Fetal fibronectin test for detecting preterm birth (GL841)

Approval

<table>
<thead>
<tr>
<th>Approval Group</th>
<th>Job Title, Chair of Committee</th>
<th>Date</th>
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<tbody>
<tr>
<td>Maternity &amp; Children’s Services Clinical Governance Committee</td>
<td>Chair, Maternity Clinical Governance Committee</td>
<td>5th June 2015</td>
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Change History

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Author, job title</th>
<th>Reason</th>
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<tbody>
<tr>
<td>1.0</td>
<td>July 2012</td>
<td>M Selinger (Consultant in fetomaternal medicine), B Jadoon, S Kausar (Specialist Registrars)</td>
<td>Trust requirement</td>
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<tr>
<td>1.1</td>
<td>Sept 2014</td>
<td>M Selinger (Consultant in fetomaternal medicine), S Kausar (Specialist Registrar)</td>
<td>Reviewed – no changes</td>
</tr>
<tr>
<td>1.2</td>
<td>May 2015</td>
<td>S Kausar (Specialist Registrar)</td>
<td>Minor change to pg</td>
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Supporting document

Why is preterm labour (PTL) important?

Preterm birth is defined as birth between 24-36 weeks, with incidence of 5%-8% in most developed and developing countries. It can be spontaneous, and follow preterm labor (50%), or preterm premature rupture of membranes (30%); or be iatrogenic.

75% of perinatal mortality occurs in preterm babies, with 60% of them are born before 32 weeks. Morbidity includes respiratory distress syndrome (RDS), bronchopulmonary dysplasia, intraventricular haemorrhage (IVH), necrotizing entero-colitis, sepsis, retinopathy, etc.

What is the risk of preterm birth (PTB) in patient presenting with signs and symptoms of PTL?

Women presenting with the signs and symptoms of PTL continue to be a clinical challenge. 90% will not deliver within 7 days and almost 70% deliver by term. Standard method of assessment of the risk for PTB in women with threatened PTL includes uterine contraction and cervical examination. Both have poor predictive value.

The early signs and symptoms are not followed in all cases, by PTB and as few as 1 in 20 PTL cases result in PTB within the next 14 days. As early signs and symptoms are non-specific and can occur in term pregnancies, false positive diagnoses on strictly clinical criteria run as high as 50% and true PTL may be missed in 15% to 20% of cases.

Initial cervical dilation of $\geq 3$ cm and at least 80% cervical effacement are strongly associated with PTB within 24 hours to 7 days. These women are assigned a diagnosis of PTL and aggressively treated to delay delivery, if possible, or prepared for delivery. Often women present with contractions without cervical change, making the diagnosis more challenging. When the cervix is dilated $< 3$ cm, the diagnosis of true PTL resulting in imminent PTB is more difficult to establish.

However, a clinical diagnosis is often unreliable and results in over-diagnosis of PTL.
What is fetal fibronectin?
Fetal fibronectin is an extracellular matrix glycoprotein, localized between chorion and decidua. It is present throughout gestation in all pregnancies.

DEFINITION:
It is a diagnostic test for detecting potential preterm labour. For women with the signs and symptoms of preterm labour without advanced cervical dilatation, a negative FFN result indicates that 96.7% of the patients will not deliver within 7 days and a positive test indicates that 12.7% might deliver within next 7 days.

Fetal fibronectin is a glycoprotein produced by fetal amnion. It is found in high concentration in amniotic fluid and throughout the membrane structure. In normal pregnancy FFN levels are high during the first 16-22 wks of gestation, then fall to a very low levels and rise again as the pregnancy approaches term. Its presence between 24-34 wks has been associated with the preterm birth within 7 days from testing.

In normal pregnancies, FFN levels are high (100 μg/ml) during the first 16 to 22 weeks of gestation, and then they fall to very low levels, and rise again (30 μg/ml) as the pregnancy approaches term. However, FFN is not normally detectable (at high levels) in cervico-vaginal secretions between the 22nd and 37th week of gestation, and in particular before the 35th week of gestation. The presence of FFN at high levels during this period may indicate disruption of the uteroplacental interface.

Concentration of fetal fibronectin protein found in blood is 1/5 that found in amniotic fluid; it is not present in urine. Hence, there is no risk of misinterpretation if contaminated with urine. Best to avoid this test if there is presence of blood.

The fetal fibronectin test is one of the best predictors to assess risk of preterm labor and preterm birth, by measuring amount of fetal fibronectin in cervico-vaginal secretions.

What is fetal fibronectin test?
The rapid version of the test is a lateral-flow, solid-phase immunosorbent assay device designed to qualitatively detect FFN in cervicovaginal specimens collected with the Adeza Biomedical Specimen Collection Kit. This test aids the assessment of PTB risk within 14 days from the time of collection in women between 24 and 35 weeks of gestation with symptoms of PTL, intact amniotic membranes, and minimal cervical dilation (<3cm).
How good is this test?
The overall sensitivity and specificity are 56% and 84% for preterm before 37 weeks. Its positive predictive value varies from about 9% to 46% (Leitich 1999). Positive predictive value for delivery within 1 week is 12.5% and before 37wks is 62.5%. Where as negative predictive is 96.7% and 81.3%, respectively.

When should we not do this test?
Delivery typically occurs imminently when the cervix is dilated more than 3 centimeters or if the amniotic membranes are ruptured. Additional diagnostic testing is usually not necessary to confirm risk for women with advanced cervical dilatation or rupture of amniotic membranes. Moderate or gross vaginal bleeding is an independent risk factor for preterm delivery and may be associated with other severe obstetrical or medical problems.

Clinical attention should be focused on identification of the origin of bleeding rather than immediate assessment of delivery risk. At this time, information is insufficient regarding the association of vaginal fetal fibronectin expression to delivery for women with cervical cerclage.

The Rapid fFN test should not be used for “symptomatic women” with one or more of the following conditions:

• advanced cervical dilatation (≥ 3 centimeters)
• rupture of amniotic membranes
• cervical cerclage
• moderate or gross vaginal bleeding

The Rapid fFN test should not be used for “asymptomatic women” with one or more of the following conditions:

• multiple gestations, e.g., twins
• cervical cerclage
• placenta previa (partial or complete)
• sexual intercourse in the preceding 24 hours
References

1) Berghella V, Hayes E, Visintine J, Baxter JK. Fetal fibronectin testing for reducing the risk of preterm birth (Review) Published in The Cochrane Library 2008, Issue 4


FETAL FIBRONECTIN TEST FOR DETECTING PRETERM LABOUR

Scope: Maternity Unit
Scope: Midwives and doctors

OBJECTIVES:

• To identify women at risk of pre-term labour (PTL).

Patient selection

• Gestation; 24-34 weeks
• History –
  o symptoms suggestive of PTL; tightening, contracting, cramping, pressure and lower backache
  o no PV bleeding
  o no VE in previous 24 hours
  o no sexual intercourse within previous 24 hours
• Examination -
  o Cx <3cms dilated
  o Intact membranes

Contraindications

• Congenital abnormality in fetus
• Cervical cerclage
Test technique

Equipment
Rapid Fetal fibronectin 10Q System
Sterile speculum

Technique

- Sterile speculum examination **without lubricant**. Avoid touching cervix with speculum.
- Use sterile swab to absorb cervico-vaginal secretions from posterior fornix for 10 seconds.
- Immers swab tip in buffer. Agitate the swab in the buffer solution and remove.
- Select ‘TEST’ Patient (1) on Main menu, enter user ID (First four letters of surname and initial letter of first name), Rapid FfN 10Q Cassette Lot and press Enter when prompted. Enter patient ID (their Hospital no) and press Enter. Insert the Rapid Ffn10Q Cassette and press Enter
- Use insulin syringe to transfer 0.2 ml of buffer solution to well of Rapid 10Q Cassette and press ‘Enter’
- After 10 minutes machine will print **positive** or **negative** result plus other information
Management

- **If the fibronectin test is negative and cervical dilatation is <3cms dilated**
  - Reassure the patient
  - Discharge back into community
  - Don’t give routine prophylactic steroids
  - Exclude other causes for irritable uterus like UTI

- **Patients that might require hospital admission despite negative test**
  - High risk patients e.g. previous preterm labour or multiple pregnancy for steroids
  - If cervix is more than 3cms dilated

- **If the fibronectin test is positive**
  - Admit
  - Inform Buscot
  - Steroids
  - Transfer out if <27 weeks after discussion with NN paediatricians
Clinical presentation

Speculum examination

PPROM OR Cervix >2cm dilated

Admit to hosp Steroids Tocolysis

Cervix < 2cm dilated and no SROM

Perform fetal fibronectin test

Positive test result- Admit to hosp Steroids

Negative test result

Discharge, and to come if contraction are stronger.