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MATERNAL AND FETAL/ INFANT PROGNOSIS AFTER INTRAUTERINE SURGERY FOR CORRECTION OF MYELOMENINGOCELE

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Abstract: Myelomeningocele is the most severe and common form of spina bifida. Historically, repair was performed after birth, but fetal surgery has emerged as a promising alternative. The 2011 MOMS study showed that intrauterine surgery reduced the need for shunt and improved motor and mental function, but also presented risks such as prematurity and maternal complications. Objective: To evaluate whether intrauterine surgery for myelomeningocele repair positively impacts maternal and fetal/child prognosis compared to postnatal repair. Methodology: Literature review in PubMed and Cochrane Library platforms with specific descriptors, excluding duplicates and irrelevant articles, resulting in 10 selected studies. The MOMS (Management of Myelomeningocele Study) study was manually added. Discussion: Comparisons between studies from Zurich and MOMS showed similar results, although fetal surgery is associated with complications such as hematomas and oligohydramnios. The experience of the surgical team is crucial for the results. Studies have shown that prenatal surgery resulted in a reduced need for cerebrospinal fluid diversion and improved mobility in children. Recent studies indicate that the fetoscopy technique can provide neurological results similar to hysterotomy, with some differences in complications and surgical time. The MOMS2 study (2012-2017) confirmed that the benefits of fetal surgery are maintained until school age, with improved physical function and self-care skills in children operated on intrauterinely. Conclusion: Intrauterine surgery for myelomeningocele correction improves child prognosis, especially in neurological development and motor function. The experience of the team and the surgical center is fundamental to the results. Additional studies are needed to compare the different surgical approaches and validate these findings with greater scientific rigor.

Keywords: myelomeningocele; intrauterine surgery; prognosis.

INTRODUCTION

Myelomeningocele is the most severe and common form of spina bifida, which is the most common congenital anomaly of the central nervous system (CNS) compatible with life. It is characterized by the extrusion of the spinal cord by a partial closure of the embryonic neural tube with an opening into a dorsal sac containing cerebrospinal fluid (CSF), with consequent lifelong disability[1,2]. Historically, the surgical procedure to correct this spinal injury was performed shortly after the child was born (postnatal repair). However, fetal surgery has proven to be a good option for surgical approach, especially after the Management of Myelomeningocele Study (MOMS), published in 2011. [3]. It is suggested that lesions in the nervous system as a whole worsen with advancing gestational age. As time progresses, paralysis of the lower limbs (LL), worsening of hydrocephalus and rhombencephalic hernia may occur[1].

Indeed, MOMS was a landmark prospective randomized controlled trial comparing prenatal to postnatal meningomyelocele repair. The work of 158 patients showed that intrauterine surgery resulted in reduced shunt requirements, improved mental development scores and motor function, and improved secondary outcomes such as the incidence of brain herniation and ambulation at 30 months. However, prenatal repair was associated with maternal and fetal risks, with higher rates of prematurity, premature rupture of membranes, intraoperative complications, higher rates of maternal transfusion at delivery, and scar defects. [1,2,3,4,5]. Furthermore, MOMS included only open fetal surgery, based on hysterotomy, in the study, while other approaches, such as fetoscopy, have subsequently emerged. Given the rapid development of these approaches,

the maximum time for evaluating children in the aforementioned study up to 30 months, and the fact that the population evaluated was restricted to only three maternal-fetal surgery centers in the USA (Children's Hospital of Philadelphia, Vanderbilt University, and University of California), evidence is needed to guarantee the safety and efficacy of intrauterine surgery for the correction of myelomeningocele[1,3].

OBJECTIVE

To assess whether intrauterine surgery for myelomeningocele correction has a positive impact on maternal and fetal/child prognosis compared to repair performed after birth.

METHODOLOGY

A literature review was carried out by searching the PubMed and Cochrane Library platforms on March 1, 2022, using the descriptors "fetal", "surgery", "myelomeningocele", and "prognosis". The filters "free full text" and "the last 5 years" were included, and the Rayyan platform was used to exclude duplicate articles. Thus, a total of 24 results were found. Of these, 14 were excluded by title, as they addressed topics that diverged from the objective of this study, and 1 article was excluded by text, as it only presented procedural techniques for prenatal correction of myelomeningocele. The study MOMS – Management of Myelomeningocele Study, published in March 2011 by Adzick NS et al., was manually added because it was frequently cited in the search results. Thus, 10 articles were selected for this review.

DISCUSSION

A study compared the results of treatment of myelomeningocele by fetal surgery in Zurich, Switzerland, with those obtained at MOMS. There was no statistically significant difference in most variables. After birth, a higher incidence of epidermoid cysts (28 vs. 3%, $p = 0.004$) and higher gestational age at birth were found in the Zurich group (35.6 vs. 34.1 weeks, $p < 0.0001$).) [5]. Two other studies have questioned the experience of the team and the surgical center in open correction of fetal myelomeningocele (fMMC) as an influence on maternal and fetal outcomes 6,7. The first evaluated the initial 8 years of the procedure in a fetal medicine center in Switzerland, stratified by training phase (2010–2014, 15 cases) and experienced phase (2014–2018, 52 cases). There was no significant difference between the two groups regarding gestational age at delivery, chorionic membrane separation, or incidence of placental abruption. Surgical complications, such as subchorionic hematoma (20 vs. 2%, $p = 0.009$), oligohydramnios (27 vs. 8%, $p = 0.046$), with MRI-confirmed leak (13 vs. 4%, not significant) were more common in the training phase[6]. The second, conducted in Poland, showed that increasing surgical team experience significantly decreased the risk of iatrogenic preterm labor (iPTL) ≤ 30 weeks of gestation (regression from 34.1% in the initial period, 2005-2011, to 23.9% in the period 2012-2015) with $p < 0.05$[7].

Worley et al. compared groups of children undergoing intrauterine versus postnatal surgery with respect to the frequency of neurosurgical procedures to treat comorbid conditions of myelomeningocele. They found that prenatal surgery was correlated with lower frequencies of CSF diversion (46% vs 79%; incidence rate = 0.61; 95% CI 0.53-0.71; $p<0.01$) and Chiari II malformation decompression (3% vs 7%; incidence rate

= 0.41; 95% CI 0.19-0.88; p=0.02) than postnatal surgery (n=644). The median age of last evaluation of these children was 4 years of age. [8]. Lala et al. used data from eight different surgical centers that performed prenatal repair of spina bifida using the SAFER percutaneous fetoscopic technique (in São Paulo (Brazil), Los Angeles (USA), Petah Tikva (Israel), Santiago (Chile), London (UK), Milan (Italy), Miami (USA) and New York (USA)). As a result, children in the prenatal repair group using SAFER percutaneous fetoscopic had similar long-term neurological outcomes in relation to what is described in the literature regarding the hysterotomy procedure. 103 children were evaluated at 12 months and 30 months. 54.13% of the children at 12 months did not require ventriculostomy, 54.2% walked independently and 61.0% did not require chronic intermittent bladder catheterization at 30 months[9].

A publication that included 127 US patients with open neural tube defects, of whom 93 underwent intrauterine surgery (51 fetoscopic and 42 open hysterotomy) and 34 underwent postnatal repair, found that prenatal repair prevents deterioration of lower limb motor function. In the prenatal surgery group, patients with intact motor function at referral (81% (75/93)) were proportionally similar to those at 6 weeks' gestation (74% (64/87)), before birth (74% (42/57)), at birth (68% (63/93)), and at 12 months of age (67% (39/58)) $p < 0.05$. Children who underwent postnatal repair showed motor worsening at the end of the third trimester of pregnancy, which remained in both study assessment cutoffs: after birth (S1 (L1–S1) vs L4 (L1–S1); $P < 0.01$) and at 12 months of age (S1 (L1–S1) vs L4 (L1–S1); $P < 0.01$) [10].

A study called MOMS2 was conducted between 2012 and 2017 at the same 3 clinical sites as MOMS and aimed to evaluate the physical functioning compared between the prenatal and postnatal repair groups of children with myelomeningocele aged 5 to 10 years. To this end, 154 children were recruited (78 children with postnatal repair and 76 with prenatal repair) and examiners assessed their physique, characteristics, self-care skills, neurological function and mobility. It was found that the benefits in physical functioning of children undergoing prenatal surgery for myelomeningocele reported at 30 months of age in MOMS persisted into school age. The prenatal repair group had better self-care skills competence (mean maximum FRESNO Scale score, 90.8% vs 85.5%), better ambulation according to the Modified Hoffer classification (51.3% prenatal vs 23.1% postnatal), faster 10-m 1-s walk test (difference in medians, 1.0; 95% CI, 0.3-1.7), superior gait quality (95% CI, 1.14-2.54), and higher-level mobility skills (95% CI, 1.97-11.18) [4].

A systematic review of 27 publications between 2011 and 2021 showed updates on myelomeningocele repair in the 10-year period after MOMS. According to the authors, the results of MOMS must be considered an early experience with fetal surgery. Many surgical centers in the post-MOMS period continued with postnatal repair with excellent results. Some studies compared fetoscopy vs. open surgery and demonstrated that the former resulted in longer surgical time, higher risk of prematurity, and the need for additional postnatal procedures. The study also reports superfluous and conflicting results, for example, gestational age at delivery in fetoscopy surgery, in one publication an average of 32 weeks and in another an average of 38 weeks.

Furthermore, the follow-up interval of children after birth fluctuated considerably, making it impossible to compare information and, due to the lack of uniformity in data reporting, it was not possible to perform a substantial statistical analysis of treatment strategies related to prognosis[2].

CONCLUSION

Intrauterine surgery for myelomeningocele repair appears to have a positive impact on infant prognosis compared to postnatal repair, especially with regard to neurological development, including lower limb motor function. The experience of the team and the surgical treatment center was closely related to maternal and fetal prognosis, considering gestational age at birth and the need for further surgical interventions after birth, which, in comparison with the postnatal approach, had divergent results. Therefore, interpretations of studies published after MOMS must be cautious, and further studies with a high level of scientific evidence need to be conducted to evaluate the advantages and disadvantages of postnatal surgery and the various subtypes of intrauterine approach for the treatment of myelomeningocele that have emerged in recent decades.

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