RESEARCH PROPOSAL FOR MASTER OF MEDICINE

(OBSTETRICS AND GYNAECOLOGY)
DEPARTMENT OF OBSTETRICS & GYNAECOLOGY
UNIVERSITY OF MALAYA

VERSION: 2.0
VERSION DATE: 13 December 2021
TIME FRAME: 1 Dec 2021 – 1 April 2023

6 Hours vs 12 Hours of Foley's Catheter Placement for Labour Induction in Multiparous Women with Unripe Cervices: A Randomised Trial

BY

NADIAH KAMARUDZMAN
MGG 190002

SUPERVISOR
PROF. DR. TAN PENG CHIONG
PROF DATUK DR. SITI ZAWIAH OMAR

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY
UNIVERSITY MALAYA MEDICAL CENTRE

CONTENTS

1.0 INTRODUCTION

In developed countries, approximately 20–25% of pregnant women will require labour induction (IOL) for various indications. (1) In considering IOL the benefits of an earlier delivery should outweigh the risks of continuing the pregnancy.(2) An unripe cervix is a risk factor for failed IOL and Caesarean delivery whereas prior vaginal delivery has the opposite impact. (3)

The two major techniques for cervical ripening are mechanical intervention and the use of pharmacologic agents.(4) Mechanical dilatation of the cervix may be via the transcervical placement of the single balloon catheter (i.e., Foley catheter). the double balloon catheter (i.e. Cook or Atard catheter) or with the use of osmotic dilator such as natural compound Laminaria, or synthetic compounds such as Lamicel and Dilapan.(5) Pharmacological forms of induction include prostaglandins and oxytocin.(6, 7) World Health Organization (WHO) strongly recommends the use of balloon catheter for induction of labor(8).

A lengthy induction process can increase adverse outcomes(1, 4, 9) and the burden on health care resources(10). Hence, it is clinically important to find an induction protocol that is efficient in order to reduce interval to delivery which in turn may increase maternal satisfaction.

Mechanical induction particularly with the single-balloon Foley catheter is widely used as the primary IOL method when cervical ripening is needed due to its low cost and reduced likelihood of uterine hyperstimulation compared to prostaglandins.(11) Studies have compared balloon catheter placement for 12 vs 24 hours finding that 12-hour placement results in shorter interval to delivery. (12, 13)

A recent study comparing 6 vs 12 hours placement with the double-balloon catheter has also shown reduction in the interval to delivery with the shorter placement period without increment in caesarean section rate. (14) Similarly, another study conducted using the double balloon catheter also but with only a single balloon inflated also shows shorter interval to delivery time in the 6-hour arm compared to the 12-hour group.(15) Both above-mentioned study used the costly double-balloon catheter. A 2017 meta-analysis (five randomized trials: 996 women) published in 2017, comparing single with double-balloon catheters for IOL shows the time from catheter insertion to delivery did not differ between the two types of catheters.(16)

A 2018 systematic review on complications from insertion to expulsion of a balloon catheter during labor induction reports adverse event rates of 0.0-0.26% with 'pain/discomfort' having the highest prevalence.(17) Foley induction ripens the cervix and progression to labour is uncommon without amniotomy and oxytocin augmentation.(18)

The aim of the present study is to compare the planned removal after 6 vs 12 hours placement of the Foley catheter in multiparas with unripe cervices scheduled for IOL with the hypothesis that the 6-hour arm will have a shorter interval to delivery and higher patient satisfaction with the induction process.

2.0 OBJECTIVE OF THE STUDY

The purpose of the study is to evaluate whether removal of foley's catheter after 6 hours compared to 12hours in multiparous women undergoing induction of labour will result in a shorter duration of intervention to delivery time and increase maternal satisfaction with the induction process.

3.0 RESEARCH HYPOTHESIS

We hypothesise that induction of labour with foley's catheter removed at 6 hours compared to 12 hours will result in a shorter interval to delivery and increase maternal satisfaction.

4.0 MATERIALS AND METHODOLOGY

4.1 STUDY DESIGN

Single centre, randomised controlled trial.

4.2 PLACE OF STUDY

Antenatal and labour ward, University Malaya Medical Centre, Kuala Lumpur.

4.3 POPULATION OF STUDY

Multiparous women planned for elective induction of labour for various indications admitted will be assessed for enrolment using the Eligibility Form.

Eligibility form

Inclusion Criteria

• Multiparous women (at least 1 vaginal delivery ≥ 24 weeks)	
• Age ≥ 18 years	
• Gestational age of ≥ 37 weeks	
• Singleton pregnancy	
• Cephalic presentation	
• Intact membrane	
• Reassuring fetal heart tracing	
• Absence of significant contraction ≥ 2 in 10 minutes	
• Successful Foley insertion for IOL	
• Bishop score ≤ 5	

Exclusion Criteria

• History of caesarean delivery or hysterotomy/ uterine perforation/ previous myomectomy	
• Latex Allergy	
• Estimated Fetal weight less than 2kg or > 4kg	
• Known major fetal malformations	
• Contraindication for vaginal delivery	
• Patient who is suspected COVID 19 infection or COVID 19 positive	

4.4 METHODS

This is a randomised control trial involving multiparas at term (≥ 37 weeks) who are planned for IOL for various indications. Participant information sheet with be given to all potential recruits and any inquiries by the participants will be answered by the recruiting care provider. Written consent will be obtained from all participants.

All participants will undergo standard assessment by the care provider before their IOL; including their personal characteristics, obstetric assessment and fetal wellbeing (using a nonstress cardiotocogram) assessment.

Insertion of Foley Catheter

Participants will be positioned in the dorsal position. Bishop score will be ascertained during the vaginal examination prior to Foley insertion. A Foley catheter size 16F is then introduced through

the external os using either by digital or speculum method (at discretion of introducer). Once the tip of the catheter has passed the internal os by 4 to 5cm, the balloon will be inflated with 80ml of water and retracted so the balloon rests on the internal cervical os. The other end of the Foley catheter will be taped without tension to the medial aspect of the women's thigh. (19)

Randomisation

Randomisation will be performed and intention to treat revealed only after successful Foley insertion. Randomisation is done by opening the lowest number, sealed and opaque envelope that is available, assigned in strict order. Randomisation sequence will be generated using a random number generator at Random.org in random blocks of 4 or 8 sequence, generated by an investigator who is not involved in recruitment. Blinding is not possible due to the nature of the intervention.

Participants will be randomised into two trial arms: Foley removal following its insertion

1. at 6 hours
   or
2. 12 hours

Trial will be closely monitored by the supervisors. Any serious adverse effects (SAE) will be reported to UMMC-MREC committee for discussion and review of the clinical trial.

Labour Induction Care

After catheter insertion, the patient will be monitored in the ward or labour suite with the cardiotocogram which is discontinued when reassuring. Standard care for Foley IOL in our centre is applied to both arms. They are allowed to ambulate. Analgesia is given upon request. Subsequent cardiotocogram is performed as indicated. Patients are transferred to labour and delivery suite if the catheter is spontaneously expelled before the designated 6 or 12 hours. The catheter is removed if spontaneous rupture of membrane occurs or there is clinical need as decided at the discretion of the care provider.

Upon Foley removal (or if spontaneously expelled before removal), a second Bishop score is recorded, artificial rupture of membranes performed, and oxytocin infusion is initiated according to standard IOL protocol (10 international units of oxytocin in 500mls of Hartmann solution, started at 6ml/hr [2 mU/min] and doubled every 30 minutes until 3–5/10 min regular painful contractions is achieved at which rate infusion rate is maintained to delivery if no untoward reaction, maximum dose at 96ml/hr [32 mU/min]). If artificial rupture of membranes is not possible or safe (i.e., fetal head at high station), oxytocin can be initiated prior to artificial rupture of membrane.

Failed ripening is diagnosed if Bishop score is ≤ 5 after removal of catheter. Patient will then be assessed and counselled by the care provider as standard care in these circumstances for medical induction with prostaglandin, oxytocin, another Foley or caesarean section. Standard care will be provided to all participants during their labour induction, intrapartum and postpartum. Care providers always have full discretion in deciding care to the participants' best interest.

Maternal satisfaction with the induction process will be assessed as soon as possible after delivery using the Visual Numerical Rating Scale scored from 0-10.

All date captured will be transcribed onto the Case Report Form.

4.5 SAMPLE SIZE CALCULATION

To calculate our sample size for the primary outcome, we obtained data from literature review on:

Primary outcome 1: Induction to delivery interval

Bleicher et al reported mean induction to delivery interval in the multiparous subgroup for 6 hours vs 12 hours double balloon placement as 18.0 hours with SD 6.8 vs 22.6 hours SD 8.2, p= 0.04 respectively, a mean reduction of 4.6 hours in favour of 6-hour placement.(14)

Using https://www.openepi.com/SampleSize/SSMean.htm and applying alpha of 0.02 (Bonferroni correction for 2 primary outcomes), t test, 80% power, 1 to 1 ratio, 18.0 hours with SD 6.8 vs 22.6 hours SD 8.2, 54 women are required per arm (total 104). Factoring in the possibility of non-normal data distribution requiring Mann Whitney U test application, we increase sample size by 15% and assuming 10% dropout, we plan to recruit 54 x 1.15/0.9 = 69 in each arm (N = 138 women)

For maternal satisfaction, assuming a 1-point difference in the 11-point 0-10 visual numerical rating scale (VNRS) to be clinically relevant. Using https://www.openepi.com/SampleSize/SSMean.htm and applying alpha of 0.02 (Bonferroni correction for 2 primary outcomes), t test, 80% power, VNRS standard deviation of 2 for both arms, 81 women are required per arm (total 162). Factoring in the Mann Whitney U test application as satisfaction score is ordinal, we increase sample size by 15% and assuming 10% dropout, we plan to recruit 81 x 1.15/0.9 = 103.5 in each arm (total of 207 women). We rounded the required sample size of participants up to N = 210 in total to adequately cover for both primary outcomes.

5.0 PRIMARY OUTCOMES

5.1 Foley's catheter insertion to delivery interval

5.2 Maternal satisfaction with the labour induction process

6.0 SECONDARY OUTCOMES

based on core outcome set for trials on induction of labour: CROWN

Maternal outcomes

Change in bishop score after intervention

Use of additional method for cervical ripening

Time to delivery after Foley's catheter removal

Mode of delivery

a) spontaneous vaginal
b) vacuum
c) forceps
d) caesarean section

Indication for caesarean section

Duration of oxytocin infusion

Maternal satisfaction-based allocation to intervention until birth (11-point VNRS)

Blood loss during delivery

Third -or fourth-degree tear

Maternal infection

Use of regional analgesia in labour?

Length of hospital stay

ICU admission

Cardiorespiratory arrest

Hysterectomy

Neonatal outcomes

Apgar score at 1 and 5 minutes

NICU admission

Cord pH

Neonatal sepsis

Birth weight

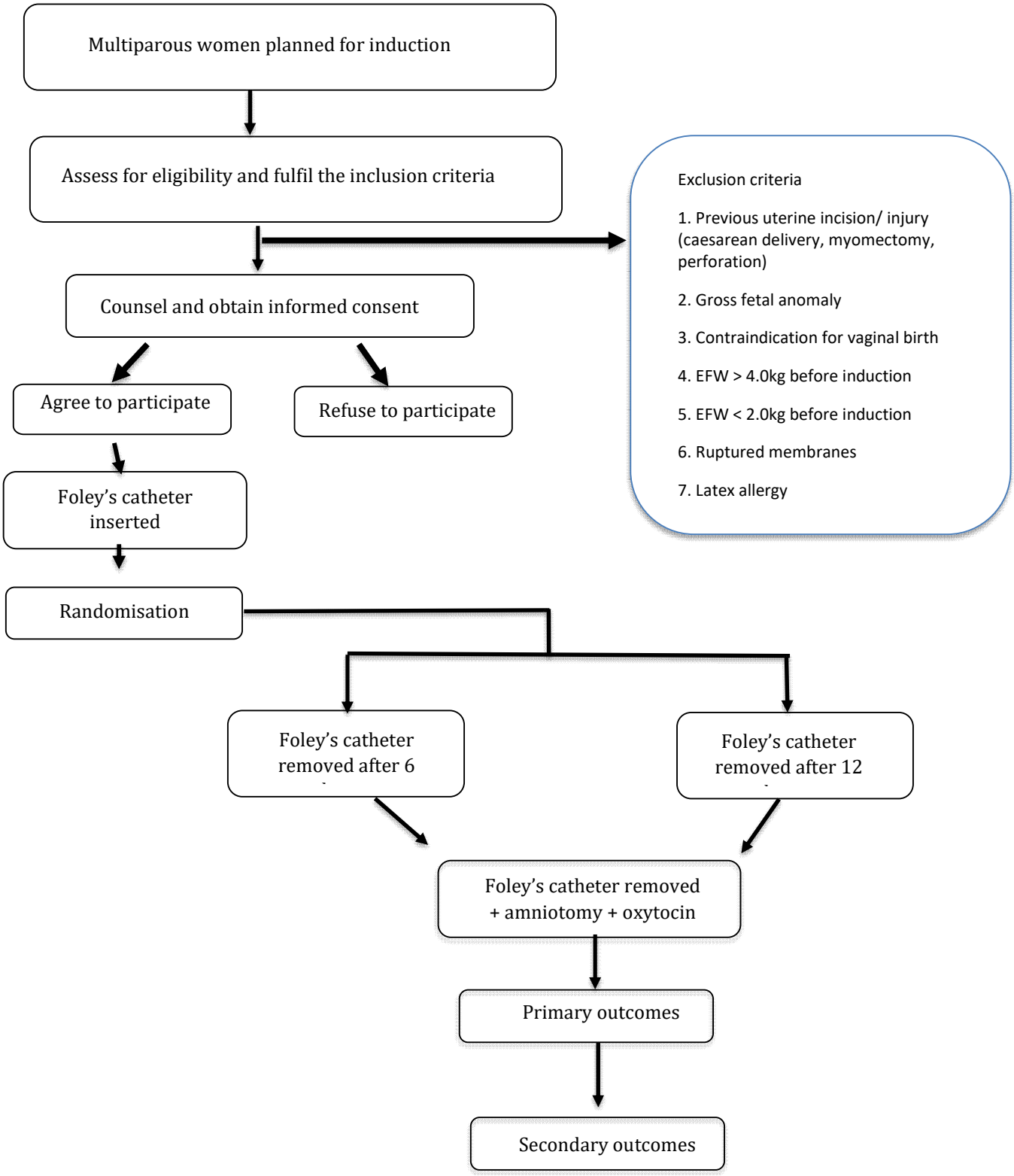
Birth trauma

Hypoxic ischaemic encephalopathy/need for therapeutic hypothermia

Trial Protocol

Patient admitted to antenatal ward or labor ward.

PROTOCOL FLOW CHART



CASE REPORT FORM

STUDY NUMBER

PATIENT STICKER

Date of recruitment: __ / __ / __ (dd/ mm/ yy)
LMP: __ / __ / __ (dd/ mm/ yy)
EDD: __ / __ / __ (dd/ mm/ yy)

Patient characteristics
D.O.B: _____ (dd/ mm/ yy)
Gravida: _____ Para: _____ Abortion: _____
Gestational age: _____
Latest recorded Weight: _____ kg
Height: _____ cm
Education level:

- Up to primary
- Secondary
- Diploma
- Degree
- Masters
- PhD

Occupation:

- Employed
- Self employed
- Student
- Housewife
- Other: _____

Ethnicity:

- Malay
- Chinese
- Indian
- Other: _____

Indication/s for IOL: _____
Pre induction Bishop Score: _____

Score	0	1	2	3
Dilatation	Closed	1-2 cm	3-4	5 cm
Length	> 4 cm	3-4 cm	1-2 cm	0
Consistency	Firm	medium	soft	-
Position	Posterior	mid	anterior	-
Station	≤ -3	-2	-1 to 0	+1, +2

Primary Outcomes:

1. **IOL to delivery interval [Date/Time delivery - Date/Time catheter inserted**

2. **Maternal satisfaction**

   Rate your satisfaction with the experience of your allocated intervention of placement (of 6 or 12 hours) of the Foley catheter for labour induction.
   Circle your score below (higher score, greater satisfaction)

0	1	2	3	4	5	6	7	8	9	10

0- totally dissatisfied

10-totally satisfied

To be assessed as soon as possible after delivery (in all cases before hospital discharge)

Dates and times

1. Date / Time catheter inserted: __ /__ / __ (dd/ mm/ yy): ___: ___ (hr:min)
2. Date / Time catheter removed/ dislodged: __ / __ / __ (dd/ mm/ yy): ___: ___ (hr:min)
3. Date / Time ARM/SROM: __ / __ / __ (dd/ mm/ yy): ___: ___ (hr:min)
4. Date / Time oxytocin infusion start (if any): __ /__ / __ (dd/ mm/ yy): ___: ___ (hr:min)
5. Date / Time oxytocin infusion stop (if before delivery):

   __ /__ / __ (dd/ mm/ yy): ___: ___ (hr:min) ☐ @ delivery
6. Date / Time of 2nd stage: _ / _ / _ (dd/ mm/ yy): __: __ (hr:min)
7. Date / Time of pushing: _ / _ / _ (dd/ mm/ yy): __: __ (hr:min)
8. Date / Time of delivery: __ / __ / __ (dd/ mm/ yy): ___: ___ (hr:min)
9. Date / Time of Hospital Discharge (as per EMR): __ / __ / __ (dd/ mm/ yy): ___: ___(hr:min)

Secondary Outcomes

Maternal Outcome

1. Bishop score at catheter removal/ dislodgement

Score	0	1	2	3
Dilatation	Closed	1-2 cm	3-4 cm	5 cm
Length	> 4 cm	3-4 cm	1-2 cm	0
Consistency	Firm	medium	soft	
Position	Posterior	midline	anterior	
Station	-3	-2	-1 to 0	+1, +2

2. Additional cervical ripening used?
   a) Foley
   b) Prostaglandin Please specify: _____
   c) Others Please specify: _____
   d) None

3. Mode of Delivery:
   a) SVD
   b) Caesarean section. Indication: _____
   c) Instrumental delivery. Indication: _____
      i. Forceps
      ii. Vacuum

4. Use of analgesia in labor?
   Circle as many as used
   a) None
   b) Entonox
   c) Opiate i.m
   d) Neuraxial analgesia
   e) Others. Please specify _____

5. Estimated blood loss at delivery: _____ ml

6. Type of perineal tear sustained:
   Intact perineum/ First°/ Second°/ Third°/ Fourth°/ Episiotomy

7. Required ICU admission
   Yes
   No
   Reason for admission: _____

8. Cardiopulmonary resuscitation (CPR) before hospital discharge
   Yes
   No

9. Hysterectomy before hospital discharge
   Yes
   No

10. Maternal fever (highest recorded temperature from IOL to discharge): _____^{0}C

11. Antibiotics given (from IOL to discharge)
   Yes Indication_____
   No

Neonatal outcome

1. Apgar Score: _____ 1 mins / _____ 5 mins

2. Cord Arterial pH: _____ Base excess : _____

3. Birth weight: _____ kg

4. Required neonatal admission:
   Yes
   No
   Place of admission: PNW / SCN / NICU / Others
   Indication for admission: _____

5. Diagnosed with Hypoxic ischaemic encephalopathy (HIE)
   Yes
   No

6. Cooling therapy for HIE
   Yes
   No

7. Neonatal sepsis diagnosed
   Yes Please specify_____
   No

8. Birth trauma
   Yes Please specify_____
   No

To be completed by participant

1) Rate your satisfaction with the experience of your allocated intervention of placement (of 6 or 12 hours) of the Foley catheter for labour induction.
   Circle your score below (higher score, greater satisfaction)

0	1	2	3	4	5	6	7	8	9	10

Totally dissatisfied

Totally satisfied

(To be assessed within 24 hours of delivery)

2) I would recommend my allocated intervention of placement (of 6 or 12 hours) of the Foley catheter for labour induction to a friend

a) Strongly agree

b) Agree

c) Neither agree nor disagree

d) Disagree

e) Strongly disagree

6.1 STATISTICAL ANALYSIS

Data will be entered into SPSS statistical software. Normally distributed continuous data will be analysed with paired Student's t test. Chi square test will be used for categorical or nominal data and Mann- Whitney U test will be used on non-normally distributed or ordinal data.

6.2 ETHICAL CONSIDERATIONS

This study is submitted to the University of Malaya Medical Centre Medical Research and Ethics committee, the local institutional review board for approval. Patient will be given and information sheet, have their oral queries addressed and written informed consent obtained to participate in the study. Patients can withdraw at any time of the study without having to providing a reason.

7.0 REFERENCES

1. ACOG Practice Bulletin No. 107: Induction of labor. Obstet Gynecol. 2009;114(2 Pt 1):386-97.
2. Caughey AB, Sundaram V, Kaimal AJ, Cheng YW, Gienger A, Little SE, et al. Maternal and neonatal outcomes of elective induction of labor. Evid Rep Technol Assess (Full Rep). 2009(176):1-257.
3. Khan NB, Ahmed I, Malik A, Sheikh L. Factors associated with failed induction of labour in a secondary care hospital. J Pak Med Assoc. 2012;62(1):6-10.
4. Jozwiak M, Bloemenkamp KW, Kelly AJ, Mol BW, Irion O, Boulvain M. Mechanical methods for induction of labour. Cochrane Database Syst Rev. 2012(3):Cd001233.
5. Gelber S, Sciscione A. Mechanical methods of cervical ripening and labor induction. Clin Obstet Gynecol. 2006;49(3):642-57.
6. Porto M. The unfavorable cervix: methods of cervical priming. Clin Obstet Gynecol. 1989;32(2):262-8.
7. 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.
8. WHO Recommendations for Induction of Labour. WHO Guidelines Approved by the Guidelines Review Committee. Geneva2011.
9. Levine LD, Downes KL, Elovitz MA, Parry S, Sammel MD, Srinivas SK. Mechanical and Pharmacologic Methods of Labor Induction: A Randomized Controlled Trial. Obstet Gynecol. 2016;128(6):1357-64.
10. Shetty A, Burt R, Rice P, Templeton A. Women's perceptions, expectations and satisfaction with induced labour--a questionnaire-based study. Eur J Obstet Gynecol Reprod Biol. 2005;123(1):56-61.
11. Rath W, Kehl S. The Renaissance of Transcervical Balloon Catheters for Cervical Ripening and Labour Induction. Geburtshilfe Frauenheilkd. 2015;75(11):1130-9.
12. Gu N, Ru T, Wang Z, Dai Y, Zheng M, Xu B, et al. Foley Catheter for Induction of Labor at Term: An Open-Label, Randomized Controlled Trial. PLoS One. 2015;10(8):e0136856.
13. Cromi A, Ghezzi F, Agosti M, Serati M, Uccella S, Arlant V, et al. Is transcervical Foley catheter actually slower than prostaglandins in ripening the cervix? A randomized study. Am J Obstet Gynecol. 2011;204(4):338.e1-7.
14. Bleicher I, Dikopoltsev E, Kadour-Ferro E, Sammour R, Gonen R, Sagi S, et al. Double-Balloon Device for 6 Compared With 12 Hours for Cervical Ripening: A Randomized Controlled Trial. Obstet Gynecol. 2020;135(5):1153-60.
15. Lassey SC, Haber HR, Kanbergs A, Robinson JN, Little SE. Six versus twelve hours of single-balloon catheter placement with oxytocin administration for labor induction: a randomized controlled trial. Am J Obstet Gynecol. 2021;224(6):611.e1-.e8.
16. Salim R, Schwartz N, Zafran N, Zuarez-Easton S, Garmi G, Romano S. Comparison of single- and double-balloon catheters for labor induction: a systematic review and meta-analysis of randomized controlled trials. J Perinatol. 2018;38(3):217-25.
17. Diederen M, Gommers J, Wilkinson C, Turnbull D, Mol B. Safety of the balloon catheter for cervical ripening in outpatient care: complications during the period from insertion to expulsion of a balloon catheter in the process of labour induction: a systematic review. BJOG. 2018;125(9):1086-95.
18. Sciscione AC, McCullough H, Manley JS, Shlossman PA, Pollock M, Colmorgen GH. A prospective, randomized comparison of Foley catheter insertion versus intracervical prostaglandin E2 gel for preinduction cervical ripening. Am J Obstet Gynecol. 1999;180(1 Pt 1):55-60.
19. Chia HM, Tan PC, Tan SP, Hamdan M, Omar SZ. Speculum versus digital insertion of Foley catheter for induction of labor in Nulliparas with unripe cervix: a randomized controlled trial. BMC Pregnancy Childbirth. 2020;20(1):330.