Investigator Catalogs Risks of Pregnancy in Older Women

BY KATE JOHNSON
Montreal Bureau

NEW ORLEANS — Women seeking infertility treatment should be warned about the increased risks associated with pregnancy at older ages, according to Barbara Luke, Sc.D., professor at the School of Nursing & Health Studies, University of Miami at Coral Gables in Florida.

In an analysis of more than 8 million singleton live births to women aged 30-54 years, her study found significantly increased risks of pregnancy complications and adverse outcomes as women aged.

The study used the U.S. Birth Cohort Linked Birth/Infant Death data set of singleton live births of 20 weeks' gestation or more between 1995 and 2000. Births to women aged 30-34 years were the reference, and the study controlled for maternal race, smoking, macrosomia, and breech or malpresentation. The highest risks were seen in women aged 45 years and older, but "many risks are significantly elevated by age 35-39 years," Dr. Luke said in an interview.

Looking at the overall population, the study found that two of the greatest health risks for older pregnant women—chronic hypertension and diabetes—may be present even before pregnancy. Chronic hypertension (hypertension developing before pregnancy or up to 20 weeks' gestation) was highest in women aged 45 or older (adjusted odds ratio of 3.7 for primiparas and 4.89 for multiparas), as was diabetes (AOR of 2.19 for primiparas and 2.58 for multiparas). Pregnancy-associated hypertension, defined as developing after 20 weeks' gestation, was another important risk in this age group (AOR 1.55 for primiparas and 2.13 for multiparas), Dr. Luke said.

Similarly, premature rupture of membranes (PROM), premature birth (less than 32 weeks' gestation), and infant death were markedly increased by age 35-39 years, with the greatest risk in women 45 years and older (AOR 1.02, 2.11, and 2.68, respectively, for primiparas and AOR 1.38, 1.77, and 1.92, respectively, for multiparas).

The risk of precipitous labor and stimulation of labor decreased with age, but the risk of excessive bleeding, dysfunctional labor, induction of labor, and prolonged labor all increased as women got older.

Primary cesarean section increased with age in both primiparas and multiparas (AOR 3.15 and 2.65 in the oldest age group), while forceps, vacuum, and vaginal deliveries actually decreased with age in the primiparous group (AOR 0.90, 0.73, and 0.32, respectively), said Dr. Luke. In the oldest multiparous group the risk of repeat section increased (AOR 1.56), forceps and vacuum deliveries increased (AOR 1.29 and 1.08), and vaginal births after cesarean section decreased (AOR 0.64).

"This is particularly worrisome since with C-section there is a doubling of the neonatal mortality rate and an increased risk of stillborn and placental complications in subsequent pregnancies," she noted.

There is also evidence of long-term health implications for women who develop pregnancy complications such as preeclampsia and preterm birth, Dr. Luke concluded. ■

Parenting Capacity Similar in Older Versus Younger Mothers

NEW ORLEANS — Women who become mothers in their 50s with egg donation are no less able to handle the physical and mental demands of parenting compared with their younger counterparts, according to a study presented at the annual meeting of the American Society for Reproductive Medicine.

"We jumped to some conclusions in the past that weren't necessarily correct about older women's reduced parenting capabilities," said the study's lead investigator, Dr. Anne Z. Steiner of the University of North Carolina in Chapel Hill.

Her study surveyed women in their 50s who had conceived and delivered after egg donation and matched them to an equal number of women in their 40s and 30s who also had conceived and delivered following in vitro fertilization. The 64 respondents (18 in their 50s, 24 in their 40s, and 22 in their 30s) had children aged 3 or 4 years old at the time of the study.

The surveys covered issues of parenting stress, using the Parenting Stress Index/Short Form questionnaire. Physical and mental function also were assessed, along with information on demographics, family structure, and child care, to determine a measure of "total parenting stress."

Overall, the study found no significant difference in physical or mental function or parental stress between the older women and their younger counterparts. Women in their 50s had a nonsignificantly lower physical function score compared with women in their 30s (55 vs. 57), but all scores were higher than the average national female score (49), said Dr. Steiner. Mental function scores were slightly higher for women in their 50s compared with women in their 30s (54 vs. 50), but again, this difference was not significant. Adjustments for race, employment status, use of child care services, age and health of the child, gestational order, and family income did not alter the findings.

"To our knowledge this is the first study to evaluate parenting in women who conceive after age 50," wrote the study's authors. "Our data do not support the hypothesis that mothers of advanced maternal age have reduced parenting capacity."

—Kate Johnson

DRUGS, PREGNANCY, AND LACTATION

New Insights in Glyburide for GD

When treatment for gestational diabetes is indicated, the drug of choice, insulin, can be problematic for some women because of the need for daily injections, which can affect compliance. The cost of therapy may also be an issue for women in lower socioeconomic groups.

The use of oral hypoglycemic agents for treating women with gestational diabetes has not been recommended in the past because many of these drugs cross the placenta, increasing the risk of neonatal hypoglycemia. But there are now several studies that provide encouraging data suggesting that the second-generation sulfonylurea glyburide is a safe option for both the woman and baby.

BY GIDEON KOREN, M.D.

The first study indicating that glyburide might be a safe option for treating gestational diabetes was conducted in 1994, using the human placental perfusion model, which entails taking the term placenta after birth and reconstructing the blood vessels of the mother and newborn to determine whether a drug crosses the placenta. The investigators showed that while most of the oral hypoglycemic drugs tested crossed the placenta, a minimal amount of glyburide passed the placenta (Am. J. Obstet. Gynecol. 1994; 171:653-60).

One of the investigators, Dr. Oded Langer, and associates conducted a randomized, controlled trial comparing insulin with glyburide in 404 women with singleton pregnancies and gestational diabetes who started treatment between 11 and 33 weeks' gestation. The study was published in 2000. Both treatments were equally effective in achieving the target level of glycemic control in the women, with 4% of women on glyburide requiring treatment with insulin.

Importantly, there were no significant differences in neonatal complications between the two groups: The percentages of babies who were large for gestational age, had macrosomia, had lung complications, were hypoglycemic, were admitted to neonatal intensive care units, or had fetal anomalies were similar in both groups. Serum insulin levels in the cord were similar in both groups, and no glyburide was detected in the cord serum of babies in the glyburide group, confirming the 1993 study (N. Engl. J. Med. 2000;343:1134-8).

A recent completed meta-analysis by Motherisk of all studies on this topic also found no evidence of an increased risk to the newborn associated with glyburide treatment, corroborating the 2000 study.

Why glyburide does not cross the placenta is an interesting question, one that several research groups are investigating. The placenta is not just a passive barrier, and it has different carrier systems that can selectively efflux different drugs from the baby back to the mother. We also know that the opposite occurs. For example, the placenta carries iron from the mother to the baby; even when the mother is anemic, the placenta ensures that the baby receives iron.

We published a paper earlier this year using the same placental perfusion model used in the 1993 study, but put glyburide on both sides of the placenta and found that it is actively pumped from the baby to the mother (Am. J. Obstet. Gynecol. 2006; 195:270-4). The central thinking now is that the most likely placental transporter for glyburide is the breast cancer–resistant protein abundantly available in the placenta.

Glyburide provides an example of a drug that has not been given to women with gestational diabetes because of the false impression that it does cross the placenta, but the available data indicate that despite being a small molecule, it does not.

These novel findings may have major implications for women with gestational diabetes who require treatment because many would be happy not to have to use insulin daily.

In many parts of the world, glyburide is already widely used for treating gestational diabetes. And although some women will require insulin, or a combination of glyburide with insulin, there are many women with gestational diabetes who will do well with glyburide. Glyburide is available as a generic, which is a significant cost advantage.

Finally, this may be one of the first examples of a medication that is considered safe to use in pregnancy because it has been found not to cross the placenta. In the future, drug therapy in pregnancy may involve the development of drugs that are pumped by the placenta back to the mother, using placental transporters to control fetal exposure (Placenta 2006;27:861-8).

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