Management of Myelomeningocele Study Clinical Trial (2003–2010)

From February 2003 to December 2010, researchers of the Management of Myelomeningocele Study, or MOMS, clinical trial compared the safety and efficacy of different treatments for a specific type of spina bifida, called myelomeningocele. Myelomeningocele, the most frequent and severe form of spina bifida, is a condition in which the bony spinal column does not develop correctly, which causes an opening of the spine, exposure of the spinal cord, and formation of a small sac containing cerebrospinal fluid. Myelomeningocele affects 3.4 infants per 10,000 live births in the United States and is fatal in ten percent of affected infants. Investigators in the MOMS trial aimed to find a more successful treatment for myelomeningocele through different types of surgery. To accomplish that, they performed prenatal, or in utero, and postnatal repair operations in their study. The MOMS researchers concluded that prenatal repair improved motor and neurologic outcomes, such as the ability to activate and coordinate the muscles and limbs, and reduced the risk for fetal death.

Myelomeningocele is a birth defect in which parts of the spinal cord and nerves are exposed through an open part of the spine. Due to their open spine, infants with myelomeningocele suffer from nerve damage and other disabilities, such as hydrocephalus. Hydrocephalus consists of an accumulation of too much cerebrospinal fluid in the brain and can cause impaired bladder control, balance problems, and progressive mental impairment. In addition to hydrocephalus, infants are often paralyzed and lose control of their bowel and bladder. When treated for myelomeningocele, infants have an increased lifespan and quality of life.

In the 1960s, physicians treated infants with spina bifida postnatally, or after birth. The physicians surgically covered the open spine immediately after the birth of the infant, but the procedure did not increase an infant's lifespan and quality of life. In 1997, Noel Bristol Tulipan, a pediatric neurosurgeon, performed one of the first prenatal repairs for myelomeningocele at the Vanderbilt University Medical Center in Nashville, Tennessee. Although Tulipan's prenatal repair was successful, there was not enough data to conclude if prenatal repair was a safer and more effective treatment method compared to the postnatal repair.

Prior to the MOMS clinical trial, more than 200 fetuses underwent the prenatal repair operation from 1997 to the beginning of the MOMS trial in 2003. Diana Farmer, a pediatric surgeon, Joseph Bruner, an obstetrician and gynecologist, and colleagues, compared the results of those 200 prenatal surgeries with the results of the postnatal repairs during the same period. Those researchers found that prenatal repair resulted in improvement of motor skills over postnatal repair. However, their results also showed that prenatal repair had an increased risk of fetal death and increased maternal risk of preterm labor. Due to those results, the National Institutes of Health sponsored the MOMS clinical trial to compare prenatal and postnatal surgery data in a more controlled environment.

In February 2003, Nick Scott Adzick, the chief surgeon and director of the Center for Fetal Diagnosis and Treatment at the Children's Hospital of Philadelphia, Pennsylvania, began the MOMS clinical trial. The trial took place at three maternal-fetal surgery centers, including Children's Hospital of Philadelphia, Vanderbilt University Medical Center in Nashville, Tennessee, and University of California, San Francisco in San Francisco, California. During the trial, all other fetal intervention centers located in the United States agreed not to perform prenatal surgery for myelomeningocele, because the MOMS researchers aimed to ensure that prenatal repair surgery was safer and more effective than postnatal surgery before other fetal intervention centers continued to use the procedure.

As part of the MOMS clinical trial, researchers screened pregnant women with fetuses diagnosed with myelomeningocele. A total of 183 pregnant women were eligible to participate in the clinical trial. The researchers then randomly assigned the 183 pregnant women to either the prenatal surgery or postnatal surgery group. Of the 183 women who were given a randomized surgery assignment, 158 pregnant women completed the study. The researchers agreed to operate on the prenatal group between nineteen and twenty-five weeks' gestation. Between nineteen and twenty-five weeks' gestation, the length of time the exposed cord may experience neural damage is minimized. In addition, the MOMS researchers planned for the pregnant women to deliver the fetus via cesarean section to protect the fetus and the mother.

For those in the prenatal repair group, the pregnant women received the prenatal repair operation between nineteen and twenty-five weeks' gestation. Surgeons from the three maternal-fetal surgery centers performed the prenatal repair operation by first giving the mother a mixture of general and epidural anesthesia. The anesthesia was used to prevent unwanted uterine contractions during the procedure. Once the anesthesia was injected, the primary surgeon used an ultrasound to locate the fetus and placenta. After locating the fetus and placenta, the surgeon made a 1-to-2 centimeter incision in the pregnant women's abdomen. Next, the surgeon passed a surgical stapler into the uterine cavity. The surgical stapler was used to make a 6-to-8 centimeter opening, thus exposing the myelomeningocele sac on the fetus. After the sac on the fetus was exposed, the surgeon manually positioned the fetus until the sac was at the center of the uterine cavity. After positioning the fetus, the surgeon administered an intramuscular, or IM, injection to the fetus to prevent the fetus from moving and feeling any pain. Then, the surgeon closed the myelomeningocele sac by suturing the skin of the fetus, then suturing the pregnant woman. Once the woman was sutured with the fetus still in her womb, the pregnancy continued until the woman delivered via cesarean section at thirty-seven weeks of gestation.

Compared to the pregnant women in the prenatal group, the women in the postnatal group did not have to receive surgery between nineteen and twenty-five weeks' gestation. Women in the postnatal group delivered via cesarean section at thirty-seven weeks of gestation to protect the fetus and the mother. In the postnatal repair group, the surgeon performed repair surgery within the first twenty-four hours of birth. During the first twenty-four hours of birth, attendants handled the infants with extreme caution to prevent further damage to their spinal cord. During postnatal surgery, the surgeon only operated on the infants. Similar to the prenatal surgery, the surgeon closed the myelomeningocele sac by suturing the infant's skin closed.

Once the researchers collected the data from 158 surgeries, they compared the results of the prenatal and postnatal operations. The prenatal group experienced a decreased risk of fetal death, and infants had a decreased need of a cerebrospinal fluid shunt by the age of twelve months. A cerebrospinal fluid shunt drains excess fluid from the brain and spreads the fluid to other parts of the body. Another primary outcome of the prenatal group was improved motor and mental function by thirty months of age. Secondary outcomes of the prenatal group included decreased presence of hindbrain herniation, where the base of the brain is pulled into the spinal canal. Furthermore, infants in the prenatal repair group had an increased chance of having the ability to walk independently when older. According to Adzick, the improvement of hindbrain herniation and the decreased need for shunting could be due to the improved flow of cerebrospinal fluid. Along with benefits of prenatal repair, several risks were presented. Such risks of prenatal repair included maternal and fetal morbidity, increased rates of preterm birth, and increased rates of preterm labor that led to either placental abruption or pulmonary edema, excess fluid in the lungs.

Based on the data, the researchers of the MOMS clinical trial determined that the prenatal repair operation was safer and more effective for fetuses diagnosed with myelomeningocele compared to the postnatal repair operation. The researchers came to that conclusion much earlier than anticipated. Though the trial was meant to continue until 200 pregnant women received treatment, the data and safety monitoring committee ended the trial early in December 2010.

Results of the MOMS clinical trial indicated that prenatal surgery was safer and more effective compared to postnatal surgery in the treatment of myelomeningocele. After the conclusion of the trial, prenatal repair was offered as a safe treatment option along with termination of the pregnancy and postnatal repair. Due to the new treatment option of prenatal repair, infants have an increased

ability to walk without orthotics or a wheelchair and have increased motor and neurologic functions. Whether a fetus receives prenatal surgery, and whether such an in utero is ethical, is largely determined by the medical team in terms of which treatment would provide the least risk of death or disability to the fetus and the mother. As of 2017, more than one hundred hospitals and clinics offer surgery to treat myelomeningocele.

Sources

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