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Induction of labour : Foley catheter revisited

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1

GENERAL INTRODUCTION

INDUCTION OF LABOUR

Induction of labour is an intervention designed to artificially start the process of cervical effacement, cervical dilation, and uterine contractions, eventually leading to the birth of the baby. It is undertaken when the risk of continuing the pregnancy outweighs the benefits. Indications for labour induction include maternal and fetal matters, or a combination of both. Common indications are post term pregnancy, hypertensive disorders, prolonged (premature) rupture of membranes, and intra uterine growth retardation of de foetus.¹

In women in whom the cervix is favourable for amniotomy, induction will generally be established by artificial rupture of membranes and subsequent oxytocin administration if necessary. However, part of the women undergoing induction of labour will have an unfavourable cervix at the start of induction. It is believed that induction, especially in these women, is associated with increased complications as compared with spontaneous labour.² The rationale behind this is that the uterus during induction is poorly prepared for labour and, as a consequence, it is more likely that labour dystocia occurs. It has long been recognised that induction of labour poses some challenges in women with an unfavourable cervix,³ and that it is important to ripen the cervix in these women. Various agents, including mechanical and pharmacological, have been proposed for ripening of the cervix, however, the optimal method has still not been established.

A BRIEF HISTORY OF LABOUR INDUCTION

Induction of labour is one of the oldest interventions in obstetrics. Reports of labour induction date back to ancient Greece, where labour was mainly induced in women with a narrow pelvis to prevent the foetus from growing too large. Hippocrates recommended two methods for labour induction, one of which is still, although very rarely, in use these days, namely nipple stimulation. He also was the first to describe succession, which involved placing the pregnant women on tree branches and tossing.⁴

Soranus of Ephese in the early 100s described rupture of membranes, next to emptying a full bladder, administration of an enema containing oil, water, and honey, and pouring egg whites into the vagina to soften and relax the cervix. He also had a midwife stay with the pregnant women, who routinely dilated the cervix with her finger. These are the first records of mechanical dilation of the cervix.^{4,5} Over the next centuries various mechanical dilators have been invented, although digital dilation of the cervix remained most often applied (Figure 1). The main problem of mechanical stretching using dilators, was the damage they brought to the cervix, as can be imagined when viewing the tools (Figure 2).^{5,6}

In the late 16th century, Justine Sigmund was said to use transplacental amniotomy to control blood loss in women with placenta praevia.⁷ This method was described in the late 17th century by Francois Mauriceau.⁸ Only in 1756

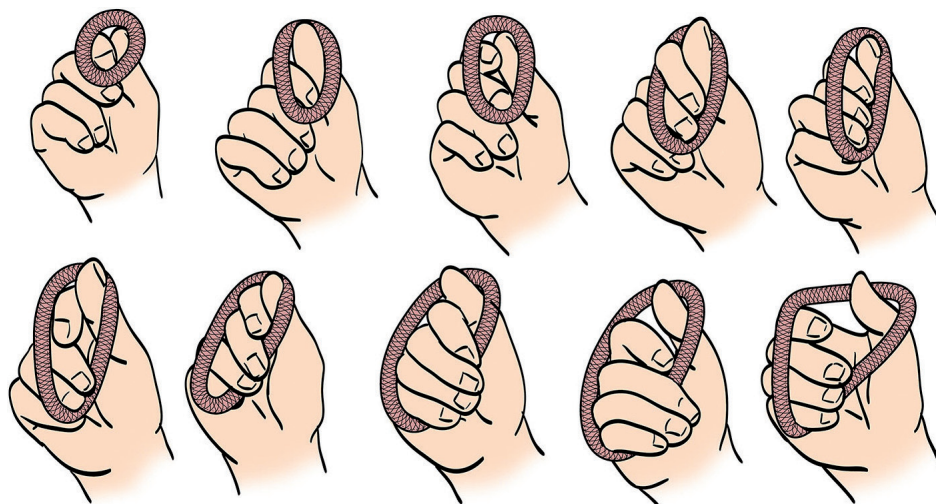


Figure 1. Digital dilation of the cervix

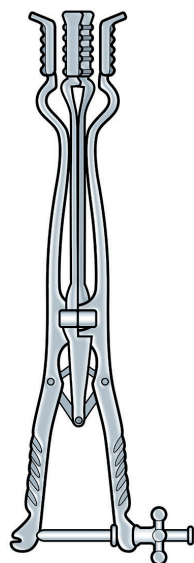


Figure 2. Bossi's dilator

Georges MacAuley⁹ started using artificial rupture of the amniotic membranes as a means to induce labour and prevent dystocia of labour in women with pelvic deformation. In the first half of the 19th century Hamilton¹⁰ introduced high amniotomy, which involved using a rubber catheter enforced with a silver fibre to rupture the membranes higher up, aiming to avoid ascending infections from the vagina. Through the 19th century artificial rupture of membranes, high or low, was the primary induction methods. It was, however abandoned in the beginning of the 1800s, to be reintroduced with the introduction of pharmacologic methods for induction.¹¹

In the late 1800s several balloon devices were described. Tarnier in 1862 described a balloon device for stretching of the cervix and uterus through introduction of the device into the lower uterine segment, that was manufactured by Charriere in Paris.^{5,12} Champetier de Ribes¹³ in 1878 described a device called a meteurynter, which was a conic bag that was placed past the cervix and filled with saline solution. Later, this device was modified and called a Voorhees meteurynter. The device consisted of a rubber covered canvas bag, which was inserted into the cervix and then inflated with water.⁶ Until the 1940s this device was described in obstetric textbooks as preferred

instrument for forcible dilation of the cervix. The first description of an ordinary urinary catheter, although at that time with a condom attached to it, was by Treub in 1890.¹¹ In 1947 Kloosterman¹⁴ wrote that the condom-catheter was still the most effective method for labour induction. In contrast to the contemporary use of the Foley catheter, most often filled with 30-80 cc (Figure 3), the catheter in the 1900s was filled with up to 500 cc of saline.¹⁵ Although described to be effective, there were substantial side-effects, such as displacement of the presenting part of the foetus and prolapse of the umbilical cord.^{15,16} It is unclear when a Foley catheter, as it is used nowadays, was first applied for labour induction, but reports of its use for cervical ripening date back to the late 1960s.^{16,17}

In the early 20th century pituitary extract became one of the primary pharmacologic agents used for induction of labour. Sir Henry Dale¹⁸ discovered that extract from the posterior pituitary gland caused uterine contractions. As this extract also contained vasopressin, its use was dangerous due to the cardiovascular, renal, and thrombotic side-effects. In 1928, Kamm and colleagues¹⁹ were able to produce Pitocin, which was largely free from vasopressin. In those days Pitocin was administered intramuscularly in high doses, which caused serious side-effects, including hypertension, water intoxication, uterine hypertonus, uterine rupture, and as a result maternal and neonatal morbidity. Theobald and colleagues²⁰ introduced in 1948 intravenous drip administration of oxytocin, which allowed titration of lower doses, although still higher doses than are used nowadays. With

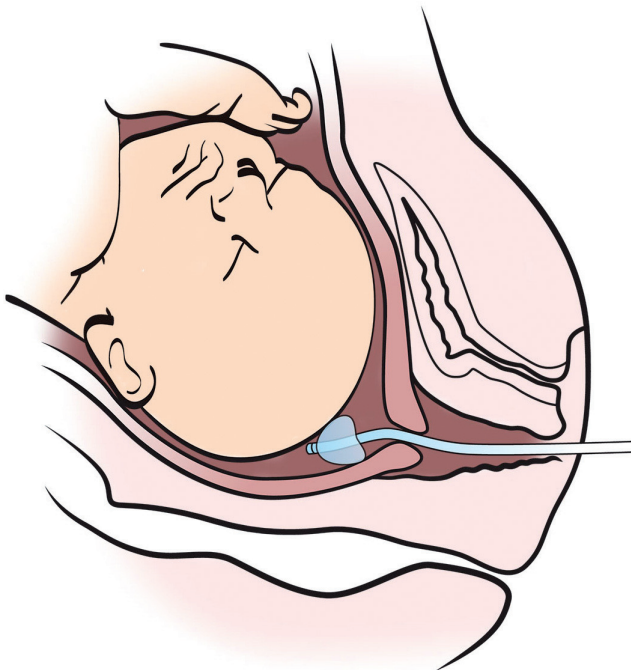


Figure 3. Foley catheter, as it is used nowadays, inserted past the internal os of the uterine cervix

the development of synthetic oxytocin by Vigneaud²¹ in 1953, for which he later was rewarded the Nobel Prize for chemistry, a new era in induction of labour started. In 1968 Turnbull and Anderson²² described titrated oxytocin infusion using a pump, which allowed lower dosing with fewer side-effects. They were also the first to prove that induction of labour with oxytocin is more effective after amniotomy.²²

Prostaglandins were discovered by two gynaecologists in New York, Raphael Kurzoak and Charles C. Lieb,²³ who in the 1930s found that fresh semen applied to myometrium specimens made muscles contract, and sometimes relax. They were later named prostaglandins in 1935 by von Euler,²⁴ who discovered that extracts from seminal vesicles and prostate glands were remarkably effective in causing contractions or relaxations in smooth muscles of various organs. The first records of induction of labour using prostaglandins date from 1968, when Karim and colleagues²⁵ first induced labour with intravenous prostaglandin F2alpha. At that time it was believed that prostaglandin (PG) E2 was a relaxant to the uterus. Calder and Embrey²⁶ were the first to induce labour with PGE2 in 1973, using extra-amniotic infusion of PGE2 through a 50 cc Foley catheter. They concluded that PGE2 softens and ripens the cervix. This initiated a series of small trials, investigating different PGE2 preparations as an induction agent, but also as a ripening agent. This resulted in a plethora of clinical trials investigating different formulations, dosing regimens, and routes of administration, without a coherent research strategy to evaluate the effectiveness and side-effects of different strategies.²⁷ Nonetheless, since the 1980s two strategies for induction of labour have generally been practiced; amniotomy followed by oxytocin infusion in case of a favourable cervix, and in case of an unfavourable cervix cervical ripening with PGE2, followed by amniotomy and augmentation with oxytocin infusion if necessary.⁶

Misoprostol, the synthetic analogue of PGE1 was originally marketed for prevention of peptic ulcer.²⁸ Studies in the late 1980s and early 1990s, however, showed that misoprostol can cause uterine contractions in early pregnancy.^{29,30} Later, a significant reduction in caesarean deliveries, and a shorter interval to delivery was shown when misoprostol was used compared to placebo and oxytocin for induction of labour.³¹ Misoprostol, which is stable in room temperature, has gained popularity in the recent decades, due to the low cost and easy storage compared to PGE2 preparations. Although still not approved for this indication by the FDA, Misoprostol is recommended for induction of labour by the American College of Obstetricians and Gynecologists (ACOG), The British Royal college of Obstetricians and Gynaecologists (RCOG), as well as the International Federation of Gynecology and Obstetrics (FIGO), and the World Health Organization (WHO).³²⁻³⁵

Mechanical methods were largely abandoned with the introduction of prostaglandins, even before proper clinical comparisons of mechanical methods with prostaglandin agents were made.

MECHANISM OF ACTION

Changes that occur in the cervix leading to its ripening during the course of pregnancy and labour are a decrease in the concentrations of collagen, and an increase in sulfated glycosaminoglycans and hyaluronic acid, leading to softening and thinning of the cervix.³⁶ Prostaglandins are thought to play a role in this process. PGE receptors can be found in the cervix as well as the myometrium. Treatment with PGE analogues has been found to cause a decrease in collagen concentration and induction of the production of hyaluronic acid by the cervical fibroblasts. This causes increased hydration and glycosaminoglycans, as seen at the spontaneous onset of labour in physiological pregnancy, leading to softening and effacement of the cervix.³⁷ As PGE receptors are also present in the myometrium, prostaglandins also have a contractile effect on the myometrium.^{38,39}

The prostaglandins that are nowadays most commonly used for induction of labour are PGE1 and PGE2. As can be seen in Figure 2., they are derived from different precursors, and have a similar, yet different structure. They therefore have different affinity to PG receptors.⁴⁰ For example, PGE2 is a ligand that has high affinity to all E-series prostanoid (EP) receptors, while misoprostol is a selective EP2/EP3 receptor agonist. Therefore, the binding of different prostaglandins to the receptors, can induce different actions, depending on the type of receptor and the dose of PG administered.⁴¹ As a result, different prostaglandins in different doses have different affinity to the various receptors and consequently different effects and potential side-effects. The various prostaglandins and their dosing and application regimens used in labour induction should therefore be investigated separately.

The mechanism of Foley catheter induction has long been unclear. In the early 1980s Keirse and colleagues⁴² elucidated that the effect of a Foley catheter is not only mechanical, but there is also a marked increase in PGF after Foley catheter placement. In the same period, Manabe and colleagues⁴³ showed that there is a rise in PGE2 and PGF in amniotic fluid after mechanical stretching of the cervix. To date, the mechanism of Foley catheter for cervical ripening has not been studied further.

POTENTIAL SIDE EFFECTS, PROS AND CONS OF FOLEY CATHETER AND PROSTAGLANDINS

Potential side effects of prostaglandins include hyperstimulation, and consequent related maternal and fetal morbidity. This includes fetal distress and asphyxia, resulting in instrumental deliveries, including vaginal instrumental deliveries and caesarean sections. Furthermore, prolonged contractions could result in uterine atony and subsequent post partum haemorrhage. As prostaglandin receptors can be found in various tissues in the human organism, systemic side-effects have also been noted. These include nausea, vomiting, diarrhoea, headaches, pyrexia, chills and shivering.⁴⁴

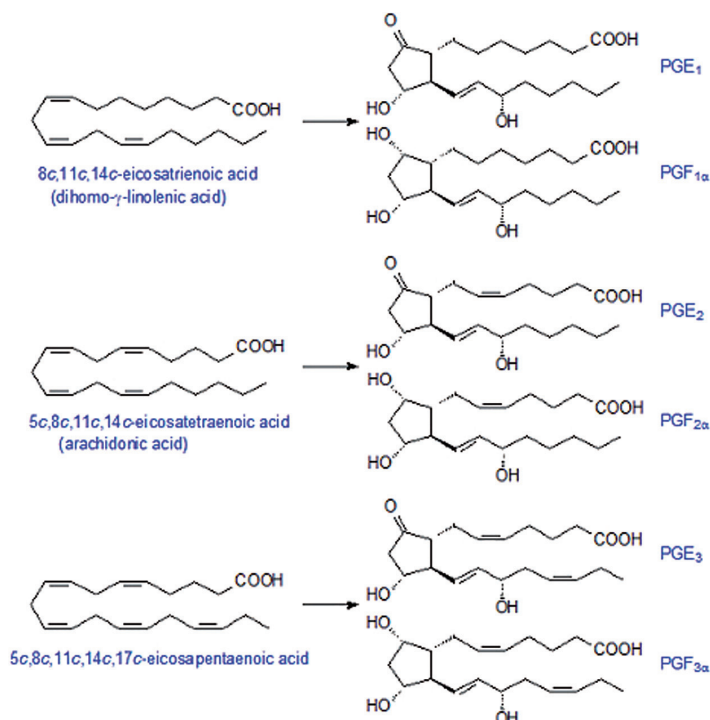


Figure 4. The prostaglandins PGE₁, PGE₂ and PGE₃ are derived from 8c,11c,14c-eicosatrienoic (dihomo- γ -linolenic), 5c,8c,11c,14c-eicosatetraenoic (arachidonic) and 5c,8c,11c,14c,17c-eicosapentaenoic acids, respectively. Numerical subscript (1 to 3) is used to denote the total number of double bonds in the alkyl substituents, and a Greek subscript (α or β) is used with prostaglandins of the PGF series to describe the stereochemistry of the hydroxyl group on carbon 9. Reproduced with permission from: <http://lipidlibrary.aocs.org/lipids/eicprost/index.htm>.

Considering Foley catheter ripening, concerns have been raised regarding increased infectious morbidity due to the introduction of a foreign object into the extra-amniotic space.⁴⁵ These, however, have not been confirmed in randomised trials.^{46,47}

It is a matter of debate whether cervical ripening and labour induction should really be seen as separate entities, as truly separating the two processes has not been possible using prostaglandin analogues, since they have an effect on the myometrium as well as the cervix.^{39,48} We believe that ripening of the cervix is merely the first step that is sometimes necessary in induction of labour. Consequently, in the current thesis, induction of labour is seen as any intervention undertaken to initiate labour, including cervical ripening.

Several authors have proposed that an ideal strategy would be one that effectuates cervical ripening before inducing contractions, as contractions during

the ripening phase are not effective in progressing labour and merely restrict blood flow to the foetus.⁴⁹⁻⁵² A method which does not cause contractions would decrease the need of fetal monitoring during ripening, and potentially reduce the risk of fetal distress, especially in fetuses with decreased placental blood flow. A possible advantage of Foley catheter compared to PG analogues, is that Foley catheter is thought to cause fewer contractions due to more physiological amounts of PGs being released. Hereby, the Foley catheter might separate the process of ripening from induction of contractions. Furthermore, when compared to PGE2 preparations, Foley catheters have substantially lower costs and are easier to store.

CURRENT STRATEGIES

Current guidelines advise the use of prostaglandin preparations, including PGE1 and E2, for induction of labour in term women with an unfavourable cervix as a first choice. Most guidelines only briefly touch on the possibility of the use of the Foley catheter. Interestingly, they provide contradictory recommendations.

The Dutch guideline advises to induce labour in women with an unfavourable cervix using prostaglandins or mechanical methods.³⁵ The ACOG guideline states that Foley catheter is a reasonable and effective alternative for prostaglandins in cervical ripening.³² On the contrary, the RCOG guideline concludes that mechanical procedures should not be used routinely for induction of labour,³⁴ and the Canadian guideline declares that the Foley catheter appears to be effective, but further research is needed.⁵³

AIM OF THIS THESIS

The aim of this thesis was to investigate the use of Foley catheter as an induction agent in women with an unfavourable cervix at term compared to pharmacological methods, mainly PGE2.

Specific research questions were:

Which are the current methods used for term induction of labour in the Netherlands?

What do we know about potential advantages and disadvantages of known methods?

Is induction with a Foley catheter more effective and safer than induction with PGE2 gel? What do we know about the safety and effectiveness of Foley catheter versus other prostaglandin preparations, such as vaginal misoprostol and slow release PGE2 vaginal inserts?

Is the use of a Foley catheter for induction of labour cost effective when compared to vaginal PGE2 gel?

Can we use Foley catheter for induction in women with a history of caesarean delivery?

OUTLINE OF THIS THESIS

Chapter two describes the methods of induction of labour used in the Netherlands in 2010, before the PROBAAT study was finalised. We conducted a nationwide enquiry to investigate the methods of labour induction in women with and without a prior caesarean birth.

Chapter three presents a systematic review and meta-analysis of studies comparing mechanical methods for induction of labour, including Foley catheter, to pharmacological methods, placebo or no intervention.

In **Chapter four** the results of the PROBAAT trial are presented. This was a multicentre randomised controlled trial comparing Foley catheter to vaginal PGE2 gel for induction of labour in term women with an unfavourable cervix.

In **Chapter five**, the results of a randomised controlled trial (PROBAAT-M) and meta-analysis of studies comparing Foley catheter to 25 microgram vaginal misoprostol are described. This randomised controlled trial was conducted parallel to the PROBAAT study.

Chapter six handles the comparison of Foley catheter versus 10 mg slow-release PGE2 inserts. This randomised controlled trial (PROBAAT-P) and meta-analysis of studies was also conducted parallel to the PROBAAT trial.

Chapter seven displays the data of an economic analysis and cost-effectiveness of Foley catheter and PGE2 gel. This cost-effectiveness study was conducted alongside the PROBAAT study, and handles, next to the main cost effectiveness question, different scenarios in which women are admitted to the antenatal ward or surveyed as out-patient during ripening.

In **Chapter eight** a model for predicting caesarean birth in women induced with an unfavourable cervix is presented. This model was a secondary analysis of the three PROBAAT studies (PROBAAT, PROBAAT-M and PROBAAT-P).

Chapter nine is a systematic review and meta-analysis of studies comparing different methods of cervical ripening and labour induction in women with a prior caesarean birth.

Chapter ten is a general discussion, in which the outcomes of the current thesis and future perspectives on mechanical methods for labour induction are conferred.

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