INTRODUCTION

Termination of pregnancy is one of the most common procedures in gynecological practice ***(Nagai et al.,2000).*** Access to safe second trimester abortion services is poor in many countries ***(Turner et al., 2008).***

Outdated second trimester abortion methods are still being used and very few studies have compared them to currently recommended methods ***(Boza et al., 2008).***

Various management protocols have been used for second trimester pregnancy termination. These include surgical techniques (dilation and evacuation) and medical approaches such as intra-amniotic prostaglandins F2 instillation, prostaglandin E2 vaginal suppositories, prostaglandin EI and high does oxytocin ***(Behrashi and Mahdian, 2008).***

Although dilation and evacuation had been used for second trimester pregnancy termination, it was an invasive method and lead to possible complications such as cervical trauma, cervical or uterine perforation, cervicovaginal fistula, sepsis and bleeding. Surgical method also needed the availability of adequately trained individuals and equipments ***(Behrashi and Mahdian, 2008).***

Many uterotonic drugs traditionally used to induce labor, prevent or manage postpartum hemorrhage such as oxytocin or other prostaglandins have been used for second trimester

pregnancy termination. In these settings, increasing access to misoprostol, a synthetic prostaglandin El analog that is used for a range of obstetric and gynecologic indications-could play an important role ***(Cristina Herdman, 2005).***

Misoprostol is a synthetic 15-deoxy-16-hydroxy-16-methyl analog of naturally occurring PGE1. It is a viscous oil susceptible to the same types of chemical degradation as natural PGE1 but stable at room temperature. This means that the drug is easily stored and transported. Misoprostol exhibits a wide range of biologic activities. It is protective of the gastric mucosa, and has vasodilator, immunosuppressive, and uterotonic effects. The uterotonic features of misoprostol are of value in pregnancy termination and in the medical management of miscarriage. Vaginal misoprostol provides safe and effective preoperative preparation for surgical dilation ***(Apuzzio et al., 2006).***

Intravaginal administration of misoprostol tablets can terminate first-trimester and second-trimester pregnancies. A large number of published controlled trials have shown that misoprostol, administered either vaginally or via the oral route, is an effective agent for cervical ripening and labor induction in patients with viable pregnancies ***(James et al., 2005).***

AIM OF THE WORK

The aim of the work is to evaluate the efficacy of adding extra-amniotic prostaglandin E1 to the intracervical Foley's catheter to induce abortion in mid-trimesteric pregnancy.

RESEARCH QUESTION

Is the addition of prostaglandin E1 injected extra-amniotically to the intracervical Foley's catheter more efficient to induce abortion in mid-trimesteric pregnancy?

RESEARCH HYPOTHESIS

The addition of prostaglandin E1 injected extra-amniotically through Foley's catheter to the intracervical balloon will be more efficient to induce abortion in mid-trimesteric pregnancy.

OUTCOME MEASURES

- **Primary outcome:**

Induction termination interval: time between applying the procedure till expulsion of uterine content. Ultrasound assessment was done to identify either abortion was complete or incomplete (remnants of conception) in which surgical interference maybe needed.

- **Secondary outcomes:**

  1- Time till expulsion of Foley's catheter.

  2- Need of surgical interference if the expulsion was incomplete.

  3- Needs of more ecobolics.

  4- Occurrence of side effects (nausea &vomiting- diarrhea-pain-fever).

  5- Hb% level after the end of the procedure.

SECOND TRIMESTER TERMINATION OF PREGNANCY

Throughout the Ages women are known to have used various herbs, salts, douches and purgatives to achieve termination of pregnancy (TOP) ***(Riddle, 1991, Bujalkova 2007).*** Milestone of second trimester MTOP were introduction of prostaglandins (PGs) in 1971 and later PG analogues ***(Wiqvist and Beygdeman, 1970; Tang and Ho 2002, Vargas and Diedrich 2009)***. Oxytocin, often administered concomitantly with mechanical methods of cervical dilatation ***(Vargas and Diedrich, 2009).***

1. Nonpharmacologic Methods

1.1 Herbal Supplements

Commonly prescribed agents (mostly on patient's request, as the herbal-supplement industry is rapidly growing) include evening primrose oil and black haw. Although evening primrose oil is the remedy most commonly used by midwives, it is unclear whether this substance can ripen the cervix. Black haw, which has been described as having a uterine tonic effect, has been used to prepare women for labor ***(Tenore, 2003).***

The oral administration of primrose (500mg three times per day for one week beginning at gestational week 37 and then once per day until labor) for purpose of advancing cervical

ripening did not shorten gestational period ***(Dove and Johnson, 1999).***

1.2 Castor Oil, Hot Baths and Enemas

Castor oil, hot baths, and enemas also have been recommended for cervical ripening. Castor oil is used as a single oral dose (60 mL). The mechanisms of action for these methods are unknown. At this time, no evidence supports the use of these three modalities as viable methods for cervical ripening or abortion induction ***(Tenore, 2003).***

1.3 Acupuncture/Transcutaneous Nerve Stimulation

Acupuncture involves the insertion of very fine needles into designated locations with the purpose of preventing or curing disease. In the Chinese system of medicine, it is thought that acupuncture stimulates channels of qi (pronounced "chee"), or energy. This energy flows along 12 meridians, with designated points along these meridians. Each point is given a name and a number and is associated with a specific organ system or function. In Western medicine, it is thought that acupuncture and transcutaneous nerve stimulation (TENS) may stimulate the release of prostaglandins and oxytocin. Most of the studies involving acupuncture were poorly designed and do not meet the rigorous criteria for analysis set forth by the Cochrane reviewers. A well-designed randomized controlled

trial (RCT) is needed to evaluate the role of acupuncture and TENS in labor induction ***(Tenore, 2003).***

Modlock et al. (2010) showed that specific points in the body play a role in cervical ripening as following:

- BL67. This point, it is claimed, can be used to stimulate uterine contractions; it is located on the little toe, near the edge of the nail, and the needle is inserted to a depth of 0.1–0.2 cm.
- LI4. It is claimed that this point can be used to help the woman push downwards and to stimulate uterine contractions; it is located in the middle of interosseous I, and the needle is inserted to a depth of 1–2 cm.
- SP6. Acupuncture at this point is claimed to promote ripening of the cervix; the point is located 3 cm above the medial malleoli, and the needle is inserted to a depth of 1.5–2.5 cm.
- GV20. This point, it is claimed, can be used for calming; it is located 7 cm (11–14 cm) from the central part of the posterior hairline, and the needle is inserted to a depth of 0.5–1 cm.

2. Mechanical Methods

Mechanical methods which were the first methods developed to ripen the cervix can be found. Among them there are different types of catheters (including the Foley's catheter)

and laminaria introduced in the cervical canal or extra-amniotic space ***(Surita et al., 2004).***

Mechanical methods were never totally abandoned but extensively replaced by pharmacological methods in the last decades. There is a trend of reintroducing it for clinical use because of some advantages and availability of sterile devices, controlling one of the principal contraindications, infection. Potential advantages of mechanical methods in comparison with pharmacological ones include easy conservation, low cost and less side effects. Nevertheless, there is contraindication of its use in pregnant women with low inserted placentas, with rupture of membranes and as it was already stated there could be higher incidence of puerperal infection and discomfort among users of these methods ***(Boulvain et al., 2008).***

All mechanical modalities share a similar mechanism of action; by offering some form of local pressure that stimulates the release of prostaglandins. The risks associated with these methods include infection (endometritis), bleeding, and placental disruption ***(Tenore, 2003).***

Despite the advantages of mechanical methods (e.g., simplicity of use, low cost, reversibility, and lack of adverse systemic effects) over pharmacologic ripening agents, these methods have gained little popularity ***(Cromi et al., 2007).***

A Cochrane meta-analysis of randomized trials comparing mechanical methods vs. pharmacologic ripening agents showed mechanical devices to be associated with a lower risk of uterine hyperstimulus ***(Boulvain et al., 2008).*** These comparative studies were designed with sufficient power to compare efficacy in reducing ripening time, induction-to-delivery time, and cesarean delivery rate, but were underpowered to draw conclusions on the safety of trans-cervical catheters. Moreover, the 60% reported rate of endometritis associated with mechanical dilators such as laminaria tents raised concerns about the risk of ascending infections ***(Cromi et al., 2007).***

A systematic review including 45 studies using mechanical methods in general compared with placebo/no treatment in addition to mechanical methods compared to prostaglandins, concluded that data are insufficient to evaluate the occurrence of vaginal delivery within 24 hours when compared with prostaglandins (intracervical, intravaginal or oral). When compared with oxytocin as a stand alone agent, mechanical methods also reduce the risk of performing a cesarean section. It further determines the lack of scientific basis for the use of extra-amniotic infusions associated to mechanical methods ***(Boulvain et al., 2008).***

2.1 Hygroscopic Dilators

Hygroscopic dilators work by absorbing water by osmosis, with a resulting change in their size and shape. When placed into the cervical canal over a period of hours (>12 hours - often overnight), they produce a mechanical dilatation, which then permits an amniotomy to be performed. These agents may also stimulate the local release of prostaglandins, which may have additional benefits on cervical ripening**.**These mechanical dilators have long been successfully used when inserted prior to pregnancy termination ***(Hale and Pion, 1972).***

They have also been used for cervical ripening before labor induction. Intuitive concerns of ascending infection have not been verified. Thus, their use appears to be safe, although anaphylaxis has followed laminaria insertion ***(Cole and Bruck, 2000).*** Dilators are attractive because of their low cost and easy placement and removal. The products available include natural osmotic dilators (e.g., Laminaria japonicum) and synthetic osmotic dilators (e.g., Lamicel). The main advantages of using hygroscopic dilators is outpatient placement ***(Tenore, 2003).***

Gilson and associates (1996) reported a rapid improvement of cervical favorability in women randomized to hygroscopic dilators prior to oxytocin induction. There was, however, no beneficial effect on the vaginal delivery rate or induction-to-expulsion times compared with those of women given oxytocin only. In a randomized study, ***Guinn and co-***

workers (2000) reported a longer induction-to-delivery time with cervical dilators plus oxytocin compared with that of extra-amniotic saline injection (EASI) plus oxytocin. Cervical dilatation has been achieved with hygroscopic osmotic cervical dilators.

Laminaria (Laminaria digitata or Laminaria japonica), a seaweed that after dehydration acquires a hygroscopic ability. Prepared in the shape of a baton it can be used as a cervical dilator. Laminaria use has been described since the Eighteenth Century but its use was abandoned due to the risk of infection. In the 70's with the new sterilization techniques its use was resumed with satisfactory results. Mechanism of action depends on the mechanical effect obtained through radial expansion which because it occurs slowly does no lesion the muscle fibers of the cervical canal. It also has a biochemical effect for it causes a foreign body reaction and local release of prostaglandins. Utilization time of laminaria may vary from 12 to 24 hours, nevertheless, because its maximum capacity of diameter increase occurs within approximately 12 hours it would be required to reassess the cervix during this period and replace the laminaria for another larger one when necessary. The clinical use for this purpose has been replaced by other more effective methods ***(Surita et al., 2004).***

The technique for placing hygroscopic dilators is as follows: the perineum and vagina are prepped with antiseptic. Using a sterile speculum examination to visualize the cervix, the dilator is introduced into the endocervix, allowing the

"tails" to fall into the vagina. Dilators are progressively placed until the endocervix is "full". The number of dilators used is noted in the medical record. A sterile gauze pad is placed in the vagina to maintain the position of the dilators ***(Tenore, 2003).***

2.2 Balloon Devices/Catheters

A Foley catheter may be placed through the internal cervical os. Downward tension that is created by taping the catheter to the thigh can lead to cervical ripening. A modification of this, termed extra-amnionic saline infusion (EASI), consists of a constant saline infusion through the catheter into the space between the internal cervical os and placental membranes (Fig. 26). Catheter placement, with or without continuous saline infusion, results in improved cervical favorability and frequently stimulates contractions ***(Guinn and associates, 2004)***. With or without saline infusion, the method led to rapid improvement in Bishop scores and shorter labors ***(Sherman et al., 1996)***.

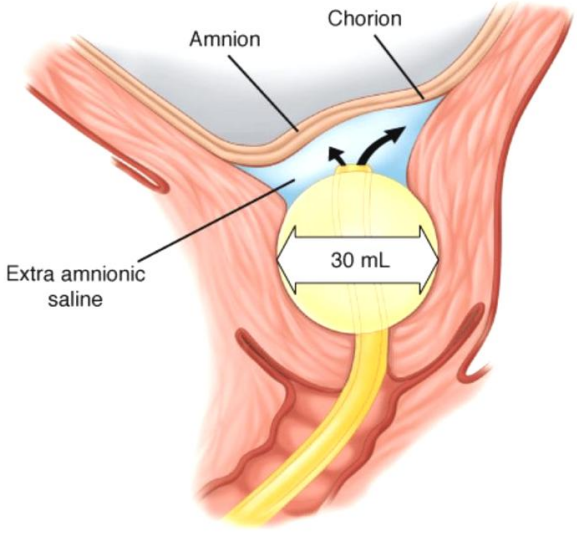

Figure (1): Extra-amnionic saline infusion (EASI) through 26F Foley catheter is placed through the cervix. The 30-mL balloon is inflated with saline and pulled snugly against the internal os, and the catheter taped to the thigh. Room-temperature normal saline is infused through the catheter port of the Foley at 30 or 40 ml/hour by intravenous infusion pump. Balloon devices provide mechanical pressure directly on the cervix as the balloon is filled. A Foley's catheter or specifically designed balloon devices can be used ***(Tenore, 2003).***

The use of a catheter in the extra-amniotic space occurred the first time in 1853 by **Krause**, a method named after him. At that time a rigid catheter was used. After that the Foley's catheter, a flexible catheter was used to induce labor in women with unripe cervices with 94% of success. At times this method is still described like the modified Krause method and because it is more acceptable and less risky it has been more utilized that the classically described method ***(Surita et al., 2004).***

The mechanism of the Foley's catheter is based on the presence of a mechanical factor acting continuously on the cervix and in addition because it separates the chorion from the decidua releasing local prostaglandins. Some of advantages of the Foley's catheter compared to other methods of cervix ripening and labor induction are: low cost, easy to use and principally the possibility of using it in women with prior cesarean sections ***(Surita et al., 2004).***

The technique is described as follows: the catheter is introduced into the endocervix by direct visualization or blindly by locating the cervix with the examining fingers and guiding the catheter over the hand and fingers through the endocervix and into the potential space between the amniotic membrane and the lower uterine segment. The balloon reservoir is inflated with 30 to 50 ml of normal saline. The balloon is retracted so that it rests on the internal os ***(Tenore, 2003)***.

Erekson et al. (2006) had described the use of a new technique for the transcervical Foley's catheter insertion for cervical ripening after they have noticed a high insertion failure rate (between 15% and 20%) and maternal discomfort during insertion which both had limited the use of transcervical Foley's catheters for cervical ripening. Their new technique was based on using a 5 French rigid catheter guide inserted into the Foley's catheter to make the catheter rigid. Without the use of the speculum, the rigid catheter guide and Foley's catheter were inserted transcervically, guided by the operator's hand. They found that the use of a rigid stylet during insertion had increased the chances of insertion success. They showed also that the ease of insertion using this technique makes the use of a Foley's catheter for cervical ripening a valuable option in patients with Bishop's score less than or equal to 4 requiring induction of abortion.

- Additional steps that may be taken: ***(Tenore, 2003)***
- Apply pressure by adding weights to the catheter end:
    - Constant pressure: attach 1 L of intravenous fluids to the catheter end and suspend it from the end of the bed.
    - Intermittent pressure: gently tug on the catheter end two to four times per hour.
- Saline infusion:
    - Inflate catheter with 40 ml of sterile water or saline.

- Infuse sterile saline at a rate of 40 ml per hour using an infusion pump. Remove six hours later or at the time of spontaneous expulsion or rupture of membranes (whichever occurs first).

- Prostaglandin E infusion:
  - Dissolved in sterile solution and injected through the catheter.

Several RCTs are comparing use of a balloon device with administration of an extra-amniotic saline infusion, laminaria, or prostaglandin E_2 (PGE2). Results from these trials indicate that each of these methods is effective for cervical ripening and each has comparable cesarean section delivery rates in women with an unfavorable cervix ***(Guinn et al., 2000).***

Ekele and Isah (2002) studied the duration that the Foley's catheter (size16-20 Fr with 30-50 balloon capacity) can safely remain in the cervical canal in patients admitted for induction of abortion with unfavorable cervices. They concluded that, the balloon of the Foley's catheter can safely remain in the extra-amniotic space for more than 24 hours if the cervix is not favorable, provided the membranes are intact and there is clinical evidence of satisfactory maternal well being. Most would be expelled within 72 hours. The maximum duration of catheter placement in their series was five days and