Low-dose HCG may improve pregnancy rates and lower OHSS in antagonist cycles: a meta-analysis

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to determine the cost-effectiveness of alternative ovarian stimulation strategies for in-vitro fertilisation. The authors concluded that generally protocols supplemented with low-dose human chorionic gonadotrophin were cost-effective. The authors also stated that a more comprehensive Markov model should be developed to evaluate the decision problem. The rounding of the pregnancy rate to one might have had a significant effect on the results, so it is not clear if the authors’ conclusions are appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to determine the cost-effectiveness of alternative ovarian stimulation strategies for in-vitro fertilisation (IVF).

Interventions
The interventions assessed were: a long agonist supplemented with low-dose human chorionic gonadotrophin (HCG); an antagonist supplemented with low-dose HCG; a non-supplemented antagonist; and a non-supplemented long agonist.

Location/setting
Greece/secondary care.

Methods
Analytical approach:
A decision-tree model was used to assess the costs and outcomes of the two interventions. The time horizon was six weeks, which was the time taken to detect an intrauterine pregnancy. The perspective was not explicitly reported.

Effectiveness data:
The authors reported that MEDLINE searches were performed in September 2007, and the references of all relevant articles were checked. The literature review also included abstracts from relevant conferences. The data, from all relevant studies, were extracted by two investigators, and disagreements were resolved by discussion. These results were combined using meta-analyses. The main clinical and effectiveness parameters, derived from these meta-analyses, were the clinical pregnancy rate and the incidence of ovarian hyperstimulation syndrome (OHSS).

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was a composite of the clinical pregnancy rate and stimulation rate. A clinical pregnancy was given the value one and a stimulation without clinical pregnancy was given the value 0.5.

Cost data:
The authors reported that the following costs were included: hospitalisations due to OHSS; follicle-stimulating hormone; agonist and antagonist; IVF; ultrasound; and work absence due to hospitalisation. Many pregnancy costs, and
antenatal, perinatal and post-partum care costs were not included. All costs were expressed in Euros (EUR).

Analysis of uncertainty:
The authors reported that a series of one- and two-way sensitivity analyses, including threshold analyses, were performed by varying the model parameters.

Results
The clinical pregnancy rate for the four interventions was rounded to the nearest integer and, for all interventions, the rate was one. The average cost per patient was EUR 957 for low-dose HCG long agonist; EUR 1,188 for low-dose HCG antagonist; EUR 1,622 for non-supplemented antagonist; and EUR 1,939 for non-supplemented long agonist.

Costs and outcomes were combined in an incremental cost-effectiveness ratio (ICER), which was the additional cost per additional clinical pregnancy. Compared with low-dose HCG agonist, the ICER for low-dose HCG antagonist was EUR 4,612. Non-supplemented antagonist was dominated as it was both more costly and less effective than another treatment. Compared with low-dose HCG antagonist, the ICER for non-supplemented long agonist was EUR 170,659.

The threshold analysis identified that if the follicle-stimulating hormone requirements were between 1,244 and 1,766.7 units, the most cost-effective intervention (using a net-benefit approach) was the low-dose HCG agonist. At rates between 1,766.7 and 1,960 units, the most cost-effective strategy was the low-dose HCG antagonist.

Authors’ conclusions
The authors concluded that, overall, low-dose HCG-supplemented protocols were cost-effective. The authors also stated that a more comprehensive Markov model should be developed to evaluate the decision problem.

CRD commentary
Interventions:
The interventions were adequately reported.

Effectiveness/benefits:
The methods used to obtain the clinical and effectiveness data from the literature were reported in great detail, including the sources searched, the inclusion criteria, the search strategy, and the methods used to extract the data and then to combine it. The authors reported that only MEDLINE was searched, in addition to conference abstracts and references from included articles, but the details reported suggest that the results of this literature review and meta-analysis were internally valid.

Costs:
The authors did not explicitly report the perspective, but productivity losses, due to hospitalisation, were included and so it appears that a societal perspective was adopted. The authors reported that a number of relevant costs were omitted, such as multiple pregnancy costs, and they did not justify these exclusions. It was unclear if these costs would have varied between interventions, which means that it is not possible to comment on whether their omissions could have biased the results. The authors did not report the sources for the costs. The price year was also not reported, except that costs were at their "present" value. The costs were incurred over a short period and discounting was not necessary. Since this abstract was published, the authors have informed us that the cost analysis focussed on FSH consumption as the major cost.

Analysis and results:
All the available evidence was synthesised in a decision-tree model. Appropriate details of the model, including a diagram, were provided. The authors performed a series of one- and two-way sensitivity analyses to test the uncertainty in their results. These analyses assessed some of the uncertainty, but probabilistic sensitivity analyses would have more thoroughly tested the overall model uncertainty. The effectiveness results were not presented clearly: it was apparent that there were differences between the four interventions, in their clinical pregnancy rates, but these estimates were rounded up, so that they were all the same (one). The authors stated that more randomised controlled trials were needed to confirm the results of their study.
Concluding remarks:

The rounding of the pregnancy rate to one might have had a significant effect on the results, so it is not clear if the authors' conclusions are appropriate.

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