Diagnostic Accuracy of Quantitative Fetal Fibronectin Versus Rapid phIGFBP-1 Assay: A Non Inferiority Study

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Introduction

Prematurity is a major cause of perinatal morbidity and mortality. Although some women will present with episodes of uterine contractions before term, only a minority of these women will subsequently go on to deliver a preterm infant. It is difficult to predict which of these women are at highest risk of preterm birth, and would therefore be most likely to benefit from expensive and invasive interventions (corticosteroids, magnesium sulfate, admission and/or transfer to a tertiary unit). The bedside tests available in Australia for prediction of preterm birth include the qualitative fetal fibronectin (fFN), quantitative fFN and Actim Partus (AP). Previous studies have compared the AP with the qualitative fFN test, which uses a cut-off value of 50ng/ml to give either a positive or negative result. These tests have similar high negative predictive values (NPV), with variable positive predictive values (PPV) of 30-40%. [1, 2] The newer quantitative fFN test gives a numerical reading of the level of fetal fibronectin in the sample, allowing the clinician to stratify the risk of preterm birth based on the numerical value. It is thought that the newer quantitative fFN may confer benefits in improved PPV compared to AP, but studies directly comparing the quantitative fFN and AP are lacking. This study aims to compare two point of care tests in their ability to accurately predict preterm birth in women presenting with contractions before term.

Methods

This prospective observational study was undertaken in a major metropolitan hospital in Melbourne, Australia. Consenting women with a singleton pregnancy and gestational age of 24+0 to 34+6 weeks, who presented with symptoms of preterm labour, had both quantitative fFN and AP swabs collected and results recorded. The primary outcomes were gestation at birth (<30 weeks, <34 weeks and <37 weeks) and time to delivery from presentation (<48hrs, <7 days, <14 days.) We compared the accuracy of each test in predicting these outcomes. Exclusion criteria were ruptured membranes, established labour (>3cm dilated), any medical indication for delivery (eg. chorioamnionitis), any contraindication to vaginal birth, and fetal anomalies. A sample size of 98 participants was required to identify a minimum detectable difference of 10% between the NPV of the quantitative fFN and AP.

The primary hypothesis was that there are no differences in the test characteristics (positive predictive value and negative predictive value) between the quantitative fFN test and the AP test.

Results

108 patients were recruited and 6 lost to follow up, resulting in 102 patients included in the analysis. Eighteen women delivered preterm (preterm birth rate 17.6%), with no deliveries prior to 30 weeks gestation. The actual agreement between the qfFN and AP was 82.4% for fFN >50, and 85.3% for qfFN >200 (Cohen's kappa 0.213 and 0.228 respectively) – agreement between the two tests was therefore low.

Outcome	Test	PPV (95% CI)	NPV (95% CI)
Delivery <48hrs	AP	0.00 (0.00, 20.59)	95.35 (88.52, 98.72)
	fFN >50	10.00 (0.25, 44.50)	96.74 (90.77, 99.32)
	fFN >200	0.00 (0.00, 52.18)	95.88 (89.78, 98.87)
Delivery <7days	AP	6.25 (0.16, 30.23)	95.35 (88.52, 98.72)
	fFN >50	20.00 (2.52, 55.61)	96.74 (90.77, 99.32)
	fFN >200	20.00 (0.51, 71.64)	95.88 (89.78, 98.87)
Delivery <14days	AP	12.50 (1.55, 38.35)	93.02 (85.43, 97.40)
	fFN >50	30.00 (6.67, 65.25)	94.57 (87.77, 98.21)
	fFN >200	40.00 (5.27, 85.34)	93.81 (87.02, 97.70)
Delivery <34/40	AP	12.50 (1.55, 38.35)	96.00 (88.75, 99.17)
	fFN >50	25.00 (3.19, 65.09)	96.39 (89.80, 99.25)
	fFN >200	50.00 (6.76, 93.24)	96.55 (90.25, 99.28)
Delivery <37/40	AP	12.50 (1.55, 38.35)	81.40 (71.55, 88.98)
	fFN >50	30.00 (6.67, 65.25)	83.70 (74.54, 90.58)
	fFN >200	40.00 (5.27, 85.34)	83.51 (74.60, 90.27)

Discussion & Conclusions

The test characteristics of the AP and the quantitative fFN were similar in our population, although the actual agreement between the tests was low. The area under the Receiver Operating Curve was <0.8 for all measured outcomes for the AP, fFN <50, fFN >50 and fFN >200.
There were no significant differences in the test characteristics between the quantitative fFN and the AP test.

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References

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