Fetal Surgery: Review

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Abstract – About 1% of all pregnancies have structural abnormalities. During the last thirty years, different experimental studies in large animals, related with the development of diagnostic imaging and fetoscopy, have prompted incredible advancement in the pathophysiology of different birth defects. Such knowledge applied to intrauterine correction of anomalies has changed the natural history of a several already deadly illnesses, prompting an extensive number of survivors. Fetal intervention, like open fetal surgery, might be demonstrated in meningomyelocele or in inherent cystic adenomatoid malformation, and in sacrococcygeal teratoma, which lead to secondary fetal hydrops. Furthermore, minimally invasive procedures using fetoscopy may have application in an inborn diaphragmatic hernia, in feto-fetal transfusion, in twin pregnancies with acardiac fetus, in the posterior urethral valve, and in hypoplasia of the cardiovascular chambers, with great outcomes. Despite minimally invasive procedures the fact that open fetal surgery and minimally invasive procedures are as yet experimental and still should be completely approved, the correct ultrasound diagnosis and the patient's referral to tertiary centers giving multidisciplinary fetal services add to the survival of fetuses with inherent diseases of generally fatal evolution.

Keywords – Congenital abnormalities/surgery; Fetus/abnormalities; Fetus/surgery; Fetoscopy.

INTRODUCTION

The presence of a genuine birth deformity is a personal and family fatality that conveys high social and financial expenses for the country. The risk of a chromosomal anomaly or structural anomaly fluctuates somewhere in the range of 0.5 and 2% of total pregnancies [1]. By far most of birth defects should be corrected at birth, and the indication for fetal intervention will rely upon the gestational age at diagnosis, the presence of associated deformities and maternal conditions. congenital deformities that are manageable to fetal treatment can be acted in the classic way, by open maternal-fetal surgery, or in a minimally invasive procedures, by means of fetoscopy [2].

Open fetal surgery is experimentally indicated in meningomyelocele or in defects that cause secondary fetal hydrops, as in congenital cystic adenomatoid malformation (MACC), when cardiac compression occurs, or in sacrococcygeal teratoma (TSC), when tumor started bleeding [3-5].

Minimally invasive procedures intervention is shown in the pregnancy of monozygotic twins with feto-fetal transfusion, in twins with one of the acardiac fetuses [6], in inborn diaphragmatic hernia [7], in bilateral obstructive uropathies and in heart diseases that lead to hypoplasia of the cardiac chambers.
EXIT (ex-utero intrapartum treatment) is a strategy, with the fetus is intubated by cesarean section before the umbilical cord is cut, which guarantees the airway route penetrability of the infant during delivery, to avoid acute respiratory failure and death at birth [8].

I. OPEN FETAL SURGERY

The improvement of intrauterine surgery happened in the mid-1980s at the University of California, San Francisco (UCSF), United States. The basis of the careful standards happened in large animal models, in which it was conceivable to comprehend the pathophysiology of a several birth defects and the potential for fetal correction. Such standards permitted the improvement of the prenatal ultrasound diagnosis, the assurance of the natural history of the defect, the making of choice rules for fetal intervention, notwithstanding the capability of sedative, tocolytic and surgical techniques that culminated in the performance of fetal surgery in humans [9-11].

The underlying involvement with UCSF for the treatment of fetal correction of intrinsic diaphragmatic hernia (HDC) utilizing open hysterotomy permitted us to infer that the course to fetal amendment was conceivable, however it included extensive maternal morbidity and high fetal mortality related to premature labor [12].

Obstetric information permitted to reason that the risk of death for the pregnant woman submitted to fetal surgery was equivalent to the risk of a cesarean section. Fetal parameters permitted us to presume that the risk was subject to the kind of intrinsic defect, and that the significant reason for fetal death was identified with premature rupture of membrane. Moreover, no pregnant woman had her fertile life compromised after fetal medical procedure, with a fertility index of 100% for patients who attempted another pregnancy. Of 45 worked patients, there was no maternal death, and 35 of them maintained fertility and new pregnancies after the initial procedure; the others didn't need a new pregnancy [13].

In the United States, the National Institute of Health (NIH) limits the sign of open fetal surgery in some college places in the multcenter study called Management of Myelomeningocele Study (MOMS) when pregnancy is somewhere in the range of 20 and 25 weeks for correction of meningomyelocele, or in rare cases of tumor masses prompting xx intrauterine hydrops. Among cases of meningomyelocele, fetal correction can prompt diminished hydrocephalus and decreased need to utilize the ventriculo-peritoneal bypass valve in the neonatal period, notwithstanding the possibility of acquiring some functional degree of spinal cord injury.

In defects that lead to secondary fetal hydrops, like MACC and TSC, there is a need to weigh the risk and the advantage between the expectation of delivery that can happen near extreme prematurity (> 26 to 28 weeks) and the chance of fetal intervention (<26 weeks).

1.1-Open fetal surgery to correct meningomyelocele

Dysraphism is a defect in the development of the neural tube, which shows itself as a failure in the complete fusion of the spinal arches of the spinal column, prompting dysplastic development of the spinal cord and meninges. Among the different types of presentation of dysraphism, there are spina bifida, meningocele and meningomyelocele (MM) [14].

This congenital anomaly is related with serious deficiencies, including motor inadequacies for its most varied degrees, skeletal deformations, bladder and intestinal incontinence, sensory deficiencies beneath the level of the lesion. Hydrocephalus, thought about the most serious alteration, occurs secondary to the Arnold-Chiari abnormality (AC), which comprises of a complex anomaly of the posterior fossa, described by permanent herniation of the bulb and cerebellum through the foramen magnum passing into the cervical spinal canal.

Hydrocephalus presents fluctuating levels of neuropsychomotor retardation, due to some degree, to the severity of the injuries that influence the spinal cord before birth, and to some extent, to the expansion in intracranial pressure [15,16]. As a result, patients born with MM have a normal life span of under 40 years and an extensive decline in their quality of life [17].

To date, it is realized that intrauterine MM adjustment in humans can switch CA, with the possibility to restrict the movement of hydrocephalus, lessening the utilization of ventriculoperitoneal leads (DVP) and the consequent complications from delayed utilization of DVP catheter. In any case, surgery for fetal correction of MM, because of its technical peculiarity, presents inherent maternal-fetal risks, like operative complications, premature labor, chorioamnionitis, rupture of uterine membranes, uterine rupture, results of tocolytics and need for cesarean deliveries for all subsequent pregnancies [18,19].
MM results from a deformity in the end of the posterior portion of the neural tube, neurulation interaction - a cycle that is finished around the 30th day of pregnancy. As indicated by the "two-hit hypothesis" theory proposed by Heffez et al. [20,21], the essential occasion that leads to the exposure of neural components causes defective development of the spinal cord, myelodysplasia, while a secondary occasion, causing erosion and necrosis of the uncovered district, prompts expanding damage with the progression of pregnancy [10,20, 21].

This speculation is affirmed by observations that the neural injury acquired during fetal life is disturbed by mechanical injury or by the chemical toxicity of the amniotic liquid [22]. Albeit the fetus has a high capacity for tissue repair, the healing of the dysgraphic defect doesn't happen in utero, it just happens successfully after birth [23]. It is the previously mentioned optional occasion that can be prevented or even turned around through fetal surgical intervention.

The rate of MM is roughly 1 for each 1,000 live births [24,25]. Fetal diagnosis is generally performed by methods for ultrasound or magnetic resonance imaging in the routine prenatal assessment, and MM would already be able to be recognized from the 16th week of pregnancy [26].

Neonatal surgical correction is the only treatment accessible for patients with MM. Nonetheless, because of the seriousness of the neural tube deformity, surgery has not been effective in the feeling of keeping away from the neurological sequelae that require uncommon consideration for the influenced children and the large expenses with medical follow-up.

In 1985, the expense of care for individuals with MM has surpassed $ 200 million every year in the United States alone [27]. What's more, even with standard surgical treatment, roughly 14% of children with the defect don't make due past 5 years old, expanding this mortality to around 35% in those with brainstem dysfunction secondary to AC malformation [28].

A several experimental models have been developed to study fetal MM. At first, we looked to examine the mechanisms of trauma that occur secondary to intrauterine exposure of the meninges. Potential etiologies that arose out of these studies include: chemical injury brought about by amniotic liquid, direct mechanical injury to the spinal cord and injury through the hydrodynamic pressure of the (CSF) in the subarachnoid space [29].

This was the primary experiment on large animals, showing that the creation and correction of intrauterine MM is practical. Such discoveries strengthened the theory that the uterine environment has significant role in the destruction of neural tissue, and that the repair of the defect may permit neurological functional preservation [22].

Viewpoints for the minimally invasive treatment for the adjustment of MM have been created in sheep models and may give subsidies to reduce the surgical trauma of open fetal surgery [30].

Albeit the revision of fetal MM is plausible and shows some encouraging viewpoints applicable to spinal cord damage and diminished utilization of DVP, the outcomes actually should be approved until admitted as an alternative surgical treatment, when compared to conventional neonatal correction.

II. MINIMALLY INVASIVE PROCEDURES WITH FETOSCOPE

2.1- Fetoscopy for congenital diaphragmatic hernia

Congenital diaphragmatic hernia (HDC) is a defect in diaphragmatic embryogenesis that influences approximately 1: 2,500 live births and establishes 8% of the main congenital anomalies [31].

HDC occurs because of a defect in the closure of the posterolateral foramen of the diaphragm, with the entry of abdominal organs to the inside of the chest. The herniation of the abdominal organs goes about as an expansive lesion, compressing the lung and leading hypoplasia and a defect in lung development [32].

HDC mortality ranges from 32 to 62%. Nonetheless, it is assessed that roughly 1 out of 2,000 conceptions don’t reach a conclusion because of associated complications and that, notwithstanding late advances in the treatment of HDC and its complications, mortality stays high because of pulmonary hypoplasia and hypertension (PH) [33, 34].

The therapeutic possibilities for HDC comprise of pre, peri and postnatal treatment and involve the surgical act followed by clinical treatment, which in severe cases may utilize pulmonary surfactant, high- frequency ventilators and extracorporeal membrane oxygenation (ECMO) to attempt limit severity of associated PH [35].
New strategies have been created with the point of promoting the development of the intrauterine lung and diminishing neonatal mortality from HDC; among them, there is the fetal trachea (OT) occlusion [36]. Experimental OT studies have shown that the inability of fetal intratracheal liquid to stream promoting growth of the fetal lung parenchyma [37] with a decrease in arterioles [38,39]. The decrease in impedance to blood stream saw in sheep with HDC proposed that there would be a chance of inversion in pulmonary hypertension. In this manner, OT seemed to reduce vascular resistance, accelerating capillary and alveolar growth, reversing changes in the pulmonary vessels of HDC [40].

The odyssey for improving lung development started with open fetal surgery procedure, which proved to be impracticable given its high mortality because of the folding of the umbilical cord vessels. The present circumstance was distinguished after the return of the liver, which was at first situated inside the chest to the fetal abdomen. At that point, still with open a surgery procedure, the idea of OT with metal clip applied externally to the trachea was presented. This intervention was very traumatic for the fetus and caused numerous neonatal complications. A similar methodology began to be performed laparoscopically and was called FETENDO; later, the OT with outer clip was replaced by the situation of an intratracheal silicone balloon.

Both for the expulsion of the clip and for the position of the intratracheal balloon, it was important to make a methodology that comprised of performing the cesarean area with staplers of absorbable threads, partially removing the embryo from the uterus, around until the epigastric region, performing surgical removal. clip (after the balloon), perform a safe tracheal intubation, followed by ligation of the umbilical cord at birth. This strategy was called EXIT [41].

FETENDO was deserted because of the high incidence of premature rupture of membranes, and its failure was ascribed to the nature of laparoscopic instruments, as there were no small caliber optics. With the improvement and capability of laparoscopic instruments, which occurred at the Catholic University of Leuven, Belgium, it was conceivable to put a similar balloon with minimally invasive material; the strategy was called FETO (from the English "fetoscopic tracheal occlusion ") [42].

The advancement of the technique for fetal OT has improved the prenatal ultrasound diagnosis, which evaluated the level of pulmonary hypoplasia by estimating the relationship between the lung area and the cranial circumference, or lung to head ratio (LHR) [43], and by intra-thoracic liver position [44]. Therefore, fetuses with HDC with LHR <1.0 and liver inside the chest (liver up) have minimal chance of survival.

The sign for FETUS, performed between the 26th and 28th weeks and eliminated at 34 weeks, is limited to the LHR underneath 1.0, related with the presence of the liver inside the chest (liver up). These standards expanded the survival of fetuses with HDC by50% [45].

Albeit the sign of FETUS has expanded the survival of fetuses with HDC, it has not yet become a standard technique for treating the defect. The combination of prenatal and postnatal procedures, particularly the capability of neonatal ventilation and a better understanding of the mechanisms of lung growth, may better approve the technique for fetal intervention, when compared with the selective neonatal treatment of babies with this defect.

2.2-Fetoscopy for fetal fetus transfusion

Twin pregnancies have a higher risk of morbidity and mortality than single pregnancies, particularly in monochorionic pregnancies [46]. The recurrence of monozygotic twins is consistent around the globe and influences roughly 3.5 by pregnancies. In the United States, it influences 1 in each 85 pregnancies, 70% of which are dizygotic and 30% homozygous [47].

Monochorionic pregnancy needs a lot of consideration in prenatal ultrasound determination, particularly in the first trimester, because of the risk of developing fetal fetus transfusion syndrome, or TTTS (from the " twin twin transfusion syndrome ") [48]. TTTS influences around 10 to 15% of monzygotic twins. The communication network between placental vessels, which causes changes in blood stream from one embryo (donor) to the other (recipient), is the main cause of TTTS [49,50].

The donor fetus is hypovolemic, oliguric, with differing levels of growth restriction and with oligohydramnios, while the recipient baby is hypervolemic, reaching hydrops, polyureic and polyhydramnios; thusly, the diagnosis of TTTS is made by inconsistency between the volume of the cavities on the prenatal ultrasound assessment, and its severity can be characterized in a several stages [51].
TTTS is related with an increased risk of miscarriage and perinatal demise. Whenever left untreated, it can reach 90% of death or cause severe sequelae at birth. The morbidity among survivors includes cardiomyopathy, renal failure and neurological sequelae, especially if one of the twins has evolved to death [47].

Traditional treatment for TTTS with the utilization of aggressive amnioreduction has shown extremely differed survival rates, as the data are generally retrospective studies, with wide variety in gestational ages at treatment [52]. Besides, the system of how amnioreduction can improve TTTS isn't known. Notwithstanding, it is realized that the seriousness of TTTS and the gestational age of the determination significantly affect survival; that is, the earlier the finding, the worse prognosis [53].

Fetoscopy laser treatment, advancing the removal of vascular anastomoses, is the best treatment accessible [54], and the outcomes have shown that the procedure is better than amnioreduction, particularly in especially in cases of earlier diagnosis [7].

2.3-Fetoscopy for acardiac twin fetus

Twin pregnancy with acardiac fetus is another uncommon sign of fetoscopic laser treatment. Acardiac fetus influences 1 in each 35,000 pregnancies and occurs just in monochorionic twins [55]. A cardiac fetus is constantly deformed, with changes in the spine and skull and, particularly from the first trimester, the phenomenon of TRAP (from the English "twin turned around blood vessel perfusion") can occur.

The TRAP grouping can be clarified as follows: the deoxygenated blood of the normal fetus goes from the heart to the placenta by means of the umbilical arteries, an arterio-blood vessel anastomosis of the placenta sends oxygen-poor blood backwards to the umbilical arteries of the acardiac fetus, entering the fetal body through the hypogastric veins. Complete blood hypo-oxygenation keeps on streaming in a retrograde manner from the chest area, and gets back to the placenta by means of the umbilical veins. A placental venous anastomosis finishes the dissemination back to the twin, as though it were a pressure pump [47]. The diagnosis of TRAP can be made with the guide of doplervelocimetry, making it conceivable to recognize the retrograde direction of the flow of the acardiac fetus [56].

Treatment can be performed by radio-ablation of the fetal umbilical cord [57] or by laser fetoscopy, which expanded the survival of the normal fetus by 80%, with 67% of pregnancies arriving at term [58].

2.4-Fetoscopy to correct fetal urinary obstruction

The rate of fetal obstetric uropathy is around 1 for each 800 pregnancies [59]. Little advancement has been made in the management of fetal obstructive uropathies, the inferior ones, which lead to bilateral renal impairment. The relationship of chromosomal anomalies with obstructive uropathies fluctuates somewhere in the range of 8 and 23% [60]. Pulmonary hypoplasia and prematurity are the significant reasons for mortality in bilateral obstructive uropathy due to oligohydramnios and, because of the distention of the fetal diaphragm brought about by the urinary tract that prevents lung growth. Mortality in the posterior urethral valve (VUP) is 45% and, when added to different reasons for lower urinary obstruction, it can reach at 95% [61-63].

The fetal ultrasound diagnosis of the obstruction can be made as early as of 16th week of gestational age and, when bilaterality, hydramnios and echo graphic parts of the renal parenchyma [64] have been diagnosis, sequential fetal bladder punctures might be demonstrated to evaluate function kidney and its level of weakness [65]. Decreased solute reabsorption, increased protein catabolism, increased substance loss and the level of hypertonicity in fetal urine are positively connected to the level of renal histological impairment [66,67].

Circumstances in which the finding is early and there is an adjustment in the echogenicity of the renal parenchyma, with deteriorating of the capacity of renal urinary organic chemistry, are liable to vesicoamniotic derivatio, in order to preserve postnatal renal function [68].

The best fetal correction experience for fetal VUP is from the Tampa Fetal Diagnosis and Therapy Institute in Florida, United States. The sign for laser removal of the urethral valve by fetoscopy is shown in early instances of loss of renal capacity [68].

Fetal urinary obstruction stays a significant experience for perinatologists. The troubles both in building up the right determination and in knowing the level of renal debilitation that is adequately identified with neonatal capacity actually should be better clarified.
Currently, a randomized controlled examination called Percutaneous Lower Urinary Tract Obstruction (PLUTO) is being created, which will survey fetal urinary biochemical markers to relate with postnatal capacities, having the option to set up the real role of fetal urinary diversion [69].

2.5-Fetoscopy for fetal aortic or pulmonary valve dilation

Fetuses with heart defects that evolve to hypoplasia of the right or left cardiovascular chamber have a 60% survival in five years [70]. Fetal valvuloplasty might be shown for progressive heart disease with poor prognosis, like serious aortic stenosis, left hypoplasia condition with intact or with atrial septum defect (ASD), and pulmonary atresia with intact ventricular septum. In the last defect, it is hypothetically possible that fetal decompression with a reasonable ventricle and fistula may result in its regression before birth, allowing circulation in both ventricles [71].

In aortic stenosis, the point of treatment is to blow up a balloon through the aortic ring, causing expansion so that there is a better ejection of blood flow through the valve [72]. In left cardiac hypoplasia with an intact or restrictive atrial septum, and the formation of a septostomy > 3 mm was related with better neonatal oxygenation and with less requirement for urgent surgery procedure, yet fetal intervention didn’t increase the survival of this defect [73].

In the United Kingdom, the National Institute for Health and Clinical Excellence (NICE) has the guide for fetal cardiovascular intervention. The improvement in the methods of fetal cardiovascular puncture and capability permit us to accept that fetal heart intervention is new frontier and has good prospects for selected cases in hypoplasia of cardiac chambers [74].

In the course of recent years, propels in fetal intervention have permitted an expansion in the survival of patients with various congenital anomalies. A significant number of these interventions are as yet viewed as experimental methods and there is a requirement for bigger arrangement and randomized studies to approve the complete use of these new treatments. Patients with prenatal diagnosis of defects and subject to intervention ought to be referred to tertiary centers of fetal medication where there is multidisciplinary checking with qualified trained professionals, to give the best treatment to the mother and the fetus.

III. CONCLUSION

Therapeutic fetal surgery has a set of experiences that presently extends for more than 50 years. All through that time, there has consistently been debate about patient choice and the ideal methodology. These discussions proceed to the present time, despite incredible advances in the strategies for open fetal surgery and the expanding alternatives for minimally invasive procedures.

Nonetheless, the genuine Achilles heel for a fetal medical procedure is the way that the human amnion doesn't heal, leading to a significant incidence of premature rupture of the membranes, amniotic liquid hole and unexpected labor. This will stay an issue until some way is found to amniotic healing, or to effectively plug the holes. As right on time as 1974, Low recommended that "the pediatric specialist ought to, in this way, not stop at neonatal nor fetal anomalies, however perhaps begin messing with removing a gene: here and embedding one there, … perpetually endeavoring to improve the quality of life … " [75]. That objective is crawling unyieldingly ever closer. It offers the chance of anticipation or early treatment. It may yet tackle the issue of healing for the amniotic layer.

The authors strongly support the concept that, where possible, progress should be based on prospective randomized trials and, where trials are not possible, accessible registries. It is to be hoped that this advice is heeded.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

AUTHORS CONTRIBUTION

Authors have equally participated and shared every item of the work.

REFERENCES


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