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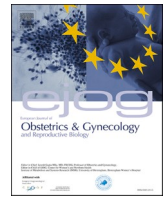
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Full length article

European guidelines on management of arrested or protracted labor in nulliparous women



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ABSTRACT

Arrested or protracted labor in nulliparous women caused by insufficient uterine contractility is a common problem in obstetrics, for which few management guidelines exist. The European Association of Perinatal Medicine nominated an expert panel, consisting of specialists in obstetrics and gynecology and midwives representing their respective professional national societies in nine European countries and patient representatives. The panel developed an evidence-based guideline for clinical practice supported by the Knowledge Institute of the Dutch Association of Medical Specialists.

Five priority clinical questions (PICO) were identified on nulliparous women, at term, with a singleton fetus, in cephalic presentation, and the diagnosis of arrested or protracted labor. For each question relevant outcome measures were defined as well as a minimal clinically important difference for each of them. Five literature searches were performed by an information specialist and articles were selected independently by two panel members. The GRADE methodology was used to write evidence summaries, considerations, and recommendations. The draft guideline was sent out for review to scientific societies involved in perinatal care in 20 European countries. Comments were answered, and the guideline was revised accordingly.

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The following procedures should be offered to women: 1) Amniotomy alone may be considered. 2) Women should be informed that there is no scientific evidence regarding the beneficial effects of immediate (<1 h) or delayed administration of oxytocin, although the first option may reduce the duration of labor. A joint decision is recommended, based on clinical judgment, and women's values and preferences. 3) A low-dose oxytocin regimen for labor augmentation should be considered. 4) Amniotomy should be considered before the administration of oxytocin infusion during the first stage of spontaneous labor. 5) Oxytocin augmentation for at least four hours with adequate uterine contractions should be considered, before an operative delivery is proposed, provided that fetal and maternal conditions are adequate.

Introduction

Arrested or protracted labor is associated with increased rates of maternal and neonatal morbidity and mortality [1–5]. Although there is no widely accepted definition of this entity, it is presumed to have a high prevalence in both low- and high resource settings, and to be an important cause of operative delivery. Despite the clinical relevance of this topic in obstetrics, few guidelines have been published to guide clinical practice. To date, there is no widely accepted definition of arrested or protracted labor. Arrested or protracted labor may be caused by cephalopelvic disproportion, malposition and malpresentation or insufficient uterine contractility. These guidelines are limited to the last category.

Artificial rupture of membranes (AROM), also referred to as amniotomy, has been traditionally used to augment uterine contractility in slowly progressing labor and is recommended by several international guidelines with or without concurrent intravenous oxytocin administration [6–9]. The World Health Organization (WHO) recommends combined amniotomy and oxytocin for labor augmentation, and advises against the isolated use of amniotomy [10]. The WHO notes that the limited available data are unable to support conclusions on the benefits or harms of routine amniotomy alone for treatment of dysfunctional labor, and that most of the studies have been performed in the setting of early amniotomy to augment or induce labor.

Intravenous oxytocin increases uterine contractility in laboring women with arrested or protracted labor and inadequate uterine contractions. In clinical practice many different schedules are used for the start, dosage and duration of oxytocin augmentation, and there is uncertainty about the order by which amniotomy and oxytocin should be used for the management of arrested or protracted labor.

In many countries, amniotomy is performed first, and if no progress is observed in the following 1–2 h, intravenous oxytocin is started. However, keeping the membranes intact could hypothetically be beneficial to control pain, and to reduce the risks of intrapartum fever, chorioamnionitis, neonatal infection, and ambiguous or abnormal cardiotocographic (CTG) patterns associated with umbilical cord compression.

It is uncertain how long oxytocin should be continued when labor progress remains inadequate in the presence of regular contractions, and what should be the threshold to recommend operative delivery in these situations. While longer duration of oxytocin administration could increase the risk of hyperstimulation, uterine rupture, and fetal hypoxia, it could also decrease the risk of operative delivery.

Several interventions for arrested or protracted labor with low risk may be tried, but are not considered in this document, e.g. one to one care, varying maternal positions, hydration, emptying the bladder, correcting malpositions.

Arrested or protracted labor is a common issue in obstetrics all over the world. For such a prevalent condition, parallel development of national guidelines would be a waste of time and effort. Therefore, under auspices of the European Association of Perinatal Medicine (EAPM) and funded by the Knowledge Institute of the Dutch Association of Medical Specialists, we made a collective effort to develop a European guideline with a multinational multidisciplinary panel.

Methods

An international expert panel for the development of the guideline was started in 2022. The panel grew during a year by networking, and finally consisted of representatives from nine national societies of obstetrics and gynecology, two representatives from the European Midwives Association and three representatives from the Dutch Midwives Association, and one patient representative from the Dutch Patient Federation, an umbrella organization for all Dutch patient organizations. All panel members were officially appointed to represent their (scientific) societies. The Code for the prevention of improper influence due to conflicts of interest was followed.

The panel made an inventory of clinical questions to be addressed based on their expert opinion and their knowledge of existing guidelines. The 'Danish national clinical guideline concerning primiparous women with dystocia (lack of progress)' published in 2015 was also used as a source of clinical questions. Five clinical questions and related PICOs were prioritized (Appendix 1).

A priori, the panel did not define the outcome measures but used the definitions used in the studies. The panel defined a Relative Risk (RR) < 0.95 or RR > 1.05 as a minimal clinically (patient) important difference for the outcomes perinatal death and encephalopathy. For the other binary outcomes, a RR < 0.8 or RR > 1.25 was considered as a minimal clinically (patient) important difference. For the continuous outcome duration of labor, a difference of 0.5 Standard Deviation (SD) was considered clinically (patient) relevant.

Four advisors and an information specialist of the Knowledge Institute of the Dutch Association of Medical Specialists supported the project, performed the literature search and evidence synthesis, and formulated conclusions according to the Grading Recommendations Assessment, Development and Evaluation (GRADE) methodology (see <https://www.gradeworkinggroup.org/>). GRADE defines four gradations for the quality of the body of scientific evidence: high, moderate, low or very low. These gradations provide information about the amount of certainty about the literature conclusions (<https://www.guidelinedevelopment.org/handbook/>). For the wording of the conclusions, we used the statements suggested by the GRADE working group [11].

The databases Medline (via OVID) and Embase (via [Embase.com](https://www.embase.com)) were searched using relevant search terms until July 2022. The detailed search strategy can be retrieved from the corresponding author. Studies were selected based on the following criteria:

- Systematic reviews, randomized controlled trials (RCTs), or comparative observational studies
- Studies including nulliparous women with term pregnancy (gestational age $\geq 37^{+0}$ weeks) and a fetus in cephalic presentation during the dilatation phase or active 1st stage of spontaneous or induced labor, with arrested or protracted labor
- Comparison of the intervention and comparison as mentioned in the individual PICOs
- Assessing one or more of the predefined outcomes
- Published between 1990 and July 2022
- Publications in English.

The panel members selected literature in pairs (independently of

each other) based on title and abstract. A second selection was performed based on full text. The studies with potentially the highest quality of research, i.e. systematic reviews and RCTs, were selected first. Individual studies were systematically assessed, based on methodological quality criteria that were determined prior to the search, so that risk of bias could be estimated. In case there were enough similarities between studies, the study data were pooled.

Members of the expert panel wrote the considerations based on the GRADE conclusions of the literature and on expert opinion, using a structured format based on the evidence-to-decision framework of the international GRADE Working Group [12,13]. The patient representative provided input on the topic ‘Values and preferences of patients (and their caregivers)’.

Recommendations provide an answer to the clinical question and are based on the best scientific evidence available and the most important considerations. The level of scientific evidence and the importance given to considerations by the guideline panel jointly determine the strength of the recommendation. In accordance with the GRADE methodology, a low level of evidence for conclusions in the systematic literature review does not rule out a strong recommendation, while a high level of evidence may be accompanied by weak recommendations. The strength of the recommendation is always determined by weighing all relevant arguments.

In the panel the considerations were discussed until consensus was reached about the recommendations, after which the guideline was sent out for review to a wide group of perinatal, obstetric and midwives organizations in 20 European countries (Appendix 2). The review comments were discussed by the panel, and if considered appropriate, the guideline text was revised. The commentary table including the panel’s responses is included in Appendix 2.

The literature search and grading of evidence was supported by the Knowledge Institute of the Dutch Association of Medical Specialists. No external funding was received.

Results

Appendix 1 contains a detailed report of the literature summaries and conclusions for the five clinical questions.

Question 1. *Should the membranes be ruptured at all or is expectant management preferable in the active stage of labor in nulliparous women at term with arrested or protracted labor?*

Recommendation

Amniotomy alone may be considered when there is arrested or protracted labor in nulliparous women at term ($\geq 37/0$ weeks) and with a fetus in cephalic presentation following a positive consent of the mother.

Considerations

The results of the literature analysis are inconclusive for the key outcomes [14,15], and it is therefore not possible to conclude from the literature whether amniotomy is or is not an effective intervention for arrested or protracted labor. The potential advantages of amniotomy are that it may speed up labor without adverse perinatal consequences, it allows a fetal electrode to be placed, and there is some evidence the intervention is favored by laboring women. The disadvantages are that it may be an ineffective intervention, it may cause umbilical cord prolapse, and that an increased chance of maternal or perinatal infection cannot be excluded.

There appears to be maternal preference in favor of amniotomy. Individual clinical interpretation of these factors, supported by an informed discussion with parent(s), is recommended.

The cost of amniotomy is minimal and this is unlikely to be an

important factor in determining its clinical role. If effective, this procedure may reduce the cost of additional interventions e.g. oxytocin infusion, epidural requests following a more prolonged course of labor, or avoidable cesarean delivery.

Amniotomy is a widely performed intervention and changing its current usage is likely to be challenging without good evidence either in favor or against its usage, despite its inconclusive effect when used alone.

There was unanimity amongst the Guideline Development Panel members around the indications and the use of amniotomy within member countries, and of the recommendation. While it is arguably inappropriate to undertake procedures without a reliable evidence base, based on the current study and wide practice, a recommendation to ban this procedure cannot be done. The panel highlights the other benefits of amniotomy than possibly accelerating the birth process, which are assessing the presence or absence of meconium, and enabling the application of a fetal electrode when required.

According to the panel, an unnecessary amniotomy may increase the risk of umbilical cord prolapse, ascending infection, and vertical transmission of certain pathogens. There are conflicting findings, however, regarding prolonged rupture of membranes and an increase of vertical transmission of hepatitis C virus (HCV), possibly untreated human immunodeficiency virus (HIV), hepatitis B virus (HBV), and other infections [16–19]. It is also acknowledged that other adverse fetomaternal effects cannot be ruled out based on the limited existing evidence.

Considering all the above it was the opinion of the Guideline Development Panel that amniotomy alone, after an informed discussion with parent(s), may be a reasonable option when arrested or protracted labor is diagnosed.

Question 2. *Should oxytocin as augmentation of labor be given immediately or delayed after diagnosing arrested or protracted labor, during the first stage of spontaneous or induced labor in nulliparous women at term?*

Recommendation

Inform the laboring woman that there is no scientific evidence about the beneficial effects of immediate (<1 h) or delayed administration of oxytocin after the diagnosis of arrested or protracted labor. It might impact the duration of labor. Decide together with the woman based on clinical judgment as well as the patient’s values and preferences.

Considerations

The literature analysis for this recommendation was based on one Cochrane review [20] that compared early use of intravenous oxytocin versus delayed use of oxytocin. Even though the evidence as derived from this study was considered low, immediate oxytocin augmentation may slightly reduce labor duration in comparison with delayed oxytocin augmentation in women with arrested or protracted labor. Most women that participated in the studies were nulliparous. There was no clinically relevant or statistically significant difference in satisfaction or childbirth experience between groups with immediate or delayed oxytocin augmentation. The evidence regarding the effect of immediate versus delayed oxytocin augmentation on perinatal death, Apgar score < 7 at 5 min, cesarean section and instrumental vaginal delivery was very low, and therefore, no conclusions were formulated. No evidence was found for the effect of immediate versus delayed oxytocin on umbilical cord (artery pH), Sarnat score, Thompson score, encephalopathy, anal sphincter rupture, incontinence, breastfeeding, bonding, and later cesarean section at maternal request.

The literature search did not yield any studies that revealed adverse effects of immediate administration of oxytocin augmentation in the first stage of labor of nulliparous women with arrested or protracted labor. No difference was found in reported outcomes, except a shorter

duration of labor in those who received immediate administration of oxytocin. This should be considered as a potential pro of an early oxytocin augmentation. No specific cons of immediate administration of oxytocin were revealed in the literature available.

Since there are no differences in satisfaction/childbirth experience identified between immediate and delayed oxytocin administration in nulliparous women with arrested or protracted labor in the dilatation phase, it is important that women are informed about both options including pros and cons as part of shared decision making. Women should not be overwhelmed by the immediate administration of oxytocin but informed to make a deliberate decision.

Some patients prefer a shorter duration of labor. For others, childbirth does not have to be as short as possible. They prefer a delivery as physiological as possible and/or believe that the process of giving birth to a child may take as long as necessary. Therefore, it is also important for women to know that there is no scientific evidence about immediate or delayed administration of oxytocin being more beneficial. Women should be assured that they are allowed to decide based on their preferences and instinct.

A longer duration of labor can be translated into increased costs associated with a longer stay in the delivery ward. The rates of cesarean section that can have a direct impact on the costs were not different between immediate and delayed oxytocin augmentation. The information about the outcomes associated with a stay at NICU, such as umbilical cord blood pH, Sarnat and Thompson scores, and encephalopathy, which create the direct economic cost, were not reported in the literature available, but we do have information about Apgar score < 7 at 5 min, which is strongly related to these outcomes as well. Since there is no clinically relevant difference in Apgar score < 7 between immediate and delayed oxytocin, we expect no difference in these outcomes and no difference in NICU admission.

There are no obstacles for this intervention that could oppose implementation. After the diagnosis of protracted or arrest of labor is made, in all situations it is possible to start augmentation of labor with oxytocin.

Cephalo-pelvic disproportion and fetal distress, however, should always be excluded before starting augmentation.

The decision to start oxytocin augmentation immediately or delayed after diagnosing arrested or protracted labor in the first stage of the labor differs between the countries and even within the countries.

Immediate administration of oxytocin (< 1 h) after diagnosing arrested or protracted labor is associated with a reduction of duration of labor compared to delayed administration of oxytocin in nulliparous women in the first stage of spontaneous labor. However, quality of the evidence is low. Therefore, immediate initiation of oxytocin augmentation after diagnosing arrested or protracted labor may be considered, based on practical arguments like logistics and a shorter duration of labor.

The evidence for the use of immediate or delayed administration of oxytocin is not available for women with induced labor. However, there is no reason to believe that these women have other pros and cons for immediate or delayed oxytocin administration than women with spontaneous labor. Therefore, the panel recommends considering giving women with spontaneous labor the same information as women with induced labor.

Question 3. *Should oxytocin augmentation be started in a high or a low dose regimen during the first stage (the dilatation phase) of labor in nulliparous women at term with arrested or protracted labor?*

Recommendation

Consider using a low dose oxytocin regimen for labor augmentation in nulliparous women at term with arrested or protracted labor.

Considerations

The Guideline Development Panel considered the dosages compared in the RCTs selected from the literature for this recommendation. The compared regimens are shown in Table 1.

Overall, the GRADE level of evidence is low to moderate, with most recommendations being of low GRADE. There are no clinically important differences in the selected crucial and important outcomes between high and low dose regimens of oxytocin for labor augmentation in nulliparous women at term with arrested or protracted labor. The only exception is a possible reduction in the risk of metabolic acidosis in children exposed to a high dose compared to a low dose of oxytocin. There are no data on the following outcomes: Sarnat score, Thomson score and encephalopathy. This makes it difficult to estimate the importance of the difference in the incidence of metabolic acidosis.

A high dose oxytocin may have no effect on the risk of a cesarean section or instrumental delivery in comparison with a low dose oxytocin (RR 0.81, 95 % CI 0.57 to 1.16 and RR 0.97, 95 % CI 0.80 to 1.18, respectively). The level of evidence, however, is low to moderate.

Another study, not included in the literature summary because the experimental intervention was pulsatile instead of continuous administration of oxytocin, reported a significant decrease in instrumental deliveries with a pulsatile regimen [25]. This study also reported fewer instrumental deliveries with a high dose compared to a low dose regimen.

In the literature summary, the incidence of hyperstimulation and the need for intra-uterine resuscitation has not been examined, but a low dose regimen may be favorable for this outcome. Tachysystole occurred more often in the high dose regimen group in the study of Selin [22], in which tachysystole was seen in 43.2 % of cases in the high dose and 33.5 % of cases in the low dose arm (RD 9.6 %, 95 % CI 4.2 to 15.1 %), without differences in the adverse neonatal outcomes. The study of Liu [25] also reported significantly less hyperstimulation with a low dose regimen. Kenyon [21] reported no evidence of an effect of a high versus low dose regimen on hyperstimulation (RR 1.47, 95 % CI 0.73 to 2.94).

A major limitation of the performed meta-analyses, is the

Table 1
Overview of dosage regimens in the included studies.

Study	Intervention (high dose)	Control (low dose)
Bidgood (1987) (Source: Kenyon, 2013 [21])	Starting dose of 7 mU oxytocin per min, increased by 7 mU/min every 15 min, to a maximum of a frequency of 7 contractions in 15 min or by abnormality in the fetal heart rate tracing	Oxytocin started at 2 mU/min, increased by 2 mU/min every 15 min, to a maximum of 40 mU/min until a table phase of uterine activity was detected or uterine activity integral exceeded 1500 kPas/15 min
Jamal (2004) (Source: Kenyon, 2013 [21])	Starting dose of 4.5 mU oxytocin per minute, increased by 4.5 mU/min every 30 min	Starting dose of 1.5 mU oxytocin per minute, increased by 1.5 mU/min every 30 min
Kenyon (2013) (Source: Kenyon, 2013 [21])	Starting dose of 4 mU oxytocin per minute, increased every 30 min to 64 mU/min	Starting dose of 2 mU oxytocin per minute, increased every 30 min to 32 mU/min
Xenakis (1995) (Source: Kenyon, 2013 [21])	Starting dose of 4 mU oxytocin per minute, increased by 4 mU/min every 15 min	Starting dose of 1 mU oxytocin per minute, increased by 1 mU/min every 30 min
Selin [22,23]	Starting dose of 6.6 mU oxytocin per minute, increased by 6.6 mU/min every 20 min. Maximum dose of 59.4 mU oxytocin per minute	Starting dose of 3.3 mU oxytocin per minute, increased by 3.3 mU/min every 20 min. Maximum dose of 29.7 mU oxytocin per minute
Dy [24]	Starting dose of 4 mU oxytocine per minute, increased every 30 min to a maximum of 40 mU/min	Starting dose of 2 mU oxytocine per minute, increased every 30 min to a maximum of 20 mU/min

heterogeneity of regimens used in the individual studies, lowering the strength of the available evidence.

The most important goal of the patient is a spontaneous delivery of a neonate without need for admission to the neonatal care unit and with a pH > 7.05 and hence no expected long-term consequences related to the birth process. There is no evidence in favor of any regimen, except for metabolic acidosis, which was less frequent in the high dose arm. This evidence, however, was reported in only one study [22] and the effect was very uncertain, shown by the wide confidence interval (RR 0.56, 95 % CI 0.19 to 1.65).

It is reassuring that there seem to be no differences in childbirth experiences between high and low dose regimens (low grade). However, there is only low-grade evidence from one study.

There are patients who prefer to give birth as naturally as possible and patients who might have a preference of receiving doses as low as possible, which is to be supported considering the available evidence. It is important for women that their preferences are considered and a choice is made based on the principles of shared decision making.

The possible additional costs of administering a higher dosage of oxytocin are low since oxytocin is a low-cost medication.

To our knowledge, no quantitative or qualitative research has been performed to evaluate the acceptability or feasibility of the intervention. We expect that the implementation of any dose regimen would be feasible, since it only entails a possible change in dosage of an indicated intervention. Patients might object to higher doses, as might physicians. Since no differences in the pre-specified outcomes have been found, the working group proposes to opt for a low dose regimen.

Physicians could compare their local protocol to the low and high dose regimens described in Table 1. If their regimen corresponds to a high dose regimen, they could consider lowering the dosage, since there are no differences in the critical and important outcomes considered in this guideline. A low dose is preferred over a high dose since the efficacy is similar and the risk of side effects is lower.

We expect no health inequity, nor do we think there are limiting factors concerning the implementation of our recommendation, except for maybe the low certainty of the evidence. Nevertheless, there are no evidence-based reasons to advise against administering a high dose regimen. Monitoring of the fetal heartbeat, as well as the frequency of the contractions (to avoid hyperstimulation) is possibly more important than adhering to a certain regimen.

The decision to use high dose or low dose oxytocin administration, provided that the condition of the fetus is stable, varies between countries, and sometimes even within countries.

Although the high dose regimen may lower the risk of metabolic acidosis, the effect is very uncertain, and the evidence is low grade. Since there was no evidence of an effect of a high vs. low dose regimen of oxytocin augmentation on other outcome measures, the panel proposes to use an as low as clinically possible dose regimen.

Question 4. *What is the best order of oxytocin augmentation or amniotomy in nulliparous women at term during the first stage of the labor after diagnosing arrested or protracted labor?*

Recommendation

Consider performing amniotomy before the administration of oxytocin infusion after diagnosing arrested or protracted labor in nulliparous women during the first stage of spontaneous labor.

Considerations

We found no studies that met our inclusion criteria. Even though no studies were included in the analysis of the literature due to a mismatch between the search results and our PICO, one study which is related to the PICO might yield some indirect evidence [26].

Nachum and colleagues [26] studied women (nulliparous and parous) at term (>37 weeks of gestation) with intact amniotic membranes and a singleton fetus in cephalic presentation who had a prolonged latent phase of labor (i.e. before approximately 5 cm cervical dilatation), not for arrested or protracted labor (i.e. slow progress after approximately 5 cm cervical dilatation). They compared the effect of 1) amniotomy, followed by oxytocin administration if no progress was observed after 2 h (n = 21); 2) oxytocin, followed by amniotomy if no progress was observed after 2 h (n = 20); and 3) both interventions performed simultaneously (n = 16). They reported a shorter duration of the first stage of labor for women who received both interventions simultaneously (mean (SD) 351 (327) minutes) than for women who received either amniotomy first (555 (307) minutes) or oxytocin first (533 (359) minutes). However, they did not report how many women needed both interventions in these two groups. This study did not report any critical neonatal outcomes. There is no literature on the order of amniotomy and oxytocin in arrested or protracted labor in women with induced labor.

There are theoretical concerns regarding the risks and disadvantages of early amniotomy. Amniotomy opens the amniotic sac, which may increase the risk of maternal and neonatal infection. Additionally, some of the natural protective mechanisms for the baby could be compromised due to the loss of amniotic fluid, potentially leading to umbilical cord compression with unclear or abnormal CTG patterns. The alternative approach is to administer oxytocin first and consider amniotomy after assessment of the progress of labor. This could decrease the risk of intrapartum fever, chorioamnionitis, intrapartum CTG changes, and neonatal infections. However, this method also has its drawbacks. Oxytocin augmentation requires equipment and precise monitoring and evaluation of labor progress, which can be resource consuming. Furthermore, pain control for the expectant mother could be challenging, especially if the labor is progressing slowly.

In summary, there is no clear answer as to whether amniotomy or oxytocin administration should come first or even simultaneously.

Nachum [26] found that women who received both amniotomy and oxytocin at the same time were more satisfied, but there was no difference between the two groups with alternate sequence of the two interventions.

The primary goal of an intervention is to ensure a safe childbirth and a positive childbirth experience. Specifically, the goal of amniotomy and/or oxytocin includes facilitating cervical dilation and progress of labor, thereby reducing the duration of labor, which can help minimize maternal exhaustion and discomfort. Further factors are minimizing risks associated with prolonged labor, such as infection or fetal distress.

Women may choose amniotomy first since it potentially reduces medication use, allowing a more natural labor progression. Alternatively, opting for intact membranes with oxytocin first could protect the fetus from infection and distress. Concerns about medicalization of the birth process may also arise. The value of these pros and cons varies among parturients. Some may prioritize a more natural birth experience, while others may prioritize a shorter labor. The certainty about these preferences can vary widely among individuals and may be influenced by cultural, psychological, and past birth experiences. Therefore, it is important to take these preferences into account and to decide according to the principles of shared decision making.

Amniotomy has little cost related to the instrument by which it is accomplished, compared to oxytocin infusion. However, if amniotomy before oxytocin would lead to more interventions or postpartum complications, this would outweigh the lower cost. No study has assessed cost-effectiveness.

Among midwives, amniotomy may be favored as a first step since the midwife may perform this independently, whereas oxytocin infusion for labor augmentation requires a doctor's prescription in most settings. Oxytocin administration is also more cumbersome as it requires more of the midwife's time to prepare the infusion, acquire intravenous access, set up the equipment to regulate the speed of infusion, and monitor CTG

continuously. However, both women, midwives, and doctors perceive the risk of complications that may occur after the membranes have been ruptured, such as infection and an abnormal CTG. However, oxytocin administration can also lead to an abnormal CTG.

The traditional approach in most European countries is to perform amniotomy first and then administer oxytocin if labor progress remains slow after a few hours. This has the advantage of being widely practiced and recommended by experienced obstetricians in many countries. In most countries, national guidelines do not routinely recommend the use of amniotomy and oxytocin during labor, although active management of labor is occasionally favored. However, if labor is suspected to be delayed, amniotomy is favored as the initial procedure. This approach also has the advantage that in countries where childbirth is midwife-centered (e.g., UK, the Netherlands), the care does not necessarily need to be transferred to medical management. If there is insufficient progress under this approach, oxytocin augmentation is an option.

Based on the existing evidence in the literature, no clear recommendation can be made regarding the order of amniotomy and oxytocin. Since amniotomy before oxytocin is the most common practice today, there is no reason to change the current practice.

Question 5. *After how many hours of oxytocin augmentation in nulliparous women at term in the first stage of labor with arrested or protracted labor should a cesarean section be performed?*

Recommendation

In arrested or protracted labor during the first stage of labor, consider continuing oxytocin augmentation for at least four hours with adequate contractions before a decision for cesarean section is made provided good fetal and maternal conditions.

Considerations

The literature search did not yield any studies comparing the effects of long versus short duration of oxytocin stimulation prior to cesarean section in nulliparous women with arrested or protracted labor, who received oxytocin augmentation in the first stage of labor. In a cohort study in women with oxytocin augmentation for labor arrest in the active phase ($n = 500$), there was a median dilatation rate of 1.4 cm/hour in nulliparous women and one of 1.8 cm/hour in parous women [27,28]. Moreover, the 5th percentile dilatation rate was 0.5 cm/hour in both groups in women with vaginal delivery, and 23/38 women (61 %) in the cohort with labor arrest > 2 h succeeded with vaginal delivery when oxytocin was continued. These data support having a > 2 -hour duration for oxytocin infusion with labor arrest but do not qualify the duration threshold otherwise.

The potential pro of a longer duration of the oxytocin infusion might be a higher success rate of vaginal delivery, whereas the cons might be a longer exposure to a drug that can result in hyperstimulation and fetal asphyxia and eventually even uterine rupture, thereby indirectly increasing the risk of cesarean section. Furthermore, it may be of significant inconvenience for the parturient to endure artificially enhanced contractions for a longer period than necessary before a cesarean section is performed.

In the NICE guideline Intrapartum Care, it is recommended to perform a vaginal exam 4 h after the oxytocin infusion has resulted in regular contractions in established labor [29]. Further obstetric review is needed to assess whether a cesarean birth is advisable if cervical dilatation has increased by less than 2 cm at this point [29]. This NICE recommendation was based primarily on indirect evidence [27,28].

It is essential to consider parental preferences as non-affirming birth experiences due to unmet expectations are common [30,31]. Most women wish a positive birth experience, where safety and psychosocial wellbeing are equally valued [31]. Any prolongation of the progress of augmentation of labor should meet all these needs. The parturient aims

for a vaginal delivery and is therefore likely willing to accept a longer duration of oxytocin stimulation (> 4 h) if this intervention increases the chance of succeeding with a vaginal delivery. It is a prerequisite to establish adequate medical and/or non-medical pain management, psychological and positional support to endure a prolonged duration of contractions.

Oxytocin is a cheap drug, and so the difference in costs between a shorter or longer duration of its use is very small. A longer treatment duration translates into increased costs associated with a prolonged stay in the delivery ward, but on the other hand, could be associated with decreased costs due to fewer cesarean sections, shorter admissions, and better maternal mental health [31]. Facility, staff load, and availability could impede the implementation of the intervention, as it is likely to result in longer labor courses.

The acceptability of the intervention depends on the expectations and needs of the woman, but is likely to be high in women who intend to deliver vaginally.

The applicability of a longer oxytocin stimulation should be carefully considered by physicians in low resource settings, as lack of access to continuous fetal surveillance, to accurate oxytocin dosing regimens, to operative delivery, or to neonatal treatment may compromise the safety of the intervention.

The minimum duration between the start of oxytocin infusion and the decision to perform a cesarean section, provided good fetal condition, varies between countries, and sometimes even within countries. In Belgium, Portugal, and Sweden there is intra-national variation. In the Netherlands, the duration is at least 2 h, in German speaking countries: 2 to 4 h, and in Denmark and Spain (in the first, active labor phase) at least 4 h of oxytocin infusion with regular contractions.

Considering the lack of data on both effects and safety of short (< 4 h) versus long (> 4 h) duration of oxytocin, it seems reasonable to extend the duration of stimulation to at least 4 h of established uterine contractility to diagnose insufficient or no progress resulting in a delivery by cesarean section. The potential of a longer duration to increase the chance of a vaginal delivery may outweigh the risks associated with a longer labor (i.e. maternal infection) including a longer exposure to oxytocin, if good maternal and fetal surveillance and treatment options are available.

We therefore recommend continuing intravenous oxytocin stimulation for at least four hours and adequate contractions in arrested or protracted labor in nulliparous women, before delivery by cesarean section is considered. The women's risks and needs as well as fetal safety should be considered in the decision to continue oxytocin infusion and performing a cesarean section after four hours.

CRedit authorship contribution statement

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Formal analysis. **Danique Middelhuis**: Writing – original draft, Formal analysis. **Linda Niesink-Boerboom**: Data curation. **Jana Tuijelaars**: Writing – review & editing, Writing – original draft, Formal analysis. **Johanna H. van der Lee**: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejogrb.2025.114064>.

References

- [1] Infante-Torres N, Molina-Alarcón M, Arias-Arias A, Rodríguez-Almagro J, Hernández-Martínez A. Relationship between prolonged second stage of labor and short-term neonatal morbidity: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2020;17(21):7762. <https://doi.org/10.3390/ijerph17217762>.
- [2] Hagiwara M, Nakanishi S, Shindo R, Obata S, Miyagi E, Aoki S. An extremely prolonged second stage of labor increases maternal complications but has no adverse effect on neonatal outcomes. *J Obstet Gynaecol Res* 2022;48(6):1364–9.
- [3] Niemczyk NA, Ren D, Stapleton SR. Associations between prolonged second stage of labor and maternal and neonatal outcomes in freestanding birth centers: a retrospective analysis. *BMC Pregnancy Childbirth*. 2022 Feb 4;22(1):99.
- [4] Pergialiotis V, Bellos I, Antsaklis A, Papapanagiotou A, Loutradis D, Daskalakis G. Maternal and neonatal outcomes following a prolonged second stage of labor: a meta-analysis of observational studies. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 2020;252:62–9.
- [5] Young C, Bhattacharya S, Woolner A, Ingram A, Smith N, Raja EA, et al. Maternal and perinatal outcomes of prolonged second stage of labour: a historical cohort study of over 51,000 women. *BMC Pregnancy Childbirth* 2023;23(1):467. <https://doi.org/10.1186/s12884-023-05733-z>. PMID: 37349683; PMCID: PMC10288707.
- [6] National Institute for Health and Care-Excellence (NICE): Intrapartum Care. Care of healthy woman and their babies during childbirth. Clinical guideline [CG 190]. NICE CG190 2014 updated 02/2017. Version 2 <https://www.nice.org.uk/guidance/cg190/evidence/full-guideline-pdf-248734770>.
- [7] Abou-Dakn M, Schäfers R, Peterwerth N, Asmushen K, Bässler-Weber S, Boes U, et al. Vaginal Birth at Term - Part 1. Guideline of the DGGG, OEGGG and SGGG (S3-Level, AWMF Registry No. 015/083, December 2020). *Geburtshilfe Frauenheilkd*. 2022 Nov 3;82(11):1143–1193.
- [8] Abou-Dakn M, Schäfers R, Peterwerth N, Asmushen K, Bässler-Weber S, Boes U, et al. Vaginal Birth at Term - Part 2. Guideline of the DGGG, OEGGG and SGGG (S3-Level, AWMF Registry No. 015/083, December 2020). *Geburtshilfe Frauenheilkd*. 2022 Nov 3;82(11):1194–1248.
- [9] ACOG Committee Opinion No. 766 Summary: Approaches to Limit Intervention During Labor and Birth. *Obstet Gynecol*. 2019 Feb;133(2):406–408.
- [10] WHO. WHO recommendations for augmentation of labour. 2014. ISBN 978 92 4 150736 3 https://iris.who.int/bitstream/handle/10665/112825/9789241507363_eng.pdf;jsessionid=EF47C4BC121DBE61E5C6168E25CDDF86?sequence=1, Glenton C, Dahm P, Garner P, Akl EA, Alper B, Brignardello-Petersen R, et al. GRADE Working Group. GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol*. 2020 Mar;119:126–135.
- [11] Alonso-Coello P, Schünemann HJ, Moher J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Working Group. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *BMJ* 2016;353:i2016.
- [12] Alonso-Coello P, Oxman AD, Moher J, Brignardello-Petersen R, Akl EA, Davoli M, et al. Working Group. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. *BMJ* 2016;353(353):i2089.
- [13] Smyth RM, Alldred SK, Markham C. Amniotomy for shortening spontaneous labour. *Cochrane Database Syst Rev*. 2013 Jan 31;(1):CD006167. Update in: *Cochrane Database Syst Rev*. 2013;(6):CD006167.
- [14] Blanch G, Lavender T, Walkinshaw S, Alfirevic Z. Dysfunctional labour: a randomised trial. *Br J Obstet Gynaecol* 1998;105(1):117–20.
- [15] Tosone G, Maraolo AE, Mascolo S, Palmiero G, Tambaro O, Orlando R. Vertical hepatitis C virus transmission: Main questions and answers. *World J Hepatol* 2014; 6(8):538–48.
- [16] Cotter AM, Brookfield KF, Duthely LM, Gonzalez Quintero VH, Potter JE, O'Sullivan MJ. Duration of membrane rupture and risk of perinatal transmission of HIV-1 in the era of combination antiretroviral therapy. *Am J Obstet Gynecol*. 2012 Dec;207(6):482.e1–5.
- [17] Bopegamage S, Kacerovsky M, Tambor V, Musilova I, Sarmirova S, Snelders E, et al. Preterm prelabour rupture of membranes (PPROM) is not associated with presence of viral genomes in the amniotic fluid. *J Clin Virol* 2013;58(3):559–63.
- [18] Cheung KW, Seto MTY, So PL, Wong D, Mak ASL, Lau WL, et al. The effect of rupture of membranes and labour on the risk of hepatitis B vertical transmission: prospective multicentre observational study. *Eur J Obstet Gynecol Reprod Biol* 2019;232:97–100.
- [19] Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2013;6:CD007123.
- [20] Kenyon S, Tokumasu H, Dowswell T, Pledge D, Mori R. High-dose versus low-dose oxytocin for augmentation of delayed labour. *Cochrane Database Syst Rev*. 2013 Jul 13;(7):CD007201.
- [21] Selin L, Wennerholm UB, Jonsson M, Dencker A, Wallin G, Wiberg-Itzel E, et al. High-dose versus low-dose of oxytocin for labour augmentation: a randomised controlled trial. *Women Birth* 2019;32(4):356–63.
- [22] Selin L, Berg M, Wennerholm UB, Dencker A. Dosage of oxytocin for augmentation of labor and women's childbirth experiences: a randomized controlled trial. *Acta Obstet Gynecol Scand* 2021;100(5):971–8.
- [23] Dy J, Rainey J, Walker MC, Fraser W, Smith GN, White RR, et al. Accelerated titration of oxytocin in nulliparous women with labour dystocia: results of the ACTION pilot randomized controlled trial. *J Obstet Gynaecol Can* 2018;40(6): 690–7.
- [24] Liu J, Yi Y, Weiwei X. Effects of increased frequency, high dose, and pulsatile oxytocin regimens on abnormal labor delivery. *Med Sci Monit* 2018;7(24): 2063–71.
- [25] Nachum Z, Garmi G, Kadan Y, Zafraan N, Shalev E, Salim R. Comparison between amniotomy, oxytocin or both for augmentation of labor in prolonged latent phase: a randomized controlled trial. *Reprod Biol Endocrinol* 2010;7(8):136.
- [26] Rouse DJ, Owen J, Hauth JC. Active-phase labor arrest: oxytocin augmentation for at least 4 hours. *ObstetGynecol* 1999;93(3):323–8.
- [27] Rouse DJ, Owen J, Savage KG, Hauth JC. Active phase labor arrest: revisiting the 2-hour minimum. *ObstetGynecol* 2001;98(4):550–4.
- [28] NICE guideline [NG235] Intrapartum care. Published: 29 September 2023. Retrieved 07/01/2024: <https://www.nice.org.uk/guidance/ng235>.
- [29] Hauck Y, Fenwick J, Downie J, Butt J. The influence of childbirth expectations on Western Australian women's perceptions of their birth experience. *Midwifery* 2007;23:235–47.
- [30] Downe S, Finlayson K, Oladapo OT, Bonet M, Gülmezoglu AM. What matters to women during childbirth: a systematic qualitative review. *PLoS One* 2018;13: e0194906.
- [31] Petrou S, Khan K. An overview of the health economic implications of elective cesarean section. *Appl Health Econ Health Policy* 2013;11:561–76.