

Prenatal Spinal Surgery Improves Outcomes

BY HEIDI SPLETE

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Prenatal surgery to repair myelomeningocele significantly reduced the need for shunts at 1 year of age and improved children's motor function at age 30 months, compared with children who had surgery after birth, based on data from a randomized trial of 183 pregnant women.

The results reflect data from 158 children who were evaluated at 12 months of age and 134 children evaluated at 30 months. Data collection is ongoing.

The surgery to repair the opening in the spine is usually performed after birth, but data from animal studies suggest that prenatal surgery could result in fewer complications, said Dr. N. Scott Adzick of the Children's Hospital of Philadelphia and his colleagues.

In the Management of Myelomeningocele Study (MOMS), 183 volunteer women with singleton pregnancies were randomized to prenatal surgery before the 26th week of pregnancy or surgery for their infants after birth (*N. Engl. J. Med.* 2011 [doi:10.1056/NEJMoa1014379]).

The children were examined for two primary outcomes. The first outcome, at age 12 months, was patient death or the need for a shunt. The second outcome, at age 30 months, was a composite score of motor function and brain development. The score was based on the Bayley Scales of Infant Development II (BSID-II) Mental Development Index and the difference between each child's actual ability and his or her expected motor function based on the severity of the spinal defects.

Death or the need for a shunt was significantly less likely in the prenatal surgery group, compared with the postnatal surgery group (68% vs. 98%). The rates of shunt placement were significantly lower in the prenatal surgery group, compared with the postnatal surgery group (40% vs. 82%).

All the fetuses in the study suffered from hindbrain herniation, in which the

VITALS

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Disclosures: The study was sponsored by the National Institutes of Health.

base of the brain is pulled into the spinal canal. But at 12 months, 36% of the children in the prenatal surgery group had no evidence of hindbrain herniation, compared with 4% in the postnatal surgery group. In addition, infants in the prenatal surgery group had lower rates of moderate or severe hindbrain herniation than did the postnatal surgery group (25% vs. 67%).

In addition, infants in the prenatal surgery group scored an average of 21% higher on measures of mental and motor function, compared with the postnatal surgery group, with primary outcome scores of 149 vs. 123, respectively.

Infants who underwent prenatal surgery were born at a mean 34.1 weeks of pregnancy, compared with a mean 37.3 weeks of pregnancy for the postnatal surgery group. Significantly more infants in the prenatal surgery group had respiratory distress syndrome, compared with the postnatal surgery group (21% vs. 6%).

In terms of secondary outcomes, children in the prenatal surgery group were more likely to be able to walk without crutches or other orthotic devices, compared with the postnatal surgery group (21% vs. 42%).

The mean age of the pregnant women was 29 years. Each fetus had a myelomeningocele located between the T1 and S1 vertebrae, evidence of hindbrain herniation, and a gestational age of 19.0-25.9 weeks. Exclusion criteria included body mass index of 35 kg/m² or higher, increased risk for preterm birth, and fetal

anomalies unrelated to the myelomeningocele.

Approximately one-third of the women in the prenatal surgery group showed uterine thinning or an area of dehiscence at the time of delivery. Women undergoing prenatal surgery must understand that they will require a cesarean delivery for the current pregnancy and any future pregnancies, the researchers added.

Myelomeningocele, a severe form of spina bifida in which the backbone and spinal canal do not close completely before birth, occurs in approximately 4 of every 10,000 births in the United States, Dr. Diana L. Farmer, division chief of pediatric surgery at the University of California, San Francisco, said in a teleconference. Dr. Farmer was one of several researchers on the study who took part in a teleconference to present the study findings.

The study was not large enough to show an impact of gestational age on the results, but data collection is ongoing. "This is a priceless cohort of patients that we will follow for a longer period of time," Dr. Farmer said. She noted that the National Institutes of Health has agreed to fund follow-up of the patients until age 6-9 years. Future studies will include whether the children in the prenatal surgery group remain free of shunts, maintain improved motor function, and require fewer procedures, compared with the postnatal group.

Although the surgery is highly specialized and more research is needed, the results suggest that ob.gyns. can recommend the procedure to appropriate patients at this time, Dr. Farmer said.

"At the present time, it would be responsible to inform families that this represents an additional option in care that they could consider. The decision to undergo fetal surgery is quite individual and different for every patient, but I think families need to know that this is one option in the armamentarium." ■

Early Results Promising

Although the results are promising, it is important to be cautious in generalizing the success of prenatal surgery for myelomeningocele to a wider population, Dr. Joe Leigh Simpson and Dr. Michael F. Greene said.

"The study by Adzick and colleagues is 'a major step in the right direction, but the still suboptimal rates of poor neonatal outcome and high maternal risk necessitate the use of less invasive approaches if such procedures are to be widely implemented,' they said.

Results might be less successful for patients treated in centers that are not as experienced in the procedure, Dr. Simpson and Dr. Greene noted.

In addition, more research is needed to determine which fetuses are more likely to benefit from the surgery, and whether performing the procedure earlier in gestation would yield even better outcomes, they added.

DR. SIMPSON is at Florida International University in Miami, and DR. GREENE is at Massachusetts General Hospital in Boston. They made their comments in an accompanying editorial (*N. Engl. J. Med.* 2011 [doi:10.1056/NEJMe1101228]). Dr. Simpson disclosed that he serves on the advisory boards for Rarecells Diagnostics, Novartis, BioDx, and Bayer HealthCare. Dr. Greene is an associate editor for the *New England Journal of Medicine*.

VIEW ON THE NEWS

Buprenorphine Is Alternative to Methadone During Pregnancy

BY MARY ANN MOON

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For opioid-dependent women who are pregnant, buprenorphine appears to offer an effective, safe, first-line alternative to methadone.

In a randomized clinical trial comparing pregnancy outcomes among women seeking treatment for opioid dependence, infants exposed in utero to buprenorphine developed significantly less severe neonatal abstinence syndrome than did infants exposed in utero to methadone, said Hendrée E. Jones, Ph.D., of

Johns Hopkins University, Baltimore, and her associates.

The study involved 175 women aged 18-41 years who were at 6-30 weeks' gestation when they entered treatment for opioid dependence at eight sites in the United States, Austria, and Canada. Eighty-six were randomly assigned to receive oral buprenorphine and 89 to receive oral methadone in a double-blind fashion.

After delivery, their neonates were assessed for signs and symptoms of neonatal abstinence syndrome (NAS) twice a day for at least 10 days.

There were five primary neo-

natal outcomes. Three of these – percentage of neonates requiring NAS treatment, peak NAS scores, and head circumference – did not differ between the two study groups. However, two of the five primary outcomes – amount of morphine required to treat NAS and length of hospital stay – favored the infants in the buprenorphine group. On average, infants exposed to buprenorphine required 89% less morphine and spent 43% less time in the hospital (10 days vs. 17.5 days) than did infants exposed to methadone.

"The benefits of buprenor-

phine in reducing the severity of NAS among neonates with this complication suggest that it should be considered a first-line treatment option in pregnancy," they said (*N. Engl. J. Med.* 2010;363:2320-31).

Despite the comparable or even superior efficacy and safety of buprenorphine, there was one important drawback with the therapy: Women were more likely to discontinue treatment for opioid dependency with buprenorphine (33%) than with methadone (18%).

Most (71%) of the women in the buprenorphine group who discontinued treatment cited

"dissatisfaction" with the drug as their reason, while only 13% of those in the methadone group did so.

Future research should focus on reducing this "dissatisfaction" as well as on identifying "subpopulations of pregnant patients who are more likely to have a response to one medication than to the other," they added.

This study was funded by grants from the National Institute on Drug Abuse. Buprenorphine tablets and the associated placebo were supplied by Reckitt Benckiser Healthcare. Dr. Jones's associates reported ties to numerous drug companies. ■