Validity of a rapid assay for antisperm antibodies in semen
Kipersztok S, Kim B D, Morris L, Drury K C, Williams R S, Rhoton-Vlasak A

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 a modified rapid immunobead-binding test (IBT) for antisperm antibodies in unwashed semen.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male partners in infertile couples at risk for the development or presence of antisperm antibodies. All the participants in this study gave written informed consent.

Setting
The study setting was a tertiary care infertility centre. The economic study was carried out in Gainesville (FL), USA.

Dates to which data relate
The dates to which the effectiveness and resource use data related were not reported. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although unclear from the paper, the costing was probably conducted prospectively on the same sample as that used in the effectiveness study.

Study sample
Power calculations were not used to determine the sample size. The sample comprised 53 men with different clinical conditions of infertility.

Study design
This was a prospective comparative study in which the sperm analyses were performed simultaneously. There were 56 semen specimens from the 53 patients. One of the authors performed the semen analysis as described by Keel (see Other Publications of Related Interest). A less than 20% motile sperm with attached immunobeads was interpreted as a negative test. Between 20 and 49% of motile sperm with attached immunobeads was interpreted as a positive test, while
a value of at least 50% was interpreted as strongly positive. The validity of the rapid assay was calculated using three values in the standard assay as 'gold' standards. More specifically, a test threshold of at least 12%, at least 30% and at least 50% antisperm antibodies attached to motile sperm. Similarly, the validity testing was calculated at each of these threshold values for the rapid test, to determine the value with the highest validity. Each standard assay was performed in conjunction with a positive and negative control. Three of the 56 semen specimens were excluded from the final analysis because the sperm motility was difficult to measure accurately using the standard test.

**Analysis of effectiveness**
The analysis of this validation study was conducted on the basis of diagnostic procedure completers only. The specimens that had a standard and a rapid test result were used to evaluate the validity of the rapid assay. The sensitivity, specificity, PPV and NPV were calculated, as described by Grimes (see Other Publications of Related Interest), for the different thresholds of the percentage of antisperm antibodies attached to motile sperm in the rapid assay. The correlation between the rapid and standard tests was assessed using the squared Pearson coefficient.

**Effectiveness results**
The prevalence of positive antisperm antibody tests in the group of patients was 16.9% (9 of 53). Positive controls had a mean antisperm antibody binding of 39%, whereas negative controls had a mean antisperm antibody binding of 4.7%.

The effectiveness results were as follows.

Group 1: for a standard test threshold of at least 20% antisperm antibody attached to motile sperm and a threshold of between at least 12% and at least 15% for the rapid assay, the sensitivity, specificity, PPV and NPV were all 100%.

Group 2: for a standard test threshold of at least 30% antisperm antibody attached to motile sperm and a threshold of between at least 12% and at least 15% for the rapid assay, the sensitivity was 100%, the specificity 93.5%, the PPV 66.7% and the NPV 100%.

Group 3: for a standard test threshold of at least 50% antisperm antibody attached to motile sperm and a threshold of at least 12% for the rapid assay, the sensitivity was 100%, the specificity 87.8%, the PPV 33.3% and the NPV 100%.

The authors provided extensive sub-group reporting of the validity tests.

The correlation results showed a positive value of r-squared in the group with antisperm antibodies (0.03), the group without antisperm antibodies (0.042) and the combined groups (0.583).

**Clinical conclusions**
The rapid test detected a greater percentage of total sperm attached to antisperm antibodies. A threshold of at least 12% bound antisperm antibodies in the rapid assay (for a standard test threshold of at least 20%) is consistent with the presence of antisperm antibodies in semen and warrants consideration for therapy. Increasing the threshold in the standard assay decreases the specificity and PPV of the rapid assay, but not the sensitivity and the NPV. In conclusion, the rapid test for antisperm antibodies has excellent validity and very good reliability in comparison with the standard IBT test.

**Measure of benefits used in the economic analysis**
No summary benefits measure was used. A cost-consequences analysis was therefore performed.

**Direct costs**
The quantities and costs were not analysed separately. The quantities measured were the total time, materials and labour for standard and rapid assays. The quantity/cost boundary was that of the laboratory. The quantities and costs were estimated from actual data, but the source and dates of these data were not reported. The price year was also not given.
Statistical analysis of costs
Statistical analysis of the costs were not performed

Indirect Costs
No indirect costs were included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were carried out.

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

Cost results
A typical standard assay, including labour and materials, cost $146. In contrast, a typical rapid assay cost $23.

Synthesis of costs and benefits
The benefits and costs were not combined. Using a threshold value of at least 12% in the rapid assay to mean clinically significant antisperm antibodies, a total of $7,592 (or 208 hours of labour) would have been saved had all 52 samples been analysed using only the rapid assay.

Authors' conclusions
This study demonstrated that a rapid test for antisperm antibodies has excellent validity and very good reliability in comparison with a standard immunobead-binding test (IBT). The test is also cost and labour efficient. A threshold of at least 12% in the rapid assay is consistent with the presence of antisperm antibodies in semen and warrants consideration for therapy.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was justified. It represented a valid and routinely conducted standard diagnostic test for antisperm antibodies in immunologic infertile patients. You should decide whether this represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a prospective comparative study, using the two alternative tests and simultaneous analyses. A single individual performed all the assays, suggesting the absence of assessor bias. The overall validity of the study is therefore likely to be high. However, the authors did not report any power calculation and, therefore, it is possible that the sample was too small to detect significant effects. The squared Pearson correlation test was used to assess agreement between the results. This appears to have been a valid method, although an interpretation of the r-squared results would have been informative to the reader. The authors highlighted the importance of clinical judgement in deciding where the diagnostic threshold of a test should be set, and that there is no unequivocal threshold of positivity in the standard IBT.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis. Thus, the analysis was categorised as a cost-consequences study.

**Validity of estimate of costs**
The analysis of the costs was carried out from the perspective of an infertility centre. The average unitary costs according to each technique were used. The source of the cost and resource consumption data was not reported in detail. The price year was not reported. No sensitivity analysis was carried out, and no statistical tests were performed on the cost data to investigate the statistical significance of the results. These factors tend to hinder the internal validity and generalisability of the cost results to other settings.

**Other issues**
The authors commented on some of the limitations of the study. For example, the sample size of different causes of infertility, the thresholds of antisperm antibody attached to motile sperm, and the interassay coefficient of variation. A single individual performed all the assays in this study.

The results were of the study were presented in full. The external validity of the study was discussed by comparing the results with those from other studies and by specifying that the results were valid for selected male partners at clinical risk for immunologic infertility cohort.

**Implications of the study**
The rapid test for antisperm antibodies has excellent validity and very good reliability in comparison with the standard IBT test. When using a rapid assay threshold of between at least 12% and at least 15% to indicate a positive result, the sensitivity, specificity, PPV and NPV are 100%. When the rapid assay is tested against higher thresholds in the standard assay, that is, decreasing the effective prevalence of the condition, the specificity and the PPV decrease. This would be translated clinically into making the wrong diagnosis of immunologic infertility in an otherwise large number of men without antisperm antibodies.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
12620434

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Autoantibodies /analysis; Costs and Cost Analysis; Humans; Immunoassay /economics /methods; Infertility, Male /immunology; Male; Microspheres; Semen /immunology; Sensitivity and Specificity; Sperm Count; Sperm Head /immunology; Sperm Motility; Sperm Tail /immunology; Spermatozoa /immunology; Time Factors

**AccessionNumber**
22003000590

**Date bibliographic record published**
30/04/2004

**Date abstract record published**
30/04/2004