Expert Predicts Routine First-Trimester Screening

There is sufficient evidence to support incorporation of aneuploidy testing into practice, expert says.

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — First-trimester screening for aneuploidy may soon become the standard of care, Robert H. Ball, M.D., predicted at a meeting on antepartum and intrapartum management sponsored by the University of California, San Francisco.

There is sufficient evidence to support the incorporation of first-trimester testing into practice, and the focus now should be on the most effective way to implement this, according to a consensus statement produced at a workshop sponsored by the National Institute of Child Health and Human Development in December 2004.

At least seven studies have shown that detection of aneuploidy can be improved by analyzing a combination of risk factors in the first trimester: maternal age, nuchal translucency measured on ultrasound, and serum testing for β-HCG and PAPP-A.

Women at risk may be offered more definitive testing earlier in pregnancy with this approach, or results of negative first-trimester screens can be integrated with second-trimester serum screening for improved aneuploidy detection in the second trimester.

"This is a big deal, no doubt about it," said Dr. Ball, a perinatologist at UCSF Children's Hospital. Most nuchal translucency screens will be done in prenatal diagnostic centers, not in physician offices.

Dr. Ball presented data at the meeting from the First and Second Trimester Evaluation of Risk for Aneuploidy (FASTER) trial, in which he was an investigator. The results have been accepted for publication in the New England Journal of Medicine.

The study obtained follow-up information for 37,002 births, from an impressive 97% of the women who enrolled and underwent first- and second-trimester screening. Aneuploidy detection rates improved when first-trimester serum screening was added to nuchal translucency measurement, compared with using nuchal translucency alone to assess risk. Detection improved further when these first-trimester results were integrated with second-trimester serum screening.

The study's size provided the power to analyze subgroups, including results based on the gestational week of screening. The best time for first-trimester screening was week 11: When screening was performed at that time, detection rates were 73% with nuchal translucency alone and 93% with the combined nuchal translucency/serum screen. After integrating the combined first-trimester screen with second-trimester screening, the detection rate was 98%.

First trimester screening may pose scheduling problems, he predicted. "That's sort of a logistical nightmare, if you think about it," because physicians will be scrambling to get patients into prenatal diagnostic centers before the 11-week window passes, he said. "I can imagine people suing because they didn't get in for their nuchal translucency screening and they have a Down syndrome kid" that might have been detected earlier.

In hopes that the integrated first- and second-trimester screening strategies might obviate the need for genetic sonograms, investigators analyzed the FASTER data with and without genetic sonogram results. They found that the likelihood of aneuploidy greatly increased with identification of at least one genetic marker on ultrasound. Genetic ultrasound results improved the overall 84% detection rate for aneuploidy using first-trimester screening alone and decreased the false-positive rate.

"Much to my chagrin, having a genetic sonogram after you've had a bucket load of other tests is actually going to be useful," Dr. Ball said. ■

Prenatal Diagnostic Test Uses Endocervical Mucus

COPENHAGEN — An investigational prenatal diagnostic test that uses fetal cells taken from maternal endocervical mucus could offer all the advantages of chorionic villus sampling, according to a study sponsored by Biocept Inc., the San Diego company that's developing the test.

"This is a completely noninvasive diagnostic test that you can do in the first trimester. It's not just a screening test, which is what the other noninvasive tests are," said study investigator Farideh Bischoff, Ph.D., of Baylor College of Medicine in Houston.

The idea of analyzing trophoblast cells taken from either maternal blood or cervical mucus has been pursued for some time. However, inefficient endocervical sampling procedures and the scarcity of trophoblasts in maternal blood have hampered previous attempts to develop a reliable prenatal test.

The Biocept test involves collecting maternal endocervical mucus with a brush similar to that used to collect samples for Pap smears. A cell capture device is used to isolate fetal trophoblasts from the mucus. Next, an antibody-based purification system filters out the maternal cells.

In a study she presented at the annual meeting of the European Society of Human Reproduction and Embryology, Dr. Bischoff described immunohistochemical staining and fluorescence in situ hybridization testing on the purified cells from 100 women.

The initial endocervical mucus sample contains very small numbers of trophoblasts and following the purification technique can strengthen the concentration to a purity of 85%-95%.

Diagnostic testing of the remaining trophoblast cells is then possible to detect chromosomal aneuploidies, she said.

"If you run a panel of probes you can detect trisomies. Alternatively, you can do DNA testing on the cells to screen for mutations. It basically allows you to do the same tests that investigators are doing with preimplantation embryos," she said.

Dr. Bischoff said Biocept is currently running a clinical evaluation study at a number of centers across the United States to compare the results of the test with those of standard chorionic villus sampling in a group of pregnant women.

—Kate Johnson

Tool Helps Women Make Decision About Invasive Prenatal Screening

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — A new computerized tool helps pregnant women decide whether they want invasive prenatal testing, Miriam Kuppermann, Ph.D., said at an antepartum and intrapartum management meeting sponsored by the University of California, San Francisco.

In a randomized, controlled trial, 496 pregnant women seen at three institutions in the San Francisco Bay area used the computerized decision-assistance tool or viewed a computer version of age-appropriate brochures the state requires clinicians give to all pregnant women. Both were available in English and Spanish. Investigators assessed the impact of the tool or the brochures in three follow-up interviews.

'The goal is to help [pregnant women] make an informed decision that is consistent with their own preferences and values.'

"We do emphasize throughout that the goal of our program is neither to get women to test nor to get them not to test. The goal is to help them make an informed decision that is consistent with their own preferences and values," Dr. Kupperman said.

Immediately after the computer session, 75% of women using the decision-assistance tool correctly estimated their risk for having a baby with Down syndrome, compared with 5% of women in the control group. A significant difference in knowledge persisted in the second follow-up interview 2 weeks later.

The state pamphlets do not provide an individual's risk for Down syndrome, so the difference in knowledge between groups is not too surprising, but it's nevertheless encouraging to see that a high percentage of women understood their risk for trisomy 21 after using the computerized tool, Dr. Kuppermann said.

Immediately after the computer session, about 50% of women in the intervention group correctly estimated their risk for miscarriage related to prenatal testing, compared with 20% of women in the control group.

The third follow-up interview, conducted at 30 weeks' gestation after any decisions about prenatal testing were made, found that women in the intervention group had less uncertainty about their decisions, reported fewer factors contributing to uncertainty, and had less decisional conflict, meaning they were more comfortable with their decisions.

Women in the intervention group were more likely to undergo invasive prenatal testing, compared with the control group. Women in this group who entered the study wanting to undergo invasive testing were more likely to change their minds and not be tested. Women who came in with little inclination to be tested were more likely to change their minds and undergo testing.

"So it's working in both directions, which makes me feel good that it's not a biased tool," she said. "We believe that our tool does lead to more informed decisions that better reflect underlying preferences."

The computerized tool first reassures women that most babies are born healthy, but it notes that 3%-4% will have a birth defect and that Down syndrome is one of the defects that can be detected by testing.

The woman enters her age, answers questions about other risk factors, and then receives an individualized risk presentation. For example, a 36-year-old woman's mid-trimester risk for carrying a fetus affected by trisomy 21 is about 4 in 1,000, so the computer might show her a photo of 1,000 balls, 4 of which are highlighted yellow to represent the risk.

In a "values clarification exercise," the woman answers questions about various aspects of testing scenarios to elicit their value to her, ranging from "absolutely critical" to "not at all important." Based on the woman's responses, the program suggests testing strategies that might fit her values and risks, and it gives summaries of strategies she chooses. "Again, there's no absolute recommendation," Dr. Kuppermann said.

She and her associates now are modifying the tool to include first-trimester screening and testing strategies and models for other genetic tests for prenatal disorders besides Down syndrome.

The tool should be ready for clinical use in 2006, she said. ■