Anti-Mullerian hormone-tailored stimulation protocols improve outcomes whilst reducing adverse effects and costs of IVF

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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
This study assessed the cost-effectiveness of serum anti-Mullerian hormone (AMH) level as an indicator of ovarian reserve in women aged 20 to 40 years, who were undergoing stimulation before in vitro fertilisation. The authors concluded that AMH-guided, controlled ovarian hyperstimulation protocols improved clinical outcomes, reduced complications, and lowered health care costs. Appropriate statistical tests were used to overcome the limitations of the retrospective study design, but caution is required when interpreting the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study assessed the cost-effectiveness of serum anti-Mullerian hormone (AMH) level as an indicator of ovarian reserve (number and quality of oocytes) in women aged 20 to 40 years, who were undergoing stimulation before in vitro fertilisation (IVF).

Interventions
The AMH-guided controlled ovarian hyperstimulation was compared against the conventional hyperstimulation, which was guided by chronological age and follicle stimulating hormone (FSH) level. In the AMH strategy, women with acceptable AMH levels were grouped into three categories (optimal, satisfactory, or low fertility), which determined their stimulation protocol; those with higher AMH levels received lower doses of gonadotrophins.

Location/setting
UK/IVF clinic.

Methods
Analytical approach:
The analysis was based on one study with a short time horizon, from stimulation to delivery. The authors did not explicitly state the perspective adopted.

Effectiveness data:
The clinical data were from a retrospective study with a historical control. This was conducted at the authors’ institution; St Mary’s Hospital, Manchester, UK. Women examined between September 2007 and September 2008 were treated based on their age and FSH levels, while those examined between December 2008 and December 2009 were treated based on their AMH levels. There were 346 women in the first group and 423 women in the second group. Women were followed-up until they gave birth. Various endpoints were used, including the rate of cancelled cycles, ovarian hyperstimulation syndrome (OHSS), failed fertilisations, pregnancy rates, and live births. Clinical outcomes were adjusted, using logistic regression, for baseline factors, such as age, previous pregnancy, male factor infertility, unexplained cause, and procedure-related factors. The impact of time differences was considered.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The main clinical endpoints were the rates of cancelled cycles, fertilisation rates, and pregnancy and live birth rates.

Cost data:
The economic analysis included the costs of the ovarian stimulation protocol and the treatment of OHSS. Only the costs of the first treatment cycle were included. The unit costs of drugs were those quoted in the British National Formulary. The costs of clinic appointments before controlled ovarian hyperstimulation were NHS reference costs. The resource quantities were from the clinical study or other published sources. All costs were in UK pounds sterling (£).

Analysis of uncertainty:
Not considered.

Results
The rate of cancelled cycles due to poor response was 4% with usual care and 3.3% with AMH guidance (adjusted $p=0.57$). The rate of OHSS leading to cycle cancellation was 6.9% with usual care and 2.3% with AMH (adjusted $p=0.004$). The incidence of failed fertilisation was 7.8% with usual care and 4.5% with AMH (adjusted $p=0.11$). The percentage of women who had embryo transfer was 78.9 with usual care and 87.5 with AMH (adjusted $p=0.003$). The rate of pregnancy per cycle started was 17.9% with usual care and 27.7% with AMH (adjusted $p=0.002$). The rate of live births per cycle started was 15.9% with usual care and 23.9% with AMH (adjusted $p=0.003$). The rate of live births per embryo transfer was 20.1% with usual care and 27.3% with AMH (adjusted $p=0.012$).

The regression analysis showed that the improvements in positive outcomes were a direct result of the AMH guidance.

The cost per patient for fertility drugs was £1,090 with usual care and £773 with AHM. Including the costs of treatment of OHSS, the total cost per patient was £1,192 with usual care and £821 with AHM.

Authors’ conclusions
The authors concluded that AMH-guided, controlled ovarian hyperstimulation protocols improved clinical outcomes, reduced the incidence of complications, and lowered health care costs. They noted that large, prospective, randomised studies should be carried out to confirm the potential cost-effectiveness of AMH-tailored IVF.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear; the proposed intervention was compared against the existing guidance for treatment. A clear description of the two options was provided.

Effectiveness/benefits:
A retrospective study was carried out to assess the clinical impact of the two options. The inclusion and exclusion criteria were reported. The two study groups were not perfectly matched at baseline in their clinical factors; statistically significant differences were observed in the causes of subfertility. The impact of these baseline differences and time factors was taken into account, using statistical analyses that were described. The study took place in one institution, which might not have been representative of the general patient population. It was unclear whether the study had sufficient power to capture significant differences for the clinical endpoints. No summary benefit measure was used and the clinical outcomes were not combined with the costs.

Costs:
The analysis was carried out from the perspective of the NHS, but this was not explicitly stated. The cost categories and their sources were consistent with a health system viewpoint. The unit costs and resource quantities were not reported. The costs were treated deterministically and no statistical analysis of them was carried out. Reflation exercises for other time periods will not be possible as the price year was not explicitly stated.

Analysis and results:
The results were clearly presented. The costs and benefits were not synthesised as a cost-consequences approach seems to have been used. The uncertainty was not investigated. Some subgroup analyses were conducted and were briefly presented in an online appendix. The authors compared their results with those of other studies, which had similar
clinical findings. It was acknowledged that future randomised studies were needed to corroborate the findings, which should be considered to be specific to the authors’ context.

Concluding remarks:
Appropriate statistical tests were used to overcome the limitations of the retrospective study design, but caution is required when interpreting the authors’ conclusions.

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