

Surgery on Fetus Reduces Complications of Spina Bifida

The Management of Myelomeningocele Study (MOMS), an NIH-funded study, shows that surgery reduces the rate of disability and increases preterm birth risk in pregnant women carrying a child with myelomeningocele, the most serious form of Spina Bifida. The Spina Bifida Association is encouraged by the study's findings and hopes that it can serve as the basis for many more studies on this complex birth defect.

Origins of the study

MOMS was a scientific study designed to compare surgery before birth (also called prenatal, maternal-fetal and in-utero surgery) and surgery after birth (also called postnatal surgery) in children with Spina Bifida. It came about because doctors had noticed that nerve function in babies with Spina Bifida seemed to worsen as a pregnancy progresses. This observation suggested that the damage to the nerves of those with Spina Bifida may be a two-part process: some damage occurring when the spinal cord and associated nerves do not develop fully in the first month of the pregnancy with additional damage occurring throughout the pregnancy.

Early studies done in animals seemed to confirm that the amount of nerve damage could be lessened if the open spine was closed early in a pregnancy. This led researchers to want to compare the safety and effectiveness of prenatal and postnatal surgery.

MOMS set out to enroll 200 women who were carrying a baby with Spina Bifida. In 100 cases the Spina Bifida would be closed between the beginning of the 19th and the end of the 25th week of pregnancy. In the other one hundred cases the baby would have surgery to close their Spina Bifida after they are born. Participating women were not "selected" for one type of surgery or the other, but were to be randomly assigned to one of the groups.

Findings

The study shows that a surgical procedure to repair a common birth defect of the spine, if undertaken while a baby is still in the uterus, greatly reduces the need to divert, or shunt, fluid away from the brain. The fetal surgical procedure also improves mobility, and increases the chances that a child will be able to walk without crutches or other devices.

However, infants who underwent this prenatal surgery were more likely to be born preterm than were the infants who had the surgery after birth, when it is typically performed. As with all infants born early, preterm infants in the study were at increased risk for breathing difficulties. Mothers who underwent the surgery during their pregnancies were at risk for uterine dehiscence, a thinning or tearing at the incision in the uterus.

The birth defect, [myelomeningocele](#), is the most serious form of Spina Bifida, a condition in which the spinal column fails to close around the spinal cord. With myelomeningocele, the spinal cord protrudes through an opening in the spine. Originally planned to enroll 200 expectant mothers carrying a child with myelomeningocele, the MOMS study was stopped after the enrollment of 183 women, because of the benefits demonstrated in the children who underwent prenatal surgery.

The study appears in the *New England Journal of Medicine* and was conducted by researchers at the Children's Hospital of Philadelphia (CHOP), The University of California, San Francisco (UCSF), Vanderbilt University Medical Center in Nashville, the George Washington University Biostatistics Center in Washington, D.C. and the NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD).

“In spite of an increased risk for preterm birth, children who underwent surgery while in the uterus did much better, on balance, than those who had surgery after birth,” said Alan E. Guttmacher, M.D., director of NICHD which funded the study. “However, caution is advised. Because the surgery is highly specialized it is best undertaken in facilities with staff having experience in the procedure.”

Effects of myelomeningocele

The study authors noted that [myelomeningocele](#) occurs in 3.4 of every 10,000 births and 10 percent of affected infants die. Spina Bifida is one of a class of birth defects known as neural tube defects, in which the brain or spine fails to develop normally in the early embryo. The condition often results in weakness or paralysis below the location of the defect on the spine.

In addition to loss of bladder and bowel control, individuals with myelomeningocele often are unable to walk unassisted or may need a wheelchair. Also, the protrusion of the spinal cord creates a change in the flow of spinal fluid that may pull the brain stem into the base of the skull, which is known as hindbrain herniation. Children with myelomeningocele are subject to blockages that hinder or shut off the circulation of cerebrospinal fluid in the brain. The resultant fluid buildup can be life threatening, and so a hollow tube, or shunt, is inserted into the brain to drain the excess fluid into the abdominal cavity. These shunts are susceptible to blockage and infection, and may require many replacements during the patient's lifetime.

Surgery for myelomeningocele has traditionally been undertaken after birth, explained the NICHD author of the study Catherine Y. Spong, M.D., chief of the pregnancy and perinatology branch. It consists of inserting the cord back into the spinal cavity and sealing the opening with sutures. Study authors N. Scott Adzick M.D. of CHOP and Diana L. Farmer, M.D. of UCSF performed the initial animal studies suggesting that surgery in the womb might prevent many of the complications of myelomeningocele.

Prenatal group versus postnatal group

Women volunteering for the current study were assigned at random to one of two groups. The first group underwent prenatal surgery to close the spinal defect in their unborn child before their 26th week of pregnancy. The second group had the surgery performed on the child after birth.

The children were examined at 12 months of age and again at 30 months. The study results were evaluated as two separate, primary outcomes. The first primary outcome took into account whether, by 12 months, a child had died, had placement of a shunt or required a shunt. The second primary outcome at 30 months was a composite from a test of mental development and an assessment of motor function. The mental development score was taken from the Bayley Scales of Infant Development II Mental Development Index. The motor assessment score was

calculated as the difference between the child's actual motor ability and the expected ability given the level of the defect on the spine.

The first primary outcome, death or the need for a shunt was much less likely in those who had prenatal surgery, occurring in 67.9 percent of the infants in the prenatal surgery group and 97.5 percent of the traditional surgery group. For the second primary outcome, the infants who underwent prenatal surgery also scored significantly higher than the infants who received traditional surgery.

In addition to evaluating the study results in terms of the two primary outcomes, the researchers also evaluated the results in terms of a number of secondary outcomes. Although the ability to walk depends on the location of the spinal malformation, children in the prenatal surgery group were more likely to be able to walk without orthotics or crutches (41.9 percent) than were children in the postnatal surgery group (20.9 percent).

Hindbrain herniation, in which the base of the brain is pulled into the spinal canal, was present during pregnancy in all of the infants who participated in the trial. However, at 12 months of age, one-third of the children (35.7 percent) who had prenatal surgery no longer had any evidence of hindbrain herniation, compared to 4.3 percent in the postnatal surgery group.

Children in the prenatal surgery group were more likely to be born preterm, at an average of 34.1 weeks of pregnancy, compared with the postnatal group, born at an average 37.3 weeks. About 20.8 percent of the infants in the prenatal surgery group had a breathing disorder associated with preterm birth (respiratory distress syndrome), which the study authors considered a consequence of being born preterm. For the postnatal surgery group, 6.3 percent had respiratory distress syndrome.

Mothers in the prenatal surgery group were also more likely to experience uterine dehiscence, a thinning or tearing in the uterine incision used for the prenatal surgery procedure. In fact, one third of all the women in the prenatal surgery group had some degree of thinning at the time of delivery. The study authors noted that prenatal incisions in the uterus increase the risk for dehiscence or outright rupture during a subsequent pregnancy, and that all women who undergo such surgery should be informed that future pregnancies should be delivered by cesarean before labor begins.

“The findings suggest that the prenatal surgery allowed for more normal development of the nervous system and fewer complications,” Dr. Spong said.

The researchers added that the surgery might pose greater risks for categories of women excluded from the study because of health concerns. For example, severely obese women (body mass index of 35 or higher) were not included in the study because of the increased risk for complications of surgery. They noted, however, that obesity is common in women carrying a child with myelomeningocele.

“Experimental outcomes from animal studies and the results from this MOMS clinical trial suggest that prenatal surgery for myelomeningocele stops exposure of the developing spinal cord

to amniotic fluid and thereby averts further neurologic damage in-utero,” Dr. Adzick said. Prenatal surgery also stops cerebrospinal fluid leak from the myelomeningocele defect which serves to reverse hindbrain herniation in-utero, and we believe that this in turn mitigates the development of hydrocephalus and the need for shunting after birth”.

Urologic component

The NICHD has indicated that the study does have a urologic component, and the findings will be forthcoming.

Folic acid recommendations

Currently, the Centers for Disease Control and Prevention recommend that all women of childbearing age are advised to consume 400 micrograms of folic acid, either in a supplement or in a fortified cereal, to reduce their risk of having a child with a neural tube defect. The CDC recommendation is available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/00019479.htm>

In 2009, an NIH study found that women with low levels of vitamin B12, found only in meat, eggs and other foods of animal origin, were at increased risk for having a child with a neural tube defect (<http://www.nichd.nih.gov/news/releases/030209-vitamin-B12.cfm>).

Information on sources of vitamin B12 and recommended daily allowances for the vitamin is available from the NIH Office of Dietary Supplements, at <http://ods.od.nih.gov/factsheets/vitaminb12/>.

Relevant Web Links: <http://www.nih.gov/news/>; <http://www.nichd.nih.gov>

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