AmnioTect™ – Detecting PROM Using a Specially Designed Panty Liner

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Abstract

Objective: To determine the performance characteristics of AmnioTect™ to detect premature rupture of membranes (PROM) by distinguishing amniotic fluid from urine, among pregnant women experiencing leaking or perineal moisture.

Study Design: Prospective multicenter observational study comparing self-assessment with blinded investigator assessment using AmnioTect™ in women presenting for PROM evaluation between December 2016 to October 2017. Eligible women were asked to wear and interpret the AmnioTect™ according to instructions for use. The same pad was independently evaluated by a blinded health care provider (HCP) and both the patient and HCP assessments were compared to standard clinical PROM evaluation by sterile speculum exam. The presence of amniotic fluid and the diagnosis of PROM was established when pooling was observed along with either positive nitrazine and/or positive ferning test. The primary outcome was to compare patient use of AmnioTect™ to clinical diagnosis and secondarily to compare patient to HCP interpretation.

Results: A total of 244 women were recruited, but only 240 were analyzed with complete results. The mean age was 27.7 years (SD: 5.46), with a range 18.2 - 40.9. The mean gestational age at enrollment was 36.7 weeks, with a range of 18.9 - 41.4 weeks. Only 3 patients were < 24 weeks and 16 (6.6%) patients were <28 weeks. The cohort was racially and educationally diverse. Only 36% of the cohort had ≥ high school education and 58% had either completed or had some high school education. The prevalence of confirmed PROM was 45% (108/240). The patient interpreted AmnioTect™ as positive in 103/108 yielding a sensitivity of 95.4% and a specificity of 96.2% (127/132). The overall concordance between the HCP reading the AmnioTect™ result and that of the patient was 99.16% (238/240). The PPV: 95.4% (103/108) and the NPV: 96.2 (127/132).

Conclusions: The performance characteristics of AmnioTect™ compare favorably when interpreted by a patient or a HCP. AmnioTect™ serves as a good screening for the outpatient detection of PROM.

The Innovation: New polymer – indicator

A new amniotic leak test liner (AmnioTect™) for detection of amniotic fluid leaks.

It contains a novel nitrazine yellow (phenolate) ion polymer with pH cut-off of ≥ 6.5, which reduces false indication due to bacterial Vaginosis (BV) and Trichomoniasis. A combination of the chemical formulation and panty liner composition reduces interference from urine and therefore increase specificity.

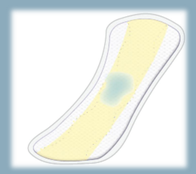
Positive result: present a gray, blue or green stain over a yellow contrast, when vaginal fluid pH ≥ 6.5.

Development of new diagnostic applications

AmnioTect™ test results :

No color change is a negative result

Blue, Green or Gray color change is a positive result.



Introduction

- The etiology of premature rupture of membranes (PROM) is not well understood, but is generally felt to be associated with inflammation and infection particularly when PROM occurs at a premature gestational age. Term prelabor rupture of membranes occurs in ~8% of pregnancies and is defined as rupture of the membranes after 37 weeks gestation, but prior to the onset of labor. Preterm premature rupture of membranes (PPROM) is responsible for > 30% of spontaneous preterm birth [1].
- Making an accurate and timely diagnosis of PROM is critical whether at term or preterm, to reduce perinatal morbidity and mortality [1, 2].
- When PROM is suspected, conventional diagnostic methods require a visit to a medical facility and exam by a healthcare professional (HCP). Standard of care requires a sterile speculum examination (SSE) to assess for pooling, amniotic fluid passage through the cervix, microscopic fern test, and pH test [3, 4]. Several point of care immunoassay tests are commercially available and are most often used as confirmatory tests when clinical results are conflicting. These immunoassays have high specificity but cases of false-negative results have been reported.
- A significant number of women experience leaking or increased perineal moisture and are uncertain of whether PROM has occurred. This can lead to a delay in seeking evaluation because of the time, effort and expense to obtain it. There is currently no home point of care test to assess PROM as there is for detection of pregnancy.

Study Design

Pregnant women were eligible to participate in the study, if they meting inclusion criteria and lacking exclusion criteria.

Inclusion criteria:
- Subjects being evaluated for leaking or feeling increased vaginal moisture.
- >18 years old.
- >16 weeks - estimated gestational age.
- Signed IRB approved informed consent form.
- Receiving medical care at investigational site for pregnancy.
- Able to read and write English or Spanish at a 6th grade level.
- Ability to distinguish blue and green colors from yellow or red.

Exclusion criteria:
- Subject is unable or unwilling to cooperate with study procedures.
- Subjects who have used the AmnioTect™ before joining the study.
- H/O frequent vaginal bleeding in the last 7 days.
- H/O vaginal intercourse within the last 12 hours.
- Subject is wet after sweating, showering etc. (must dry vaginal area).
- Diagnosis or symptoms consistent with Bacterial Vaginosis or Trichomoniasis infection within the last 3 days.
- Use of any vaginal product(s) such as lubricants in the past 12 hours.
- Any antibiotic treatment which could reduce vaginal lactobacillus in the past 7 days.

Methods

- Subjects presenting with complaints of leaking and meeting study criteria were recruited to participate.
- After signing an institutionally approved consent form they were asked to place an AmnioTect™ liner for up to 12 hours or until wetness was felt.
- After wetness was felt, the subjects was advised to remove the liner and wait 15 minutes before interpreting any color change and record their interpretation.
- A blinded HCP next evaluated the complaints of leaking employing the standard diagnostic protocol used to determine PROM. A SSE was performed to assess for vaginal pooling, ferning, and pH test with pH paper. Many patients were further evaluated with an immunoassay in situations where there was conflicting clinical results. The clinical HCP was blinded to the AmnioTect™ liner results.
- A research HCP blinded to the subject's AmnioTect™ liner interpretation, made their own assessment of color change in the liner.
- The results of the standard clinical diagnosis were compared with the subject's and the research HCP's independent interpretation of the AmnioTect™ test liner results. These comparisons were used to calculate the sensitivity, specificity, PPV and NPV of the amniotic leak test liner (n=240).
- Subjects interpretation of the AmnioTect™ were compared to the research HCP interpretation.

Results

Study population: A total of 244 women were recruited, but only 240 were analyzed with complete results. Four women were excluded for the following reasons: three had liners that were contaminated with blood compromising the integrity of the clinical diagnosis and the interpretation of the amniotic leak test liner results (subject and clinician). The fourth patient unintentionally threw out the amniotic leak test liner before reading the results. The mean age was 27.7 years (SD: 5.46), with a range 18.2 - 40.9. The mean gestational age at enrollment was 36.7 weeks, with a range of 18.9 - 41.4 weeks.
The prevalence of confirmed PROM, using standard clinical diagnosis, was 45% (108/240).

AmnioTect™ Subject Results Reading Vs. Standard Clinical Diagnosis

AmnioTect™ Subject Result	Final Clinical Diagnosis		
	Positive	Negative	Total
Positive	103 True Positive	5 False Positive	108
Negative	5 False Negative	127 True Negative	132
Total	108	132	240
Sensitivity = 95.4%		Specificity =96.2%	
PPV = 95.4%		NPV = 96.2%	

The patient interpreted AmnioTect™ as positive in 103/108 yielding a sensitivity of 95.4% and a specificity of 96.2% (127/132). The positive predictive value was 95.4% (103/108), and the negative predictive value was 96.2% (127/132).

AmnioTect™ HCP Results Reading Vs. Standard Clinical Diagnosis

AmnioTect™ HCP Result	Final Clinical Diagnosis		
	Positive	Negative	Total
Positive	104 True Positive	4 False Positive	108
Negative	4 False Negative	128 True Negative	132
Total	108	132	240
Sensitivity = 96.3%		Specificity =97.0%	
PPV = 96.3%		NPV = 97.0%	

The HCP interpreted AmnioTect™ as positive in 104/108 yielding a sensitivity of 96.3% and a specificity of 97% (128/132). The positive predictive value was 96.3% (104/108), and the negative predictive value was 97% (128/132).

Comparison between Patients and Clinicians Results Reading

AmnioTect™ Subject Result	AmnioTect™ Clinician Result Reading		
	Positive	Negative	Total
Positive	107	1	108
Negative	1	131	132
Total	108	132	240

The overall agreement between the HCP reading and the patient reading is 99.16% (138/240).

Conclusions

- The performance characteristics of AmnioTect™ compare favorably with standard clinical diagnostic testing yielding high sensitivity, specificity, PPV, and NPV.
- There is a high correlation between the patient and HCP interpretation of the AmnioTect™ results.
- These results suggest that AmnioTect™ may serve as a good screening test for outpatient detection of PROM.

References

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