

INTRODUCTION

Induction of labour is a common procedure in obstetrics, occurring in up to 30% of pregnancies (*Laws et al., 2002 and National Collaborating Centre for Women's and Children's Health, 2008*). The success of induction depends on the state of the cervix before commencement with the most favourable outcomes occurring in cervixes which are soft and effaced (*Riskin-Mashiah and Wilkins, 1999*). A cervix that is closed, firm and difficult to distend increases the likelihood of failed induction, longer duration of labour and caesarean section (*Vahratian et al., 2005*).

The ideal methods for cervical ripening are those that are safe for both the mother and fetus, incur a low cost, have minimal maternal discomfort, and do not require extensive monitoring. A wide variety of methods are available. These methods may be divided into pharmacological and mechanical methods. Although many methods are used to ripen the cervix before induction is attempted, there is little consensus on the best method (*National Collaborating Centre for Women's and Children's Health, 2008; Boulvain et al., 2001; Kelly et al., 2003; Royal College of Obstetricians and Gynaecologists, 2001 and Prager et al., 2008*).

Common cervical ripening methods include biochemical and mechanical agents. Synthetic prostaglandins such as prostaglandin E₁ analogue (PGE₁) imitate normal physiological cervical ripening and increase the sensitivity of

the uterine myometrium to oxytocin (*Riskin-Mashiah and Wilkins, 1999 and Kelly et al., 2003*). While PGE₁ analogue reduces the likelihood of caesarean section compared with placebo, the fourfold increase in risk of uterine hyperstimulation with fetal heart changes is concerning (*Kelly et al., 2003*).

Nonpharmacologic approaches to cervical ripening and labor induction have included herbal compounds, castor oil, hot baths, enemas, sexual intercourse, breast stimulation, acupuncture, acupressure, transcutaneous nerve stimulation, and mechanical and surgical modalities. Of these nonpharmacologic methods, only the mechanical (hygroscopic and balloon dilators) and surgical (stripping of the membranes and amniotomy) methods have proven efficacy for cervical ripening or induction of labor. The potential risks associated with mechanical methods include infection, bleeding, membrane rupture, and placental disruption. Stripping of the membranes promotes onset of labour but does not seem to produce important benefits on maternal and neonatal outcomes, and thus must be weighed against patient discomfort and other adverse effects such as bleeding, accidental rupture of membranes, infection, and uterine irritability. Risks associated with this amniotomy include umbilical cord prolapse or compression, maternal or neonatal infection, FHR deceleration, bleeding from placenta previa or low lying placenta, and possible fetal injury (*RCOG, 2001; Crane et al., 2001; Sanchez-Ramos*

and Hsieh, 2003; Tenore, 2003).

Mechanical ripening devices apply pressure on the internal os of the cervix, overstretching the lower uterine segment and indirectly increasing localized secretion of prostaglandin (**Boulvain et al., 2001**). These devices are easy to insert, relatively low cost, and have few adverse effects. Furthermore, studies have shown no increased risk of perinatal infections with the use of a single balloon (Foley) catheter for cervical ripening (**Cromi et al., 2007**). A number of randomized controlled trials have investigated the efficacy of Foley catheters. While the risk of caesarean section is reduced when foley catheters are compared with oxytocin, comparison with PGE₂ is inconclusive (**Boulvain et al., 2001**).

The double balloon device was first used by Jack Atad for pre induction cervical ripening, first they reported their experience with 50 cases and they reported that this method was safe and effective. This was followed by a case series provided by **Atad et al. (1997)** at which 250 cases underwent pre induction cervical ripening using the double balloon device, in this case series, significant ripening and dilatation of the unfavorable cervix occurred in 92% of patients, vaginal delivery was achieved following a mean of 6.9 h following removal of the Atad ripener device in 84% and they reported a caesarean section rate of 16% for women induced with an unfavourable cervix.

The mechanism of action of the double balloon

catheter may be by two ways. Gradual mechanical cervical dilatation is achieved by the pressure applied on both the external and internal os due to the inflated balloons. The cervical pressure of the internal uterine balloon may cause release of endogenous prostaglandins from the adjacent deciduas.

The method most commonly used to identify readiness for onset of labour is the Bishop score which includes quantitative measures of consistency and dilation of the cervix, and station and position of the presenting part.

This study was undertaken to compare the efficacy and safety of the two methods (Double balloon catheter versus prostaglandin E1 analogue) for cervical ripening in term pregnancy and up to our knowledge, this is the first study comparing these methods for pre-induction cervical ripening.

AIM OF THE WORK

To compare efficacy and safety of two methods: double balloon device and vaginal PGE1 analogue for ripening and dilating the unfavorable cervix for induction of labor in term pregnancy.

ANATOMY OF UTERINE CERVIX

The uterus is located in the pelvic cavity in non-pregnant women and also during first trimester of pregnancy, then later with advancement of pregnancy, it becomes an abdominal organ. It is situated between the bladder on its anterior surface and the rectum on its posterior surface. The uterus resembles a flattened pear in shape. It consists of two major but unequal parts: An upper triangular portion, the body, or corpus, and a lower, cylindrical, or fusiform portion, the cervix, which projects into the vagina (*McMinn, 1990; Leppert, 1992 and Cunningham et al., 2005*).

In the premenarchal girl, the body of the uterus is only half as long as the cervix. In nulliparous women, the cervix-is only a little more than a third of the total length of the organ. After menopause, uterine size decreases as a consequence of atrophy of both myometrium and endometrium (*Cunningham et al., 2005*).

The cervix is bounded at its cephalic end by the internal os and at its caudal end by the external os. The internal os is located at the peritoneal reflection of the bladder. The whole cervical length is about 2.5-3 cm and its wall is about 1 cm thick throughout its length. The cervix is divided into two portions, the portio vaginalis and

the portio supravaginalis, according to the segments that lie respectively below and above vaginal reflection. The vaginal reflection is located at about the junction of the lower and middle thirds of the cervix (**Cunningham et al., 2005**). The uterine supports (the pubocervical fascia anteriorly, the uterosacral ligaments posteriorly and the transverse cervical or cardinal ligament laterally) are attached to the cervix immediately superior to the vaginal reflection in the non-pregnant women (**Dan forth, 1983**).

Embryology:

The squamous epithelium of the portion vaginals and the mucous membrane of the cervical canal are developed from the Mullerian ducts (**O'Rahilly, 1977**). In the early fetal life a layer of mesenchyme surrounds these structures and with time this mesenchyme forms the cervical stroma (**Davies and Kusama, 1962**). Differentiation of the cervix from the uterine body begins with the 10th week of the intrauterine life and it is clearly recognized as a separate entity by the 20th week of life. In a 22-week fetus the smooth muscle is well differentiated in the corpus uteri but absent from the wall of the cervix. Within 2 weeks of birth, the reduction of hormonal stimulation results in a reduction in length of the uterus to about 25-mm; two thirds of this length is still the cervix (**Hughesdon, 1952**).

Histology of the uterine cervix:

The Cervical epithelium:

The cervical epithelium generally contains stratified squamous epithelium, characteristic of the ectocervix and mucous-secreting columnar epithelium characteristic of the endocervical canal. However, the intersection where these two epithelia meet (the squamocolumnar junction) is geographically variable and dependent on hormonal stimulation. It is this dynamic interface, the transformation zone that is most vulnerable to the development of squamous neoplasia (*Johanthan et al., 2002*). The mucosa of the cervical canal is composed of a single layer of very high ciliated columnar epithelium that rests on a thin basement membrane. Numerous cervical glands extend from the surface of the endocervical mucosa directly into the subjacent connective tissue. These glands furnish the thick cervical secretions (*Cunningham et al., 2005*).

The Cervical Connective Tissue:

The extra-cellular matrix is made up of collagen fibers and elastin separated by ground substance. The collagen gives the tissue tensile strength; the elastin gives the tissue elasticity. Water, glyco-saminoglycans, and proteoglycans are important constituents of the uterine cervical matrix as well, especially dermatan sulfate, hyaluronic acid, and heparin sulfate (*Golichowski et al., 1980; Woessner and Kokenysi, 1997*).

Collagen: Collagen fibers of the cervix represent 82% of total cervical proteins (**Danforth, 1983**). The basic molecule (also called tropocollagen) has a molecular weight of about 300.000 Dalton (**Uldbjerg et al., 1983**). The cervical fibrous connective tissue may be considered as a fiber-reinforced composite material in which tightly packed collagen fibers are embedded in a gel-like ground substance. In the human cervix the fiber orientation is organized into three distinct zones that blend smoothly into each other on passing radially outward from the canal. (**Aspden et al., 1988**).

Elastic tissue: Elastin is the major component in elastic fibers. The constitute 1% of total fibrous tissue of the cervix. The ratio of elastin to collagen is higher at the area of the internal os, meaning that there are more elastic fibers compared with collagen at the internal os. Elastin, in its closed state, allows the uterus to retain the fetus during gestation. With mechanical stress, the elastin component can distend to twice its length to allow the cervix to dilate for parturition, elastin may also be important in returning the cervix to a non-pregnant shape following delivery (**Phyllis and Leppert, 1995**).

Proteoglycans and Glycosaminoglycans:

Proteoglycans are proteins that contain covalently linked glycosaminoglycans. A GAG is an unbranched polysaccharide made up of repeating disaccharides, one

component of which is always an amino sugar (hence the name GAG). The other component of the repeating disaccharide (except in the case of keratin sulfate) is a uronic acid (*Murray et al., 1996*).

Physiology of the cervix:

Cervix has several demanding functions. First, it serves as a barrier that separates the vaginal bacterial flora from the uterine cavity. It has been shown that cervical mucus demonstrates antibacterial activity which may protect the fetus against ascending infections (*Hein et al., 2001*). Second; it provides mechanical resistance to ensure a normal development of the fetus. This function is modulated by sexual steroid hormones and achieved by anabolic processes in the collagen and proteoglycan metabolism (*Winkler and Rath, 1999*).

As pregnancy advances collagen bundles, smooth muscle and fibroblasts come into alignment, presumably to increase the resistance of the tissue in response to the increasing load of the fetus (*Yu and Leppert, 1991*).

The competent cervix is firm and its canal is closed. During the last 3-4 weeks of pregnancy, substantial remodeling of the extra-cellular matrix takes place to prepare the cervix to open at birth (*Kleissl et al., 1978*). This process, which is called cervical ripening, is controlled by hormones, and involves catabolic processes

leading to degradation of collagen. (*Stjernholm et al., 1997*). With the onset of pregnancy vascularity and water content are increasing and a secretory transformation of fibroblasts takes place. Mediators, such as prostaglandins and interleukin-8 (IL-8, or neutrophil chemotactic factor), may induce neutrophil migration from vessels into stroma (*Barclay et al., 1993*), which initiate inflammatory-like processes with release of proinflammatory cytokines and matrix-metalloproteinases (MMPs). MMPs are known to play a central role in the degradation of extracellular matrix components. They originate from cervical fibroblasts and invading leukocytes (*Stygar et al., 2002*).

The total amount of glycosaminoglycans increases, with the highest values observed with the onset of labor (*Osmers et al., 1993*), and a relative increase in the glucuronic acid-containing GAG heparan sulfate (*Uldbjevg et al., 1983*). During labor the increased distensibility of the cervix is achieved by the increased concentration of hyaluronic acid, which causes the tissue to swell, and by the decreased concentration of dermatan sulfate (*Osmers et al., 1993*). Hyaluronic acid also weakens the affinity of fibronectin to collagen, which is a contribution to the loosening of the collagen framework at term. During labor, as the cervix effaces, the upper part of the cervix with its internal os moves laterally to become indistinguishable from the lower segment of the uterus, which suggests that the internal os of the cervix is the place of maximal softening (*Dan forth, 1983*).

The opening of the cervix from 2 to 10 cm is achieved gradually; with each contraction of the myometrium the cervix dilates, but in the interval between the contractions most of the stretching is recovered (**Leppert et al., 1995**). The process of dilatation is assisted by the viscoelastic behavior of the cervix and occurs passively when the presenting part of the fetus is pushed against it during the contractions. Immediately after birth the collagen fibers are diminished and separated into their fibrils and the cervix is extremely soft. Within 1 month the cervix returns to its non-pregnant shape (**Danforth, 1983**).

Uterine Cervix in Pregnancy:

The role of the cervix shifts between two opposing functions during pregnancy. In order to hold the products of conception inside the uterus, the cervix has to resist tension and remain closed and rigid throughout most of gestation. At term, however, a drastic change in cervical function is required in order to accommodate stretch and delivery (**Leppert, 1992**).

Mechanical changes during pregnancy:

The clinical changes that occur in the cervix during normal pregnancy are quite dramatic. Before the urine pregnancy test becomes positive, increased cervical softening may be detected and usually enlarges two to three folds in diameter (**Mclnnes et al., 1980**).

The lower segment of the uterine body, which is formed during the second trimester, originates from the isthmic portion above the fibro-muscular junction (*Danforth, 1974*).

Structural and Biochemical Changes during pregnancy:

Collagen: During pregnancy the collagen concentration is halved (40-60%) (*Granstrom et al., 1989*), and its extractability increases due to changes in the proteoglycan composition, an increase in acidic relative to neutral proteins. These changes are responsible for the softening of the cervix (Goodell's sign) and the isthmus (Hegar's sign). Histologically the collagen fibers appear thinner and more spread out (*Uldfbjerg et al., 1990*).

Immunohistochemical analysis revealed that type I collagen might play an important role in the maintenance of pregnancy and that decreased expression of this collagen could be associated with the process of uterine cervical ripening (*Iwahashi et al., 2003*).

A remarkable change in macroscopic properties is accomplished through subtle shifts in biochemical constituents; the total collagen content remains almost unchanged, while more significant changes are seen in collagen cross linking and the relative quantities of sulfated glycosaminoglycan and hyalouronic acid (*Myers et al., 2007*). Cervical ripening is a combination of increased

collagen synthesis and increased percentage of collagen denaturation, whereas at parturition, an increased digestion of the denatured collagen leads to increased collagen loss from the cervical connective tissue (**Breeveld-Dwarkasing et al., 2003**).

Elastin: The total content of uterine elastin increased throughout gestation, reaching maximal levels at day 19 of gestation, which were three times those of on-gravid tissue. Following involution, the elastin content decreased rapidly to near baseline values by 5 days postpartum (**Sharrow et al., 1989**). The elastic system fibres are increased in the cervix at the end of pregnancy. They may be involved in the immediate shape-recovering of the cervix after delivery as well as in helping to strengthen the anchoring of the epithelium to the lamina propria, thus minimizing birth trauma (**Battlehner et al., 2003**).

Proteoglycans and Glycosaminoglycans: During pregnancy, the keratin sulfate content increased significantly and the contents of the chondroitin sulfates and dermatan sulfate have decreased. During labour, keratin sulfate, chondroitin 4- and 6-sulfates, and dermatan sulfate did not change. Hyaluronate content of a postpartum cervix was significantly higher than in non-pregnant women (**Von Maillot et al., 1979**). Dermatan sulfate is quantitatively the most important glycosaminoglycan in the cervix of both pregnant and non-pregnant, and there is a significant

decrease in the concentration of both dermatan sulfate and chondroitin sulfates occurred in the biopsies obtained just after delivery (*Kokenyesi et al., 1990*).

During pregnancy, hyaluronic acid (HA) concentration in the human cervix is very low, but increases rapidly at the onset of labour. It is an endogenous regulator of interleukin-1 (IL-1). HA induced cervical ripening in both pregnant and non-pregnant animals and cervical water content was significantly increased. Tissue collagen was markedly decreased (*EI-Maradny et al., 1997*). A randomized trial has found positive association between intracervical administration of hyaluronidase and the ripening of the cervix. The association may also be extended to a decrease in the duration of labor and an increase in the chance of vaginal delivery (*Spallicci et al., 2007*).