NICE advice

AmnioSense for unexplained vaginal wetness in pregnancy

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is AmnioSense. It is used for identifying leaking amniotic fluid in pregnant women with unexplained vaginal wetness.
- The **innovative aspects** are that AmnioSense is a non-invasive test that uses a pH-dependent colour changing strip to identify amniotic fluid. The test can be used in a clinical or home environment.
- The intended **place in therapy** would be as well as standard care in pregnant women with unexplained vaginal wetness.
- The **main points from the evidence** summarised in this briefing are from 4 studies: 1 observational study and 3 repeated measures comparative studies including a total of 729 pregnant women in a clinical setting. They show that AmnioSense is as effective as standard care in identifying amniotic fluid in women with unexplained vaginal wetness.

- **Key uncertainties** around the evidence or technology are the lack of studies comparing the current version of the technology with standard care. There are also no published studies to show equivalence between the current and previous versions of the technology.
- The **cost** of AmnioSense is £1.59 per unit (exclusive of VAT). The **resource impact** would be greater than standard care. The technology may be capacity releasing because of a shift from secondary care to primary and community care but there are no published studies to support this claim.

The technology

AmnioSense (Common Sense Ltd) is a non-invasive diagnostic pad. The pad is designed to assess unexplained vaginal wetness during pregnancy. Vaginal wetness can result from leaking amniotic fluid and may indicate amniotic membrane rupture. Premature membrane rupture needs urgent medical attention.

AmnioSense attaches to underwear and can be worn for up to 12 hours. The liner has a central polymer-embedded strip which changes colour when it comes into contact with fluid of pH 6.5 or higher. A healthy vagina has a pH value of 3.5 to 4.5 but amniotic fluid and urine have pH values higher than 6.5. When in contact with urine or amniotic fluid, the central strip changes colour from yellow to blue or green. If ammonia is present above a certain level, the strip reverts to yellow within 15 minutes, distinguishing urine from amniotic fluid. When wetness is felt, the liner is removed and left to dry. If after 15 minutes the colour of the strip is blue, green or grey, the user should seek medical attention. In the presence of amniotic fluid, the colour of the liner will stay changed for up to 2 hours.

Innovations

AmnioSense is a non-invasive technology that aims to detect amniotic fluid in small volumes of vaginal wetness over a long period of time. The technology is currently the only home test for the detection of amniotic fluid. Standard care for pregnant women experiencing unexplained vaginal wetness is an invasive procedure to check that the amniotic membrane is intact.

Current care pathway

NICE's guideline on intrapartum care recommends that women experiencing unidentified vaginal wetness have a speculum examination to detect ruptured amniotic membranes in cases where the cause for vaginal wetness is unclear. Before the procedure, the woman is asked to lie down for 30 minutes to allow for pooling of amniotic fluid. A speculum is then used to examine the vagina and detect any pooling of amniotic fluid. Where pooling is present, the woman is diagnosed with ruptured membranes and her condition is managed accordingly. Where no pooling is detected, it is assumed the membranes are still intact and the woman may be discharged. The total time to complete a speculum examination, including time allowed for amniotic pooling, is up to 1 hour. Diagnosis confirmation may be sought through nitrazine (pH) testing, amniotic fluid crystallisation testing (fern testing), biomarker testing and ultrasound examination of the uterus. However, these assessments are not routine practice in the NHS.

Population, setting and intended user

AmnioSense is intended for pregnant women who have unexplained vaginal wetness. The technology is targeted towards women who are in their second or third trimester of pregnancy.

The technology is designed to be used by primary and community care clinical staff or at home by pregnant women. Instructions for use of the technology are included in the packaging.

Costs

The technology costs £1.59 per pad, excluding VAT, and is sold in boxes of 12 or 50 individually sealed pads. Women who have a positive test result using AmnioSense will need a speculum examination.

Costs of standard care

The cost of a disposable speculum is £0.89. As well as the cost of the speculum, there is also a cost associated with the procedure. The approximate cost of the procedure is £65 according to the NHS reference costs 2017/18 for specialised fetal invasive diagnostic procedures.

Resource consequences

AmnioSense has been launched in the UK. The cost of the technology is greater than standard of care. The company anticipates the technology will be resource releasing for the NHS because of fewer speculum examinations, the need for fewer higher-grade staff and a shift in care setting from secondary to primary and community. Instructions for using the technology are included in the cost, no additional training is needed.

Regulatory information

AmnioSense is CE marked as an in vitro diagnostic device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

AmnioSense is designed to be used by pregnant women; sex and pregnancy are protected characteristics under the Equality Act (2010).

Clinical and technical evidence

This technology was originally evaluated by NICE and was published as NICE medical technologies guidance 15 (MTG15). All NICE guidance is subject to review. Following the review of MTG15, the guidance was withdrawn because of changes to the technology. NICE have commissioned this briefing based on the new version of the technology.

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Four studies with a total of 729 women were included in this briefing.

This briefing includes 1 observational study and 3 repeated measures, comparative studies. Also, the results of an unpublished study are reported in the user leaflet on the company's website. The study investigated the use of the current version of AmnioSense (branded as AL-SENSE in the US) in 232 pregnant women and reported a sensitivity of 97.06% (99/102; 95% confidence interval [CI] 91.64 to 99.39) and specificity of 96.92% (126/130; 95% CI 92.31 to 99.16).

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

The studies have appropriate sample sizes and the outcome measures are relevant for evaluating the clinical efficacy of a diagnostic technology. The evidence base includes 1 UK-based study. The remaining 3 studies were done outside of the UK and results may not be generalisable to the NHS. The 3 comparative studies were done using a previous version of the technology, limiting their value. The 1 study evaluating the current technology is an observational study published as a poster abstract and does not report sensitivity and specificity figures. However, these can be calculated from the available data. Currently, there are no published equivalence studies comparing the various versions of the technology.

Table 1 Summary of selected studies

Stringer and Hornbuckle (2016)	
Study size, design and location	Poster abstract of an observational study reporting outcomes of 148 symptomatic pregnant women over 20 weeks of pregnancy after using AmnioSense as a SROM screening tool. Australia.
Intervention and comparator(s)	AmnioSense (under an alternative brand name, AL-SENSE).

Key outcomes	39 women had a positive AmnioSense test result, 36 of whom had a diagnosis confirmed within 48 hours resulting in a sensitivity of 94.7%. The remaining 109 received negative results. There were 90 women with negative results who were discharged. Of these, 6 women re-presented within 12 hours, 2 were subsequently diagnosed with SROM resulting in a specificity of 97.2%. No adverse events recorded. Compared with a retrospective group, using AmnioSense resulted in 39 minutes less in the assessment unit.
Strengths and limitations	This study has reasonable sample size and reports the number of confirmed positive diagnoses and adverse events after using AmnioSense. The study does not compare direct use of the technology with standard screening tools, and sample demographics were not reported. Sensitivity and specificity of AmnioSense were not reported. Retrospective comparisons can be confounded by uncontrolled variables. The study was done in Australia so results may not be generalisable to the UK.
Bornstein et al. (2009)	
Study size, design and location	A blinded, repeated measures study evaluating the reliability of Vision ALD in identifying leaking amniotic fluid in 339 pregnant women over 16 weeks of pregnancy. Israel and US.
Intervention and comparator(s)	Vision ALD (previous version of technology under alternative brand name, AmniScreen). Standard diagnosis including visualisation of vaginal pooling, crystallisation and nitrazine testing.
Key outcomes	Vision ALD displayed a sensitivity of 96% (154/161) and a specificity of 84% (125/148). Overall, agreement between the patient's interpretation of the Vision ALD result and the healthcare professional was 97%.

Strengths and limitations	The study was a large, multicentre, blinded study comparing the results of the Vision ALD with current standard of care diagnostic techniques. Results of the technology were interpreted by the patient and a healthcare professional who was blinded to the subject's interpretation. This design allows for generalisability for patient use. Confidence intervals have not been calculated. The study uses an earlier version of the technology and was conducted outside of the UK so results may not be generalisable. This study was supported by the company.
Mulhair et al. (2009)	
Study size, design and location	A blinded, repeated measures, prospective cohort study comparing the outcomes of Vision ALD and a speculum examination in 139 women between 18 and 42 weeks of pregnancy. UK.
Intervention and comparator(s)	Vision ALD (previous version of technology under alternative brand name, AmnioSense). Speculum examination.
Key outcomes	Vision ALD correctly identified intact membranes in 52 women and ruptured membranes in 58 women. Vision ALD resulted in 28 false positives, 7 of which were associated with a positive high vaginal swab result. There was 1 woman who had a false negative result. Vision ALD showed a sensitivity of 98% (58/59; 95% CI 91 to 100) and specificity of 65% (52/80; 95% CI 54 to 75).
Strengths and limitations	This study is a well-designed comparator study. The outcomes measures of prevalence, sensitivity and specificity are relevant to the evaluation of the technology. The study was appropriately powered and was done in the UK. There was a higher percentage of Caucasian subjects in the cohort compared with the population and subgroups were insufficiently powered for analyses. The study was done in a clinical setting and is not generalisable to home use. This study was done using an earlier version of the technology.
Bornstein et al. (2006)	

Study size, design and location	103 women attending a labour and delivery ward were categorised into 3 groups: positive control, negative control and study group. The diagnostic efficacy of Vision ALD was tested in each group and compared with standard care diagnostic procedures. Israel.
Intervention and comparator(s)	Vision ALD (previous version of technology under alternative brand name, AL-SENSE). Standard diagnosis including visualisation of vaginal pooling, crystallisation and nitrazine testing.
Key outcomes	In the study group (n=34), Vision ALD had a sensitivity of 100% (10/10; 95% CI 69.15 to 100) and a specificity of 75% (18/24; 95% CI 65.47 to 93.24) in detecting PROM. In the positive control group (n=42), all women correctly had a positive result using the technology. In the negative control group (n=27), Vision ALD correctly identified 23 of 25 negative cases, 2 women of the 27 had ruptured membranes. The overall agreement between the Vision ALD test result and the clinical diagnosis was 82.35%.
Strengths and limitations	The study compares use of the Vision ALD liner with relevant clinical diagnosis. Appropriate outcome measures were reported. The technology was tested across a range of clinical presentations. The study was done with an earlier version of the technology and was done in Israel so results may not be generalisable to the UK. The study was partially supported by a grant from the company.
Abbreviations: CI, confidence interval; PROM, premature rupture of membranes; SROM, spontaneous rupture of membranes; Vision ALD, vision amniotic lead detector.	

Recent and ongoing studies

- Pivotal study of the Rx AL-SENSE liner for amniotic fluid leakage screening (PRALS) in the second and third trimesters of pregnancy. ClinicalTrials.gov identifier: NCT02959268. Status: complete. Indication: pregnant women. Devices: AL-SENSE, Common Sense Ltd (marketed as AmnioSense in the UK). Completed October 2017. Location: US.

- Proof of AmnioSense Blue in home usage and as a hospital standard of care for amniotic fluid leak detection. ClinicalTrials.gov identifier: NCT03177135. Status: not yet recruiting. Indication: pregnant women with unexplained vaginal wetness. Devices: AmnioSense, Common Sense Ltd. Estimated completion in January 2018. Location: None stated.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Four specialists were involved in the production of this briefing. Three specialists are familiar with the product, 1 of which has used the technology. One specialist is unfamiliar with the technology.

Level of innovation

Three specialists consider the concept to be novel and convenient for patients, 1 of whom states there are currently no tests for use outside of a secondary care setting. Two specialists commented that some trusts use diagnostic biomarker tests following an inconclusive speculum examination. One welcomes the technology for the use of excluding ruptured membranes and reducing hospital referrals.

Potential patient impact

Two specialists believe the technology would be beneficial to all women with vaginal wetness, another believes the technology would benefit all women in their third trimester. Three commented that the technology would give women confidence and reassurance. Three specialists believe the technology would result in fewer unnecessary journeys to hospitals for intimate procedures. Two consider the technology to be particularly useful for women at risk of preterm labour.

Potential system impact

Three specialists think the technology would result in a decrease in unnecessary speculum

examinations and fewer referrals to secondary care. Two believe the technology will likely result in an increase in staff capacity resulting in cost savings, 1 commented that bed availability will be increased and the other believes the technology will be time saving. One thinks false positives could result in increased stress for women as well as cost increases because of further investigations and increased consultant time. One feels unable to speculate about the cost-saving potential without figures detailing the number of cases of unnecessary speculum examinations.

General comments

One specialist feels further evidence is needed to confirm the most recent version of the technology is as reliable as the versions used in the evidence base. One specialist raises concerns that the sensitivity and specificity is less than 100% and feels the technology should be used with the assistance of midwives and further investigations to be completed if symptoms continue. One raises concerns about the effect of tap water on the test result. The user instructions say tap water can interfere with test results and a retest should be done if wetness is related to recent bathing. One specialist supports the technology provided women have robust training in using the product.

Patient organisation comments

A representative from Little Heartbeats believes that current tests for preterm premature rupture of membranes (PPROM) are unreliable and result in misdiagnoses. The representative commented that current tests rely on women who are actively leaking amniotic fluid during their antenatal day clinic visit and feel that a reliable home test would be more beneficial. Subgroups that Little Heartbeats consider would benefit from the technology include:

- women leaking amniotic fluid inconsistently or very quickly
- women whose concerns are not fully investigated
- women with PPROM before or soon after 24 weeks of pregnancy.

Little Heartbeats does not recognise any potential disadvantages that might arise from using the technology. They consider that more education about PPROM is necessary and could potentially act as a barrier to the introduction of this technology.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Jenny Carter, senior research midwife, department of women and children's health, King's College London. Co-authored the Mulhair et al. (2009) publication.
- Professor Lesley Page, visiting professor, Florence Nightingale School of Nursing and Midwifery, King's College London; and honorary research fellow, Oxford Brookes University. Advised on the Mulhair et al. (2009) publication.
- Christine Harding, consultant midwife, Royal Berkshire NHS Foundation Trust. NICE multiple obstetric and guidelines committee member.
- Lisa Smith, consultant midwife, Princess Anne Hospital. NICE multiple obstetric and guidelines committee member.

Representatives from the following patient organisations contributed to this briefing:

- Little Heartbeats.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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