Increasing the effectiveness of external cephalic version

Velzel, J.

Citation for published version (APA):
Chapter 1

General introduction
General introduction

The ultimate goal in obstetrical care is to achieve that a mother delivers a healthy baby at the end of her pregnancy and remains in optimal physical and mental condition. Women, when problems arise or are anticipated during pregnancy and delivery, require appropriate counseling in order to come to informed decision making to obtain the optimal fetal and maternal health goals. This thesis provides novel insights to improve individualized informed decision making for the prevention of breech presentation at term delivery. Breech presentation at term compared to vertex position with headfirst has potentially worse outcome for both mother and child.

Clinical management of breech presentation at term: vaginal birth or caesarean delivery?

At term, in three to four per cent of all singleton pregnancies the fetus presents itself in breech position. In only 15% of the women with a breech presentation, an identifiable factor exists such as uterine malformation, placenta praevia, polyhydramnios, (congenital) abnormalities of the fetus like anencephaly and disorders accompanied by motor impairment that are reported to be associated with breech presentation. Compared to birth in cephalic position, vaginal breech delivery of healthy fetuses is associated with increased risk of neonatal birth trauma, low Apgar scores and neonatal mortality. The results of the Term Breech Trial, a randomized controlled trial (RCT) comparing the mode of delivery in term breech presentations, showed a clear reduction in overall risk of perinatal and neonatal mortality and morbidity in favor of elective caesarean delivery compared to planned vaginal breech delivery (respectively 0.3% v 1.3%, RR 0.23, 95% CI 0.07 to 0.81 and 1.4% v 3.8%, RR 0.33, 95% CI 0.19 to 0.56). Publication had an unprecedented large impact on daily clinical practice even though results correspond to a number needed to treat of 100, which means performing 100 elective caesarean deliveries to prevent one perinatal or neonatal death. So gain in newborn health was judged superior to the accompanied increased risk for the mother because of the associated abdominal surgery. In addition, the 2-year follow up of this study demonstrated no difference in ‘neonatal death or neurodevelopmental delay’ (RR 1.09, 95% CI 0.52 to 2.3). The authors concluded that a policy of elective caesarean delivery is substantially better, especially in Western countries and in clinical practice this policy was adopted quickly. Although the results of this study seemed to confirm the presumption that an elective caesarean delivery could reduce neonatal morbidity and mortality, criticism on the trial followed. This critique mostly regarded methodological issues such as case selection, incomplete follow-up and questions on clinical competence of personnel responsible for breech delivery in the participating hospitals. The PREMODA study group conducted a prospective cohort study on breech delivery in 174 hospitals where breech delivery was still common practice. This study demonstrated
no significant differences in perinatal and neonatal mortality between both modes of delivery (OR 0.64, 95% CI 0.13 to 3.1). The authors concluded that a planned vaginal breech delivery remains a safe option and can be offered to women in hospitals when strict criteria are met before and during labor. However, a recent published meta-analysis, including cohort studies and RCTs, confirmed the findings of the Term Breech Trial.\(^{10}\) This study showed that in absolute risks, perinatal mortality is approximately 2.0/1000 with planned vaginal breech birth and 0.5/1000 with caesarean delivery. The authors however also pointed out the relatively low absolute risks of vaginal breech delivery leading to a high number needed to treat (approximately 67) with caesarean delivery having negative effects on mothers' health and outcome of future pregnancies. They stated that their study underscored the importance of the practice of individualized decision making on the mode of delivery in a term breech presentation.

Even though there is an ongoing discussion in literature about the preferred mode of delivery, clinical practice indicates that clinicians' and patients' choice is unambiguous in breech presentation at term since after publication of the Term Breech Trial, caesarean delivery rates for breech delivery increased significantly worldwide. In the Netherlands, the rate of elective caesarean delivery for breech presentation in the years before this publication varied between 20 and 25%, and from 2001 onwards, it is more than 60%.\(^{11,12}\) In Sweden, the UK and Australia, this percentage shifted up to 80-95%.\(^{13-15}\) Nowadays, in Western countries, breech presentation is the third most common indication for caesarean delivery and is responsible of 15% of all caesarean deliveries.\(^ {16}\)

The ongoing debate on this topic is understandable, considering the maternal downsides that come with caesarean delivery being the proposed safest route of delivery for the fetus. Women undergoing caesarean delivery are at higher risk of mortality and morbidity compared with women after vaginal delivery.\(^ {17}\) A large population-based study from Canada found a threefold risk of short-term combined severe maternal morbidities for caesarean delivery as compared to vaginal delivery (2.7% v 0.9%).\(^ {18}\) Serious maternal morbidity was found like hemorrhage requiring hysterectomy or transfusion, uterine rupture, anesthetic complications, assisted ventilation, venous thromboembolic event and major infection. Also, there were concerns regarding future pregnancies in the light of the increased incidence of abnormal placentation, which can lead to hemorrhage requiring hysterectomy, and rupture of the uterine scar, which is highly associated with perinatal death (6% to 10% of all uterine ruptures).\(^ {19-23}\) Therefore, family planning is an important topic in counseling women with breech presentation near term as a study by Vlemmix et al (unpublished observation) demonstrates that elective caesarean delivery for term pregnancy leads to a significant increase in maternal morbidity, and adverse neonatal outcome in subsequent pregnancies.
Since currently one in three women give birth by caesarean delivery in the United States, the American College of Obstetricians and Gynecologist published jointly with the Society of Maternal-Fetal Medicine an obstetric care consensus recommending prevention of the elective caesarean delivery. They conclude on an existence of global overuse of caesarean delivery because of the rapid increase of caesarean births in the last decade without the clear evidence of decreases in neonatal morbidity or mortality. Prevention of breech at term would solve the dilemma discussed in this paragraph.

Prevention of breech presentation at term: overview
As fetal breech presentation is the reason for a caesarean delivery in approximately 15% of all cases, prevention is an important issue. Though theoretically vaginal breech delivery could reduce the number of caesarean deliveries and has to be discussed as an option with women, logically reducing the number of breech babies at term is a strategy to invest. Several methods to achieve this are described in literature and are based on different mechanisms. A preventive measure to reduce the incidence of breech presentation at term is postural management from 32 weeks of gestation onwards. This includes knee-chest position, and a supine position with the pelvis elevated with a wedge-shaped cushion for several minutes to one hour per day. However, a Cochrane review from 2012 concluded insufficient evidence to support the use of postural management as standard treatment. Moxibustion therapy is believed to increase fetal movement and could result in a spontaneous version to cephalic presentation from 32 weeks of gestation onwards. External cephalic version (ECV) is an obstetrical procedure in which a baby is manipulated by applying pressure externally through the gravid abdomen into a cephalic position. It requires training and manual skills. ECV is proven to be effective and reduces non-cephalic birth (pooled RR 0.42, 95% CI 0.29 to 0.61) and caesarean delivery (pooled RR 0.57, 95% CI 0.40 to 0.80). Sources from the time of Aristotle suggest that it has been practiced since the classical antiquity. In post medieval literature, ECV is first described in 1807. It became routine practice for breech presentation, and after a period of declined interests between 1960 and 1980, due to publications reporting on high rates of reversions and fetal complications, the revival of the use of ECV came in the early 1980’s.

ECV is considered a safe procedure with few contraindications and can prevent breech delivery in 40-60% of cases. The complication rate is low, with reported serious perinatal complications of 2.0/1000, including still-birth and placental abruption. In case of still-birth, there does not seem to be a relationship with ECV, as it equals the reported still-birth rate in the general population. It is important to compare perinatal risk associated with ECV with adverse outcome associated with the alternatives to ECV, namely perinatal mortality in planned vaginal breech birth (2.0/1000) and elective caesarean delivery (0.5/1000). As the ultimate goal of ECV is to achieve vaginal cephalic birth, there remains,
However, controversy on the question whether the risk of caesarean delivery is increased for women with a fetus in cephalic position after a successful version compared with women with a spontaneous cephalic presentation. A review by Chan et al in 2004 found a two times increased risk for caesarean delivery in women after a successful external cephalic version. Since 2004 many studies on ECV were published, therefore an update on mode of delivery after successful ECV is needed and could shed more light on this issue.

At present, ECV is recommended to all women with an uncomplicated breech pregnancy near term. Furthermore, Tan et al demonstrated ECV to be cost-effective when the probability of successful ECV was greater than 32%. Then, the question remains: is there room for improvement?

**There is still room for improvement of ECV both in the way it is executed and implemented**

To enhance success rates of ECV procedures, several strategies have been proposed. These methods include the use of tocolytic medication or epidural or spinal analgesia to increase uterine relaxation and amnioinfusion to increase fetal room to maneuver and methods not based on principles used in Western regular medicine like moxibustion therapy.

Several studies have shown that uterine relaxation with tocolytic medication is effective. Types of tocolytics described in literature are nitric oxide, beta-mimetics, oxytocin receptor blockers and calcium channel blockers. The majority of studies that evaluated the effectiveness of tocolytics have used beta-mimetics and meta-analysis of randomized controlled trials demonstrated that the use of beta-mimetics can enhance the ECV success rate compared with placebo (nine studies, pooled RR 1.6, 95% CI 1.2 to 2.0) for cephalic presentation after ECV attempt. However, beta-mimetics have known adverse maternal cardiovascular side effects in terms of flushing, chest pain and palpitations, and as a result the implementation of routine uterine relaxation is low. Patients’ willingness to undergo ECV was evaluated in a vignette study by Vlemmix et al. This study showed that the use of intravenous uterus relaxants with side effects decreased the chance of opting for ECV. Therefore, evaluating alternative tocolytic medication could be useful. A possible tocolytic agent that has not been evaluated for ECV is an oxytocin receptor antagonist. This type of drug could be considered for ECV as its been used as uterine relaxant to delay or prevent preterm birth and has fewer maternal side effects compared to other tocolytics. To our knowledge, there are no randomized controlled trials assessing the effectiveness of an oxytocin receptor antagonist in ECV until now.
In addition to planning this type of trials and in the absence of trials that compare all pharmacological interventions, a network meta-analysis could be helpful. This analysis allows to rank treatments by effectiveness in combining direct (available from standard pairwise meta-analysis) and indirect evidence. Even when the results of direct evidence are conclusive, combining them with the results of indirect evidence may contribute to a more refined and precise estimate of the outcome since it maximizes existing information within the network of treatment comparisons. Furthermore, since routine administration of tocolytic medication always carries a risk for unwanted side-effects, careful weighing who benefits most is needed in providing the best a priori chance of success.

Another used method to prevent breech presentation is the use of moxibustion, part of Complementary and Alternative Medicine (CAM). CAM is defined as non-mainstream practices or products used as primary treatment or as a complement to mainstream health care. In healthy pregnant women, CAM treatments have been reported to help lower stress, improve sleep, and reduce pain, and some care providers regularly refer pregnant patients to yoga classes, massage therapists, and other CAM practitioners, though this is found only in low impact literature. Notwithstanding this lack of solid evidence, a survey among pregnant women and physicians revealed that up to 49% of women consult a CAM practitioner, of which only half discloses this to their physician. In addition, breech presentation is one of the most common topics in pregnancy to consult a CAM practitioner for treatment with moxibustion therapy alone or in combination with acupuncture to establish cephalic presentation.

Moxibustion therapy is a traditional Chinese medical intervention that uses the heat generated by burning herbal preparations containing Artemisia vulgaris (mugwort) to stimulate the acupoint BL67 (beside the outer corner of the fifth toenail). The exact mechanism cannot be understood with Western physiological principles, however, it is thought that this method increases fetal activity and can be applied to correct breech presentation from 32 weeks of gestation onwards. A recent published Cochrane review in 2012 found limited evidence to support the beneficial effect of moxibustion, applied alone or in combination with acupuncture or postural measures, compared to observation alone or postural measures. However, this review did not distinguish between studies offering ECV or not. As moxibustion in practice is used from 32 weeks which is prior to a possible ECV attempt, executed from 36 weeks of gestation, potentially both could be recommended provided a beneficial effect is present. We decided that there is a need to determine the effectiveness of moxibustion as a complementary treatment for women eligible for an ECV attempt in order to be able to answer questions from clients in daily practice.
Implementation of ECV in clinical practice: barriers and facilitators
Considering the safety and effectiveness of the ECV procedure, all eligible women should be offered this treatment option. However, a study on the implementation of ECV in the Netherlands in 2014 showed that the implementation rate varied between 8% and 84%, with an average of 72%.47 In the United States, the implementation of ECV is even lower. A nationwide cohort study showed that only 5% of the women with breech presentation had a successful version. Assuming an average ECV success rate of 40% would imply that only 13% received an ECV attempt.48 These low implementation rates are both doctor and patient related. Among professionals the main barriers are a lack of knowledge and skills to inform and counsel patients.49 For patients the success rate and expected pain are the most important factors influencing the willingness to opt for ECV.37 Higher success rates of vaginal delivery after successful ECV increased women's willingness (OR 3.4, 95% CI 2.0 to 5.7). As the success rate of ECV varies from approximately 35% up to 86% in the literature with an average of 50–60%17, an a priori chance of success estimate can be helpful to counsel women for an ECV.

Previous studies have shown that clinical and ultrasound characteristics are associated with success or failure of an ECV procedure.50,51 The clinical factors multiparity, non engagement of the breech, a relaxed uterus and a palpable fetal head were associated with successful ECV. Ultrasound factors predictive for successful ECV were posterior placenta localization, complete breech position and an amniotic fluid index >10 cm. In literature, there are several prediction models that enable individualized prediction of the outcome of an ECV attempt. For implementing in clinical practice, it is important to assess their quality by determining which predictors they used and determining their performance. Accurate and individualized prediction of the outcome of an ECV attempt is helpful for optimal and accurate shared decision making.

Objective and outline of the thesis
The aims of the presented studies in this thesis address the following research questions:
• What is the effectiveness of atosiban as a uterine relaxant for ECV compared to fenoterol?
• Which tocolytic agents are reported to be the most effective for ECV?
• Is moxibustion alone or in combination with acupuncture to correct breech presentation in combination with ECV effective?
• Can we determine who benefits most of tocolysis with beta-mimetics for ECV?
• Which prediction model performs best in predicting successful ECV?
• Can we develop a clinical prediction model for ECV that performs better in predicting successful version and beneficial neonatal outcome compared to existing models?
• Is there an increased risk for caesarean section after external cephalic version resulting in cephalic presentation compared to spontaneous cephalic presentation?
In chapter 2 we report on the results of a randomized controlled trial assessing the effectiveness of the oxytocin receptor antagonist atosiban as a uterine relaxant for ECV compared to the beta-mimetic fenoterol.

In chapter 3 we describe the results of a network meta-analysis that was performed to identify the most effective tocolytic agent for uterine relaxation for ECV.

In chapter 4 we systematically review the medical literature reporting on the use of moxibustion alone or in combination with acupuncture to correct breech presentation in combination with ECV.

In chapter 5 we report on a secondary analysis of a randomized controlled trial to determine who benefits most of tocolysis with beta-mimetics for ECV.

In chapter 6 we demonstrate the results of a systematic review of medical literature on prediction models for successful ECV.

In chapter 7 we present a model for the prediction of successful ECV based on clinical variables determined alongside a randomized controlled trial.

In chapter 8 we demonstrate the results of a systematic review of medical literature on the mode of delivery after ECV.

In chapter 9 we discuss the results of the studies presented in this thesis and give clinical implications and implications for future research in this field.