

# Comparison of cervical assessment, fetal fibronectin and fetal breathing in the diagnosis of preterm labour

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*Summary:* The management of threatened preterm labour is hampered by an inability to differentiate accurately true from false labour at an early stage. We compared the performance of vaginal assessment, fetal breathing movements and the detection of fetal fibronectin (Ffn) in the prediction of true preterm labour among 25 singleton pregnancies admitted with regular uterine activity, cervical dilatation < 4 cms and intact membranes at 25 to 35 weeks of gestation. A Bishop score of < 2 or a negative Ffn test was highly predictive (100%) of false preterm labour whereas fetal breathing movement detection was less reliable. The positive predictive value of cervical assessment alone was considerably improved with the addition of Ffn testing. The introduction of Ffn testing of cervico-vaginal secretions could result in a more rational use of tocolysis.

*Key words:* Fetal breathing; Fetal fibronectin; Preterm labour.

## INTRODUCTION

Preterm labour and delivery remains the single most important cause of perinatal morbidity and mortality despite advances in peri-natal and neonatal care. Whereas a significant proportion of preterm births are the result of identifiable obstetric complications such as hypertension and placental abruption, so-called 'idiopathic' preterm labour and delivery remains a common obstetric problem. The

current management of preterm labour centres around tocolysis with beta-agonists or indomethacin and the administration of corticosteroids, all of which may have adverse maternal and fetal effects. However, only a small proportion of cases presenting with preterm uterine activity will establish and proceed to preterm delivery. Differentiating between those in true and false preterm labour would allow for a more rational use of tocolytic agents with a reduction in iatrogenic morbidity.

Cervical assessment forms the cornerstone of diagnosing progressive labour and early changes in cervical effacement and consistency may be of value in predicting true preterm labour. Absence of fetal breathing movements (FBM) has also been demonstrated to precede preterm labour and has been proposed as a test to differentiate true from false preterm labour (<sup>1</sup>). More recently, detecting fetal

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fibronectin (Ffn) in cervico-vaginal secretions has also shown promise in differentiating true from false preterm labour<sup>(2)</sup>.

This study was designed to evaluate the relative merits of cervical scoring, FBM and Ffn testing in the diagnosis of true and false preterm labour amongst women presenting with preterm uterine activity.

## MATERIALS AND METHODS

During a six month period in 1994, women attending our delivery unit at Ninewells Hospital, Dundee with a singleton pregnancy at 25 to 35 weeks' gestation (determined by routine 18 week ultrasound) with regular uterine activity of  $> 5$  contractions per hour were included in the study. Exclusion criteria were ruptured membranes, vaginal bleeding, clinical chorio-amnionitis, maternal diabetes mellitus, history suggestive of cervical incompetence or cervical dilatation  $> 4$  cms. There were 25 such cases who underwent vaginal examination, Ffn testing and FBM testing by one of us (IPS). A modified Bishop score was recorded<sup>(3)</sup> and reported to the attending staff. Ffn testing employed a commercially available kit requiring a sample of posterior vaginal fornix secretions obtained by swabbing (Membrane Assay Kit, Adeza Biomedical, Sunnyvale, Calif.). FBM were considered absent if a period of  $< 30$  seconds of sustained breathing was seen during 30 minutes of continuous scanning with portable real-time ultrasound (Hitachi EUB 405). Ffn and FBM testing is not routine practice in our department and the results were not revealed to the attending staff. Patient management was according to the established practice of administering intravenous ritodrine and intra-muscular corticosteroids to the mother when considered appropriate.

## RESULTS

Twenty five cases fulfilled the entry criteria during the study period when one of us (IPS) was available. The mean maternal age was 25 years (range 16 to 40) and 12 cases (48%) were primigravidae. The mean gestational age at presentation was  $31 \pm 4$  weeks (range  $25 \pm 4$  to  $34 \pm 4$ ). The mean number of contractions per hour at presentation was 13. Seven cases (28%) received ritodrine, eight (32%)

received prophylactic antibiotic therapy and 19 (76%) received corticosteroids. Caesarean section was performed in six cases (24%) and there were no perinatal deaths. Five cases delivered at less than 37 completed weeks of gestation of which three cases delivered within one week of admission. There were no significant differences in maternal age, gestational age and frequency of uterine activity between the cases delivering  $< 1$  week and  $> 1$  week from presentation. All three cases delivering  $< 1$  week received tocolysis and corticosteroids with two receiving prophylactic antibiotics.

The test performances of a Bishop score of  $> 2$  at initial cervical assessment, positive Ffn test and absence of FBM for delivery within one week of admission are presented in Table 1. As a single test, cervical assessment to Ffn reliably identifies all cases of false preterm labour with no false negative results. This is clearly important since the majority of cases were not in true labour. The positive predictive value of cervical assessment could not be improved by changing the threshold of the Bishop score adopted but can be considerably improved with the addition of Ffn testing. In this way, the number of false positive results is reduced from the six obtained with cervical assessment alone to only one when Ffn testing is added.

Table 1. - *Test performance of cervical assessment, Fetal Breathing Movements (FBM) and Fetal fibronectin (Ffn) in identifying pregnancies delivering within one week of admission.*

	Sens. (%)	Spec. (%)	+pred. (%)	-pred. (%)
Cervical assessment (Bishop score $> 2$ )	100	73	33	100
Absent FBM	33	86	25	90
Ffn positive	100	86	50	100
Bishop score $> 2$ and Ffn positive	100	95	75	100

## DISCUSSION

The primary prevention of preterm labour through education, increased antenatal care and alterations in work practises has largely been unsuccessful to date (<sup>4</sup>). Secondary prevention entails the prevention of preterm delivery when signs of preterm labour appear and it is clearly desirable to be able to differentiate between true and false preterm labour at an early stage for a number of reasons. Current tocolytic practice can result in adverse maternal effects with beta-agonists (<sup>5</sup>) and fetal effects such as premature closure of the ductus arteriosus and impaired renal function are described following antenatal indomethacin (<sup>6, 7</sup>). Antenatal corticosteroids reduce the incidence of hyaline membrane disease (<sup>8</sup>) and are not associated with subsequent adverse effects in infancy (<sup>9</sup>) but may result in maternal hyperglycaemia and even pulmonary oedema when used in combination with beta-mimetic agents (<sup>5</sup>).

Cervical assessment is central to diagnosing progressive labour and is incorporated into scoring systems aimed at predicting preterm delivery (<sup>10</sup>). The assessment of subtle, early cervical changes is prone to intra and inter-observer variation which will limit its value as a test in the routine clinical situation. An objective assessment of cervical change can be obtained with the cervicotonometer and there is an increased risk of preterm delivery among women experiencing preterm uterine activity if cervical maturation assessed in this way is advanced (<sup>11</sup>). Unfortunately, the positive predictive value of the cervicotonometer measurements was poor and it is unclear as to whether this technique would be widely applicable or acceptable.

Fetal breathing movements detected by ultrasound are absent prior to preterm la-

bour and delivery and their absence has been proposed as a predictor of true preterm labour (<sup>1, 12</sup>).

The presumed mechanism is that increased levels of circulating prostaglandin associated with labour inhibit fetal respiration, a phenomenon demonstrated in fetal lambs (<sup>13</sup>). In our series, FBM performed relatively poorly with false positive and false negative results. Together with the time, effort and equipment required to establish the presence or absence of FBM with confidence, we feel that FBM testing alone cannot be considered sufficiently accurate to base management decisions on.

Fetal fibronectin is a protein found in amniotic fluid, placental tissue and the extracellular substance of the decidua basalis next to the placental intervillous space (<sup>2</sup>). The virtual disappearance of fetal fibronectin from the vaginal secretions by 22 weeks gestation coincides with fusion of the chorion and decidua capsularis with the decidua parietalis of the uterine wall. The reappearance of fibronectin before labour may represent the separation of the chorion from the decidua prior to the onset of labour (<sup>14</sup>). Furthermore, Ffn production by human chorion cells *in vitro* is stimulated by inflammatory mediators and products which in themselves may be responsible for a proportion of preterm deliveries (<sup>15</sup>). Whatever mechanism is in operation, in 117 women presenting with preterm uterine activity and intact membranes, Lockweed *et al.* (<sup>2</sup>) found that the presence of fetal fibronectin in the cervico-vaginal secretions was a good indicator of those who subsequently went on to deliver prematurely and a negative result was highly predictive of the pregnancy continuing until term. Morrison *et al.* (<sup>16</sup>), investigating eventual delivery following an episode of preterm uterine activity (false labour) considered a negative Ffn result to be re-

assuring with only one of 14 cases delivering preterm. Our study confirms the usefulness of Ffn testing in the prediction of preterm delivery, either as an initial test applied to all cases or to improve the positive predictive value of cervical assessment.

## CONCLUSION

To our knowledge, this is the first study to compare directly cervical assessment, FBM and Ffn testing in the prediction of true and false preterm labour and delivery. We deliberately adopted criteria which excluded cases with contra-indications to tocolytic therapy and a gestational age range where tocolytic and corticosteroid therapy would normally be considered. From our study, it is not possible to determine whether tocolysis influenced the admission to delivery interval and therefore the test characteristics. It does seem unlikely however, since intra-venous ritodrine results in a 24 to 48 hour delay in delivery only<sup>(17)</sup>.

Care is necessary in interpreting the positive predictive value of the tests since only three of the twenty five cases delivered within one week of admission, a proportion similar to another study of similar cases<sup>(12)</sup> and which serves to highlight the difficulty in diagnosing true preterm labour at an early stage. However, a negative Ffn test or Bishop score < 2 is very highly predictive of false labour among these cases. If these findings are confirmed by larger studies then a more rational approach to the prescription of tocolytic agents and corticosteroids can be adopted with an anticipated reduction in maternal and fetal morbidity.

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