MOMS trial

A randomized clinical trial (MOMS trial) showed that prenatal correction of open spina bifida (OSB) via open fetal surgery was associated with improved infant neurological outcomes relative to postnatal repair, but at the expense of increased maternal morbidity.

The MOMS Trial is a Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) sponsored study of prenatal and postnatal closure of myelomeningocele; a collaboration of The Children's Hospital of Philadelphia, the University of California at San Francisco, Vanderbilt University Medical Center in Nashville and the George Washington University in Washington, D.C.

History

1980 - Fetal surgical techniques using animal models were first developed at the University of California, San Francisco by Dr. Michael R. Harrison, Dr. N. Scott Adzick and colleagues.

1994 - The surgical model that is most similar to simulating the human disease is the fetal lamb model of myelomeningocele (MMC) introduced by Meuli and Adzick in 1994. The MMC-like defect was surgically created at 75 days of gestation (term 145 to 150 days) by a lumbo-sacral laminectomy. Approximately 3 weeks after creation of the defect a reversed latissimus dorsi flap was used to cover the exposed neural placode and the animals were delivered by cesarean section just prior term. Human MMC-like lesions with similar neurological deficit were found in the control newborn lambs. In contrast, animals that underwent closure had near-normal neurological function and well-preserved cytoarchitecture of the covered spinal cord on histopathological examination. Despite mild paraparesis, they were able to stand, walk, perform demanding motor test and demonstrated no signs of incontinence. Furthermore, sensory function of the hind limbs was present clinically and confirmed electrophysiologically. Further studies.showed that this model when combined with a lumbar spinal cord myelotomy leads to the hindbrain herniation characteristic of the Chiari II malformation and that in utero surgery restores normal hindbrain anatomy.

Surgeons at Vanderbilt University, led by Dr. Joseph Bruner, attempted to close spina bifida in 4 human fetuses using a skin graft from the mother using specialized telescope called a laparoscope. Four cases were performed before stopping the procedure - two of the four fetuses died.

1998 - Dr. N. Scott Adzick and team at The Children’s Hospital of Philadelphia performed open fetal surgery for spina bifida in an early gestation fetus (22 week gestation fetus) with a successful outcome.

Surgeons at Vanderbilt University, led by Dr. Noel Tulipan, made an incision in the mother's uterus to obtain better exposure to fetuses of 28 to 30 weeks gestation. All 4 fetuses were born premature but with evidence of reversal of their chiari II malformation. Only 2 of the 4 required ventricular shunts after birth. Fetal surgery after 25 weeks has not shown benefit in subsequent studies.

Subsequently, 4 medical centers conducted 253 open spina bifida repairs prior to the MOMs trial. The outcomes were mixed and the only comparison groups were other children that had not undergone repair after birth in the past.

In February 2003, the National Institutes of Health began the Management of Myelomeningocele Study (MOMS). Three centers (Vanderbilt University, Children's Hospital of Philadelphia and the

University of California at San Francisco) were chosen to participate in the study of 183 fetuses which were randomized, 91 for fetal repair and 92 for postnatal repair. The study took 8 years to complete at a cost of $22.5 million.

Of the 1,087 fetuses and mothers initially screened for the study, 183 met all the inclusion criteria. The Children's Hospital of Philadelphia treated 77 patients, University of California at San Francisco treated 54 and Vanderbilt University treated 52.

Prenatal surgery was done at the assigned center between 19 and 25 weeks of pregnancy. Deliveries for both groups were performed by C-section at the assigned MOMS Center at approximately 37 weeks of pregnancy. The infants in the postnatal surgery group had their spina bifida closed at the MOMS Center as soon as possible after delivery, usually within 48 hours.

Medical information on the mothers and babies were gathered throughout the study and follow-up of their progress continued until the child reached at least two and a half years of age. Two outcomes were considered. The first, at 12 months, was death or need for a ventricular shunt. The second, measured at 30 months, was a composite score of standardized tests for mental and motor development.

Outcomes of the Trial

An interim analysis conducted in December 2010, made public in February 2011, and released in the New England Journal of Medicine in March 2011, showed a statistically significant benefit to the surgery and closed the trial.

The trial demonstrated that outcomes after prenatal spina bifida treatment are improved to the degree that the benefits of the surgery outweigh the maternal risks. Although this is a value judgement rather than a certain statement because one maternal uterine dehiscence may be more significant that multiple small Chiari malformation improvements. Results were reported in the New England Journal of Medicine by Adzick et al.

Specifically, the study found that:

Babies that underwent fetal repair of spina bifida were half as likely to need a ventricular shunt. Chiari malformation was less common in the fetal repair group. Standardized test scores for motor skills were superior in the fetal surgery group, and twice as many children were walking independently at 30 months as compared to the postnatal surgery group.

Based on these outcomes, fetal repair of spina bifida is now considered a standard of care at some fetal centers. However, prenatal repair is a complex and challenging procedure, requiring the most expert, comprehensive care for both mother and fetus.

The surgical team's level of experience in all aspects of care surrounding the operation are of paramount importance. Therapy that is highly dependent on the provider is of limited benefit to the wider population.