In conclusion, we have developed and validated a simple, rapid, and specific method for the determination of ORA in urine. The method can be used for routine screening of hyperammonemia or urea cycle patients and may also be used for heterozygosity testing for OCTD.

References

Accuracy of the Rapid Fetal Fibronectin TLi System in Predicting Preterm Delivery, Veronica Luzzi, Kelly Hankins, and Ann M. Gronowski (Department of Pathology and Immunology, Division of Laboratory Medicine, Washington University School of Medicine, 660 South Euclid Ave., Box 8118, St Louis, MO 63110; * author for correspondence: fax 314-362-1461, e-mail gronowski@pathology.wustl.edu)

Numerous studies have demonstrated that fetal fibronectin (fFN) is an excellent marker of preterm delivery with a negative predictive value (NPV) >99% for predicting delivery within 7 or 14 days in symptomatic women (1–3). Interestingly, these studies have been performed by sending the sample to Adeza Biomedical for testing using an ELISA microtiter plate or by a rapid colloidal gold test marketed only outside the US. In the US, however, the only method available for rapid fFN analysis is the TLi™ system (Adeza Biomedical). Our objective was to assess the utility of the TLi rapid fFN system to predict delivery in symptomatic patients within 7, 14, or 21 days.

We used 501 cervicovaginal samples consecutively received in the Barnes-Jewish Hospital Laboratory for physician-ordered fFN analysis during an 18-month period for the study (February 2001–August 2002). From this cohort, charts for 243 patients were available for review. This constitutes the group of patients who delivered at Barnes-Jewish Hospital. Study inclusion criteria included the following: signs and symptoms of preterm labor, intact membranes, cervical dilation <3 cm, and fFN collection at 24–35 weeks. These are all criteria for fFN specimen collection included in the manufacturer's package insert. Patients who had delivered by cesarean section or other forms of induced delivery within 21 days of fFN were excluded. If fFN measurement was performed more than once, for simplicity we arbitrarily chose the measurement made closest to delivery to be included in the study. A total of 15 patients had more than one fFN measurement performed. fFN measurements were performed according to the manufacturer's instructions. Briefly, the patient sample was extracted from the Dacron swab into an extraction buffer (provided by the manufacturer), incubated at 37 °C in a water bath for 10 min, and filtered through a plunger filter (provided by the manufacturer). A 200-μL portion of the filtered sample was applied to the Rapid fFN cassette, and at 20 min the TLi analyzer quantified the intensity of the lines. The instrument then provided a positive or negative result. Institutional Review Board approval was obtained for this study.

Of 133 patients who met the inclusion criteria, 38 were positive for fFN and 95 were negative. The mean (SD) maternal ages at delivery for the positive and negative groups were 25.5 (5.8) and 24.1 (6.1) years, respectively (age ranges, 16.2–40.8 and 12.9–41.4 years, respectively). The mean gestational ages at the time of collection for the positive and negative groups were 29.6 weeks (SD, 2.4; range, 24.1–33.3 weeks) and 30.0 weeks (SD, 2.8; range, 25.3–34.4 weeks), respectively. The mean gestational ages at the time of delivery for the positive and the negative groups were 35.3 weeks (SD, 3.7; range, 24.7–39.8 weeks) and 37.4 weeks (SD, 2.1; range, 30.9–40 weeks), respectively. The mean times from collection to delivery for the positive and negative groups were 39.9 days (SD, 22.5; range, 0–91 days) and 51.4 days (SD, 22.7; range, 2–107 days), respectively. Unpaired t-tests showed that only the gestational age at the time of delivery and the time from collection to delivery were significantly different between the fFN-positive and -negative groups (P = 0.003 and 0.017, respectively).

The NPV, positive predictive value (PPV), specificity, and sensitivity for predicting delivery within 7, 14, and 21 days of testing are shown in Table 1. We also calculated the likelihood ratio for a positive result [sensitivity/(1 – specificity)]; the likelihood ratio was 2.12 for birth within

Table 1. NPV, PPV, specificity, and sensitivity of TLi Rapid fFN for predicting delivery in symptomatic patients.

<table>
<thead>
<tr>
<th>Days to delivery</th>
<th>&lt;7</th>
<th>&gt;7</th>
<th>&lt;14</th>
<th>&gt;14</th>
<th>&lt;21</th>
<th>&gt;21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive fFN, n</td>
<td>4</td>
<td>34</td>
<td>6</td>
<td>32</td>
<td>9</td>
<td>29</td>
</tr>
<tr>
<td>Negative fFN, n</td>
<td>3</td>
<td>92</td>
<td>6</td>
<td>89</td>
<td>6</td>
<td>89</td>
</tr>
<tr>
<td>Total, n</td>
<td>7</td>
<td>126</td>
<td>12</td>
<td>121</td>
<td>15</td>
<td>118</td>
</tr>
<tr>
<td>NPV, %</td>
<td>96.8</td>
<td>93.7</td>
<td>93.7</td>
<td>93.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPV, %</td>
<td>10.5</td>
<td>15.8</td>
<td>23.7</td>
<td>23.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity, %</td>
<td>73</td>
<td>73.6</td>
<td>75.4</td>
<td>75.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>57</td>
<td>50</td>
<td>60</td>
<td></td>
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</tbody>
</table>
7 days, 1.92 for birth within 14 days, and 2.4 for birth within 21 days. The likelihood ratio for a negative result \([1 - \text{sensitivity}/\text{specificity}]\) was 0.59 for birth within 7 days, 0.68 for birth within 14 days, and 0.53 for birth within 21 days. The data in Table 1 are similar to those obtained in previous studies using the ELISA-based assay. Joffe et al. (1) reported a NPV of 99.6% and a PPV of 9.1% for 243 patients who delivered within 7 days with gestational ages between 24 and 35 weeks of gestation. Iams et al. (2) reported a NPV of 99.3% and a PPV of 38.9% for 192 patients who delivered within 7 days with gestational ages between 24 and 34 weeks of gestation. This group also calculated a NPV of 95% and a PPV of 40% for patients delivering within 14 days. Peaceman et al. (3) examined 763 patients with gestational ages of 24–34 weeks and reported a NPV of 99.5% and a PPV of 12.7% for patients who delivered within 7 days and a NPV of 99.2% and a PPV of 16.7% for patients who delivered in within 14 days.

In our study, the NPV of fFN using the TLi system compared well with data from previous reports using ELISA-based assays. For patients who delivered within 7, 14, and 21 days, the NPVs were 96.8%, 93.7%, and 93.7%, respectively.

Parts of this work were presented at the AACC Annual Meeting, July 28–August 1, 2002, Orlando, FL.

References

Macroprolactin Detection by Precipitation with Protein A-Sepharose: A Rapid Screening Method Compared with Polyethylene Glycol Precipitation, Rémy Sapin and Gilles Ker etezz (1 Laboratoire Universitaire de Biophysique, Unité d’Analyses Endocrinienne, ULP/CNRS UMR 7004, Faculté de Médecine de Strasbourg Cedex, France; 2 Immunech Beckman Coulter, 13276 Marseille Cedex 9, France; * address correspondence to this author at: Institut de Physique Biologique, Faculté de Médecine, F-67085 Strasbourg Cedex, France; fax 33-3-90-24-40-57, e-mail sapin@ipb.u-strasbg.fr)

Prolactin (PRL) circulates in serum in three major molecular sizes identifiable by gel-filtration chromatography: monomeric PRL (23 kDa), big PRL (45–60 kDa), and big big PRL or macroprolactin (150–170 kDa). Macroprolactin is mainly a complex of PRL with human immunoglobulins G (hIgG) (1–4), but aggregates of PRL may also be present (4). Identification of macroprolactin, which has reduced bioactivity but can be the cause of high PRL values in patient samples, can help resolve diagnostic confusion and avoid expensive investigations and inappropriate treatment. It is generally admitted that all samples showing apparent hyperprolactinemia should be examined for macroprolactin.

The immunoassays used to determine prolactinemia react variously with macroprolactin (5). With high-reacting assays such as the Elecsys® PRL assay from Roche Diagnostics, polyethylene glycol (PEG) precipitation has been validated as a rapid technique to detect macroprolactin (6). However, the PRL PEG precipitation test suffers from high nonspecific precipitation [~14–16% (7, 8)], and results of this test may not be definitive in any case, making it necessary to define a gray zone (6, 9). Comparison of the results of a high-reacting method with those of low-reacting methods, such as the ADVIA:Centaur or ACS:180 PRL assays (Bayer Diagnostics), has also been proposed as a screening method (10). However, results obtained for macroprolactinemic sera have been shown to appear sample dependent, particularly with the Bayer assays (7, 11), and the presence of macroprolactin can not be excluded by comparing the results obtained with a high- and a low-reacting method.

Recently, a screening method based on the recognition of the hlgG component of macroprolactin by goat anti-human IgG-agarose (binding capacity, 1.5 mg hIgG/mL of resin) has been validated with the Elecsys assay (12). This method incorporates a 2-h incubation time and a 20-fold dilution of the serum, which may prevent its use in samples with moderate hyperprolactinemia (<1000 mIU/L). In the present study we describe the application of a simple and rapid method based on precipitation of hlgG-PRL complexes by a protein A-Sepharose suspension with high hlgG binding capacity (16 mg/mL of resin). Protein A is a polypeptide that binds the Fc region of human immunoglobulin molecules, especially hlgG1, hlgG3, and hlgG4 but only a fraction of hlgG3 (13). This method involves a short incubation time and a threefold dilution factor only. Results obtained with this new method were compared with those obtained with the PEG precipitation test.

Prolactin was measured in 116 sera from hyperprolactinemic individuals (PRL >600 mIU/L); 23 men (age range, 12–79 years) and 93 women (age range, 8–90 years). These sera were selected on the basis of their PEG-precipitated PRL values (7–96%) to study the whole range of values. The PRL concentrations in these samples were between 636 and 24,400 mIU/L. The procedures were in accordance with the Helsinki Declaration of 1975 and the subsequent 1996 amendments.

We used the automated Elecsys PRL immunoassay on the Elecsys 2010 analyzer. The PRL standard was the third International Reference Preparation WHO 84/500. PEG precipitation was performed as described previously (8). This method involves a twofold dilution. Results were expressed as the percentage of PEG-precipitated PRL (10).