OBSTETRICS

The Management of Myelomeningocele Study: obstetrical outcomes and risk factors for obstetrical complications following prenatal surgery

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BACKGROUND: The Management of Myelomeningocele Study was a multicenter randomized trial to compare prenatal and standard postnatal closure of myelomeningocele. The trial was stopped early at recommendation of the data and safety monitoring committee and outcome data for 158 of the 183 randomized women published.

OBJECTIVE: In this report, pregnancy outcomes for the complete trial cohort are presented. We also sought to analyze risk factors for adverse pregnancy outcome among those women who underwent prenatal myelomeningocele repair.

STUDY DESIGN: Pregnancy outcomes were compared between the 2 surgery groups. For women who underwent prenatal surgery, antecedent demographic, surgical, and pregnancy complication risk factors were evaluated for the following outcomes: premature spontaneous membrane rupture ≤34 weeks 0 days (preterm premature rupture of membranes), spontaneous membrane rupture at any gestational age, preterm delivery at ≤34 weeks 0 days, nonintact hysterotomy (minimal uterine wall tissue between fetal membranes and uterine serosa, or partial or complete dehiscence at delivery), and chorioamniotic membrane separation. Risk factors were evaluated using χ^2 and Wilcoxon tests and multivariable logistic regression.

RESULTS: A total of 183 women were randomized: 91 to prenatal and 92 to postnatal surgery groups. Analysis of the complete cohort confirmed initial findings: that prenatal surgery was associated with an increased risk for membrane separation, oligohydramnios, spontaneous membrane rupture, spontaneous onset of labor, and earlier gestational age at birth. In multivariable logistic regression of the prenatal surgery group adjusting for clinical center, earlier gestational age at surgery and chorioamniotic membrane separation were associated with increased risk of spontaneous membrane rupture (odds ratio, 1.49; 95% confidence interval, 1.01—2.22; and odds ratio, 2.96, 95% confidence interval, 1.05—8.35, respectively). Oligohydramnios was associated with an increased risk of subsequent preterm delivery (odds ratio, 9.21; 95% confidence interval, 2.19—38.78). Nulliparity was a risk factor for nonintact hysterotomy (odds ratio, 3.68; 95% confidence interval, 1.35—10.05).

CONCLUSION: Despite the confirmed benefits of prenatal surgery, considerable maternal and fetal risk exists compared with postnatal repair. Early gestational age at surgery and development of chorioamniotic membrane separation are risk factors for ruptured membranes. Oligohydramnios is a risk factor for preterm delivery and nulliparity is a risk factor for nonintact hysterotomy at delivery.

Key words: fetal myelomeningocele, fetal spina bifida, fetal therapy, prenatal surgery

Introduction

The National Institutes of Health-sponsored Management of Myelomeningocele Study (MOMS) was initiated in 2003 to compare the safety and efficacy of prenatal repair of myelomeningocele with that of standard postnatal repair. The trial was stopped in 2010 before reaching the target sample size, at the recommendation of its data and safety monitoring committee according to prespecified stopping rules for the efficacy of prenatal surgery. Results of the trial were reported[1] based on 158 women who had undergone randomization before July 1, 2009, as this was the cohort analyzed for the data and safety monitoring committee. Findings in that report demonstrated a significant improvement in the primary outcomes at 12 and 30 months of age, and in multiple secondary outcomes, including reversal of hindbrain herniation and ambulation by 30 months, in the prenatal repair group. However, prenatal surgical intervention was associated with significantly higher rates of oligohydramnios and chorioamniotic separation, as well as spontaneous membrane rupture (SROM) and preterm delivery (PTD) ($P < .001$). Moreover, of those in the prenatal surgery group, only 64% had an intact, well-healed hysterotomy site from the prenatal repair surgery observed at cesarean delivery.

The initial MOMS report summarized the pregnancy outcomes of 86% of the 183 randomized women. The primary objective of the current report is to update the final pregnancy outcome results from the MOMS trial, as well as to analyze risk factors for preterm premature rupture of membranes (PPROM), SROM at any gestation, early preterm delivery (PTD), and uterine dehiscence among those women who underwent prenatal repair. It is the authors' view that these additional components are anticipated to enhance the knowledge of benefits, risk assessment, and informed consent process for future families considering fetal myelomeningocele repair, where maternal and fetal characteristics match those set forth in the inclusion and exclusion criteria of the trial.

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Materials and Methods

Study population and design

Patient recruitment, study procedures, details of the primary and secondary outcome parameters, as well as the perioperative management algorithm for prenatal myelomeningocele surgery were described in detail in the previous MOMS trial publication.[1] Briefly, eligible pregnant women with a fetus diagnosed with myelomeningocele and between 19−25 weeks of gestation were randomized at 1 of the 3 MOMS clinical centers to either prenatal or postnatal surgical repair. Women randomized to the postnatal surgery group went home and returned at 37 weeks of gestation to their maternal-fetal surgery center for cesarean delivery and postnatal repair by the center's neurosurgical team. Given the anticipated increased risk of preterm labor, patients randomized to prenatal myelomeningocele surgery remained close to the MOMS center to permit standardized management after the surgery, including tocolysis therapy, weekly ultrasound evaluations, and delivery at 37 weeks of gestation if still undelivered. In addition to the usual content of a prenatal care visit and assessment of postsurgery maternal well-being, a targeted ultrasound was performed to evaluate amniotic fluid volume and the status of the hysterotomy and membranes, to assess for potential oligohydramnios, dehiscence, or chorioamniotic membrane separation (CMS), during the weekly outpatient visits.

When CMS was seen by ultrasound, patients were placed initially on outpatient bed rest. If the membrane separation progressed and extended to the placental cord insertion site, patients were admitted and placed on bed rest, with fetal heart rate testing obtained every shift or if decreased fetal movement was reported by the patient. Diagnosis of oligohydramnios was managed by hospital admission with assessment of fetal heart rate or nonstress tests every shift when the amniotic fluid index was <5 cm. Tocolytic therapy using indomethacin <32 weeks' gestation and/or magnesium sulfate was initiated for palpable contractions with documented cervical change. Preterm labor unresponsive to tocolytics or due to chorioamnionitis, suspected uterine rupture, placental abruption, or a nonreassuring fetal status was treated by cesarean delivery. If the patient experienced rupture of membranes at <34 weeks of gestation, she was managed expectantly until 34 weeks of gestation at which time she was delivered by cesarean delivery. If preterm labor was diagnosed and the likelihood of delivery was high <32 weeks (eg, PPROM, vaginal spotting, or nonreassuring antepartum fetal surveillance), a single course of betamethasone therapy was given to minimize complications of prematurity.

At 37 weeks' gestation, delivery took place by elective cesarean delivery because of the presence of the hysterotomy scar. Although the same abdominal laparotomy incision was used for the cesarean delivery as for the prenatal surgery, the fetus was preferably delivered via a lower uterine segment incision.

Statistical analysis

The updated analysis comparing the prenatal vs postnatal repair groups was performed according to the intention-to-treat principle. Relative risks and 95% confidence intervals were calculated.

For the analysis within the prenatal repair group of risk factors for adverse

TABLE 1
Demographic data and baseline characteristics

	Prenatal surgery N = 91	Postnatal surgery N = 92
Fetal sex female	42 (46.2)	57 (62.0)
Gestational age at randomization, wk	23.7 ± 1.4	23.9 ± 1.3
Maternal age at screening, y	29.2 ± 5.2	28.7 ± 4.8
Race/ethnicity		
White non-Hispanic	85 (93.4)	86 (93.5)
Black non-Hispanic	1 (1.1)	1 (1.1)
Hispanic	3 (3.3)	4 (4.3)
Other	2 (2.2)	1 (1.1)
Married or living with partner	84 (92.3)	86 (93.5)
Education, y	14.9 ± 1.7	14.9 ± 1.7
Body mass index at screening, kg/m^2	26.3 ± 3.7	26.3 ± 3.9
Currently smoking	6 (6.6)	5 (5.4)
Either parent with familial history of NTD	9 (9.9)	16 (17.4)
Nulliparous	37 (40.7)	37 (40.2)
Previous uterine surgeries, including cesarean	12 (13.2)	11 (12.0)
Cervical length—transvaginal, mm	39.5 ± 7.6	39.4 ± 5.9
Anterior placenta	43 (47.3)	39 (42.4)
Lesion level L3 or lower	62 (68.1)	76 (82.6)
Any clubfoot on ultrasound	24 (26.4)	19 (20.7)

Intent-to-treat analysis of full randomized cohort.

Data presented as n (%) or mean ± SD.

mm, millimeters; *N*, number; *NTD*, neural tube defect; *wk*, weeks; *y*, years.

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