Contingent Screen 'Attractive' for Down Detection

The method shows a favorable rate of identification while reducing the need for second-trimester screening.

BY SHARON WORCESTER
Southeast Bureau

MIAMI BEACH — Contingent screening is an attractive option for prenatal detection of trisomy 21, Dr. Fergal Malone said at the annual meeting of the Society for Maternal-Fetal Medicine.

This screening method was analyzed using data from the First and Second Trimester Evaluation of Risk (FASTER) trial, a National Institute of Child Health and Human Development-funded study of pregnant women who underwent screening in both trimesters.

The outcomes of contingent screening were compared with the outcomes of two other commonly described screening methods: stepwise sequential screening and integrated screening in more than 32,000 women in the FASTER trial population.

The results of the analysis showed that contingent screening had a detection rate of 93%, with a false-positive rate of 4% in a relative comparison of the three methods for detection of trisomy 21 in the FASTER population. The first-trimester detection rate was 65%, with 2% of patients requiring chorionic villus sampling (CVS), and the second-trimester detection rate was 28%, with another 3% of patients requiring amniocentesis.

Only 22% of patients required additional screening in the second trimester, said Dr. Malone of the Royal College of Surgeons in Dublin.

Stepwise sequential screening had a 95% detection rate with a 5% false-positive rate and a 65% early detection rate. But 98% of patients were required to return for second-trimester screening to achieve these target rates.

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DR. MALONE

Integrated screening had a comparable 92% detection rate, with a false-positive rate of 5%. This method provided no early detection, and required that 100% of patients return for second-trimester screening.

The contingent screening approach assigns patients to one of three trisomy 21 risk groups based on the first-trimester ultrasound measurement of nuchal translucence and the first-trimester serum measurement of pregnancy-associated plasma protein-A (PAPP-A) and free β-hCG.

Patients in the highest risk group (greater than 1:30 risk in this study) undergo CVS, those in the lowest risk group (less than 1:1,500 risk) receive no further testing, and those in the borderline risk group (between 1:30 and 1:1,500 risk) undergo quad screening (serum alpha fetoprotein, hCG, unconjugated estriol, and inhibin A) in the second trimester and receive a final risk assessment based on all the measures, with a risk cutoff for further testing of 1:270, Dr. Malone explained.

Stepwise sequential screening divides patients into two risk groups that are based on nuchal translucency, PAPP-A, and free β-hCG measures in the first trimester, with those with a risk of greater than 1:30 receiving immediate CVS, and all others returning for second-trimester quad screening.

Integrated screening consists of nuchal translucency and PAPP-A screening in the first trimester, with no risk assessment given at that time, and quad screening in the second trimester.

A risk assessment that is based upon all the measures is given following the second-trimester screening, with a cutoff of 1:270 for additional screening. This method raises ethical concerns about withholding results during the first trimester and possibly causing a delay in a patient's potential decision to terminate due to aneuploidy.

"While contingent screening appears very attractive, there are some practical issues that need to be considered before endorsing this approach for widespread implementation," Dr. Malone stressed.

For example, the outcomes reported require that patients precisely follow the risk cutoffs used in this study.

The question is whether a woman with a risk of 1:31 versus the cutoff of 1:30 would forego chorionic villus sampling and wait for second-trimester screening results.

If the patients do not accept and follow these risk cutoff values precisely, the actual observed performance of contingent screening will be less efficient, he explained.

Other practical concerns regarding contingent screening include the effects of borderline-risk patients who fail to return for later screening and the fact that most patients screened by this method would have no neural-tube-defect risk assessment performed; steps would need to be taken to establish alternate methods for such screening, such as sonographic central nervous system anatomy evaluation, or single-marker alpha-fetoprotein testing, he said.

Contingent screening appears to effectively balance the benefits of first-trimester screening while focusing the added value of second-trimester screening measures on just a small segment of the population of pregnant women, Dr. Malone said.

"But before widespread use of this screening can be endorsed, prospective implementation studies will be required to confirm its efficacy in actual clinical practice," he concluded. ■

Maternal SSRI Use Tied to Increased Neonatal Hypertension Risk

BY MELINDA TANZOLA
Contributing Writer

Use of selective serotonin reuptake inhibitors during pregnancy is associated with neonatal abstinence syndrome and a slightly increased risk of persistent pulmonary hypertension of the newborn, according to results of two recently published studies.

In a case-control study, infants of women who took SSRIs in the second half of pregnancy were five to six times more likely to develop persistent pulmonary hypertension of the newborn (PPHN), with an overall incidence of 1 case for every 100 exposed infants (N. Engl. J. Med. 2006;354:579-87).

In an accompanying editorial, Dr. James L. Mills wrote that "the association is very unlikely to be due to chance … the current study was well designed and carefully executed." (N. Engl. J. Med. 2006;354:636-8).

In an interview, however, Dr. Gideon Koren of the Motherisk Program in Toronto, who was not involved in either study, cautioned against placing too much significance on the finding. "If you look more carefully at the numbers, it all hinges on two to three cases. These are very small numbers and although this is a large study, [PPHN] is a very rare condition," he said.

PPHN, which affects 1-2 infants per 1,000 live births, causes significant morbidity and mortality. In the case-control study, Dr. Christina D. Chambers of the University of California, San Diego, and her associates investigated the association between SSRI use and PPHN in 377 women whose infants had PPHN and 836 matched controls.

Within 6 months after delivery, participants were interviewed by nurses unaware of the study hypothesis. Interviewers collected detailed information on demographics, medications taken during pregnancy, and other risk factors.

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Fourteen cases of PPHN were noted among women taking SSRIs after the 20th week of gestation, compared with six cases in control infants (adjusted odds ratio 6.1). PPHN was three times more likely with antidepressant use after the 20th week of pregnancy, five times more likely if the antidepressant was an SSRI, and six times more likely after adjustment for confounding variables. No elevation in risk was observed with SSRI use earlier in pregnancy or when non-SSRI antidepressants were used.

The investigators noted that 3% of infants with PPHN died. Dr. Koren said that he spoke with the study investigators, who told him that none of the infants who died were exposed to SSRIs in utero, a fact that is not noted in the published study.

Dr. Koren cautioned that "it would be sad if because of this study, women discontinue SSRIs in late pregnancy, as [depression] can be life threatening for some and a cause of high rates of morbidity. The best predictor of postpartum depression is depression in late pregnancy."

An unrelated cohort study found that 30% of 60 infants exposed to SSRIs in utero experienced some degree of neonatal abstinence syndrome; none of 60 control infants showed any symptoms of the syndrome. Among the exposed infants, 10 exhibited mild symptoms and 8 had severe symptoms of neonatal abstinence, according to Dr. Rachel Levinson-Castiel of the Schneider Children's Medical Center of Israel in Petah Tiqwa, and her associates (Arch. Pediatr. Adolesc. Med. 2006;160:173-6).

The most common symptoms, measured using the Finnegan score, included tremors (in 37 SSRI-exposed infants vs. 11 control infants), gastrointestinal disturbances (34 vs. 2), sleep disturbance (21 vs. 2), high-pitched cry (18 vs. 0), and hypertonicity or myoclonus (14 vs. 1). Most symptoms peaked within the first 48 hours after delivery, although maximal scores were observed through day 4.

Although the small study size precluded an evaluation of dose effects for most SSRIs, the investigators found a significant association between paroxetine dose and the degree of neonatal abstinence syndrome symptoms. Infants exposed to doses less than 20 mg showed no signs of the syndrome.

While neonatal abstinence syndrome is indeed a result of withdrawal in most infants, Dr. Koren added that in some cases, the symptoms are instead due to a high level of drug in the neonate.

"This is important because if it is a lack of drug [causing the symptoms], you may want to give the baby an SSRI, whereas if it is poisoning you cannot give the drug," he said.

The study investigators suggested that infants exposed to SSRIs in utero be followed carefully after delivery. "After birth, close monitoring is mandatory. Early discharge of SSRI-exposed infants should be avoided and observation continued until symptoms subside." ■