Induction of labour

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Abstract

Induction of labour describes the artificial stimulation of the onset of labour and occurs in up to 20% of pregnancies in the United Kingdom. Both mechanical and pharmacological methods of induction of labour exist. In the vast majority of women, the recommended method of induction of labour is by the use of vaginal prostaglandin E2. Induction of labour is associated with less maternal satisfaction and potentially increased rates of instrumental delivery and caesarean section compared with spontaneous vaginal delivery. Therefore, the decision for induction of labour should not be undertaken lightly and appropriate counselling of the mother with appropriate documentation of the provision of information in addition to the indications, risks, benefits and alternatives to induction of labour is advocated.

Keywords caesarean section; induction of labour; oxytocin; prostaglandin

Introduction

Induction of labour is a method of prematurely or artificially stimulating the onset of labour prior to the onset of spontaneous labour. The incidence of induction of labour has increased over recent decades, mainly due to an accumulating body of evidence highlighting the risks to the fetus of pregnancy lasting beyond 41 completed weeks of gestation and a decreased threshold for practitioners to recommend intervention of induction of labour for a variety of indications. Approximately 5%–10% of women will continue their pregnancy beyond 294 days or 42 completed weeks of pregnancy. These women are considered post-term and are one of the main contributors to the high incidence of induction of labour. The incidence of induction of labour varies from country to country, ranging from approximately 6% in third world countries such as Nigeria to approximately 20% in the United Kingdom. Induction of labour may be one of the commonest interventions in obstetrics, but it is not without risks and should not be undertaken lightly. Recent randomised controlled trials involving induction of labour for conditions such as large for gestational age or pre-eclampsia at 37 weeks' gestation suggest that induction of labour is not associated with increased caesarean section rates. Nonetheless, of all women who are induced, less than two-thirds will give birth without further intervention; approximately 15% will have an instrumental delivery and over 20% will deliver by emergency caesarean section. In addition, studies have demonstrated that a vast majority of women (>70%) would prefer not to have induction of labour by any means. It is therefore imperative that women be counselled appropriately antenatally regarding induction of labour, risks, benefits and alternatives.

Physiology of labour

The process of labour is a complex physiological process, and there is still a lack of basic understanding of the factors which trigger labour naturally. There are however two critical components of labour, cervical ripening and myometrial contractions, which ultimately result in cervical effacement and dilatation and expulsion of the fetus, placenta and membranes.

The normal human cervix measures approximately three and a half centimetres in length and is composed of 80–85% extracellular connective tissue and 10–15% smooth muscle. The predominant molecules of the extracellular matrix are type 1 and type 3 collagen. Intercalated among these collagen molecules are glycosaminoglycans and proteoglycans, hyaluronic acid, dermatan sulphate and heparin sulfate. Fibronectin and elastin also run among the collagen fibres and it is the release of fibronectin from the interface between the chorion and the decidua that is utilised in tests used to predict preterm labour.

It is necessary for the cervix to undergo several changes in order to stimulate the onset of labour and allow dilatation to occur. This process is known as cervical ripening and is the result of a series of complex biochemical reactions resulting in the cervix becoming soft and pliable. Late in pregnancy, hyaluronic acid, cervical collagenase and elastase increase in the cervix. This results in an increase of water molecules which intercalate among the collagen fibres. The amount of dermatan sulphate and chondroitin sulphate decreases, leading to reduced bridging among the collagen fibres. These changes, combined with decreased collagen fibre alignment, decreased collagen fibre strength, and diminished tensile strength of the extracellular cervical matrix, result in the ripening process. Near term, collagen turnover increases and degradation of newly synthesized collagen increases, resulting in decreased collagen content in the cervix. The process of cervical ripening is induced by cytokines, nitric oxide synthesis enzymes and prostaglandins and hormones such as progesterone, relaxin and oestrogen.

An increase in the enzyme cyclo-oxygenase-2, leads to increased local production of prostaglandin E2 (PGE2) in the cervix. The increase in PGE2 results in numerous changes to the cervix, including dilatation of small vessels in the cervix, an increase in interleukin (IL) 8 release and an increase in collagen degradation mediated by increased chemotaxis for leukocytes. Cervical ripening also involves prostaglandin F2-alpha which stimulates an increase in glycosaminoglycans. There is also increased activity of matrix metalloproteinases 2 and 9, enzymes that degrade extracellular matrix proteins.

The nitric oxide (NO) system also likely plays an integral role in the cervical ripening process and onset of labour. In the myometrium, nitric oxide synthase (NOS) activity is higher prior to the onset of labour and decreases during labour. In contrast, in

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the cervix prior to cervical ripening, NOS activity is low and then increases at the time of labour, associated with cervical ripening. In the human cervix, ripening is associated with an increase in induced NOS (iNOS) and brain NOS expression in the cervix.

Cervical ripening is followed by myometrial contractions which result in progressive effacement and dilatation of the cervix. The stimulus which initiates onset of myometrial contractions is unclear. It is likely that the myometrium, which is relatively quiescent prior to the onset of labour, becomes more sensitive to endogenous signalling molecules, which then trigger myometrial contractions. Coordinated myometrial contractions are achieved by gap junctions between myometrial smooth muscle cells, allowing the myometrium to act as a functional syncytium.

Prevention of induction of labour

Accurate dating of pregnancy using early antenatal ultrasound is widely accepted to help prevent high rates of induction of labour, most likely by avoiding misclassification.

The NICE guidelines on induction of labour recommend that at the 38 week antenatal visit women be informed of the potential for their pregnancy to continue beyond term; interventions such as membrane sweeping that may reduce post term pregnancies and the rationale, risks, benefits and alternatives to induction of labour should be discussed. This proactive approach may reduce the incidence of induction of labour by allowing a woman to consider the alternatives available to her, encourage her to look at a variety of sources of information, and give her time to discuss the information with her partner before coming to a decision.

To further reduce the incidence of induction of labour, it is recommended that all women are offered a sweep of the membranes after 37 weeks of gestation. Sweeping (or stripping) of the membranes involves inserting the examiner's finger through the internal os of the cervix and rotating it circumferentially. This manipulation is thought to result in the release of PGE2 from the cervix and also the release of prostaglandin F2α from the decidua and adjacent membranes. Vaginal spotting, mild abdominal cramps and slight maternal discomfort are the commonest side effects of this outpatient procedure and successive trials have conclusively demonstrated the safety of this procedure. In addition to increasing the onset of spontaneous onset of labour, sweeping of the membranes may also increase successful vaginal delivery rates. Additional membrane sweeping may be offered if there is no spontaneous onset of labour, however, the extra benefits of this remain unclear. The NICE guidelines recommend that membrane sweeping be offered to nulliparous women from between 40 and 41 weeks' gestation and multiparous women from 41 weeks. However, in practice, the sweeping of membranes is often offered earlier. There is no evidence that membrane sweeping more than once per week reduces rates of induction.

Indications for induction of labour

Labour may be induced for maternal or fetal indications. The decision to induce is made after consideration of maternal factors such as well being, cervical assessment, parity, previous mode of delivery and fetal factors such as gestational age, growth and well being of the fetus. Numerous indications exist for the induction of labour. Commonly accepted indications for induction of labour are presented in Table 1. Specific groups who may benefit include physiological 'post-dates'- pregnancies, advanced maternal age, maternal conditions such as pre-eclampsia and diabetes, and fetal intrauterine growth restriction.

- **'Post dates' pregnancies**

Traditionally, pregnancy has been allowed to continue up until 42 completed weeks of gestation and beyond. The Royal College of Obstetricians and Gynaecologists now recommend a policy of labour induction at 41 completed weeks of pregnancy rather than awaiting the spontaneous onset of labour. The NICE guidelines recommend that women with uncomplicated pregnancy should be offered induction of labour between 41^{+0} and 42^{+0} weeks' gestation. A recent large Cochrane systematic review and meta-analysis of low risk pregnancies found that induction at 41 weeks compared to expectant management results in fewer perinatal deaths (including stillbirth) and lower caesarean section rates. The absolute risk of perinatal mortality remains very small following 41 weeks' gestation. There is insufficient data to recommend routine induction of labour at 40 weeks' gestation as maternal–fetal benefits such as a reduction in the incidence of stillbirth have not been conclusively proven.

Indications for induction of labour

Maternal indications	• Post-term pregnancy • Pregnancy induced hypertension or pre-eclampsia greater than 37 weeks' gestation. • Obstetric cholestasis where bile acids >100 μmol/L >37 weeks • Maternal diabetes >40 weeks' gestation • Advanced maternal age, >39 weeks.
Fetal indications	• Intrauterine growth restriction. • Intrauterine fetal death. • Fetal macrosomia. Increasingly women are been offered induction of labour for suspected fetal macrosomia. However, there is insufficient evidence that induction of labour improves maternal or fetal outcomes and this is not recommended by the NICE guidelines.
Membrane and placental indications	• Preterm prelabour rupture of membranes greater than 37 weeks' gestation with no spontaneous onset of labour occurring within 24 h. • Preterm prelabour rupture of the membranes <37 weeks if any signs or symptoms of chorioamnionitis are present

Table 1

The potentially increased costs of a policy of routine induction of labour at 40 weeks, consequent on increases in neonatal care have also not been properly evaluated.

Should a woman decline induction of labour following 42 weeks' gestation, NICE recommend that the women be offered at least twice weekly CTG monitoring and ultrasound assessment of the maximum amniotic fluid pool depth.

The ARRIVE study was a multicentre randomised controlled trial which randomly assigned low-risk nulliparous women who were at 38 weeks 0 days−38 weeks 6 days of gestation to labour induction at 39 weeks 0 days−39 weeks 4 days or to expectant management. The study recruited over six thousand women, 3062 of whom were assigned to labour induction, and 3044 were assigned to expectant management. The primary outcome was a composite of perinatal death or severe neonatal complications. The primary outcome occurred in 4.3% of neonates in the induction group and in 5.4% in the expectant-management group (relative risk, 0.80; 95% confidence interval [CI], 0.64 to 1.00). The frequency of caesarean section delivery was significantly lower in the induction group than in the expectant-management group (18.6% vs. 22.2%; relative risk, 0.84; 95% CI, 0.76 to 0.93).

- **Intrauterine growth restriction (IUGR)**

In the Green−top Guideline No. 31, 2nd Edition entitled "The Investigation and Management of the Small−for−Gestational −Age Fetus", induction of labour is recommended by 37 weeks' gestation provided Doppler studies are normal up until this gestation. A Cochrane review of induction versus expectant management for infants suspected of fetal compromise or IUGR at term found that there was no benefit to a policy of induction for early delivery, but this was based on just three randomised trials. Saving Babies' Lives A care bundle for reducing stillbirth provides an algorithm and Risk Assessment Tool for Screening and Surveillance of fetal growth in singleton pregnancies. This provides advice on the differentiation between the pathological SGA fetus that is at increased risk of stillbirth compared with the SGA fetus which is more likely to be constitutionally small and alternatives to delivery at 37 weeks' gestation.

- **Pre-eclampsia**

Provided there are no other contraindications to induction of labour, it is recommended for women who develop pre-eclampsia once they reach 37 weeks' gestation (HYPITAT study).

- **Diabetes mellitus (gestational and pre-existing)**

There are specific risks associated with a prolonged pregnancy (>40 weeks) in mothers with diabetes. Risks to the fetus include an increased risk of stillbirth. The reason for this is unclear but it is theorised that suboptimal gylcaemic control may lead to fetal distress, hyperinsulinemia, hyperlactinaemia and acidosis, which may cause fetal death. The NICE guideline on Diabetes in Pregnancy advises that induction of labour be offered to women with type 1 or type 2 diabetes from 37 weeks' gestation.

- **Advanced maternal age**

Twenty per cent of live births in the UK are to women over the age of 35. These women have an increased rate of stillbirth, with the risk of stillbirth in a woman > 35 at 39 + 0 equivalent to the risk of stillbirth in a women aged 25−29 at 41 + 0 weeks. The RCOG issued a scientific impact paper on the induction of labour at term in older women in which it is suggested that the pros and cons of induction of labour be discussed and induction of labour considered or offered to women ≥40 years of age at 39−40 weeks' gestation. There is concern that a blanket policy of induction may lead to an increase in caesarean section rates. However, a meta-analysis published in 2016 demonstrated no significant increase in caesarean section rates in women >35 who are induced at term.

Regardless of the indication, induction of labour has a significant health impact on the woman and her baby, particularly if the cervix is unfavourable. Hence NICE do not recommend induction of labour on maternal request alone, nor do they recommend induction of labour because a mother simply has a history of precipitate labour. If induction of labour is to be offered to the mother, then there should be clear evidence that the induction of labour is beneficial to the mother and/or the fetus. Therefore, the decision to undertake induction of labour needs to be thoroughly discussed with the mother and alternatives and risks clearly explained and documented.

Reduced fetal movements

Reduced fetal movements around term is a common presentation and often an indication for induction of labour, either due to perceived increased risks by clinicians or anxiety by patients. The AFFIRM study tested the hypothesis that the introduction of a reduced fetal movement care package for pregnant women and clinicians would alter the incidence of stillbirth. A stepped wedge cluster randomised trial was done in the UK and Ireland involving 37 hospitals which collected data from 409,175 pregnancies. The introduction of the specific care package did not reduce the risk of stillbirth with the incidence of stillbirth being 4·40 per 1000 births during the control period and 4·06 per 1000 births in the intervention period (adjusted odds ratio [aOR] 0·90, 95% CI 0·75−1·07; p = 0·23).

Suspected macrosomia

With increasing use of ultrasound in obstetrics, the occurrence of the non-diabetic suspected macrosomic fetus is increasing. As macrosomia brings with it an increased risk of shoulder dystocia, increasingly this finding is considered an indication for induction of labour. Boulvain et al. performed a randomised controlled trial between Oct 1, 2002, and Jan 1, 2009, in 19 tertiary-care centres in France, Switzerland, and Belgium. Women with singleton fetuses whose estimated weight exceeded the 95th percentile were randomised to receive induction of labour within 3 days between 37 (+0) weeks and 38 (+6) weeks of gestation, or expectant management. Results demonstrated a reduction in the risk of shoulder dystocia or associated morbidity (n = 8) compared with expectant management (n = 25; relative risk [RR] 0·32, 95% CI 0·15−0·71; p = 0·004). No differences were observed in caesarean section rates and women in the induction arm a higher likelihood of spontaneous vaginal delivery.

Prelabour rupture of membranes

Preterm pre-labour ruptured membranes close to term is associated with increased risk of neonatal infection, but immediate delivery is associated with risks of prematurity. The PPROMT trial was a multicentre randomised controlled trial done at 65 centres across 11 countries in which 1839 women were recruited

and randomly assigned: 924 to the immediate birth group and 915 to the expectant management group. The authors concluded that in the absence of overt signs of infection or fetal compromise, a policy of expectant management with appropriate surveillance of maternal and fetal wellbeing should be followed in pregnant women who present with ruptured membranes close to term.

Hannah et al. investigated term PROM and demonstrated that induction of labour with intravenous oxytocin results in a lower risk of maternal infection than does expectant management. Women view induction of labour more positively than expectant management.

Contra-indications to induction of labour

The common contra-indications to induction of labour presented in Table 2 are also generally considered to be indications for caesarean section. In addition to these contraindications, other scenarios exist in which caution should be exercised and senior obstetric opinion may be sought. These include a high or mobile presenting part, multiple pregnancy, polyhydramnios, previous low transverse caesarean section and unstable lie. These pregnancies require very close monitoring during the induction process, if induced, with continuous fetal monitoring and a low threshold for cessation of the induction process and delivery by caesarean section.

Contraindications to induction of labour

Maternal contraindications to induction of labour	• Previous transmural uterine surgery in which the full thickness of the myometrium has being disrupted, e.g. myomectomy • Previous multiple caesarean sections (>2 previous caesarean sections is considered a contraindication for an induction of labour). • Previous classical caesarean section. • Unexplained maternal pyrexia. • Regular contractions • Active herpes • Previous traumatic or difficult delivery
Fetal contraindications to induction of labour	• Malpresentation such as a face or brow presentation • A breech presentation is considered by most to be a contraindication to induction of labour. External cephalic version should instead be offered and delivery by caesarean section considered if the baby remains breech. • Transverse fetal lie • Cord prolapse. • Non-reassuring fetal state such as evidence of severe fetal growth restriction.
Placental contraindications to induction of labour	• Placenta praevia • Vasa praevia • Unexplained vaginal bleeding.

Table 2

Methods of induction of labour

Recommended methods for induction of labour depend on many factors. One of the main determinants is the presence or absence of a scar on the uterus. Other factors influencing the method of induction of labour include a cervical assessment using Bishop's score, parity and patient and obstetrician preference. The most useful predictor of success in induction of labour is the Bishop score, a score of cervical favourability, or ripeness. The cervix is considered to be favourable when the Bishop score (Table 3) is five or greater and the majority of inductions of labour will be effective when the cervix is favourable. Regardless of the method of induction used, if the Bishop score is high, reflecting a high degree of cervical ripeness, induction of labour usually can usually be achieved relatively quickly, generally with a successful vaginal delivery as the outcome. In contrast, if the Bishop score is very low it is much more difficult to induce labour and these efforts are much more likely to fail. If the cervix is not considered to be favourable then a priming agent is generally administered to induce cervical ripening. Cervical ripening results in the softening and an increase in the distensibility of the cervix, ultimately leading to the effacement and dilatation of the cervix.

Methods for induction of labour may be divided into mechanical and pharmacological.

- **Mechanical methods for induction of labour**

Although discussed in this review it must be emphasised that the NICE guidelines recommend that mechanical procedures should not be used routinely for the induction of labour. This is because in women with an unfavourable cervix, mechanical methods for induction of labour do not result in an increased incidence of vaginal birth or reduce the caesarean section rate. Also, there is limited available evidence investigating the effects of mechanical methods for induction of labour in women with a favourable cervix compared with placebo or no treatment or with prostaglandins. However, mechanical methods have some advantages such as a low risk of fetal heart rate abnormalities, low risk of systemic side effects and convenient storage (not requiring refrigeration) and studies such as those by Gupta et al. have demonstrated that osmotic dilators. The risk of

(Modified) Bishop's score. A score of 5–6 or more is considered favourable

Cervical Parameter	Score			
	0	1	2	3
Position of cervix	Posterior	Mid-position	Anterior	–
Consistency of cervix	Firm	Medium	Soft	–
Station of presenting part (relative to ischial spines)	-3 cm	-2 cm	-1/0 cm	+1/+2 cm
Cervical Dilatation	0 cm	1–2 cm	3–4 cm	5–6 cm
Effacement	0–30%	31–50%	51–80%	>80%
Or				
Cervical length (Modified Bishop's Score)	4 cm	2–4 cm	1–2 cm	<1 cm

Table 3

hyperstimulation is also reduced with mechanical methods compared with prostaglandins. Disadvantages of mechanical methods include discomfort during insertion. Despite concerns, it appears that in the absence of prelabour rupture of membranes, mechanical methods for induction of labour do not result in an increase in the risk of ascending infection and chorioamnionitis. Mechanical methods for induction of labour include insertion of a balloon catheter, extra-amniotic saline infusion and the use of hygroscopic dilators.

Historically, insertion of a 30 ml–50 ml Foley catheter filled with saline in the uterus was the commonest mode of induction of labour. However, this has been superceded by the advent of prostaglandins in the past three decades. The catheter may be inserted using a ring forceps, the balloon is inflated following removal of the forceps and the catheter is retracted so the inflated balloon rests against the cervix. This saline filled balloon results in pressure to the lower segment of the uterus and the cervix resulting in the local production of prostaglandins. Generally, the catheter is inserted, inflated and left in situ for 12–24 h. Catheter insertion may be combined with a saline solution as an extra-amniotic infusion but this is not generally performed. Extra-amniotic saline infusion (EASI) is a method of induction of labour in which sterile saline is infused continuously into the amniotic space via a catheter. EASI does not appear to increase the risk of chorioamnionitis but is invasive and not generally performed in the UK.

Hygroscopic dilators are dilators which may be placed in the cervix and dilate secondary to water absorption. Several dilators may be inserted into the cervix and they expand over 12–24 h as they absorb water resulting in the opening of the cervix. Although, these dilators physically dilate the cervix, and evidence is limited, they do not appear to improve the outcome of induction of labour.

Amniotomy is a mechanical method for induction of labour which is used routinely in induction of labour following cervical ripening with either pharmacological or mechanical methods. Amniotomy involves the rupturing of the membranes using an amnihook. Naturally, to perform an amniotomy, the cervix must be dilated. However, amniotomy alone or in combination with oxytocin should not be used as a primary method for induction of labour unless the use of PGE2 is contraindicated.

- **Pharmacological methods for induction of labour**

Pharmacological methods for induction of labour include prostaglandins (oral and vaginal) and oxytocin. Pharmacological methods for induction of labour are the preferred method for induction of labour in the UK, most likely due to less patient discomfort and better efficacy compared to mechanical methods.

Vaginal prostaglandin E2 (PGE2) is the recommended method of induction of labour in the absence of any contraindications. PGE2 may be administered as a gel, tablet or controlled release pessary and all these preparations appear to have similar efficacies. Each 3 g gel (2.5 ml) contains 1 mg or 2 mg dinoprostone. The gel should be inserted high into the posterior fornix with care to avoid administration into the cervical canal. The patient should then be instructed to remain recumbent for at least 30 min. In primigravida patients with a Bishop score of 5 or less, an initial dose of 2 mg may be administered vaginally. In other patients an initial dose of 1 mg should be administered vaginally. A second dose of 1 mg or 2 mg may be administered after 6 h following repeat cervical assessment. It is advised not to exceed a maximum dose of 4 mg in 24 h. However, the optimal dose and frequency of administration remains unclear.

An alternative preparation of dinoprostone is Cervidil, which contains 10 mg of dinoprostone embedded in a mesh. In the UK this is often in the form of Propess®. This is also placed in the posterior fornix and allows for controlled release of dinoprostone over 12–24 h, after which it is removed. The advantage of this mode of administration is that in the result of hyperstimulation the mesh may be removed immediately.

Adverse reactions to dinoprostone are rare. The commonest include vomiting, nausea and diarrhoea. Other rarer adverse reactions include uterine hyperstimulation, fetal distress, maternal hypertension, bronchospasm, backache, rash and amniotic fluid embolism. Uterine hyperstimulation may respond to the administration of 250 μg terbutaline subcutaneously to relax the uterus. Senior obstetric opinion should be sought prior to administration of a tocolytic in response to uterine hyperstimulation.

A prostaglandin E1 analog called misoprostol has also been used in the induction of labour. However, misoprostol is only recommended for induction of labour in the presence of intrauterine fetal death. A 25 μg misoprostol tablet can be inserted in the vagina every 4 h although doses depend on the gestation. A Cochrane review demonstrated that vaginal misoprostol appears to be more effective than conventional methods of cervical ripening and labour induction. Advantages over PGE2 analogues include its low cost and stability at room temperature, making it particularly suitable for induction of labour in low resource settings. However, the safety profile of vaginal misoprostol remains to be proven as there appears to be an increase in the occurrence of uterine hyperstimulation. The risk of uterine rupture associated with the use of misoprostol is unclear. Oral misoprostol appears to be safer than vaginal misoprostol, with similar efficacy. It is increasing in use worldwide, and indeed is recommended by the WHO as a first line induction agent. However, it is not currently licensed for this use. Regardless of the type of prostaglandin used, women should be informed of the risk of uterine hyperstimulation.

Oxytocin

Oxytocin is a polypeptide hormone produced in the hypothalamus and secreted by the posterior pituitary. Exogenous oxytocin (Syntocinon) may be administered intravenously and results in uterine contractions. Generally, the dose is titrated, with increasing doses administered every approximately 30 min until regular contractions occur of approximately 1 min in duration every 3 min. Risks of oxytocin include, hyponatremia (oxytocin is an ADH analogue), tachycardia and hypotension, fetal distress and uterine hyperstimulation. Oxytocin alone or in combination with amniotomy is not recommended for induction of labour. A Cochrane review concluded that prostaglandins were more successful in achieving a vaginal birth within 24 h. In addition, oxytocin induction may increase the rate of interventions in labour. Oxytocin induction of labour may have a role to play in high-risk patients whose fetuses may be at increased risk for intolerance of labour but further research into this area is required.

Antiprogesterones

Mifepristone (formerly known as RU486) is a very effective antiprogesterone and antiglucocorticoid that works by binding to progesterone and glucocorticoid receptors. Randomized trials have shown it to be very effective in inducing labour. The use of mifepristone is only recommended following intrauterine fetal death and is used as a priming agent prior to the administration of Misoprostol. NICE recommend oral mifepristone followed by either vaginal PGE2 or vaginal misoprostol for induction in the presence of IUFD (suggested FIGO protocol at http://www.misoprostol.org/File/Misoprostol_Dosage%20Recommendations%202012.pdf).

In addition to these methods for induction of labour, the following methods for induction of labour are not recommended: oral or intravenous or intracervical PGE2, hyaluronidase, corticosteroids, oestrogen and vaginal nitric oxide donors. There is also insufficient evidence to recommend any of the following non-pharmacological methods of induction of labour: herbal supplements, acupuncture, castor oil, homeopathy, sexual intercourse, curries, enemas and hot baths.

Outpatient induction of labour

Induction of labour is usually carried out in hospital but some methods may be suitable for use with women treated as outpatients, and allowed to go home to wait for labour to progress. A Cochrane review published in 2017 (Vogel et al.) concluded that Induction of labour in outpatient settings appears feasible and important adverse events seem rare, however, in general there is insufficient evidence to detect differences. There was some evidence that compared to placebo or no treatment, induction agents administered on an outpatient basis reduced the need for further interventions to induce labour, and shortened the interval from intervention to birth.

Risks associated with induction of labour

The majority of women induced will have a successful vaginal delivery of a healthy infant. However, complications may arise following induction of labour. These include.

- Hyperstimulation of the uterus may occur following administration of Prostaglandin gel. Women with high Bishops scores and multiparous women with previous successful vaginal deliveries may be more susceptible to hyperstimulation of the uterus. Should hyperstimulation of the uterus occur, tocolysis using a uterine relaxant such as terbutaline may be considered in combination with cessation of oxytocin infusion, maternal oxygen and intravenous fluids and placing the mother in the left lateral position.
- Uterine rupture. Women may be particularly at risk of uterine rupture if there is a history of previous uterine surgery including caesarean sections.
- Fetal immaturity is a risk of induction of labour, in particular when an accurate gestational age has not been established. This risk can be minimised by ensuring timely and accurate booking visits with ultrasound dating of pregnancy. Because earlier delivery even just a few weeks before term has been shown to affect both IQ and educational attainment, it is critical that indications for induction of labour are evidence based and necessary.
- Caesarean sections. There is no consensus at present on the effect of induction on caesarean section rates. Clinical trials investigating the induction of labour have demonstrated increased, decreased and no change in caesarean section rates. A Cochrane review by Gülmezoglu et al. in 2009 concluded that based on evidence from more than 5000 women who participated in these included trials, caesarean section rates and assisted vaginal delivery rates are not increased by induction of labour. One systematic review that assessed the effects of induction of labour versus expectant management from 37 to 42 weeks of gestation demonstrated that the induction group was significantly less likely to have caesarean birth (RR 0.58, 95% CI 0.34 to 0.99) but more likely to require assisted vaginal birth. A recent systematic review and meta-analysis of 37 RCTs by Wood et al. concluded that induction of labour in women with intact membranes reduces the risk of caesarean section but suggests this may be due to non-treatment effects. Definitive conclusions on the risks of caesarean section following induction of labour are difficult as many trials differ in criteria such as cervical ripeness, modes of induction of labour, threshold for fetal distress and the use of fetal monitoring. The AFFIRM study (reduced fetal movements study) demonstrated higher caesarean Section (28.3 vs 25.5%) and Induction of labour rates (40.7 vs 35.8%) compared with control groups whereas the ARRIVE study (induction of low risk nulliparous women) demonstrated a significantly lower caesarean section rate 18.6% vs. 22.2%) in induced women.
- Artificial rupture of membranes via amniotomy carries the rare but grave risk of umbilical cord prolapse. Risk factors include polyhydramnios, prematurity and a high presenting head. This necessitates immediate emergency delivery by caesarean section. This complication may be avoided by adequate assessment of engagement of the head prior to amniotomy, palpation for umbilical cord presentation at the time of vaginal examination and assessment of Bishop's score and avoidance of artificial rupture of the membranes in the presence of a high head.

Induction of labour in women with previous caesarean sections

With rising caesarean section rates it is not uncommon to encounter induction of labour in women with a previous caesarean section and no previous successful vaginal delivery. Between 50% and 70% of women with a previous caesarean section and no previous successful vaginal delivery will have a successful vaginal delivery in their second pregnancy. There is limited good quality evidence available regarding the ideal management of these women. However, it appears that vaginal PGE2 followed by amniotomy may provide a more effective method of induction of labour compared with amniotomy plus

intravenous oxytocin. Vaginal misoprostol is associated with a higher frequency of uterine rupture compared with intravenous oxytocin and should not be used.

The NICE guidelines recommend that if delivery is indicated, women who have had a previous caesarean section may be offered induction of labour with vaginal PGE2. However, women with previous caesarean sections should be counselled regarding the increased risk of need for emergency caesarean section and the increased risk of uterine rupture.

The risk of uterine rupture varies according to the method of induction. Overall, the Royal College of Obstetricians and Gynaecologists recommends that women are quoted a risk of uterine rupture of 74/10,000 planned vaginal birth after caesarean section.

The potential increase in the risk of uterine rupture with the use of PGE2 is unclear. In a prospective four year observational study, Landon et al., demonstrated that prostaglandin induction was not associated with a significantly increased risk of uterine rupture compared with non-prostaglandin induction incurred. A second large Scottish study demonstrated a statistically significantly higher uterine rupture risk (87/10,000 versus 29/10,000) and a higher risk of perinatal death from uterine rupture (11.2/10,000 versus 4.5/10,000). Finally Stock et al. performed a population-based retrospective cohort study of singleton births greater than 39 weeks' gestation, in women with one previous caesarean delivery, in Scotland from 1981 to 2007 (n = 46,176). 40% of women who underwent induction of labour from 39 to 41 weeks' gestation were ultimately delivered by caesarean section. When compared to expectant management, induction of labour was associated with lower odds of caesarean delivery, no significant effect on the odds of perinatal mortality but greater odds of neonatal unit admission. Whether, mechanical methods of induction of labour may be used safely in women with previous caesarean section is unclear with very limited available evidence.

If using PGE2 in women with previous caesarean sections, it may be advisable to consider restricting the dose and adopting a lower threshold of total prostaglandin dose exposure.

Monitoring and pain relief associated with induction of labour

When induction of labour is performed, continuous monitoring of the fetus using continuous fetal heart monitoring and of maternal contractions should be used. Prior to induction of labour, a baseline cardiotocogram (CTG) should be performed to confirm fetal well-being and a Bishop's score recorded. Following administration of PGE2, a repeat CTG should be performed and following this, intermittent auscultation may be used. Intermittent auscultation should occur at every maternal assessment and once contractions start the fetal heart should be auscultated after a contraction for at least 1 min, at least every 15 min, and the rate should be recorded as an average. Box 1 highlights instances when it is appropriate to switch to continuous fetal monitoring.

Six hours following administration of PGE2 gel or 24 h following insertion of a Propess pessary®, a repeat assessment should be performed, a Bishop's score re-evaluated and a decision made to either administer further PGE2, perform an amniotomy ± oxytocin, stop the induction process or consider alternative options such as delivery by caesarean section.

Induction of labour is considered to be more painful than labour occurring spontaneously. Women should be counselled regarding this at the time of decision for induction of labour. Pain relief options for women who are undergoing an induction of labour are the same as for women who have gone into spontaneous labour and range from conservative techniques such as mobilisation and hot baths to pharmacological options such as nitrous oxide and epidurals.

Indications for switching from intermittent fetal auscultation to continuous fetal monitoring. (Adapted from NICE clinical guideline Intrapartum Care 55)

- The presence of meconium stained liquor.
- Abnormal fetal heart rate defined as a fetal heart rate less than 110 beats per minute or greater than 160 beats per minute or any decelerations occurring after a contraction
- Maternal pyrexia (defined as 38.0 °C once or 37.5 °C on two occasions 2 h apart)
- Unexplained fresh bleeding developing during labour
- The augmentation of labour with oxytocin.
- Maternal request

Box 1

Failed induction of labour

Failed induction is defined by the NICE guidelines as labour not starting after one cycle of treatment. If labour has not started after one cycle of treatment the clinician should reassess the woman's condition and pregnancy in general, assess fetal well-being with electronic fetal monitoring and provide support and make decisions in accordance with the woman's wishes and clinical circumstances. Options following failed induction of labour include a further attempt to induce labour, potentially following a purposeful delay, after consultation with the patient, or performing a caesarean section.

Conclusion

Labour involves a complex series of events and conclusive recommendations regarding induction of labour are limited due to a basic lack of understanding of the physiologic events that are involved in the process of labour, a wide biological variation observed between women normal labour and a large selection of heterogeneous trials which use different clinical endpoints rendering the evidence difficult to interpret. Induction of labour is best undertaken when continuing the pregnancy is thought to be associated with greater maternal or fetal risk than inducing labour. Where possible, it is advisable to avoid induction of labour. When induction of labour is being considered, women should be appropriately counselled regarding indications, risks, benefits and alternatives. PGE2 is the recommended mode of induction in the majority of women. Further research is needed to identify those fetuses most at risk of morbidity and stillbirth and ultimately those fetuses who warrant early intervention and induction of labour. Research is also required to assess the cost effectiveness of induction of labour verses expectant management, alternatives to encourage spontaneous onset of labour and the identification of those women most likely to have a successful induction of labour. ◆

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Practice points

- Healthcare professionals should counsel women regarding the potential for, the risks, benefits and alternatives to induction of labour. Women should be provided with information on induction of labour, then allowed time to discuss the information before reaching a decision. Healthcare professionals should provide a range of sources of information and offer sufficient time to allow women to ask questions.
- Women with uncomplicated pregnancies should be given every opportunity to go into spontaneous labour, hence avoiding the need to for an induction of labour.
- The Bishop's score is the best available tool for predicting the probability of a successful induction.
- Women should be informed that induced labour is likely to be more painful than labour which has a spontaneous onset.
- Vaginal prostaglandin E2 is the recommended method for induction in the majority of women.
- Further research is needed to identify subsets of women and fetuses most likely to benefit from induction of labour, alternative approaches to and optimal methods for induction of labour.