

## *Leading Article*

### **Trends in induction of labour: implications for Sri Lanka**

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#### **Abstract**

The methods used for induction of labour (IOL) and the indications for IOL have markedly changed over the last 20 centuries. Mammary stimulation and mechanical dilation of the cervical canal was described more than 20 centuries ago. Since then, the methods used include: amniotomy; strong purgatives and various herbal preparations; a pituitary extract; amniotomy combined with synthetic oxytocin; artificial separation of membranes; a supra cervical balloon catheter; vaginal prostaglandins; hygroscopic cervical dilatation. Currently, there is a great interest in oral prostaglandins and supracervical balloon catheters as well as the possibility of IOL in

an outpatient setting. The indications for IOL 20 centuries ago were probably for maternal reasons, and fetal reasons are likely to have been added much later. During the 20<sup>th</sup> century, social reasons also become indications for IOL. Recently, routine IOL at or above 37 weeks' gestation has been recommended to reduce perinatal mortality including still births. Almost all the methods used globally for IOL and the indications for IOL, are applicable to Sri Lanka. However, before implementing them in Sri Lanka, their justification, feasibility, safety, and acceptability to the pregnant women and their care givers, must be carefully assessed.

#### **Introduction**

It is reported that Hippocrates described mammary stimulation and mechanical dilation of the cervical canal more than 20 centuries ago and that Soranus described artificial rupture of membranes (amniotomy) for induction of labour (IOL), during the second century. Thereafter, up to the 17<sup>th</sup> century, combinations of amniotomy, manual and instrumental dilatation of cervix and the use of purgatives and various types of herbal

medications have been used for IOL<sup>1</sup>. Artificial separation of membranes (ASM) to stimulate the local production of prostaglandins, has apparently been first described by James Hamilton in 1810<sup>2</sup>, while a pituitary extract has been tried by Bell in 1909 but soon abandoned due to its serious adverse effects<sup>1</sup>.

The synthesis of oxytocin in 1955 by an American Biochemist Vincent du Vigneaud, who was awarded the Nobel Prize in Chemistry for his work, was a seminal event<sup>3</sup>. This revolutionized IOL, and amniotomy combined with the intra venous infusions of synthetic oxytocin became the commonest method for IOL, world wide, until another landmark event which occurred in the history of IOL; the advent of prostaglandins in 1968, as a result of the work by Karim and colleagues from Uganda<sup>1</sup>. Embrey and Mollison in 1967 described the supra cervical placement of a Foley catheter for ripening of the cervix to make it favourable for IOL<sup>1</sup>. Although vaginal prostaglandins were being increasingly used, ASM, supra cervical Foley catheter and hygroscopic cervical dilatory methods were again being used by the 1990s. Currently, there is a great interest in low dose oral misoprostol (OM), a synthetic methyl analogue of prostaglandin E<sub>1</sub> and supracervical balloon catheters, as well as the possibility of IOL in an outpatient setting.

If continuing the pregnancy is considered to be dangerous for the mother or the fetus or both (eg severe pre-eclampsia, post term pregnancies etc), IOL would be indicated. The indications for IOL 20 centuries ago would most probably have been for maternal reasons. The addition of fetal reasons, as an indication for IOL, is likely to have occurred much later. During the 20<sup>th</sup> century, social reasons i.e the convenience for the mother or care giver or both, became indications for IOL, and IOL is being increasingly carried out currently without a definite obstetric reason. Recently, routine IOL at or above 37 weeks' gestation has also been recommended, with a view to reducing perinatal mortality including still births, even among low-risk women. Almost all the methods globally used for IOL and the indications for IOL, are applicable to Sri Lanka. However, before implementing them in Sri Lanka, their justification,

feasibility, safety, and acceptability to the pregnant women and their care givers, must be carefully assessed. The method of IOL needs to be individualised, to suit the differing needs and preferences of different women in different contexts, ensuring its effectiveness as well as its safety to both the mother and her fetus.

## **Historical methods: implications for Sri Lanka**

### ***Mammary stimulation and sexual intercourse***

Mammary stimulation is known to cause the release of oxytocin from the posterior pituitary, and prostaglandins, which were originally thought to originate from the prostate (and hence its name) are produced by the seminal vesicles. However, there is lack of evidence to justify the use of mammary stimulation and sexual intercourse as methods of IOL<sup>4</sup>.

### ***Amniotomy***

Although amniotomy for IOL was first described by Soranus in the second century, English literature refers to it as the "English Method" of IOL and the credit for it is given to Thomas Denman who has apparently reported it in 1756<sup>2</sup>. Amniotomy continues to be used as a method of IOL worldwide. It only involves the mastering of a simple skill, and as it can be carried out with instruments freely available in any maternity unit, it is suitable for Sri Lanka too. However contraindication for amniotomy should be excluded (eg cervico vaginal infections and fetal, death *in utero* other than consequent to placental abruption), women suitable for amniotomy should be carefully selected, strict aseptic techniques must be adopted and prolapse of the umbilical cord should be prevented.

### ***Manual and instrumental dilatation of cervix and the use of purgatives and various types of herbal medications***

These methods are no longer recommended because of the availability of more effective, safe and acceptable methods of IOL<sup>4</sup>.

### ***Artificial Separation of Membranes***

It is currently recommended that ASM, also referred to as sweeping of membranes, which was describe in the 19<sup>th</sup> century, should be offered to all women at term, as it stimulates the local production of prostaglandin, and leads to “ripening of the cervix” which could initiate spontaneous onset of labour and thereby reduce the need for formal IOL with a more effective method subsequently, or at least facilitate IOL by reducing the induction delivery interval<sup>5</sup>. It is important to counsel women undergoing ASM about the possible discomfort, mild vaginal bleeding and intermittent uterine contractions after the procedure. Although ASM was abandoned by many obstetricians during the 1980s, due to fears of possible maternal and neonatal infections, such an increased risk has not been found and it is considered to be safe even in Group B Streptococcus carriers<sup>2</sup>. Therefore, this simple, “no cost” procedure should be carried out in Sri Lanka. Nevertheless, it is essential not to perform an ASM in a woman who has clinical evidence of a cervico vaginal infection and to thoroughly clean the vagina and cervix with povidone iodine, prior to ASM.

### **Methods from the 20<sup>th</sup> century and for the future: implications for Sri Lanka**

#### ***Amniotomy combined with intravenous infusions of synthetic oxytocin***

This was the most popular method of IOL in the second half of the 20<sup>th</sup> century and it continues to be a relatively cheap, frequently used method of IOL globally, including Sri Lanka. A recent systematic

review and network meta-analysis (SR and NMA) has shown that this method is very effective and has high rates of vaginal delivery in 24 hours (VD 24), in women with favourable cervixes<sup>4</sup>. It is important to ensure that IOL is carried out using a detailed, specific guideline, in addition to a protocol for oxytocin dosage, under the direct supervision of an experienced obstetrician. Pharmacokinetic studies have demonstrated that it is important to have an interval of approximately 40 minutes between increments and to monitor the uterine contractions and the fetus carefully<sup>6</sup>. The use of oxytocin for IOL should be continuously monitored in all maternity units, because if it is used incorrectly, it can become a very dangerous medication, with serious adverse consequences, such as hyper stimulation or fluid overload, carrying increased risks to the mother and her fetus.

#### ***Nitric Oxide Donors administered vaginally***

Prior to spontaneous onset of labour, there is structural remodeling or ripening of the cervix, which progresses to the onset of labour as a continuous process without a clear demarcation between the two processes. Nitric oxide (NO), interacting with numerous substances, has an important role in initiating cervical ripening and subsequent spontaneous onset of labour. At the beginning of the 21<sup>st</sup> Century, there was a great interest in the possibility of using vaginally administered NO donors for pre induction cervical ripening, especially in women with unfavourable cervixes, to facilitate subsequent IOL. The feasibility of IOL in an outpatient setting had also become of interest by the beginning of the 21<sup>st</sup> Century. Therefore, vaginally administered NO donors (eg. isosorbide mono nitrate) appeared to be ideal agents for pre induction cervical ripening, because they could be self-administered by the women in their own homes, and maternal or fetal well-being monitoring was not needed as

there was no risk of uterine hyperstimulation<sup>7</sup>. It has been shown that NO donors are better than placebos in causing pre induction cervical ripening between 12-24 hour of administration, and are suitable for use in an outpatient setting<sup>8</sup>. Therefore, this strategy, which is cheap and has only mild side effects such as headache and nausea which can be managed with simple medications, could be implemented in Sri Lanka.

### ***Hygroscopic cervical dilatation***

Hygroscopic cervical dilatation with the use of sterile Laminaria rods (made from the sea weed *Laminaria japonica*), could also be used for pre induction cervical ripening in women with cervixes unfavourable for IOL. This method is currently popular in Japan, where the use of vaginal prostaglandins is not permitted. The synthetic Dilapan S could also be used effectively for this purpose<sup>2</sup>. However, in Sri Lanka, the use of a supracervical Foley catheter would be more appropriate for pre induction cervical ripening as Foley catheters are freely available and cheap, and they can also result in IOL<sup>9,10</sup>.

### ***Supra cervical Foley catheter***

A large multicenter randomised control trial (RCT) carried out in the Netherlands has shown that a supra cervical Foley catheter can be safely kept in situ for up to four days, and by then it is not inferior to low dose OM in leading to IOL and vaginal delivery<sup>11</sup>. The recent SR and NMA has shown that a supra cervical Foley catheter was the method of IOL least likely to cause uterine hyperstimulation with fetal heart rate (FHR) changes, and next to vaginal misoprostol, had the lowest occurrence of caesarean delivery (CD)<sup>4</sup>. In Sri Lanka, although a supra cervical Foley catheter is used by many obstetricians, it is often removed early (often after a maximum of 24 hours), after which another method of IOL is used, and at times this results in failed IOL and CD. In RCTs

carried out in Sri Lanka and Africa, the supra cervical Foley catheter was safely kept *in situ* for up to two and three days respectively<sup>11, 12</sup>. Furthermore, the risk of adverse events such as rupture of membranes, prolapse of umbilical cord, intra uterine infection and hyperstimulation occurring during the period between insertion and expulsion of a balloon catheter in cervical ripening has been shown to be low<sup>13</sup>. Therefore, early removal of supra cervical catheters should be discouraged. It is important that all medical officers attached to tertiary care maternity units in Sri Lanka are trained to insert supra cervical Foley catheters properly.

### ***Vaginal and Intra Cervical Prostaglandins***

The description of intravenous infusion of prostaglandin (PG) F<sub>2</sub> alpha, as an alternative to intravenous infusions of synthetic oxytocin<sup>14</sup>, led to increased research in to the role of PGs for IOL. The recent SR and NMA has shown that vaginal misoprostol was the most effective method of IOL in order to achieve VD 24 and had the lowest occurrence of CD but it had the highest occurrence of uterine hyperstimulation with FHR changes. Among the PGs, the occurrence of hyperstimulation with FHR changes was less with intracervical dinoprostone (PGE<sub>2</sub>) and least with OM<sup>4</sup>. In Sri Lanka, vaginal pessaries with 3mg of PGE<sub>2</sub> are frequently being used for IOL since the 1980s but the intracervical gel with 2mg of PGE<sub>2</sub> is available only in the private sector. One distinct advantage of the use of PG for IOL is that it can be used irrespective of the "favourability of the cervix" which has been hitherto assessed by the Bishop Score and its modifications, prior to amniotomy and intravenous synthetic oxytocin infusions for IOL.

### ***Oral Misoprostol***

In addition to having a lower risk of uterine hyperstimulation with FHR changes, in comparison to vaginal misoprostol, the recent SR and NMA has also shown that the use of titrated, low-dose OM solutions resulted in the lowest CD rates compared to the rest of the techniques, except for vaginal misoprostol, and that OM, which is much cheaper than vaginal PG, is also probably the most cost-effective method of IOL with the highest utility value for mothers and fetuses<sup>4</sup>. However, because there is a possibility that buccal or sublingual misoprostol could be even more cost-effective than OM, it has been suggested that future RCTs should be designed to detect the most cost-effective method of using misoprostol. It has also been recommended that exploration of women's views of the process of IOL should be an integral part of future RCTs to measure utility value from the perspective of the mother and her fetus<sup>4</sup>. Although the European Quality of Life-5 Dimensions instrument has been recommended for this purpose, any instrument used will need to be validated depending on the community in which the women are being assessed.

In Galle, Sri Lanka, a RCT has shown that three doses of OM 50µg four hourly per day for 48 hours was a feasible and effective method of IOL<sup>10</sup>. In comparison to titrated doses of OM, the intermittent doses of OM would be more convenient, cheap and appropriate for implementation in maternity units with heavy workloads, as found in Sri Lanka. Intermittent OM doses are also used in the Netherlands<sup>11</sup>

### ***Outpatient Induction of Labour***

Currently there is a great deal of interest in the possibility of IOL in an outpatient setting<sup>12,13,15-19</sup>. In Sri Lanka, a supra cervical Foley catheter is used only as an inpatient procedure. However it has been shown that in women, especially nullipara, requiring IOL, the insertion of a supra

cervical Foley catheter and sending them home until the catheter is expelled, while adopting suitable measures for the prevention and early detection and treatment of possible complications, which have been shown to be minimal, is safe and effective<sup>13,15</sup>. The main advantage of this method is that it is a cheap procedure which does not require intensive fetal monitoring because the risk of uterine hyperstimulation is extremely low<sup>4</sup>. It could be adopted even in Sri Lanka, for low-risk nulliparous women residing in close proximity to hospital and having access to easy transport to the hospital concerned, with telephone communications from the hospital and intermittent home visits by a community midwife. It has been calculated that if it is used as an outpatient procedure, it would be much more cost effective compared to inpatient low dose OM<sup>19</sup>. The "Sending home versus staying in the hospital for induction of labour using a Foley catheter at term: a non-inferiority randomised controlled trial (HOME Trial)" will be conducted in Sri Lanka in the near future<sup>20</sup>.

A survey carried out in the United Kingdom in 2014, where supra cervical balloon catheters are not used, found that approximately 16% of units had used and another 46% hoped to use slow-release PG E<sub>2</sub> pessaries for outpatient IOL<sup>16</sup>. All women are not happy to have IOL at home. Some women feel more comfortable and safer in the hospital, while others, especially those residing in close proximity to hospital prefer to have IOL in the comfortable, familiar home environment, having the support of their partners and attending to their day-to-day activities while awaiting the onset of labour. Women having IOL at home have reported physical and emotional comforts helping them cope better with their labour, leading to good birth experiences<sup>17,18</sup>. However, IOL at home with PG needs careful monitoring because of the higher risk of uterine hyperstimulation compared to a supra

cervical Foley catheter. Although continuous trans abdominal fetal ECG telemonitoring was reassuring, women still depended on effective, intermittent telephone communications from hospital staff to provide a “virtual presence” of a health professional in the home, when undergoing IOL with slow-release PGE<sub>2</sub> pessaries<sup>18</sup>. In Sri Lanka, IOL at home with PG would not be appropriate, especially because of the prohibitive costs of the equipment which would be needed to effectively monitor these women at home.

### ***Vaginal Delivery in 24 hours***

The outcome of IOL is frequently assessed by VD 24. However, although women may prefer to have a shorter induction to delivery interval, the primary aim of IOL would be to have a safe vaginal delivery. Therefore, a supra cervical Foley catheter or oral misoprostol may be preferable to vaginal misoprostol for IOL in women with intact membranes and an “unfavourable” cervix

### ***Indications for induction of labour***

In addition to maternal or fetal or combined materno- fetal indications for IOL. social

## **Conclusions**

Methods used for IOL as well as the reasons for carrying out an IOL, have changed over the last 20 centuries. Some historical methods eg amniotomy continue to be frequently carried out to date and the principle of pre induction cervical dilatation is also applicable to date although more sophisticated, hygroscopic methods such as Laminaria rods and Dilapan S are currently used. The ASM which was described in the 19<sup>th</sup> century has also been recommended again from the latter part of the 20<sup>th</sup> century. Amniotomy combined with intravenous synthetic oxytocin infusions, introduced in the latter part of the 20<sup>th</sup> century continues to be a very effective

reasons i.e for the convenience of the mother or care giver or both, have become indications for IOL during the latter part of the 20<sup>th</sup> century, and IOL is currently being increasingly carried out without a definite obstetric reason. Furthermore, from the latter part of the 20<sup>th</sup> century, routine IOL at or above 37 weeks’ gestation has also been recommended, with a view to reducing perinatal mortality including still births, even among low- risk women<sup>21</sup>. In a study carried out in the United States of America in 2018, almost half the women were in favour of IOL at term without any obstetric indication<sup>22</sup>. Whatever the reason for IOL, a careful assessment of the benefits versus the risks of IOL must be carried out to avoid a CD for failed IOL, unless urgent delivery is indicated in any case, for obstetric reasons. The woman and her partner must be actively involved in the decision- making process. They should be provided with sufficient knowledge to understand the reasons for IOL and the process involved, so that they can make an informed choice regarding the need, timing and the method of IOL, and not feel as if they are pressured to undergo IOL and are a part of a production line of a commodity<sup>17,18,22,23</sup>.

method of IOL for women with favourable cervixes. Pre induction cervical ripening has been described with the use of vaginally administered NO donors as well supra cervical Foley catheters. The use of PG has enabled IOL in women with cervixes unfavourable for an amniotomy. It is likely that oral or buccal or sublingual misoprostol will become the standard method of IOL in the future and that IOL will also be carried out at in the woman’s home with the use of a supracervical Foley catheter or with slow release vaginal PGE<sub>2</sub> and telemonitoring of the woman and her fetus. In 2008, Sri Lanka was estimated to have the highest rate of IOL in the world

(35.5%)<sup>24</sup>, and in keeping with global trends, this rate is likely to have increased thereafter. Therefore, it is imperative that all clinicians involved with IOL are knowledgeable and acquire experience in the newer methods of IOL, and are able to practise evidence based medicine, which

involves individualised management based on: current best available evidence; the experience of the clinician and the facilities available; the patients' preferences. This would improve not only the maternal and perinatal outcomes of IOL but also the birth experiences of women undergoing IOL

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