Ultrasound or ultrasound and hormonal determinations for in vitro fertilization monitoring

Murad N M

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
Using ultrasound only protocol for patients monitored for ovarian stimulation in in vitro fertilisation and embryo transfer (IVF ET). Under the ultrasound-only protocol patients were monitored, starting on day 5 of the menstrual cycle (day 3 of hyperstimulation) and then every other day; the monitoring involved counting the number of follicles which had developed, and measuring their diameter and the endometrial thickness until the dominant follicle reached its critical diameter (greater than 16 mm) and endometrial thickness was greater than 8 mm, at which point 10,000 IU of human chorionic gonadotropin (hCG) were administered.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients undergoing ovarian stimulation with human menopausal gonadotropin (hMG) and human chorionic gonadotropin (hCG) protocol. The excluded cases were as follows: (1) Severe male factor infertility (sperm count less than 10 millions/ml, motility less than 30% and normal form sperm less than 4%) due to the unavailability of the intracytoplasmic sperm insemination (ICSI) procedure; (2) Polycystic ovarian disease due to patients being hyperstimulated by a different protocol with possibility of influencing the end results; and (3) High responders to hMG injection due to being desensitised by gonadotropin-releasing hormone agonist (GnRh-a) before hyperstimulation.

Setting
Hospital. The economic study was carried out in Jordan.

Dates to which data relate
Effectiveness and resource use data corresponded to patients treated between December 1995 and June 1997. The price year was not explicitly specified.

Source of effectiveness data
The evidence for the final clinical outcomes was derived from a single study.

Link between effectiveness and cost data
Costing was undertaken on the same patient sample as that used in the effectiveness analysis. It was not explicitly reported whether the costing was performed prospectively or retrospectively.
Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 206 patients; the first 110 (mean (SD) age 32.4 (3.7) years) being monitored daily using the ultrasound only protocol (Group I), while the remaining 96 (mean (SD) age 31.6 (4.9) years) were monitored every day by a combination protocol (Group II). The total number of patients who underwent retrieval in Group I was 110, and in Group II, 87.

Study design
The study was a prospective cohort study, carried out in a single centre. The duration of the follow-up appears to have been until discharge from hospital. The loss to follow-up appears to have been 9 patients in Group II due to a premature LH surge detected by LH estimation. All patients who developed a premature LH surge or a decrease in E_2 level, with more than 30% of the level on the day after hCG administration, were removed from the study.

Analysis of effectiveness
The principle used in the analysis of effectiveness appears to have been treatment completers only. The health outcomes were pregnancy rate, taking home baby rate, and ovarian hyperstimulation syndrome (OHSS) rate. The number of mature oocytes, fertilised oocytes, and immature and post-mature oocytes were also reported. The study groups were found to be comparable in terms of mean age, duration of infertility and number of hMG ampules administered.

Effectiveness results
Group II had statistically better outcomes in terms of the number of mature oocytes (p<0.0072) and fertilised oocytes (p<0.0057), while Group I demonstrated significantly better results in terms of immature oocytes (p<0.0001) and post-mature oocytes (p<0.0015). The clinical pregnancy rate was 23.4% in Group I versus 22.9% in Group II (NS). The corresponding rates in terms of taking home baby rate were 14.8% in Group I and 14.3% in Group II (NS). OHSS developed in only two patients - one in each group.

Clinical conclusions
This study showed that daily hormonal determination can be eliminated, and the frequency of ultrasound monitoring can be reduced without affecting the clinical pregnancy rate or the taking home baby rate.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis and, since the alternative monitoring strategies were found to have equal efficacy, the economic analysis was conducted on a cost-minimisation basis.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the monitoring costs of hormonal determination, ultrasound, and patient's transportation to the IVF unit. The perspective adopted in the cost analysis was not explicitly specified. The price year was not explicitly specified.

Statistical analysis of costs
Statistical analyses were performed to compare cost components and total costs between the study groups.

Indirect Costs
Not considered.

Currency
Jordanian dinars (JD). The exchange rate was reported to be US$1 = 0.70 JD.

**Sensitivity analysis**
Not conducted.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The mean total monitoring cost was JD78 in Group I versus JD222 in Group II, (p<0.0001).

**Synthesis of costs and benefits**
Costs and benefits were not combined since the intervention (ultrasound monitoring only) was the dominant strategy (equal efficacy and lower costs).

**Authors' conclusions**
The ultrasound-only monitoring protocol proved to be cheaper, more convenient and less time consuming for both the patients and the IVF team. However, no significant difference was found regarding the clinical pregnancy rate or the taking home baby rate between the two protocols.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the choice of the comparator (the combination protocol). It was deemed to be the commonly used approach in the context in question. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The internal validity of the effectiveness results can not be guaranteed due to the non-randomised nature of the study design and the lack of power calculations to ensure adequate power for the study to detect potential differences. The effectiveness analysis appears to have been based on the principle of treatment completers only, hence introducing some potential bias into the study. The study groups were comparable with respect to age, duration of infertility and number of hMG ampules administered. The degree to which the patient sample was representative of the study population should be evaluated in the light of the exclusion of some subgroups of cases to avoid the development of OHSS. Despite the exclusion of these subgroups, two cases of severe OHSS occurred in the study; it was deemed that the development of OHSS cannot be prevented in all IVF cycles.

**Validity of estimate of measure of benefit**
The analysis of benefits was based on therapeutic equivalence of treatment alternatives. The economic analysis therefore only included costs.

**Validity of estimate of costs**
Some quantities were reported separately from the costs. Insufficient details of methods of cost estimation were given (such as the sources of cost data, the procedure of data collection regarding resource use and unit costs, the costs being based on true costs or charge data, the perspective adopted in the cost analysis, and price year). The effects of different monitoring procedures on indirect costs (productivity loss) were not addressed. It is not clear whether all important costs were included in the analysis. Statistical analyses were performed on cost data but not on resource use. The conversion rate from Jordanian currency to US dollars was reported but no mention was made of the reference year.
Other issues
Uncertainties in the data were not accounted for by sensitivity analysis. The issue of generalisability to other settings or countries was not addressed. Some comparisons were made with other studies.

Implications of the study
A significant economic benefit was obtained by using the ultrasound monitoring protocol over the combined monitoring protocol, and this is vital in a developing country such as Jordan.

Source of funding
None stated.

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