EUROPEAN ASSOCIATION OF PERINATAL MEDICINE
http://www.europerinatal.eu/

EUROPEAN GUIDELINES ON PERINATAL CARE

PERIPARTUM CARE

OXYTOCIN FOR INDUCTION AND AUGMENTATION OF LABOR

Writing group: Inês Nunes (Portugal), Corinne Dupont (France), Susanna Timonen (Finland).
Guideline panel: Vanessa Cole (UK), Christiane Schwarz (Germany), Anneke Kwee (Netherlands), Diogo Ayres-de-Campos (Portugal),BrankaYli (Norway), Austin Ugwumadu (UK), Christophe Vayssiere (France), Emmanuel Roth (France), National Society representatives. Approved 2021.

Summary of recommendations

1. Oxytocin for induction or augmentation of labor should not be started when there is a previous scar on the body of the uterus (such as previous classical cesarean section or myomectomy) or in any condition where labor or vaginal delivery are contraindicated. (**Moderate quality evidence +++-**; **Strong recommendation**). Oxytocin should not be started before 1 hour has elapsed since amniotomy, 6 hours since the last application of dinoprostone gel, 4 hours since application of the last misoprostol tablet, and 30 minutes since removal of a dinoprostonevaginal insert.**(Low quality evidence ++--; Moderate recommendation)**.

2. Cardiotocography (CTG) should be performed and a normal pattern without tachysystole should be documented for at least 30 minutes before oxytocin is used. Continuous CTG, with adequate monitoring of both fetal heart rate and uterine contractions, should be maintained for as long as oxytocin is used, and thereafter until delivery (**Low++-- to moderate +++- quality evidence; Strong recommendation**).

3. For labor induction, amniotomy should be followed 1-hour later by oxytocin infusion, unless adequate uterine contractility has meanwhile ensued. For augmentation of labor, if the membranes are intact and there are conditions for a safe amniotomy, the latter should be considered before oxytocin is started**(Very low quality of evidence +---; Weak recommendation)**.

4. Oxytocin should be administered intravenously using the following regimen: 5IU oxytocin diluted in 500mL of 0.9% normal saline (each mL contains 10 mIU of oxytocin), in an infusion pump at increasing rates, as shown in Table 1, until a frequency of 3-4 contractions per 10 min is reached, a non-reassuring CTG pattern ensues, or maximum ratesare reached(**Low quality evidence ++--; Strong recommendation**). If the frequency of contractions exceeds 5 in 10 min, the infusion rate should be reduced, even if a normal CTG pattern is present. With a non-reassuring CTG pattern, urgent clinical assessment by an obstetrician is indicated, and strong consideration should be given to reducing or stopping the oxytocin infusion. The minimal effective dose of oxytocin should always be used.**(Low ++-- to Moderate +++- quality evidence;Strong recommendation)**.

Table 1. Recommended oxytocin incremental regimen

	No uterinescar		Previousuterinescar	
Time	**mIU/min**	**mL/hour**	**mIU/min**	**mL/hour**
Start	2	12	1	6
0.5hour	4	24	2	12
1 hour	6	36	3	18
1.5 hours	8	48	4	24
2 hours	10	60	5	30
2.5 hours	12	72	6	36
3 hours	14	84	7	42
3.5 hours	16	96	8	48
Medical review				
4 hours	18	108	9	54
4.5 hours	20	120	10	60
5 hours	22	132	**Maximum dose**	
5.5 hours	24	144		
6 hours	26	156		
6.5 hours	28	168		
7 hours	30	180		
	Maximum Dose			

5. Use of oxytocin for induction or augmentation of labor should be regularly audited (**Low quality evidence ++--; Strong**

recommendation).

Introduction

Oxytocin is a neuropeptide produced in the supraoptic and paraventricular nuclei of the hypothalamus. It is a potent uterotonic agent that stimulates the smooth muscles of the uterus and also causes contraction of the myoepithelial cells surrounding the mammary alveoli, leading to milk ejection during lactation.[1-6] The effects of oxytocin are modulated by the circulating levels of the hormone, but also by the levels of oxytocinase (an enzyme that degrades oxytocin), the number and activity of oxytocin receptors. At the onset of labor, there is an upregulation of oxytocin receptor mRNA levels and the density of myometrial oxytocin receptors reaches a peak.[7]

Induction of labor is defined as the artificial initiation of uterine contractions before their spontaneous onset, with the purpose of accomplishing vaginal birth. For induction of labor to be successful, cervical ripening, a biomechanical process whereby the cervix becomes soft and compliant, needs to have taken place. The latter may occur naturally or as a result of physical or pharmacological interventions, which are outside the scope of this guideline. Augmentation of labor is the process of stimulating the uterus to increase the frequency, duration and intensity of contractions after the onset of labor. It is commonly used to treat protracted or arrested labor, when inadequate uterine contractions are thought to be the underlying cause.

A synthetic analogue of oxytocin is commonly used in clinical practiceto induceor augment labor. The solution for injection is colorless and generally available in ampoules containing 5IU in 1ml or 10IU in 1ml. Forthe purpose of labor induction and augmentation it should only be used by intravenous (IV) infusion. With intravenous use, the half-life of oxytocin is around 3-12 minutes, depending mostly on its dilution. At an appropriate infusion rate, a gradual response in uterine contractions is elicited within 3-5 minutes, reaching a steady state within 20-40 minutes. [8-9] Discontinuation or reduction ofthe infusion rate leads to a rapid decline incontractile activity. At low infusion rates it causes rhythmic uterine contractions. In higher doses it also has a direct relaxing effect on vascular smooth muscle resulting in transient hypotension, reflex tachycardia and flushing.

The uterus is more sensitive to oxytocin as pregnancy advances, in younger women, in parous women, in women with lower body mass index, in women with spontaneous labor, and after prostaglandin administration.[10-13]Increased responsiveness also occurs in the late first stage and in the second stage of labor.[14] However, there is a large biological variability in the infusion dose required to cause adequate uterine contractions.[2]For this reason, there is noabsolute safe rate, and there is a constant needto titratethe infusion rate against the frequency of uterine contractions.[15-18]

In 2007, the Institute for Safe Medication Practices added oxytocin to its list of high-alert medications.[19] Errors involving oxytocin administration are most frequently related to the lack of timely recognition of excessive uterine activity, but also to mistaken administration of IV fluids containing oxytocin, excessive doses leading to transient maternal hypotension, and inappropriate administration to women with less than 39 completed weeks of gestation. Other risks and side effects associated with the use of oxytocin are: nausea and vomiting; post-partum hemorrhage (PPH),especially when a high dose is used during labor, when increment intervals are short, or when the patient does not receive prophylactic oxytocin in the third stage of labor; water intoxication with maternal and neonatal hyponatremia (use of high doses of oxytocin with large amounts of electrolyte-free fluid, related with its anti-diuretic activity); maternal hypotension or cardiac rhythm disturbances (as a result of interactions with inhalation anesthetics such as cycloprophane, enflurane, halothane and isoflurane); and an increased uterotonic effect when associated with prostaglandins.[20-22]All of these risks are preventable if safe care practices are used.

Induction and augmentation of labor should only be performed when there is a clear medical indication for these procedures, and the expected benefits outweigh the potential harms. Moreover, appropriatestaff, facilities, and equipment need to be present before they are considered, including people with sufficient experience in cardiotocographic (CTG) monitoring and with the capacity to perform an urgent cesarean delivery.

Recommendations

1. Oxytocin for induction or augmentation of labor should not be started when there is a previous scar on the body of the uterus (such as previous classical cesarean section or myomectomy) or in any condition where labor or vaginal delivery are

contraindicated. (**Moderate quality evidence +++-**; **Strong recommendation**). Oxytocin should not be started before 1 hour has elapsed since amniotomy, 6 hours since the last application of dinoprostone gel, 4 hours since application of the last misoprostol tablet, and 30 minutes since removal of a dinoprostone vaginal insert. **(Low quality evidence ++-; Moderate recommendation).**

Uterine rupture secondary to treatment with oxytocin is 2.5 to 14.0 times more likely to occur in multiparous women in the context of a previous uterine scar (*circa*1.4-2.1 %), when compared with spontaneous labor (*circa*0.15-0.6%), and increases with higher doses of oxytocin used.[23-25] In nulliparous women it is extremely rare for the uterus to rupture in the absence of a scar(*circa*0.0045-0.05%).[26] There are a few case-reports and one retrospective case-control study documenting a *circa*2-foldincreased risk of uterine rupture with oxytocin use in such situations, and it is hypothesized to occur mainly when oxytocin perfusion rate is increased despite the occurrence of adequate uterine activity.[26]The minimum time interval between prostaglandin administration or amniotomy,and the initiation of oxytocin infusion has not been scientifically determined.[27]Therefore the recommendations contained in this guideline are based in the reported half-lives of the different drugs and extrapolations from the recommended therapeutic regimens.According to the manufacturers' guidelines, after use of 1.5 mg dinoprostonegelin intracervical application or 2.5 mg dinoprostone gel in vaginal application, oxytocin induction should be delayed for 6–12 hours, because theeffect of prostaglandins on uterine contractilityis heightened with oxytocin.

2. Cardiotocography (CTG) should be performed and a normal pattern without tachysystole should be documented for at least 30 minutes before oxytocin is used. Continuous CTG, with adequate monitoring of both fetal heart rate and uterine contractions, should be maintained for as long as oxytocin is used, and thereafter until delivery (**Low++-- to moderate +++-quality evidence; Strong recommendation**).

The main risk associated with oxytocin infusion isexcessive uterineactivity, which is usually only detectable as tachysystole (more than 5 contractions in two successive 10 min periods or more than 15 contractions in 30 min). Excessive uterine contractility can result in fetalhypoxia, as the interval between contractions is important for re-establishment of fetal oxygenation. There are data to suggest that, in spontaneous labor it takes up to 90 seconds after a contraction for fetal oxygenation to be restored[28], while in oxytocin-augmented labors this recovery period averages 138 seconds.[29-31]Excessive uterine activity should be avoided, irrespective of whether CTG changes are present or not. [18]This complicationcan occur both at low or high oxytocin infusion rates.

It is important to document a normalpattern without tachysystole before oxytocin is started, to identify the situations in which its use may be dangerous or unnecessary. Oxytocin should not be started when there is a non-reassuring CTG. Evaluation of the CTG tracing and the decision to start oxytocin is the responsibility of an obstetrician and should be recorded in the clinical records.

The decision to induce a pregnant woman with a previous low transverse cesarean section, twins, preterm fetus, fetal growth restriction, as well as a pregnancy with previous cardiovascular disease should be made by a senior obstetrician, and recorded in the clinical records.

3. For labor induction, amniotomy should be followed 1-hour later by oxytocin infusion, unless adequate uterine contractility has meanwhile ensued. For augmentation of labor, if the membranes are intact and there are conditions for a safe amniotomy, the latter should be considered before oxytocin is started (**Very low quality of evidence +---; Weak recommendation)**.

There is insufficient evidence on the efficacy and safety of amniotomy alone for labor induction.[27, 32]Although itcan be used for this purpose when the cervix isfavorable (modified Bishop score of 6 or above), there is an unpredictable and sometimes very long interval before the onset of contractions. Therefore, amniotomy should be followed 1-hour later by oxytocin infusion, unless adequate uterine contractility has meanwhile ensued.

Augmentation of labor should not be considered without a clear diagnosis of labor dystocia, as both early amniotomy and routine oxytocin administration during spontaneous labor have not been shown to confer benefits to perinatal outcomes, interventions or birth experiences.[33-35]Before oxytocin infusion is started for labor

augmentation, the status of the fetal membranes should be evaluated. If these are intact and there are conditions to perform a safe amniotomy, consideration should be given to perform this procedure first, as itmay be sufficient to accelerate labor, and thus the risks of oxytocin infusion can be avoided. At least 1-hour should be allowed to evaluate the effect of amniotomy on uterine contractility before oxytocin is started.

In a systematic review of randomised controlled trials (RCTs) evaluatingwomen with slow progress in the first stage of labor, the use of oxytocin when compared with placebo resulted in a *circa* 2-hour reduction in the total duration of labor, an increase in uterine hyperstimulation with CTG changes, and no difference in perinatal outcomes or intervention rates.[36]A systematic review of RCTs comparing the discontinuation versus the continuation of intravenous oxytocin in the active phase of induced labors, reported that the latter results in a *circa* 25-min decreased duration of the active phase of labor and a trend towards decreased chorioamnionitis, but a 85% increase in tachysystole with CTG changes, a 31% increase in cesarean delivery, and no difference in perinatal outcomes.[37]It must be emphasized that abnormal CTG findings and intervention rates may be heavily influenced by oxytocin infusion protocols and by healthcare reactions to abnormal CTG findings.

4. Oxytocin should be administered intravenously using the following regimen: 5 IU oxytocin diluted in 500 mL of 0.9% normal saline (each mL contains 10 mIU of oxytocin), in an infusion pump at increasing rates, as shown in Table 1, until a frequency of 3-4 contractions per 10 min is reached, a non-reassuring CTG pattern ensues, or maximum rates are reached (**Low quality evidence ++--; Strong recommendation**). If the frequency of contractions exceeds 5 in 10 min, the infusion rate should be reduced, even if a normal CTG pattern is present. With a non-reassuring CTG pattern, urgent clinical assessment by an obstetrician is indicated, and strong consideration should be given to reducing or stopping the oxytocin infusion. The minimal effective dose of oxytocin should always be used. **(Low ++--** to **Moderate +++- quality evidence;Strong recommendation)**.

Currently there is no generalized agreement on the recommended regimen for oxytocininfusion, and different guidelines proposedifferent regimens.[38-50]Existing evidence suggests that no oxytocin regimen is superior to others. In a systematic review of RCTs, a high dose regimen was associated with significant reductions in the length of labor, and cesarean deliveries, as well as an increase in spontaneous vaginal births.[46]However, few data were recorded on adverse outcomes for mothers and newborns, so the evidence was not considered strong enough to make firm recommendations.

A major concern is that different oxytocin infusion regimens maybe used in the same delivery unit, thus increasing the risk of medication errors.The use ofa single oxytocin infusion regimen in delivery units has been shown to minimize risks[21,51,52]. In this guideline, a low-dose regimen is proposed, based mainly on safety issues (Table 1). When referring to infusion rates of oxytocin, both milliunits/min (mIU/min) or milliliters/hour (mL/hour) may be used, but each delivery unit should decide which of these will be used by all staff.

The person preparing the oxytocin infusion bag should place an “Oxytocin” drug additive label on it, signing, dating and timing it. The oxytocin starting and increment infusion rates are displayed in Table 1. Note that when there is a previous uterine scar, the infusion rates are lower.

The infusion rate should be titrated according to the frequency of uterine contractions, CTG findings and progress of labor.The minimal effective dose of oxytocin should always be used to obtain 3-4 contractions every 10 min and adequate progress of labor.Maternal heart rate and the CTG tracingshould be evaluated prior to the start or any increase in the infusion rate.Adequate quality of the fetal heart rate and uterine contraction signal needs to be guaranteed.The infusion rate should be reduced if the frequency of contractions exceeds 5 in 10 min, even when a normal CTG pattern is present. With a non-reassuring CTG pattern, urgent clinical assessment by an obstetrician is indicated, and strong consideration should be given to reducing or stopping the oxytocin infusion.

External monitoring of uterine contractions with a tocodynamometer is the technology usually available in conventional CTG monitors. This only reliably records the frequency of uterine contractions; other characteristicssuch as duration, intensity, basal tone, and relaxation time between contractions, are also important for fetal oxygenation, but can only be monitored with an intrauterine pressure catheter.[31,53]

Excessive uterine contractility can usually be reversed by reducing or stopping the oxytocin infusion,and if a rapid response is required, by starting acute tocolysis with beta-adrenergicagonists (salbutamol, terbutaline, ritodrine), atosiban, or nitroglycerine.[31]If rapid normalization of the CTG pattern does not occur, immediate operative delivery

needs to be considered. If oxytocin infusion is discontinued for any reason CTG monitoring should continue until delivery. A decision to recommence oxytocin is the responsibility of a senior obstetrician.

5. Use of oxytocin for labor induction and augmentation should be regularly audited (**Low quality evidence ++--; Strong recommendation**).

It is the responsibility of healthcare professionals administering oxytocin infusion to record all related clinical findings and proceduresappropriately in the patient's notes, including the timing of increment doses.[54]Regular audit of women undergoing labor induction or augmentation is important to identify communication problems, issues related to guideline implementation, adverseoutcomes and intervention rates.[54]Thisshould includean evaluation of severe PPH, uterine rupture, cesarean delivery, metabolic acidosis, low 5-min Apgar score, and hypoxic-ischemic encephalopathy.

Methodology used in the development of this guideline

The writing group conducted searches in Medline and the Cochrane Library for articles related to thistopic. These were limited to studies involving humans and articles published in English between January 1988 and February 2020. The searches were completed manually by consulting the reference list in the identified publications and other guidelines related to the topic. The writing group synthesized the evidence and elaborated the first draft of the manuscript, proposing recommendations according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. The guideline panel members were asked to comment and modify the text in three successive interactions until a final version of the manuscript was reached. All panel members who agreed with the final version and gave their consent forco-authorship are listed in the document.

References

1.Jonsson M, Nordén SL, Hanson U."Analysis of malpractice claims with a focus on oxytocin use in labor." ActaObstetGynecol Scand. 2007;86(3):315–9.

2. Clark S, Belfort M, Saade G, Hankins G, Miller D, Frye D, et al."Implementation of a conservative checklist-based protocol for oxytocin administration: maternal and newborn outcomes." Am J ObstetGynecol.2007;197(5):480.e1–5.

3.Jonsson M, Nordén-Lindeberg S, Ostlund I, Hanson U. "Acidemia at birth, related to obstetric characteristics and to oxytocin use, during the last two hours of labor." ActaObstetGynecolScand. 2008;87(7):745–50.

4. Clark SL, Simpson KR, Knox GE, Garite TJ. "Oxytocin: new perspectives on an old drug." Am J Obstet Gynecol.2009;200(1):35.e1–6.

5.Clark SL, Meyers JA, Frye DK, Perlin JA. "Patient safety in obstetrics--the Hospital Corporation of America experience." Am J ObstetGynecol. 2011;204(4):283–7.

6. Prasad MR, Funai E. "Oxytocin use during active labor: too much of a good thing?" Am J Obstet Gynecol.2012; 207(6):439–40.

7. Blanks AM, Thornton S. "The role of oxytocin in parturition." BJOG. 2003; 110 Suppl 20:46–51.

8.Seitchik J, Amico J, Robinson AG, Castillo M."Oxytocin augmentation of dysfunctional labor. IV. Oxytocin pharmacokinetics." Am J Obstet Gynecol. 1984;150(3):225–8.

9.Novartis. Syntocinon®. (2009) Apr 6;:1–10 http://www.novartis.com.au/pi_pdf/syt.pdf.

10. Caldeyro-Barcia R, Poseiro JJ. "Physiology of the uterine contraction". ClinObstet Gynecol. 1960;3:386–408. (Level III)

11. Satin AJ, Leveno KJ, Sherman ML, McIntire DD. "Factors affecting the dose response to oxytocin for labor stimulation". Am J Obstet Gynecol.1992;166:1260–1. (Level II-3)

12. Zhang J, Bricker L, Wray S, Quenby S. "Poor uterine contractility in obese women."BJOG.2007;114(3):343-348.

13. Hill M, Reed KL, Cohen WR."Oxytocin utilization for labor induction in obese and lean women". J Perinat Med. 2015;43(6):703-706.

14. Thorngren-Jerneck K, Herbst A. "Perinatal factors associated with cerebral palsy in children born in Sweden". Obstet Gynecol. 2006;108:1499-505.

15. Bakker PCAM, Kurver PHJ, Kuik DJ, Van Geijn HP. "Elevated uterine activity increases the risk of fetal acidosis at birth." Am J Obstet Gynecol. 2007;196(4):313.e1–6.

16. Simpson KR, James DC. "Effects of oxytocin-induced uterine hyperstimulation during labor on fetal oxygen status and fetal heart rate patterns." Am J Obstet Gynecol. 2008;199(1):34.e1–5.

17. Frey H, Meister M, Kleweis S, Stuart J. "Discussion: "Tachysystole in term labor" by Heuser et al". Am J Obstet Gynecol. 2013;209(1):e6–7.

18. Heuser CC, Knight S, Esplin MS, Eller AG, Holmgren CM, Manuck TA, et al. "Tachysystole in term labor: incidence, risk factors, outcomes,

and effect on fetal heart tracings." Am J Obstet Gynecol. 2013;209(1):32.e1–6.
19. Institute for Safe Medication Practices 2020 - https://www.ismp.org/resources/errors-associated-oxytocin-use-multi-organization-analysis-ismp-and-ismp-canada
20. Rousseau A, Burguet A. "Oxytocin administration during spontaneous labor: guidelines for clinical practice. Chapter 5: maternal risk and adverse effects of using oxytocin augmentation during spontaneous labor." J GynecolObstet Hum Reprod. 2017;46(6):509-521.
21. Buchanan SL, Patterson JA, Roberts CL, Morris JM, Ford JB. "Trends and morbidity associated with oxytocin use in labor in nulliparas at term." Aust N Z J ObstetGynaecol. 2012;52(2):173-8.
22. 'Oxytocin to accelerate or induce labor', Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland and the Clinical Strategy and Programmes Division, Health Service Executive, (2019) Robson M *et al.*
23. Sentilhes L, Vayssière C, Beucher G, Deneux-Tharaux C, Deruelle P, Diemunsch P, *et al*."Delivery for women with a previous cesarean: guidelines for clinical practice from the French College of Gynecologists and Obstetricians (CNGOF)". Eur J ObstetGynecolReprod Biol. 2013;170(1):25-32.
24. Cahill AG, Stamilio DM, Odibo AO, Peipert JF, Stevens EJ, Macones GA. Does a maximum dose of oxytocin affect risk for uterine rupture in candidates for vaginal birth after cesarean delivery? Am J ObstetGynecol 2007;197:495.e1-495.e5.
25. Dekker G, Chan A, Luke C, Priest K, Riley M, Halliday J, et al. Risk of uterine rupture in Australian women attempting vaginal birth after one prior caesarean section: a retrospective population-based cohort study. BJOG 2010;117:1358–1365.
26. Gibbins KJ, Weber T, Holmgren CM, et al. "Maternal and fetal morbidity associated with uterine rupture of the unscarred uterus." Am J Obstet Gynecol. 2015;213:382.e1.
27. ACOG Practice Bulletin No 107 'Induction of labor' (2009). Obstet Gynecol. 2009,114(2 Pt 1):386-397.
28. McNamara H, Johson N. "The effect of uterine contractions on fetal oxygen saturation. BJOG. 1995;102(8):644-7.
29. Peebles DM, Spencer JA, Edwards AD, Wyatt JS, Reynolds EO, Cope M, et al. "Relation between frequency of uterine contractions and human fetal cerebral oxygen saturation studied during labor by near infrared spectroscopy."BJOG. 1994;101 (1):44-8.
30. Ayres-de-Campos D, Arulkumaran S; FIGO Intrapartum Fetal Monitoring Expert ConsensusPanel. "FIGO consensus guidelines on intrapartum fetal monitoring: Physiology of fetal oxygenation and the main goals of intrapartum fetal monitoring". Int J Gynaecol Obstet. 2015;131(1):5-8.
31. Ayres-de-Campos D, Spong CY, Chandraharan E; FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. "FIGO consensus guidelines on intrapartum fetal monitoring: Cardiotocography". Int J Gynaecol Obstet. 2015;131(1):13-24.
32. Moldin PG, Sundell G. "Induction of labor: a randomised clinical trial of amniotomy versus amniotomy with oxytocin infusion". BJOG. 1996;103:306–12. (Level I)
33. WHO recommendations for augmentation of labor. (2014). **ISBN:** 9789241507363
34. Barasinski C, Vendittelli F. "Oxytocin administration during spontaneous labor: guidelines for clinical practice. Chapter 3: interventions associated with oxytocin administration during spontaneous labor." J GynecolObstet Hum Reprod. 2017;46(6):489-497.
35. Gaucher L, Le Ray C. "Oxytocin administration during spontaneous labor: guidelines for clinical practice. Chapter 2: indications of oxytocin according the first and second stages of spontaneous labor."J GynecolObstet Hum Reprod. 2017;46(6):479-487.
36. Bugg GJ, Siddiqui F, Thornton JG. "Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labor." Cochrane Database Syst Rev. 2013 Jun 23;(6):CD007123.
37. Boie S, Glavind J, Velu AV, Mol BWJ, Uldbjerg N, de Graaf I, et al.Discontinuation of intravenous oxytocin in the active phase of induced labour. Cochrane Database Syst Rev. 2018 Aug 20;8(8):CD012274.
38. Foster TC, Jacobson JD, Valenzuela GJ."Oxytocin augmentation of labor: a comparison of 15- and 30-minute dose increment intervals." Obstet Gynecol.1988;71(2):147–9.
39. Akoury HA, MacDonald FJ, Brodie G, Caddick R, Chaudhry NM, Frize M. "Oxytocin acceleration of labor and perinatal outcome in nulliparas." Obstet Gynecol. 1991;78(2):227–30.
40. Lazor LZ, Philipson EH, Ingardia CJ, Kobetitsch ES, Curry SL. "A randomized comparison of 15- and 40-minute dosing protocols for labor augmentation and induction." Obstet Gynecol.1993;82(6):1009–12.
41. Merrill DC, Zlatnik FJ. "Randomized, double-masked comparison of oxytocin dosage in induction and acceleration of labor." Obstet Gynecol.1999;94(3):455–63.
42. Voutsos L. "Oxytocin: less opinion, more studies." Am J Obstet Gynecol.2009;201(3):e9; authorreplye9
43. Wei S-Q, Luo Z-C, Qi H-P, Xu H, Fraser WD. "High-dose vs low-dose oxytocin for labor acceleration: a systematic review." Am J Obstet Gynecol.2010;203(4):296–304.
44. Zhang J, Branch DW, Ramirez MM, Laughon SK, Reddy U, Hoffman M, et al. "Oxytocin Regimen for Labor Acceleration, Labor Progression, and Perinatal Outcomes." Obstet Gynecol.2011;118(2, Part 1):249–56.
45. Kenyon S, Armstrong N, Johnston T, Walkinshaw S, Petrou S, Howman A, et al. "Standard- or high-dose oxytocin for nulliparous women with confirmed delay in labor: quantitative and qualitative results from a pilot randomised controlled trial." BJOG; 2013;120(11):1403–12.
46. Kenyon S, Tokumasu H, Dowswell T, Pledge D, Mori R. "High-dose versus low dose oxytocin for acceleration of delayed labor." Cochrane Database Syst Rev. 2013 Jul 13;(7):CD007201.
47. Budden A, Chen LJY, Henry A. "High-dose versus low-dose oxytocin infusion regimens for induction of labor at term." Cochrane Database Syst Rev. 2014 Oct 9;(10):CD009701.
48. Norwegian Guidelines. (2014) "Stimuleringavrier." Mar 25:1–3.

49. NICE Guideline 190. (2014) "Intrapartum Care." Nov 28:1–839.
50. Society of Obstetricians and Gynaecologists of Canada. (2013) "Induction of Labor." *Journal of Obstetrics and Gynaecology Canada*; 35(9).
51. Freeman RK, Nageotte M. "A protocol for use of oxytocin." Am J Obstet Gynecol. 2007;1;197(5):445–6.
52. Hayes EJ, Weinstein L. "Improving patient safety and uniformity of care by a standardized regimen for the use of oxytocin." Am J Obstet Gynecol. 2008;198(6):622.e1–7.

53. ACOG Practice Bulletin No. 106 (2009): Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2009;114(1):192.
54. Dupont C, Carayol M, Le Ray C, Deneux-Tharaux C, Riethmuller D; "Clinical Practice Guidelines Group. Oxytocin Administration During Spontaneous Labor: Guidelines for Clinical Practice. Guidelines Short Text". J GynecolObstet Hum Reprod. 2017;46(6): 539-543.