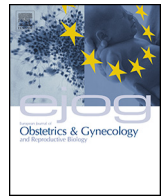




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Review article

Delivery after fetal death in women with earlier cesarean section. A review

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ABSTRACT

The clinical management of intrauterine fetal demise (IUFD) in women with a previous cesarean delivery presents a dilemma for the obstetrician. With the current reluctance of obstetricians to perform vaginal birth after cesarean (VBAC) and the paucity of data to counsel women regarding maternal risks, management options are limited by physician's clinical experience and biases. In the setting of fetal demise, maternal safety becomes the primary concern. Medicolegal pressures may prevent physicians from attempting a trial of labor in this situation.

In this review we will a focus on frequency of birth with IUFD after cesarean section (CS), we discuss the options (VBAC vs CS), different complications, methods for induction of vaginal birth as well as risk factors of vaginal birth and cesarean delivery.

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Definition

In this article we describe obstetric outcomes in a group of patients with singleton pregnancies with a prior CS and an antepartum IUFD of equal or greater than 22 weeks of gestation or 500 g. In some articles the lowest level of gestational age of new-born is 20 weeks, but for example in African countries the lowest gestational age is 28 weeks.

Incidence

The reported incidence of stillbirths varies significantly between studies from different countries and depends on the

definitions used. From a global estimate of 2.6 million stillbirths in 2015 with a stillbirth rate of 18.4 per 1000 births, the majority occurred in the developing world. For example, India accounted for the highest number of stillbirths [1].

With the rising rate of CS, for example in the USA now reaching over 30 % and fetal demise occurring in 0.6 % of deliveries, the occurrence of a fetal demise in a patient with a prior CS is becoming more prevalent [2]. Based on a study from USA, from a sample of 45,988 women who had a singleton gestation and a history of CS, 209 (0.45 %) were identified with a singleton antepartum IUFD of equal to or greater than 20 weeks of gestation or 500 g [2].

Vaginal versus cesarean delivery

In the Nordic countries the primary goal is to deliver vaginally in cases of an IUFD after a previous CS. However, considering safety

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and legal issues, the situation is different in other countries for example in USA. Medicolegal pressures may prevent physicians from attempting a trial of labor in this situation. In the setting of fetal demise, maternal safety becomes the primary concern.

In the stressful situation of an IUFD, the options are either to await the onset of spontaneous labor or to induce labor. It may take several weeks for spontaneous expulsion. It is well known that complex emotional factors are associated with fetal loss. Retention of the fetus can be associated with emotional distress, intrauterine infection if membranes are ruptured, and a time related risk of consumptive coagulopathy. This becomes more difficult when IUFD occurs in a woman with a prior CS [2]. For example, in an Indian study, a large majority (84.6 %) of women with an IUFD required induction of labor [3]. This study is quite small, and the results need to be confirmed in future studies.

In women with IUFD and prior CS, prevention of maternal morbidity is important. Repeated CS, in women who plan future pregnancies, may increase the risk of uterine rupture, placenta accreta and morbidity related to multiple abdominal surgeries. Women who deliver vaginally successfully have less postpartum discomfort, shorter hospital stays and shorter periods of disability than women who undergo repeated CS [4]. Further, compared with vaginal delivery, women are at higher risk of endometritis, blood transfusions, and intensive care unit admissions after CS [3,4], as well as neonates for respiratory morbidity and lacerations. In some cases, a CS is an easy way out of a complicated situation.

Women with a prior uterine scar represent a unique group and treatment must be individualized. For women with a previous low transverse incision, and a uterus greater than 28-week size, oxytocin protocols may be utilized and cervical ripening with Foley balloon may be considered as per ACOG recommendations [4].

The number of earlier CS varies a lot, for example Ramirez et al. presents in her article that the women with one earlier CS was 71.8 %, two CS 22.0 %, and three or more CS 6.2 % [2].

A lot of positive reports of induction of labor have been published recently. Ramirez et al. studied a group of patients (n = 209) with prior CS presented with an IUFD. The trial of labor (TOLAC) was attempted in 75.6 % (158/209), and VBAC success rate was 86.7 %. [2]

In another study, women with IUFD and prior CS trial of labor following induction with extra amniotic saline instillation and prostaglandins was found to be effective. 33 women were given trial of labor [3]. 28 of these women had induction of labor with mechanical and pharmacological methods while 5 women had spontaneous onset of labor. Authors could achieve successful vaginal delivery in 19 (57.67 %) of the 33 women with prior cesarean who were given a trial. Authors had two cases of uterine rupture in TOLAC group [3].

Methods for trial of labor

Patients may elect for a repeat CS in the setting of a stillbirth, but the risks and benefits must carefully be considered and discussed with the patient. Ideally, elective CS should be avoided. Regardless of the route of delivery of a stillbirth, clinicians should be sensitive to the emotional difficulties and needs of families suffering a stillbirth. All women should be included in choosing their individual management plan be it in an expectant management or induction of labor [4]. Overall, data from USA suggest that induction of labor in women with an IUFD and previous CS is associated with a high success rate and shorter hospital stay and it should be considered an option to repeat CS [2].

It is well known that complex emotional factors are associated with fetal loss. Once intrauterine death is confirmed, the majority of women hope for expulsion of the dead fetus as early as possible. [3]

In the stressful situation of an IUFD, the options are either to await the onset of spontaneous labor or to induce labor. It may take several weeks for spontaneous expulsion. Retention of the fetus can be associated with emotional distress, intrauterine infection if membranes are ruptured and a time related risk of consumptive coagulopathy [5]. Coagulation abnormalities occur in about 3–4% of patients with uncomplicated stillbirth [5] when the latency period is prolonged several weeks.

In general, in the setting of fetal demise, maternal safety becomes the primary concern, and fetal distress is not the main problem. On the other hand, the trial of labor takes place significantly earlier than if the fetus is alive. An advantage is that the fetal weight close to 30 weeks, is less than during later pregnancy. For example, in USA in cases of earlier CS and fetal demise, the women who attempted TOLAC had an average gestational age of 30.2 ± 6.6 weeks [2], and at this time the induction could be more challenging, and close to the term, augmentation of labor is achieved in many cases with oxytocin. Oxytocin is less effective for the induction of labor remote from term. [6]

According to previous studies, misoprostol administered vaginally will increase the risk of uterine rupture [7,8]. However, some new studies show that induction of labor with oral solution of misoprostol after one previous CS is a safe and effective method well comparable with the use of a balloon catheter, despite a more unfavourable status of the cervix [6]. Therefore, prostaglandins may be valuable in this clinical situation. Prostaglandins have been shown to be safe and effective in termination of pregnancies prior to 28 weeks of gestation in women with prior cesarean deliveries, without resulting in uterine rupture or hysterectomy [6]. Misoprostol is a prostaglandin analogue, used for induction of labor worldwide. Since 2012, misoprostol, administered as an oral solution, is the recommended method for induction of labor in Sweden [6]. The success rate of VBAC after one previous CS in women with induction of labor is remarkably high, almost 70 % with both balloon catheter and oral solution of misoprostol, regardless of unfavourable cervix status [6].

Though both mifepristone-misoprostol combination regimen and misoprostol alone regimen for induction of labour in IUFD have been recommended by different international associations, there is no consensus regarding the ideal regimens [4].

For women with a previous low transverse incision and a uterus less than 28-weeks size, the usual protocols for misoprostol induction at less than 28 weeks may be used [4]. For women with a previous low transverse incision, and a uterus greater than 28-week size, oxytocin protocols may be utilized and cervical ripening with Foley balloon may be considered as per ACOG recommendations [4].

Generally, in women with a previous CS, lower doses should be used and doubling of doses should not occur [6]. In contrast, induction of labor was achieved most with oxytocin in combination with artificial rupture of membranes, various prostaglandin agents, laminaria, or Foley catheter. The median number of tablets of misoprostol was significantly higher for termination of pregnancy than for fetal death in utero (4 vs. 2; $p = 0.002$) [5].

In a new study from India, most women received prostaglandin analogues along with mifepristone [3]. A combination of mifepristone and misoprostol was a remarkably effective and safe method of induction of labor after a IUFD [3]. Some clinics never use prostaglandins or oxytocin for cervical ripening in women with history of CS; instead, they use a Foley catheter when needed [9].

Misoprostol is prepared as an oral solution, one tablet of 200 µg misoprostol was dissolved in 20 mL of water. The solution thus held 10 µg of misoprostol. This method of administration has been tested by the Swedish Institute of Pharmacology [6] and approved to be accurate in terms of correct dosage. A dose of 2.5 mL / 25 µg of

misoprostol was administered orally to the women every two hours until frequent painful contractions were obtained. The dose could be repeated up to eight times if necessary (maximum 200ug in 24 h) [6].

Women who receive prostaglandins are much more likely to have an unfavourable cervix than women induced with oxytocin or who enter labor spontaneously [6]. In our opinion it is important to have a various selection of methods for TOLAC especially when the cervix is unfavourable.

Complications

Uterine rupture is a well-known but unusual complication in vaginal deliveries with a history of earlier CS. To be able to estimate the risk of uterine rupture in rare cases with earlier CS and IUFD, we should first look at the risk with earlier CS without IUFD.

Published data on these risks vary considerably, the highest rate of uterine rupture being 9.7 % in patients with a history of CS [8]. However, modern articles estimate the risk of uterine rupture to be at least two-fold when labor is induced. In Sweden, women can deliver vaginally after one previous CS, regardless if labor starts spontaneously or is induced [6]. The incidence of uterine rupture among women with one previous CS is assumed to be 0.5–0.9% [10–12] compared to 0.02 % in women without any history of CS [13]. A recent metaanalysis of 16 observational trials reported a low uterine rupture rate of 0.28 % in women receiving misoprostol for second-trimester termination [5].

The cornerstone of concerns over TOLAC is the risk of uterine rupture, with its implied catastrophic consequences for both the mother and new-born. A total of seven cases of uterine rupture were recorded and additional 16 cases of uterine dehiscence – an incidence of 0.10 % for both diagnoses and 0.03 % for uterine rupture [9]. None of these cases required CS, no maternal, intrapartum nor neonatal death was recorded. All seven cases of ruptured uterus (0.5 % of trials) were diagnosed during labor, spontaneous for the most part [9].

According to previous studies, misoprostol administrated vaginally will increase the risk of uterine rupture [13,14]. Misoprostol in all forms has therefore been discouraged in various guidelines on labor induction in women with previous CS even though the scientific knowledge is limited [4,15]. However, the evidence is unclear and based on only small studies where only vaginally administrated misoprostol has been studied.

Kaczmarczyk et al. [13] described in their large population-based cohort study, a 5% and 60-fold increase in neonatal mortality in their uterine rupture group whereas others report a 16-fold increase in neonatal mortality in the uterine rupture cohort, with a total of 3 (0.90 %) deaths within 28 days of birth. Nonetheless if uterine rupture is to occur, neonates have a dramatically higher risk of morbidity and mortality [13]. An analysis of data from Japan revealed that the rates of TOLAC and uterine rupture were 5.0% and 0.46 %, respectively [14]. Further, Dommergues et al. [15] noted that the rate of uterine rupture was significantly higher when there was a history of CS: 3% (3 in 103 women) vs. 0.35 % (3 in 853 women). Lately, the risk of uterine rupture during TOLAC was reported at 0.5–0.9 % in spontaneous labor [6]. This risk was approximately doubled in cases of augmented or induced labor [6].

In a study from Israel [9], 22,670 deliveries were registered, with a 18.2 % rate of cesarean section. 2890 women had a single cesarean scar; of them 1206 delivered vaginally and 194 were re-operated during unsuccessful TOLAC. Seven cases of uterine rupture and 16 cases of dehiscence were recorded. There were no maternal, intrapartum or neonatal deaths, and no cesarean hysterectomy [9]. There was one re-laparotomy, one intensive care unit admission, and one blood transfusion; one neonate was

admitted to neonatal intensive care unit. TOLAC was successful in 86.1 % of cases [9].

If the delivery was induced, the proportion of uterine ruptures was 2.0 % (6/295) with orally administrated misoprostol, 2.1 % (7/335) with balloon catheter and 5.0 % (14/281) when prostaglandins were used in a study from Sweden [6]. No difference in the proportion of uterine ruptures was shown when orally administrated misoprostol and balloon catheter were compared ($p = 0.64$) [6]. Orally administrated misoprostol and balloon catheter give a high success rate of vaginal deliveries (almost 70 %) despite an unfavorable cervix [6].

For women with earlier CS and IUFD, the frequency of uterine rupture in the study of Ajini et al. was 3.6 % as the reported rates of uterine rupture in women with previous CS who underwent induction of labor [3]. Uterine rupture occurred in five women (2.4%), and in 3.0% (27/910) of the women with induction of labor had a uterine rupture. Further, Ramirez et al. [2] reported that none of those being induced after an IUFD and CS required hysterectomy. The rate of uterine rupture was quite high 4.8 % [95 % CI: 1.2–14.2]. The women with uterine rupture had an average gestational age of 32.8 ± 7.1 weeks and birth weight of 2196 ± 1584 g [2]. This was accomplished with a high proportion of labor inductions and an overall increased risk of uterine rupture overall (24/1000) and after labor induction (34/1000) compared with trial of labor for a live fetus (7/1000) [11].

In the study from India [3], among the 44 women with previous CS, 11 underwent elective CS. 19 women (57.6 %) out of 33 cases of trial of labour after CS had a successful vaginal delivery. There were two cases of ruptured uterus. The frequency of uterine rupture in this study, which was 3.56 %, is similar to the reported rates of uterine rupture in women with previous CS who underwent induction of labor [3].

The rate of *severe bleeding* during delivery is low. Based on an article from France, bleeding during delivery requiring a transfusion occurred in 2 cases (3.0 %; 95 % CI: 0.5–11.3) [5]. The studies cited show a rate of blood transfusion that ranged from 0 to 11.4 % during termination of pregnancy when there was a history of CS [16]. Based on the results from India, the rate of blood transfusion was 8% [3].

The application of laminaria tents may, however, increase risk of *infection* [17] although this was not the case in another study [5].

There are just a few reports that discuss this problem, and there is a great need to publish articles in this field. The rarity of the situation is a limiting factor, and perhaps large national register studies could be a solution.

Conclusion

Delivery after an earlier CS remains a challenge especially if a fetal demise complicates the new pregnancy. The choice must be made between an induction for vaginal delivery and a CS. A vaginal delivery is both effective and safe. If an induction is needed, oral solution of misoprostol or a balloon catheter and, regardless of unfavourable cervix status, is recommended. Uterine rupture after previous low segment transverse cesarean is rarely catastrophic, and in modern articles none of the cases with uterine rupture requires cesarean hysterectomy.

Declaration of Competing Interest

The authors report no declarations of interest.

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