Overview of using Propranolol and Oxytocin on Induction and Outcome of Labor

Ali El Shabrawy Ali,MostafaAbdoAhmed, Mai MostafaZaitoun, Mohamed Sobhy Mohamed Gamal-Eldin*
Department of Obstetrics &Gynecology, Faculty of Medicine,Zagazig University, Egypt
***Corresponding author:** Mohamed Sobhy Mohamed Gamal-Eldin, **E-Mail:** sobhi255@gmail.com

Abstract

Labor and delivery both are not passive events by which 'uterine contractions push a solid object through a fixed aperture'. The ability of the fetus to successfully manipulate the pelvis during labor and delivery depends upon a complex interaction of three variablesincluding uterine contractions, fetus passage, and both bony pelvis and pelvic soft tissues. The sequential activation of signals that serve to augment the labor process suggest that it cannot be possible to determine any one signaling mechanism as being responsible for the initiation of labor.Prolonged labor can lead to maternal and neonatal complications.Induction of labour is generally preferred when there are no contraindications to labor and vaginal birth, given the increased maternal risks associated with cesarean delivery. Various hormones and neuropeptides and can affect myometrial contractility. The concentration of some of these agents changes in maternal serum during pregnancy suggesting that they might act in an endocrine fashion, while others are produced locally within myometrial smooth muscle cells and act in anautocrine/paracrine manner. However, their role in the initiation and maintenance of labor at term remains controversial.The aim of the present study to review the role of oral propranolol and/or oxytocin on induction of Labor and the related complications.

Keywords: LaborInduction; Propranolol; Oxytocin ;complications
DOI Number: 10.14704/nq.2022.20.6.NQ22788 **NeuroQuantology 2022; 20(6):7922-7930**

Introduction

Labor defined as a physiological process including a sequential, integrated set of changes within the myometrium, uterine cervix and decidua and that occur gradually over a period of days and may extend to weeks **(1).**Labor is a clinical diagnosis, it involves the presence of regular phasic uterine contractions which increase in intensity and frequency, and progressive cervica1 effacement and dilatation. The myometrial contractility pattern changes in labor from "contractures" (long-lasting, low frequency activity) to "contractions" (high intensity, high frequency activity) **(2)**.

Duration of labor varies widely depending on demographic, clinical, genetic factors, uterine activity, fetal 1ie or presentation and number of fetus. The mean duration of human singleton pregnancy is 280 days (40 weeks) calculated from the first day of the 1ast menstrual period**(3)**.

Delivery before the onset of labor is indicated when the maternal/fetal risks associated with continuing the pregnancy are thought to be greater than the maternal/fetal risks associated with early delivery. However, the relative risk of continuing the pregnancy versus early delivery can rarely be determined with precision. It is influenced by factors such as gestational age, presence/absence of fetal lung maturity, severity of the maternal or fetal clinical condition**(4)**.

Induction of Labor

Induction of labor refers to techniques for stimulating uterine contractions to accomplish delivery prior to the onset of spontaneous labor **(5)**.Examples of some common conditions where induction is often indicated include post-term pregnancy, premature rupture of membranes, preeclampsia, eclampsia, fetal demise, aternal diabetes, fetal growth restriction, chorioamnionitis, abruptio placentae,

*e*ISSN 1303-5150

oligohydramnios, cholestasis of pregnancy, alloimmunization with fetal anemia and twins **(4)**.

For most patients at ≥39 weeks of gestation, we suggest avoiding elective induction of labor. The major concerns associated with elective induction at full term are the potentially increased length of labor, the potential for patient/provider impatience and cesarean delivery during a long latent phase, cost, and neonatal morbidity if gestational age is actually less than 39 weeks of gestation, which is the minimum gestational age that elective induction should be considered **(6)**. There are, however, potential advantages to scheduled induction of labor at full term, such as reductions in stillbirth and further fetal growth leading to macrosomia and its consequences **(7)**.

A thorough evaluation of maternal and fetal status is important before undertaking labor induction to make sure the indication is appropriate and confirm the absence of contraindications to labor or vaginal delivery. The evaluation includes reviewing the estimate of gestational age, determining fetal presentation, estimating fetal size and potential for shoulder dystocia, performing a cervical examination to decide whether a cervical ripening agent is indicated, evaluating the fetal heart rate pattern to ensure that the fetus will tolerate initiation of labor, and reviewing the patient's pregnancy and medical history for risk factors for potential problems that may develop during labor and delivery eg, risk factors for postpartum hemorrhage **(8)**.

There is general consensus that the maternal/fetal risks associated with labor and vaginal delivery, and induction of labor are greater than the risks associated with cesarean delivery. Therefore, induction of labor is contraindicated in case of prior classical or other high risk cesarean incision, prior uterine rupture, prior transmural uterine incision entering the uterine cavity, active genital herpes infection, placenta previa or vasa previa, umbilical cord prolapses, transverse fetal lie, invasive cervical cancer and category III fetal heart rate. All of these may be associated with an increased risk of maternal or fetal morbidity during induction**(9)**.

Predicting a successful induction:

Generally, an induction is considered successful when it results in an uncomplicated vaginal birth within 24 hours of beginning oxytocin. However, depending on the trial, a successful outcome may be defined as vaginal delivery within 48 hours or by the cesarean delivery rate **(10)**.

Cervical status immediately before oxytocin administration is a key factor for predicting the likelihood of successful induction and the Bishop score appears to be the best available tool for assessing cervical statusor sonographic measurement of cervical length, and that dilation is the most important element of the Bishop score **(11)**.

The modified Bishop score is the cervical assessment system most commonly used in clinical practice that tabulates a score based upon the station of the presenting part and four characteristics of the cervix: dilatation, effacement, consistency, and position **(Table 1)**. Cervical scoring systems other than the bishop score exist, but are rarely used for predicting labor outcome (eg, Fields system; Burnett, Caldor, and Friedman modifications of the bishop system **(12**).

Table (1): Modified Bishop scoring system(13):

	0	1	2	3
Dilation, cm	**Closed**	**1 to 2**	**3 to 4**	**≥5 to 6**
Effacement, %	**0 to 30**	**40 to 50**	**60 to 70**	**≥80**
Station*	**-3**	**-2**	**-1, 0**	**+1, +2**
Cervical consistency	**Firm**	**Medium**	**Soft**	
Position of the cervix	**Posterior**	**Midposition**	**Anterior**	

*e*ISSN 1303-5150

A Bishop score ≥8 suggests the chances of having a vaginal delivery are good and the cervix is considered favorable or ripe for induction. If the Bishop score is low, variably defined as ≤3 to 6, the chances of having a vaginal delivery are lower, and the cervix is considered unfavorable or unripe for induction. A simplified Bishop score can be calculated using only dilation, station, and effacement. Using these three variables, a simplified Bishop score ≥5 has a similar predictive value for vaginal delivery as a classic Bishop score ≥8. Based on a -3 to +3 scale; most evidence supports the concept that women with a high Bishop score (≥8) have a similar likelihood of vaginal delivery whether labor begins spontaneously or is induced. On the other hand, when the bishop score is low (we use ≤6), induction is less likely to be successful than spontaneous labor and associated with a higher rate of cesarean delivery **(13,14)**.

Other methods including the role of fetal fibronectin (fFN) as a tool for selecting women likely to have a successful induction is uncertain **(15)**.

More data, including cost-benefit analysis, are needed before this test can be recommended for choosing candidates for semi-elective induction. Sonographic assessment of cervical length for predicting the outcome of labor induction has been evaluated in numerous studies. In a systematic review of 20 prospective studies, cervical length did not perform significantly better than Bishop score for predicting a successful induction. These data are limited by substantial heterogeneity among the studies. As with fFN, the role of ultrasound examination as a tool for selecting women likely to have a successful induction is uncertain. More data, including cost-benefit analysis, are needed before this test can be recommended in choosing candidates for semi-elective induction **(16)**.

Noncervical characteristics of the population being induced also impact prediction of successful induction. Induction is more likely to be successful in term pregnancies. This factors including multiparous women regardless of Bishop Score, women with ruptured membranes, women with a previous vaginal delivery, tall and non-obese women, women with an infant <4000 g and women without comorbidities associated with placental insufficiency**(17)**.

Technique:

The following are broad lines to approach induction of labor: (I)Preinduction cervical ripening if the cervix is unfavorable. Misoprostol 25 mcg is used every three to four hours administered vaginally, but use of other cervical ripening agents and regimens is also reasonable. (II) Oxytocin infusion using a low-dose protocol. (III) Early amniotomy, as long as the head is engaged. (IV) Avoidance of latent phase cesarean delivery by use of strict criteria for failed induction**(18)**.A consistent approach to labor induction may reduce the rate of cesarean delivery **(19)**.

I. Preinduction cervical ripening

Because oxytocin is less successful when used in women with a low Bishop score, a ripening process is generally used prior to administering oxytocin to women with unfavorable cervices. If prostaglandin E_2 or E_1 is administered to promote cervical ripening, this alone initiates labor in approximately 50 percent of women, and obviates the need for oxytocin **(20)**.

II. Oxytocin infusion

Administration of oxytocin is probably the most common method of labor induction. Because it is less successful when used in women with a low Bishop score, a ripening process generally should be used prior to administering oxytocin to women with unfavorable cervixes**(21)**.

.

Oxytocin is a polypeptide hormone produced in the hypothalamus and secreted from the posterior lobe of the pituitary gland in a pulsatile fashion. It is identical to its synthetic analog, which is among the most potent uterotonic agents known **(22).**

The optimum regimen for oxytocin administration is controversial and no protocol

has been subjected to the scientific scrutiny necessary to demonstrate its superiority in both efficacy and safety over another **(23)**.

Protocols differ as to initial dose (0.5 to 6 mU/min), time period between dose increments (10 to 60 minutes), and maximum dose (16 to 64 mU/minute), but success rates for varying protocols are strikingly similar **(24)**.

High-dose regimens are associated with a higher rate of tachysystole than low-dose regimens and, in some studies, this has resulted in a higher rate of cesarean delivery for nonreassuring fetal heart rate tracings, but no significant difference in neonatal outcomes **(25)**.

The dose is typically increased until there is normal progression of labor, or strong contractions occurring at two- to three-minute intervals, or uterine activity reaches 150 to 350 Montevideo units (ie, the peak strength of contractions in mmHg measured by an internal monitor multiplied by their frequency per 10 minutes). There is no benefit to increasing the dose after one of these endpoints has been achieved. The oxytocin infusion should be maintained until delivery based on clinical experience and data from a noninferiority study and a randomized trial that discontinuation prolongs labor **(26)**.

Low-dose protocols attempt to mimic a physiologic approach. The dose of oxytocin is initiated at 0.5 to 1 mU per minute and increased by 1 mU per minute at 30- to 40-minute intervals. This interval was based upon studies showing approximately 40 minutes were required for any particular dose of oxytocin to reach a steady-state concentration and maximal uterine contractile response **(24)**. Slightly higher doses (begin at 1 to 2 mU/min and increase by 1 to 2 mU/min) and shorter incremental time intervals (15 to 30 minutes) have also been recommended **(27)**.

A maximum oxytocin dose has not been established; however, most labor units do not go above 40 mU/min. The most common complication of the high-dose regimen is uterine tachysystole. Pulsatile administration of intravenous oxytocin at 6- to 10-minute intervals is effective and may better simulate normal labor than continuous oxytocin administration **(28)**.

III. Early amniotomy

Amniotomy is performed as soon as possible after beginning oxytocin. In a randomized trial, routine early amniotomy (defined as cervical dilation ≤4 cm) in nulliparous labor induction shortened the time to delivery by >2 hours and increased the proportion of deliveries within 24 hours (68 versus 56 percent; RR 0.72, 95% CI 0.59-0.89) compared with "usual care" **(29)**.

Alternatives to oxytocin in women with a favorable cervix

1. Amniotomy:

Amniotomy alone may be an effective method of labor induction, but can only be performed in women with a partially dilated and effaced cervix **(30)**. However, in a systematic review of randomized trials, the combination of amniotomy and intravenous oxytocin administration was more effective for labor induction than amniotomy alone. With the combined regimen, fewer women were undelivered at 24 hours than with amniotomy alone (RR 0.13, 95% CI 0.04-0.41)**(31)**.

2. Prostaglandin E1 or E2

In women with a favorable cervix, the relative advantage of prostaglandins versus oxytocin for induction of labor are unclear, and there is minimal information on other agents. Until more dataon safety and efficacy are available, using of prostaglandins to induce labor in women with favorable cervixes is avoided **(31)**.

3. Membrane stripping

Stripping or sweeping of the membranes involves inserting the examiner's finger beyond the internal cervical os and then rotating the finger circumferentially along the lower uterine segment to detach the fetal membranes from the decidua. It is typically performed during an office visit when the patient and clinician want to hasten the onset of spontaneous labor and the cervix is partially dilated **(10)**.

4. Breast stimulation

Breast/nipple stimulation causes uterine contractions and has been used to induce labor. A 2005 systematic review found that this technique appeared to be effective for initiating labor within 72 hours in women with favorable cervixes, but was not useful in women with an unfavorable cervix **(32)**.

5. Nonstandard approaches

There is a paucity of data regarding the safety and/or efficacy of glucocorticoids, castor oil, hyaluronidase, isosorbidemononitrate, acupuncture, evening primrose oil, herbal preparations, or sexual intercourse for labor induction **(33)**.

Propranolol:

Propranolol is one of the beta-adrenergic receptor antagonists which are a class of drugs that are particularly used to control cardiac arrhythmias **(34)**. Beta receptors are placed on cells of the heart muscles, uterus, smooth muscles, airways, kidneys, arteries and other tissues that are a major part of the sympathetic nervous system and initiate stress responses, especially when they are stimulated by epinephrine. Beta blockers interact with the binding of the hormone to the receptor of epinephrine and other stress hormones, and weaken the effects of stress hormones **(35)**.

There haven't been enough studies done in humans to be certain how the drug might affect the fetus. However, prolonged usage of β-blocking agents in general reduces perfusion of the placenta which may cause adverse outcomes for the neonate, this includes pulmonary or cardiac complications, or premature birth. The newborn may develop additional adverse effects such as hypoglycemia and bradycardia**(36)**.Most β-blocking agents appear in the milk of lactating mother. However, propranolol is almost bound to proteins in the bloodstream and is distributed into breast milk at very low levels **(37).**

Oral propranolol plus oxytocin versus oxytocin

In a randomized, double-blind, controlled trial performed on pregnant women at gestational age of 40-42 weeks were allocated to receive 20 mg oral dose of propranolol or placebo plus oxytocin infusion (73 participants in each group). They found that mean duration of active phase and the second stage of labor were significantly shorter in the propranolol group than in the placebo group on both the first and the second days of induction. The mean duration of third stage of labor was shorter in the propranolol group than in the placebo group, but the difference was not significant statistically on the first (P = 0.159) and second (P = 0.065) days. Frequency of cesarean section deliveries significantly decreased in the propranolol plus oxytocin group compared to the placebo plus oxytocin group (P = 0.005, P = 0.015) on the first and the second days, respectively**(38)**.

Also, **Sobhy et al. (39)** reported thatadministration of oral propranolol combined with oxytocin during latent phase of labor is an effective agent in shortening the labor duration and decreasing the rate of cesarean section with no considerable side effects neither to the mother nor to her newborn has been recorded. Several studies are in agreement with the effective outcomes by using oral propranolol plus oxytocin infusion for induction of labour**(40-43)**.

Failed Induction:

An induction is considered successful when it results in an uncomplicated vaginal birth within 24 hours of beginning oxytocin. However, there is no universal standard for failed induction; the key principle is to allow adequate time for cervical ripening and development of an active labor pattern before determining that the induction has failed. This minimizes the number of cesarean deliveries performed for failed induction in patients who are progressing slowly because they are still in the latent (cervical ripening) phase of labor **(44).**

A workshop convened by the United States National Institute of Child Health and Human Development, Society of Maternal-Fetal Medicine, and American College of Obstetricians and Gynecologists proposed that failed induction be defined by the following criteria:

-Membranes should be artificially ruptured, if safe and feasible. After rupture of membranes, the induction may be considered a failure if regular contractions and cervical change do not

occur after at least 12 to 18 hours of oxytocin administration.

-If membranes are intact, induction may be considered a failure if regular contractions approximately every three minutes are not generated and cervical change does not occur after at least 24 hours of oxytocin administration.

-The time devoted to cervical ripening is not included when calculating the length of induction or diagnosing failed induction. The workshop's goal was to provide evidenced-based criteria for reducing the number of cesarean deliveries performed for failed induction in the latent phase of labor. By allowing the latent phase to extend for 24 hours or more and administering oxytocin for 12 to 18 hours after membrane rupture, many of these cesarean deliveries can be avoided **(8)**.

Complications:

1. Tachysystole

The term tachysystole to describe >5 contractions in 10 minutes, averaged over a 30-minute window The presence or absence of associated fetal heart rate changes should also be stated. There are no uniform worldwide definitions for such terms as tachysystole, hyperstimulation, and hypertonus. Clinicians should be mindful of the semantic differences in the literature. For example, the term "uterine hyperstimulation without fetal heart rate changes" has been used to describe uterine tachysystole (>5 contractions in 10 minutes for at least 30 minutes) or uterine hypersystole/ hypertonus (a contraction lasting at least 2 minutes) with a normal fetal heart rate. The term "uterine hyperstimulation with fetal heart rate changes" has been used to denote uterine hyperstimulation with fetal heart rate changes such as persistent decelerations, tachycardia, or decreased short-term variability**(4)**.

Rarely, tachysystole causes uterine rupture; this is more common in multigravidas than primigravidas. In one retrospective review of 905 women from a single institution in six randomized trials using a variety of approaches to cervical ripening and labor induction, women with ≥3 episodes of tachysystole had a similar rate of adverse outcome as those with no episodes of tachysystole (defined as >6uterine contractions in each of two consecutive 10-minute windows). The perinatal outcomes included cesarean rate, Apgar score at five minutes, and low cord pH**(45)**.

Management if FHR changes are presentwith tachysystole byplacing the woman in the left lateral position, administering oxygen (10 L/min of oxygen via nonrebreather mask), and increasing intravenous fluids (eg, fluid bolus of 500 mL of lactated Ringer's solution or more) also appear to be of benefit. After tachysystole and fetal heart rate changes have resolved, oxytocin can be resumed, if needed. No studies have evaluated the optimum approach to resuming the drug. One approach resumes oxytocin at one-half the previous dose if it has been discontinued for less than 30 minutes, and at the initial dose ordered if it has been discontinued for more than 30 minutes **(46)**.

Management when FHR changes are not presentiftachysystole is not accompanied by fetal heart rate changes, the oxytocin infusion rate should still be re-evaluted. Decreasing the dose to titrate to an appropriate contraction frequency or discontinuation for a brief period of time are both reasonable options. If oxytocin is briefly discontinued, a lower dose should be used when the infusion is resumed. There are no reliable data on which to base a dosage recommendation, so clinicians must use their best clinical judgment in these situations. For women who demonstrate tachysystole with frequent low amplitude contractions without the sensation of pain, it is reasonable to resume oxytocin at the penultimate level. For women with symptomatic tachysystole, a greater reduction in dose is prudent **(47)**.

2. Uterine rupture

The relative risk of uterine rupture is increased during labor induction, but the absolute risk is low and most cases occur in women with a scarred uterus. In a series including over 226,000 births, 41 true uterine

ruptures (2/10,000 births) occurred: 27 (66 percent) were in women with prior uterine surgery (20 cesarean deliveries, 7 other uterine surgeries) and 14 (34 percent) were in women with an unscarred uterus; 12 of the 14 ruptures in unscarred uteruses occurred in women exposed to oxytocics for induction or augmentation of labor **(48)**.

3. Amniotic fluid embolism

A population-based retrospective cohort study including 3 million deliveries reported that medical induction of labor was associated with an increased risk of amniotic fluid embolism (adjusted odds ratio 1.8, 95% CI 1.2-2.7) **(49)**. However, the absolute risk was small, 10.3 per 100,000 births with medical induction versus 5.2 per 100,000 births without medical induction. Moreover, given that these women were induced for medical indications, not inducing labor could potentially result in greater maternal-fetal morbidity/mortality than inducing labor.

4. Other

Induction of labor at term does not appear to be a risk factor for spontaneous preterm birth in the subsequent pregnancy **(50**).

Conclusion:

Oxytocinin combined with oral propranolol have an effective role in during latent phase of labor with shortening the labor duration.

Conflict of interest: The authors declare no conflict of interest.

Author contribution: Authors contributed equally in the study.

REFERENCES

1- **Errol R, Charles J and Vaness A:** physiology of parturition: a review of literature somepomed.org article content 2015;30/38/31328.
2- **Nathanielsz PW, Giussani DA and Wu WX:** Stimulation of the switch in myometrial activity from contractures to contractions in the pregnant sheep and nonhuman primate. Equine Vet J 1997; 83.
3- **Terkawi AS, Jackson WM, Thiet MP, et al:** Oxytocin and catechol-O-methyltransferase receptor genotype predict the length of the first stage of labor. Am J ObstetGynecol 2012; 207(3):184-190.
4- **Spong, C. Y., Mercer, B. M., D'Alton, M., Kilpatrick, S., Blackwell, S., &Saade.** Timing of indicated late-preterm and early-term birth. Obstetrics and gynecology, 2011, 118.2 Pt 1: 323.
5- **Osterman MJ and Martin JA:** Recent declines in induction of labor by gestational age. NCHS Data Brief 2014; 1.
6- **Clark SL, Miller DD, Belfort MA, et al:** Neonatal and maternal outcomes associated with elective term delivery. Am J ObstetGynecol 2009; 200:156.
7- **Darmstadt, G. L., Yakoob, M. Y., Haws, R. A., Menezes, E. V., Soomro, T., & Bhutta, Z. A.** Reducing stillbirths: interventions during labour. BMC pregnancy and childbirth, 2009; 9(1), 1-43.
8- **Kramer, M. S., Berg, C., Abenhaim, H., Dahhou, M., Rouleau, J., Mehrabadi, A., Joseph, K. S.** Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. American journal of obstetrics and gynecology,2013; 209(5), 449-e1.
9- **Barber EL:** Indications contributing to the increasing cesarean delivery rate. Obstetrics and gynecology, 2011, 118.1: 29-38.
10- **Kilpatrick S and Etoi G.** "Normal labor and delivery." Obstetrics: Normal and problem pregnancies 5 2007; 303-321.
11- **Verhoeven CJ, Opmeer BC, Oei SG, et al:**Transvaginalsonographic assessment of cervical length and wedging for predicting outcome of labor induction at term: a systematic review and meta-analysis. Ultrasound ObstetGynecol 2013; 42:500.
12- **Baacke KA and Edwards RK:**Preinduction cervical assessment. ClinObstetGynecol 2006: 49:564.
13- **Yelikar, K., &Deshpande, S**. Induction of Labor. In Labour Room Emergencies (pp. 201-212). Springer, Singapore,2020.
14- **Antsaklis, Panos**. "Intrapartum Ultrasound and Bishop Score: A New Obstetric

*e*ISSN 1303-5150

Tool." Intrapartum Ultrasonography for Labor Management. Springer, Cham, 2021. 75-84.

15- **Ahner R, Egarter C, Kiss H.** Fetal fibronectin as a selection criterion for induction of term labor. Am J ObstetGynecol 1995; 173:1513.

16- **Hatfield AS, Sanchez-Ramos L and Kaunitz AM:** Sonographic cervical assessment to predict the success of labor induction: a systematic review with metaanalysis. Am J ObstetGynecol 2007; 197:186.

17- **Gibson KS and Waters TP:** Measures of success: Prediction of successful labor induction. SeminPerinatol 2015; 39:475.

18- **Viteri OA and Baha MS.** "Challenges and Limitations of Clinical Trials on Labor Induction: A Review of the Literature." American Journal of Perinatology Reports 8.04 2018: e365-e378).

19- **Rhinehart-Ventura J, Eppes C, Sangi-Haghpeykar H, et al:** Evaluation of outcomes after implementation of an induction-of-labor protocol. Am J ObstetGynecol 2014; 211:301. e1.

20- **Thomas J, Fairclough A, Kavanagh J, et al:** Vaginal prostaglandin (PGE2 and PGF2a): for induction of labour at term. Cochrane Database Syst Rev 2014; CD003101.

21- **Alfirevic Z, Kelly AJ and Dowswell T:** Intravenous oxytocin alone for cervical ripening and induction of labour. Cochrane Database Syst Rev 2009; CD003246.

22- **Arrowsmith S and Wray S:** Oxytocin: its mechanism of action and receptor signalling in the myometrium. J Neuroendocrinol 2014: 26:356.

23- **Hayes EJ and Weinstein L:** Improving patient safety and uniformity of care by a standardized regimen for the use of oxytocin. Am J ObstetGynecol 2008; 198:622. e1.

24- **Selin, L**. Delayed Labour-risk factors, use of oxytocin and outcomes, 2008.

25- **Smith JG and Merrill DC:** Oxytocin for induction of labor. ClinObstetGynecol 2006; 49:594.

26- **Diven LC, Rochon ML, Gogle J, et al**. Oxytocin discontinuation during active labor in women who undergo labor induction. Am J ObstetGynecol 2012; 207:471. e1.

27- **Patka, J. H., Lodolce, A. E., Johnston, A. K**. High-versus low-dose oxytocin for augmentation or induction of labor. Annals of Pharmacotherapy, 2005; 39(1), 95-101.

28- T

29- **Macones GA, Cahill A, Stamilio DM, et al:** The efficacy of early amniotomy in nulliparous labor induction: a randomized controlled trial. Am J Obstet Gynecol;2012, 207: 403.e1.

30- **Bricker L and Luckas M:**Amniotomy alone for induction of labour. Cochrane Database Syst Rev 2000; CD002862.

31- **Howarth GR and Botha DJ:**Amniotomy plus intravenous oxytocin for induction of labour. Cochrane Database Syst Rev 2001; CD003250.

32- **Kavanagh J, Kelly AJ and Thomas J:** Breast stimulation for cervical ripening and induction of labour. Cochrane Database Syst Rev; 2005: CD003392.

33- **Smith CA, Crowther CA and Grant SJ:** Acupuncture for induction of labour. Cochrane Database Syst Rev 2013; CD002962.

34- **Cruickshanks KJ, Nondahl DM, Tweed TS, et al:** Education, occupation, noise exposure history and the 10-yr cumulative incidence of hearing impairment in older adults. Hearing research; 2010; 264(1-2): 3-9.

35- **Arcangelo VP and Peterson AM:**Pharmaco-therapeutics for advanced practice: a practical approach. Lippincott Williams & Wilkins 2006: 205.

36- **Sweetman and Sean C, ed:** "Cardiovascular Drugs". Martindale: The complete drug reference (36th ed.): London: Pharmaceutical Press 2009;1226–1381.

37- **Sean C and Sweetmaned:** "Cardiovascular Drugs". Martindale: The complete drug reference (36th ed.): London: Pharmaceutical Press 2005;1226–1381.

38- **Direkvand-Moghadam, A., Jaafarpour, M., Khani, A., Taheri, S., &Delpisheh, A.** The effect of oral propranolol plus oxytocin versus oxytocin only on the process and outcome of labor: A double-blind randomized trial. Iranian

*e*ISSN 1303-5150

journal of nursing and midwifery research, 2014; 19(5), 491.

39- **Sobhy, M., Ali, A. E. S., Ahmed, M. A., Zaitoun, M. M.** The Effect of Oral Propranolol plus Oxytocin Versus Oxytocin alone on Induction and Outcome of Labor. The Egyptian Journal of Hospital Medicine,2022; 88(1), 3363-3368.

40- **Vasilios P, Maximos F, Anastasia P.** Propranolol and oxytocin versus oxytocin alone for induction and augmentation of labor: a meta-analysis of randomized trials. Arch Gynecol Obstet., 2016; 293(4):721-9.

41- **Pergialiotis V, Frountzas M, Prodromidou A.**Propranolol and oxytocin versus oxytocin alone for induction and augmentation of labor: a meta-analysis of randomized trials. Arch Gynecol Obstet.,2016; 293:721–729.

42- **Hanafy M, Abdel-Hakamand F, Mohammed M.**Maternal and Fetal Outcomes after Oxytocin and oral Propranolol for augmentation of labor. Life Sci J.,2019;16(1):43-48.

43- **Bigelow C,Pan S,Overbey J.**Propranolol for Induction of Labor in Nulliparas trial a double-blind, randomized, placebo-controlled trial. American Journal of Obstetrics & Gynecology MFM,2021; 3(2): 100301. https://doi.org/10.1016/j.ajogmf.2020.100301.

44- **Rouse DJ, Owen J and Hauth JC:** Criteria for failed labor induction: prospective evaluation of a standardized protocol. ObstetGynecol 2000; 96:671.

45- **Bofill JA, Darby MM, Castillo J, et al:**Tachysystole Following Cervical Ripening and Induction of Labor Is Not Associated with Adverse Outcomes. GynecolObstet Invest 2016; 82(5): 487-493.

46- **Pullen KM, Riley ET, Waller SA, et al:** Randomized comparison of intravenous terbutalinevs nitroglycerin for acute intrapartum fetal resuscitation. Am J ObstetGynecol 2007; 197:414. e1.

47- **Westgate JA.** "The intrapartum deceleration in center stage: a physiologic approach to the interpretation of fetal heart rate changes in labor." American journal of obstetrics and gynecology 197.3, 2007: 236-e1).

48- **Porreco RP, Clark SL, Belfort MA, et al:** The changing specter of uterine rupture. Am J ObstetGynecol 2009; 200:269. e1.

49- **Kramer MS, Rouleau J, Baskett TF, et al:** Amniotic-fluid embolism and medical induction of labour: a retrospective, population-based cohort study. Lancet; 2006, 368:1444.

50- **Levine LD, Bogner HR, Hirshberg A, et al:** Term induction of labor and subsequent preterm birth. Am J ObstetGynecol; 2014, 210:354.e1.

*e*ISSN 1303-5150