Is fluorescence polarization reliable and cost efficient in a fetal lung maturity cascade

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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
Use of the TDxFLM test in a cascade system (TDxFLM test-L/S (lecithin/sphingomyelin) ratio cascade with results 70 mg/gm or greater indicating maturity) for assessment of fetal lung maturity. Effectively, the proposed cascade involved replacing the shake and foam stability index portion of the cascade with the TDxFLM test.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Pregnant women at 24 weeks' or longer gestation undergoing transabdominal amniocentesis for assessment of fetal pulmonary maturity. The exclusion criteria were amniotic fluid specimens obtained from the vagina, specimens contaminated with blood or meconium, frozen samples, patients suspected of having clinical chorioamnionitis or having a positive amniotic fluid culture.

Setting
Hospital. The economic study was carried out in California, USA.

Dates to which data relate
No dates were specified.

Source of effectiveness data
The evidence for final outcomes was based on a single study.

Link between effectiveness and cost data
The costing appears to have been undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were used to determine the sample size. Based on the assumed true rate of 1% of the positive tests having hyaline membrane disease in the population, to show a falsely mature test, a sample size of 100 infants delivered within 72 hours of the amniocentesis was required. Of a total of 161 amniotic fluid samples obtained (which resulted in 176 newborns) 46 samples had only the L/S ratio performed or did not have a TDxFLM test performed. The remaining 115 specimens were run as a maturity cascade and had a TDxFLM test performed. 108 newborns were delivered within
72 hours of the amniocentesis. The mean estimated gestational age at the time of amniocentesis was 35.9 (+/- 2.1; range: 30 - 39.4) weeks.

**Study design**
This was a prospective, single-blinded, self-control study, carried out in a single centre. The duration of the follow-up was not explicitly stated but appears to have been at least 72 hours after fetal pulmonary maturity assessment, during which the infants were born and respiratory distress syndrome (RDS) was diagnosed based on the clinical signs (tachypnea, retractions, grunting, nasal flaring, and the need for supplemental oxygen for over 24 hours to maintain adequate oxygen tension) and chest x-ray. Loss to follow-up was not reported. Uncontaminated amniotic fluid was obtained by transabdominal amniocentesis for fetal lung maturity assessment. Strict clinical and radiographic parameters were used to compare the results of the two alternative test cascades with regard to hyaline membrane disease. A pediatric radiologist, blinded to each infant's clinical course, read x-ray films from the neonates on completion of the study chest x-ray. All clinicians involved were kept blinded to the results of the TDxFLM test, and these results were not used in clinical management.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness was not explicitly specified. The clinical outcomes were sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and efficiency (as defined by combined predictive values of mature and immature test results). The percentage of cases with positive results, and the number of cases of hyaline membrane disease were among the outcomes reported. Maternal indication was the leading indication for amniocentesis.

**Effectiveness results**
The number of cases with positive shake or foam stability index was 40 (35%) and the remainder (75 cases) necessitated a L/S ratio because of negative results. The number of cases with positive TDxFLM test results was 42 (37%). The number of cases with hyaline membrane disease was 7 in 108 newborns. 87 out of 108 newborns had a mature original cascade, compared to 85 with the use of the proposed TDxFLM test-L/S ratio cascade, with one case of respiratory distress syndrome and hyaline membrane disease. For the maturity cascade, sensitivity was 86%, specificity was 84%, PPV was 27%, NPV was 99%, and efficiency was 86%. For the proposed TDxFLM test-L/S ratio cascade, the values were sensitivity 86%, specificity 83%, PPV 23%, NPV 99%, and efficiency 85%.

**Clinical conclusions**
As with many other tests, the TDxFLM test has significant false immature rates. However, because of the objective, accurate, reliable, quick, and standardised nature of the test, it lends itself to a cascade system of pulmonary maturity assessment.

**Modelling**
A decision analytic model was used to represent schematically the alternative test outcomes and to estimate the costs and effects associated with the alternative test cascades.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. Since the alternative test cascades were equivalent in terms of the main test outcomes, the economic study proceeded as a cost-minimisation analysis.

**Direct costs**
Costs were not discounted due to the short time frame of the cost analysis. Quantities were reported separately from the costs only in terms of turnaround time. Unit costs for each individual test were reported separately. The cost analysis
covered the costs of materials and turnaround time (the time allotment involved both the labour and the test run time) with the latter component not being converted into a monetary value. The perspective adopted in the cost analysis was not explicitly specified. The reference laboratory in the study institution provided information regarding the individual laboratory test. The date to which the price data referred was not explicitly specified. Laboratory technician time was not converted into a monetary value since it was conjectured that it might vary from institution to institution.

**Indirect Costs**
Not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
An analysis was performed to assess the effects of eliminating the shake test portion in a cascade system in terms of turnaround time and costs.

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

**Cost results**
The average cost per patient was $33.55 for the original maturity cascade versus $26 for the proposed TDxFLM test-L/S ratio cascade. This yields a 24% reduction in the cost of maturity testing with no delay in turnaround time (average time per patient, 3.23 versus 3.29 hours).

**Synthesis of costs and benefits**
Costs and benefits were not combined since the use of the proposed TDxFLM test-L/S ratio cascade was the (weakly) dominant strategy (equivalent efficacy associated with lower costs). The elimination of the shake test portion was associated with a 13% increase in turnaround time while the cost reduction associated with the use of TDxFLM test-L/S ratio cascade was 36%.

**Authors' conclusions**
In summary, the TDxFLM test is an objective, reliable, quick, inexpensive, and safe test for the assessment of fetal pulmonary maturity. The use of the TDxFLM test in a cascade system is cost efficient for both those institutions already providing fetal pulmonary maturity testing and for those institutions that currently are not.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the choice of the comparator (the original maturity cascade). It was the usual practice in the context in question.

**Validity of estimate of measure of effectiveness**
The effectiveness results are likely to be internally valid given the prospective nature of the study design and the power calculations performed to ensure an adequate sample size. The study sample appears to be representative of the study population.

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

**Validity of estimate of costs**
Quantities were reported separately from the costs only in terms of turnaround time. Adequate details of the methods of cost estimation were not given. Price dates were not given and it is not clear whether any relevant cost components were omitted. It is not clear whether charges or true costs were used.

**Other issues**
The authors’ conclusion appears to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. Appropriate comparisons were made with other studies. The study covered only the uncontaminated specimens and this appears to be reflected in the generalisation made in the authors’ comments.

**Implications of the study**
The authors felt that the role of the TDxFLM test in the case of contaminated specimens should be more extensively studied. The authors also felt that the cut-off value (the 50 to 70 mg/gm range) for the TDxFLM test to increase sensitivity warrants further evaluation.

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