived FSH gonadotrophins. Additional factors should be considered when choosing a gonadotrophin regimen, including the cost, patient acceptability, safety and drug availability.

CRD commentary

This meta-analysis posed a reasonably well-defined question, based on appropriate inclusion criteria relating to the interventions, participants and study design. The search of the published literature appeared adequate. The authors do not appear to have searched for unpublished or non-English language papers, but they did present a funnel plot that indicated publication bias was unlikely to have influenced their results. The level of concealment of treatment allocation was recorded for each included study, but this information was not incorporated into the synthesis. However, few studies scored poorly on this, and these studies did not have results that were extreme or systematically different from the higher quality RCTs. The authors' conclusions seem appropriate given the evidence presented.

Implications of the review for practice and research

The authors did not state any implications for practice or further research.

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