Proteomic Analysis May Predict Preterm Labor

BY KATE JOHNSON
Montreal Bureau

Biomarkers of intra-amniotic infection and inflammation can be rapidly detected in amniotic fluid using proteomic analysis. And the identification of a distinctive biomarker profile can predict imminent preterm delivery with 100% accuracy, opening the door to future treatments, results of a recent study suggest.

"We are probably at a turning point in the history of preterm labor diagnosis," lead author Irina Buhimschi, M.D., of Yale University, New Haven, and her associates wrote (BJOG 2005;112:173-81). She conducted the research with Catalin S. Buhimschi, M.D., also of Yale, and Rob Christner of Ciphergen Biosystems, Fremont, Calif.

"We think this proteomic analysis will be the diagnostic platform of the future from which many diseases will be diagnosed," Dr. Irina Buhimschi commented in an interview.

The discovery could help identify preterm labor patients who might benefit from intervention "before the battle is completely lost," she explained.

Although amniotic fluid cultures can detect infection, they have limited clinical utility because results are not quickly available. "By the time you have the result, the patient has already delivered, and the baby is in neonatal intensive care—so the only benefit of the test is to confirm the decision of the physician. In the case of [proteomic analysis], the result can be available within 50 minutes or less and has the potential of being useful for clinical decision making," she said.

Using proteomic analysis, the team analyzed frozen amniotic fluid samples from 77 women with symptoms of preterm labor or preterm, premature rupture of membranes, and a known outcome (stage 1). The findings were then applied to samples from 24 symptomatic patients whose outcomes were not known to the investigators (stage 2).

The analysis identified a distinctive profile of four proteins present in patients who went on to preterm delivery but absent in patients whose symptoms subsided and who did not give birth prematurely.

This profile consisted of three out of four biomarkers of infection and inflammation, including human neutrophil defensin-1 and -2 and calgranulins A and C.

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"If there were just two of the biomarkers present, the symptoms might either spontaneously resolve or get worse. It was only when three or four were present that imminent delivery could be predicted," Dr. Buhimschi said.

The analysis involved a sophisticated algorithm called mass restricted (MR) analysis, and patients were given an MR score based on their levels of these four proteins.

The scoring system had 100% sensitivity and specificity for predicting which patients would deliver prematurely. Patients with an MR score of 3-4 had a median amniocentesis-to-delivery interval of 2 days, compared with a median of 51 days for patients with MR scores of 0-2.

Although it is generally accepted that a large proportion of preterm deliveries are caused by infection and inflammation, previous attempts at treating all preterm labor patients with antibiotics have failed to reverse the process. This may be partly because patients whose preterm labor is caused by factors other than infection and inflammation do not respond to antibiotic therapy, Dr. Buhimschi said.

"It is reasonable to think that those who respond to antibiotics will be only those in whom the preterm labor is caused by an infection and inflammation—and our approach is able to identify those patients," she said. In addition, the identification of specific biomarkers of preterm delivery holds potential for research into pathology-specific treatments, she said.

The research was funded by the National Institutes of Health and Ciphergen Biosystems. Dr. Buhimschi said the NIH has agreed to fund further investigations into the application of this research. ■

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