Noninvasive Test May ID Intra-Amniotic Infection

BY PATRICE WENDLING

CHICAGO — A noninvasive test that discriminates between the presence and absence of intra-amniotic infection in women with preterm labor could reduce the need for amniocentesis in this population, according to Dr. C. Andrew Combs.

The test, based on five distinct proteins in cervicovaginal fluid, also may be useful in the management of preterm labor, which is dependent on infection status. Antibiotics and prompt delivery are indicated when infection is present, while tocolysis and prenatal steroids are used when it is absent, he said at the annual meeting of the Society for Maternal-Fetal Medicine.

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Major Finding: A test based on five marker proteins in cervicovaginal fluid was able to discriminate intra-amniotic infection in 13 of 14 cases in which infection was present and in 7 of 84 in which infection was absent, resulting in a sensitivity of 93%, specificity of 92%, positive predictive value of 65%, and negative predictive value of 99%.

Data Source: Multicenter trial involving 105 women with preterm labor.

Disclosures: Dr. Combs has received honorarium from ProteoGenix Inc., the sponsor of the study.

Amniocentesis is often needed to make an accurate diagnosis of intra-amniotic infection (IAI), but is frequently refused by women in preterm labor because of the associated risk of miscarriage. Even when amniocentesis is used, rapid results are somewhat limited, said Dr. Combs, a perinatalogist in group practice in Campbell, Calif.

IAI is subclinical in 80% of cases, and clinical signs such as fever, uterine tenderness, white blood count, and tachycardia are often absent. A culture takes 2-5 days and is negative in up to one-third of IAI cases, he said. Finally, cultures specific for *Mycoplasma* and *Ureaplasma* species, which may be important in many of these infections, are not available in most hospital laboratories.

Dr. Combs and his associates hypothesized that proteins in cervicovaginal fluid would be differentially expressed in infected vs. noninfected cases, and tested this hypothesis in a multicenter trial involving 105 women with preterm labor at a gestational age of more than 22 weeks with intact membranes. IAI was present in 14 (13%) based on a positive amniocentesis fluid culture and/or 16S ribosomal DNA polymerase chain reaction test result. Cervicovaginal swabs were used for protein analysis.

Screening was performed on 178 proteins likely to have an association with IAI, with 42 entered into statistical models. Five proteins were included in a final model: one plasma protein, two cytokine/chemokines, one cell adhesion protein, and one peroxidase. Dr. Combs declined to specifically identify the proteins, citing proprietary reasons on behalf of ProteoGenix Inc. (Costa Mesa, Calif.), which sponsored the study and is developing a commercial test.

The final model had a "mediocre" area under the receiver operating characteristic curve of 0.84 with only a single protein, improving to 0.94 with three proteins and to 0.98 with all five proteins, Dr. Combs said.The five-marker test was positive in 13 of 14 cases in which infection was present and in 7 of 84 cases in which infection was absent, resulting in a sensitivity of 93%, specificity of 92%, positive predictive value of 65%, and negative predictive value of 99%.

"We think this is an excellent diagnostic performance," he said.

An audience member expressed concern about using a test with such a low positive predictive value. Dr. Combs said he shared this skepticism if the test were used as the basis for prescribing antibiotics and delivering the infant in a mother with an intra-amniotic infection. He added that he would use a positive result to direct him to perform amniocentesis.

Validation of the test is underway in an independent population, with 300 patients already enrolled, he said. ■