Economic evaluation of highly purified menotropin compared with recombinant follicle-stimulating hormone in assisted reproduction

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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.

Health technology
The use of highly purified menotropin (hMG) and recombinant follicle stimulating hormone (FSH) for ovarian stimulation in patients undergoing in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women aged 18 to 36 years, with regular ovulatory menstrual cycles of 24 to 36 days, who were candidates for IVF or ICSI, and who had proven infertility for more than 1 year (except for proven bilateral occlusion or male factor). Women were excluded if they had body mass index of less than 18.0 or greater than 29.0, had a history of severe ovarian hyperstimulation syndrome (Type III), or were known to use illegal drugs, drink excessive alcohol (more than 30 units per week), or smoke more than 10 cigarettes per day. They were also excluded if they had undergone more than three unsuccessful IVF or ICSI cycles, or were considered a poor responder to gonadotropin stimulated procedures (defined as a development of fewer than four follicles, or more than 20 days of gonadotropin stimulation until human chorionic gonadotropin criteria were met).

Setting
The setting was tertiary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were derived from a study published in 2002. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness evidence was derived from a published single study, (The European and Israeli Study Group on Highly Purified Menotropin versus Recombinant Follicle-Stimulating Hormone, see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.
Study sample
There was limited information on the sample selection process since most of the details had been published elsewhere. There were 781 patients, 396 in the hMG group and 385 in the FSH group. The women in the hMG group had a mean age of 31 (+/- 4) years and 94.9% were white. The women in the FSH group had a mean age of 31 (+/- 4) years and 93.4% were white.

Study design
This was a prospective, randomised clinical trial that was carried out in 22 centres in 6 countries (Belgium, Germany, Israel, the Netherlands, Switzerland and the UK). No information on the method of randomisation was provided. The patients were followed up to at least 10 weeks. The outcome assessment was not blinded. The authors stated that 92% of the highly purified hMG group and 88% of the recombinant FSH group remained in the study long enough to undergo oocyte retrieval. This difference was not statistically significant.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary outcome measure was the rate of ongoing pregnancy, as assessed by a serum or urine pregnancy test and confirmed by ultrasonography 10 or more weeks after oocyte retrieval. Safety data were also assessed in the primary trial, but were not reported in the current analysis, although the authors stated that both treatments were well tolerated. The authors stated that the two groups were well matched for all baseline characteristics.

Effectiveness results
The rate of ongoing pregnancy at 10 weeks or more was 0.22 (95% confidence interval, CI: 0.18 - 0.27) in the hMG group and 0.19 (95% CI: 0.15 - 0.23) in the FSH group. The difference was not statistically significant.

Clinical conclusions
The effectiveness analysis showed that highly purified hMG and recombinant FSH were equally effective in terms of the ongoing pregnancy rate.

Measure of benefits used in the economic analysis
The summary benefit measure was the ongoing pregnancy rate. This was derived directly from the effectiveness study.

Direct costs
Discounting was not relevant as the costs were incurred during less than 2 years. The unit costs were presented separately from the quantities of resources used. The health services included in the economic evaluation were study drugs, other medications as part of the IVF or ICSI procedure, visits to the clinic, visits requiring injections, ultrasound examinations, blood tests and other diagnostic procedures, and oocyte retrieval, fertilisation and implantation procedures. Medication, physician visits, and hospital stay for the treatment of adverse events were also included. The drug costs included the most economical prescription available that matched the drug, brand, dose and route of administration. Depot injections were treated as a single day’s treatment by using the full cost of the depot formulation. The cost/resource boundary of the UK NHS was adopted. The costs were estimated from multiple sources, such as the finance department of the University Hospitals Coventry and Warwickshire, Personal Social Services Research Unit, National Health Service Reference costs, and the British National Formulary. The price year was not explicitly reported.

Statistical analysis of costs
Bootstrapped CIs for the total costs were estimated.
Indirect Costs
The indirect costs were not considered.

Currency
UK pounds sterling (€).

Sensitivity analysis
Sensitivity analyses were carried out to investigate the impact of using an alternative source of costs (i.e. patients' charges). The use of discounting from drug list prices was also assessed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The resource usage of the groups was fairly comparable.

The estimated total costs per patient were £2,424 (95% CI: 2,356 - 2,495) with highly purified hMG and £2,745 (95% CI: 2,658 - 2,830) with recombinant FSH. The difference in costs of £322 (95% CI: 208 - 435) was statistically significant, (p<0.001). The difference was mainly due to the different drug acquisition costs.

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated to combine the costs and benefits of the interventions under evaluation.

The average cost per ongoing pregnancy was £10,781 (95% CI: 9,056 - 12,919) with highly purified hMG and £14,284 (95% CI: 11,883 - 17,891) with recombinant FSH.

The authors stated that the use of alternative sources of costs (patients' charges) or price discounts did not change the main conclusions of the analysis.

Authors' conclusions
Highly purified menotropin (hMG) used for ovarian stimulation in women undergoing in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) was as effective as recombinant follicle stimulating hormone (FSH), but the costs were significantly lower, mainly due to savings associated with lower hMG acquisition costs. The authors stated that, since their centre had a fixed budget, the use of highly purified hMG would translate into a 13% increase in the number of cycles that could be offered.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators. Both treatments represented regimens for ovarian stimulation in patients undergoing IVF or ICSI as recommended by recent UK guidelines. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a well-conducted clinical trial. Limited information on the study was provided as it had already been published. However, the internal validity of the study appears to have been high due to the strong design (multi-centre, randomised trial) and the large sample size. The basis of the analysis was intention to treat, which further enhances the reliability of the estimates used in the analysis. The authors stated that the efficacy study had
sufficient power to detect statistically significant differences between the groups.

**Validity of estimate of measure of benefit**
The summary benefit measure represents a widely used end point for treatments for infertility. However, it was specific to the disease considered in the study and would, therefore, be difficult to compare with the benefits of other health care interventions.

**Validity of estimate of costs**
The authors explicitly stated the perspective adopted in the study. Given that perspective, it appears that all the relevant categories of costs have been included in the analysis. A detailed breakdown of the cost items was provided. The unit costs were presented separately from the quantities of resources used, which enhanced the possibility of replicating the study. The source of the cost data was reported for each category. The authors calculated CIs around the total costs, although the unit costs were treated as point estimates. Overall, the cost analysis was carried out satisfactorily.

**Other issues**
The authors made few comparisons of their findings with those from other studies. In terms of the generalisability of the study results to other settings, it was noted that the estimated costs could "be broadly applicable to privately funded patients, particularly those managed on a not-for-profit basis". The study referred to women undergoing ovarian stimulation for IVF or ICSI and this was reflected in the authors' conclusions.

**Implications of the study**
The authors suggested that future research should investigate the cost-effectiveness of repeated cycles if appropriate data from robust clinical trials become available.

**Source of funding**
Funded by Ferring Pharmaceuticals.

**Bibliographic details**

**PubMedID**
14607557

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Clinical Trials, Phase III as Topic; Cost Control; Cost-Benefit Analysis; Drug Costs; Female; Fertility Agents, Female /economics /isolation & purification; Fertilization in Vitro; Follicle Stimulating Hormone /economics; Health
Resources /utilization; Humans; Menotropins /economics /isolation & purification; Multicenter Studies as Topic; Pregnancy; Randomized Controlled Trials as Topic; Recombinant Proteins /economics; Sperm Injections, Intracytoplasmic; Treatment Outcome

**AccessionNumber**

22003001502

**Date bibliographic record published**

31/03/2005

**Date abstract record published**

31/03/2005