Outcomes of new quality standards of follitropin alfa on ovarian stimulation: meta-analysis of previous studies

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CRD summary

The authors concluded that follitropin alfa filled by mass was as safe as follitropin alfa filled by international units and required a smaller dose over a shorter period to produce more oocytes and final embryos. Inadequate assessment of study quality plus lack of reporting of patient characteristics made it difficult to judge the reliability or generalisability of the reported results.

Authors' objectives

To evaluate the efficacy and safety of ovarian stimulation using follitropin alpha filled by mass (FbM) compared with follitropin alfa filled by international units (FbIU).

Searching

PubMed, EMBASE, The Cochrane Library, Web of Science and Current Contents Connect Databases were searched for studies without restrictions. Search terms were reported, but search dates were not. Relevant publications were scanned. Studies published only as abstracts were included.

Study selection

Clinical controlled studies that compared the two forms of recombinant human follicle stimulating hormone (FbM versus FbIU) for ovarian stimulation were eligible for inclusion.

Review outcomes were average dose, days of treatment, oestradiol peak, number of follicles greater than 14mm, number of extracted oocytes, number of embryos obtained and clinical pregnancies as efficacy outcomes and number of cases of ovarian hyperstimulation syndrome (OHSS) as the safety outcome.

Two reviewers independently selected studies.

Assessment of study quality

The authors stated that they assessed study quality and the level of evidence according to Oxford Centre for Evidence-Based Medicine recommendations. Only the level of blinding in randomised controlled trials (RCTs) was reported.

The authors did not state how many reviewers assessed validity.

Data extraction

Two reviewers independently extracted data.

Methods of synthesis

Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated for dichotomous data. Pooled weighted mean differences (WMD) with 95% confidence intervals were calculated for continuous data. Fixed-effect models were used. Heterogeneity was assessed using the I^2 statistic. Heterogeneity was examined using sensitivity analysis.

Results of the review

Six studies were included (n=1,327 patients): four RCTs (n=1,055 patients) and two case-control studies (n=272 patients). Two of the RCTs were double-blinded and the assessor was blinded in a third RCT.

Compared to follitropin alfa FbIU, follitropin alfa FbM was associated with improvements in the following outcomes: a significantly lower dose (WMD -230.29 IU, 95% CI -326 to -134.5; four studies, n=1,019); significantly fewer days of treatment (WMD –0.48, 95% CI -0.69 to -0.27; five studies, n=1,150); significantly greater number of oocytes (WMD

0.84, 95% CI 0.18 to 1.51; five studies, n=1,150); and a significantly greater number of embryos (WMD 0.88, 95% CI 0.40 to 1.37; three studies, n=875).

There was no statistically significant difference between follitropin alfa FbM and FbIU in the number of follicles greater than 14mm (three studies, n=403), number of clinical pregnancies (three studies, n=558) or cases of OHSS (four studies, n=1,128).

Follitropin alfa FbM was associated with a significantly higher peak level of oestradiol (WMD 613.08pmol/L, 95% CI 142.4 to 1083.7; five studies, n=1,150).

No significant heterogeneity was found for any of the analyses (I^2<50%).

Authors' conclusions

Follitropin alfa filled by mass was as safe as follitropin alfa filled by international units and required a smaller dose over a shorter period to produce more oocytes and final embryos.

CRD commentary

The review question was clearly stated and inclusion criteria were appropriately defined for intervention and outcomes. Inclusion criteria for study design were broad. Several relevant sources were searched and attempts were made to minimise publication bias by including studies reported only as abstracts. It was unclear whether attempts were made to minimise language bias. Methods were used to minimise reviewer errors and bias in the selection of studies and extraction of data. Study validity was not adequately assessed, which made it difficult to judge the reliability of results. No information was provided about participants, which made it difficult to determine the likely generalisability of findings. Pooling RCTs and case-control studies may not have been appropriate and there was no subgroup analysis limited to RCTs. Confidence intervals of treatment differences were wide, which reflected uncertainly about the point differences. Some limitations of the evidence were discussed. Inadequate assessment of study quality combined with lack of reporting of patient characteristics made it difficult to judge the reliability or generalisability of the reported results.

Implications of the review for practice and research

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

Research: The authors stated that additional clinical studies were required to determine the effect of follitropin alfa FbM on other outcomes such as the quality of oocytes and implanted embryos.

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