

OUTCOME OF HIGH RISK PREGNANCY
FOLLOWING INDUCTION OF LABOUR

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LIST OF ABBREVIATIONS

CTG	CARDIOTOCOGRAPHY
COX-1	CYCLO-OXYGENASE-1
COX-2	CYCLO-OXYGENASE-2
CHORIOAM	CHORIOAMNIONITIS
DM&GDM	DIABETES MELLITUS AND GESTATIONAL DIABETES MELLITUS
HPT	HYPERTENSIVE
ROM	RUPTURE OF MEMBRANE
TMSL	THICK MECONIUM STAINED LIQUOR
MMSL	MODERATE MECONIUM STAINED LIQUOR
MSAF	MECONIUM STAINED AMNIOTIC FLUID
NICU	NEONATAL INTENSIVE CARE UNIT
PGE2	PROSTAGLANDIN E2
PGF2	PROSTAGLANDIN F2
PGI2	PROSTACYCLIN
PPH	POSTPARTUM HAEMORRHAGE
SVD	SPONTANEOUS VAGINAL DELIVERY
LSCS	LOWER SEGMENT CAESAREAN SECTION
ARM	ARTIFICIAL RUPTURE OF MEMBRANE

IUGR

INTRAUTERINE GROWTH RESTRICTION

G

GRAVIDA

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Dr Siti Muslihat bt Kadir

1) INTRODUCTION TO THE HOSPITAL KUALA TRENGGANU

The state of Terengganu is located in the East Coast of Peninsular Malaysia, facing the South China Sea covering 1,295,517.1 kilometres square. With stretches of white sandy beaches along the coast, make Terengganu one of the most popular tourist destinations. The main economical activities are fisheries and petroleum industry.

Kuala Terengganu Hospital, which is the only referral hospital for the state, also serves 7 districts. It is located about 2 kilometres away from the town of Kuala Terengganu and has the total of 786 beds. The hospital is made up of 2 main areas, i.e. the new 8-storey hospital complex and the old hospital where both are facing the beautiful South China Sea.

The Obstetrics and Gynaecology Department is functioning with 2 consultants, 2 specialist, 3 medical officers, 7 post graduate masters candidates (Universiti Sains Malaysia and Universiti Kebangsaan Malaysia) and 12 house officers. There are 1 matron, 4 sisters, 78 nurses and 64 support staff.

1.1 MATERNITY COMPLEX (OBSTETRIC SECTION)

Obstetric section is situated mainly at level 1 and partly at the ground floor and level 2 of the main building. It includes the clinics, Day care centre, Admission centre, Antenatal ward, Postnatal ward, Labour suites and maternity Operation Theatre.

There are 4 wards to accommodate the obstetric patients, 1 antenatal ward (36 bedded), 2 postnatal wards (36 bedded-high risk ward and 24 bedded – low risk ward) and 1 first class ward (10 bedded mixed Obstetric ward). Admission centre served to ensure appropriate admission and also minimize delay in clerking. In 1999 the centre received 13 094 patients. The Bed Occupancy Rate for the antenatal ward is almost always above 100%.

The Labour Suite has 12 delivery beds where 3 beds are reserved for patients requiring close monitoring during tocolytic therapy or bleeding placenta praevia in which expectant management is carried out. Besides that, there is a 2-bedded room for patients with severe Pre eclampsia/ Eclampsia.

This hospital also adopts the ‘ husband friendly hospital’. The response is good and an average of 150 husbands will be with their wives during labour every month.

Adjoining to the labour suite is the maternity theatre where elective and emergency Caesarean section are carried out from 8.00 am to 3.00 pm. Five dedicated maternity staff run the services.

The Day care service has reduced the number of clinic attendance and unnecessary admission. In 1999 there were 1466 attendance to the day care centre. There are 3 antenatal clinic sessions per week i.e. antenatal booking; combined clinic and antenatal follow up clinic. There is also 1 postnatal clinic session weekly. The total attendance annually is about 10,000.

1.2 GYNAECOLOGY SECTION

Gynaecology also contributes to the workload in the Department. Besides having the gynaecology clinic, the specialised clinic, infertility and oncology services are also available. The total attendance for the gynaecology clinic is more than 5000 patients per year.

2 ABSTRACT

2.1 BAHASA MALAYSIA VERSION

OBJEKTIF

Tujuan kajian ini dilakukan adalah untuk mengetahui tentang data demografi, kadar bersalin secara induksi, cara bagaimana induksi dilakukan, masalah yang memerlukan induksi di jalankan serta mengetahui kesan induksi ke atas ibu dan bayi yang bakal dilahirkan bagi kes-kes obstetrik yang berisiko tinggi. Kajian ini juga dilakukan untuk menentukan samada preinduksi Bishop skor memberi kesan kepada ibu dan anak didalam kandungan.

Metodologi

Satu kajian bersilang telah dijalankan di Hospital Kuala Trengganu bermula pada 1hb Jun 1999 selama 3 bulan. Sebanyak 712 orang pesakit telah dimasukkan ke dalam kajian, 356 di dalam kumpulan bersalin secara induksi dan 356 lagi bersalin secara spontan tetapi mempunyai masalah perubatan yang sama. Pemerhatian yang direkodkan adalah umur, bangsa, pariti, graviditi, jangkamasa mengandung, preinduksi Bishop skor, cara bersalin, keadaan air mentuban dan komplikasi kepada ibu dan bayi.

Keputusan

Tiada perbezaan yang ketara dari segi usia dan graviditi diantara kedua-dua kumpulan. Tetapi jangkamasa mengandung antara 37/52 hingga 41/52 lebih ketara di dalam kumpulan bersalin secara induksi dan kandungan yang tidak cukup matang <37/52 serta yang lebih dari >41/52 adalah lebih ketara didalam kumpulan yang bersalin secara spontan.

Kadar bersalin secara induksi adalah 12%. Masalah perubatan atau masalah obstetrik yang paling banyak memerlukan kelahiran secara induksi adalah kandungan lebih dari jangka (44.4%) dan penyakit darah tinggi (30.1%). Cara induksi dilakukan adalah melalui kemasukan ubat Prostaglandin ke dalam salur faraj, pemecahan selaput air mentuban dan ubat oxytocin kedalam aliran vena.

Kadar purata preinduksi Bishop skor adalah 5.4. Preinduksi Bishop skor tidak memberi kesan yang ketara terhadap ibu dan bayi tetapi 'unfavourable' preinduksi Bishop skor memainkan peranan penting dalam menentukan cara bersalin. Kadar kelahiran secara pembedahan adalah tinggi (19%) bagi kes yang mempunyai bishop skor yang kurang daripada 3/13 berbanding dengan hanya (5.5%) bagi Bishop skor yang lebih daripada 6/13. Mengikut kajian juga bersalin secara induksi mempunyai kadar bersalin secara pembedahan yang lebih ketara tingginya jika di bandingkan dengan bersalin secara spontan.

✳ [Tiada perbezaan yang ketara di antara kedua-dua kumpulan dari segi jangkamasa bersalin, komplikasi kepada ibu (seperti kadar pendarahan selepas bersalin, hyperstimulasi kepada rahim, rahim luka, 'abruptio placenta' ataupun 'cord prolapse') dan komplikasi kepada bayi (seperti kadar Apgar skor yang rendah dan kemasukan ke unit rawatan rapi)]

Tiada perbezaan yang ketara diantara kehadiran 'meconium' di dalam air mentuban di kedua-dua kumpulan yang bersalin secara 'induced' ataupun spontan. Kehadiran 'TMSL' didalam kedua-dua kumpulan meningkatkan kadar kelahiran secara pembedahan dan mempunyai Apgar skor yang rendah pada 1 minit kelahiran.

Secara keseluruhan, bersalin secara induksi bagi kes- kes yang berisiko tinggi adalah selamat dan tidak memberi kesan yang memudaratkan kepada ibu dan bayi.

ABSTRACT

ENGLISH VERSION

Objective:

The objective of the study was to determine the demographic data, rate, method of induction, indications and the outcome of the induction in the high-risk obstetrics cases,

and to find out whether the preinduction cervical score will adversely affect the maternal and foetal outcome.

Method

A cross sectional study was carried out at the Hospital Kuala Trengganu at 1st June 1999 for a 3 months duration. A sample size of 712 cases were included in the study in which 356 were in the induction group were compared to the spontaneous labour group, who also had similar underlying medical or obstetric problems. The outcome measured were age, gestational age, parity, gravidity, ethnic group, indication of induction, methods of induction, preinduction cervical score, mode of delivery, state of liquor, maternal and prenatal outcome.

Result

There was no significant difference in terms of mean maternal age and gravidity between the induction group and spontaneous labour group. Gestational age of 37/52 to 41/52 was significantly higher in induction group, whereas preterm and postdate more than 41/52 were statistically higher in the spontaneous group.

The induction rate was 12%. The most common indications for induction of labour were postdated pregnancy and hypertension. The 3 most common methods of induction were Prostaglandin E2, Artificial rupture of membrane and oxytocin.

The mean Bishop score was 5.4. The preinduction Bishop score had not significantly associated with maternal and prenatal outcome, but an unfavourable Bishop score become one of the factors in determine the mode of delivery. In cases with a poor preinduction Bishop score ($\leq 3/13$) had a higher caesarean section rate (19%) compared to the favourable score only had (5.5%) Induction of labour significantly had a higher rate of caesarean section compared to spontaneous labour.

[There is no significant difference in between the two groups in term of the duration of labor, maternal complications such as postpartum haemorrhage, uterine hyperstimulation, cord prolapsed, uterine rupture and abruptio placenta or fetal complications such as low Apgar score and admission to the intensive care unit.]

Induction of labour had not associated with a higher incidence of meconium stained amniotic fluid, but thick meconium stained liquor significantly associated with caesarean section and depressed Apgar score at 1 min of life.

Induction of labour in high-risk cases is safe and it doesn't have the adverse maternal and prenatal outcomes.

3) HIGH RISK PREGNANCY OUTCOME FOLLOWING INDUCTION OF LABOUR

3.1 INTRODUCTION

INDUCTION OF LABOUR

Induction of labour is the common procedure in obstetrics and often undertaken in the interest of the mother and the foetus. It is indicated when the continuation of a pregnancy presents risks to either mother or fetus, or both, that are greater than those of delivery.

It's defined as the artificial initiation of uterine contraction prior to their spontaneous onset leading to progressive dilatation and effacement of the cervix and delivery of the baby.

INDUCTION RATE

The rate of induction varies widely in different countries, and even between individual obstetricians within the same unit. The differences may be due to several factors:

- a) Differences in the incidence of the indication of induction.
- b) Definitions
- c) Availability of the resources as well as to unexplained differences in opinion and practice.

Rate between 10-25% are common in industrialized countries.

3.2 INDICATION OF INDUCTION

The Australian Council of Healthcare Standards (ACHS), in concert with The Royal Australian College of Obstetricians and Gynaecologists (RACOG) has developed a list of ‘defined’ indications for induction of labour, which form the basis Obstetric Clinical Indicator number 1(1). There were as follows:

- 1) Diabetes Mellitus
- 2) Rupture of membrane >24 hours, not in labour
- 3) Hypertensive disorders (including chronic renal disease)
- 4) Intrauterine growth restriction
- 5) Iso immunization
- 6) Fetal Distress (as diagnosed by CTG)
- 7) Fetal demise
- 8) Chorioamnionitis
- 9) Prolonged pregnancy

The indication of induction were based on the above list (ACHS/RACOG) however fetal demise, fetal distress as diagnosed by CTG were excluded in this study.

In our practice, post-date pregnancy was induced at 41 weeks and beyond. Previous one lower caesarean section is allowed to vaginal delivery and induction of labour is performed if indicated, under close supervision. We do not practice induction as requested by patient.

PREMATURE SPONTANEOUS RUPTURE OF MEMBRANE. (PPROM)

Prelabour rupture of membrane at term is less complicated than preterm. Most patients will deliver spontaneously and without intervention only about 2-5% remain undelivered after 48 hours (Egan & O'Herlihy, Grant & Keirse 1989). Early induction leads to greater analgesic requirements and longer labours, higher incidences of operative vaginal and caesarean delivery. However induction of mothers undelivered more than 24 hours after spontaneous rupture of membrane represent a reasonable compromise and majorities followed by vaginal delivery.

DIABETES

In the UK survey of diabetic mothers (Lowy and Beard, 1982) 51% of mothers were delivered before 38 weeks. Of the mothers studied, 41% were delivered by caesarean section and 29% were induced. There is increasing evidence that diabetic pregnancies can be allowed to go into spontaneous labour, provided that their diabetic control is good and has an uncomplicated pregnancy (O'Connor 1994). However in the presence of polyhydramnion and macrosomia delivery should be considered at 37 weeks.

HYPERTENSION

In pre-eclampsia, provided that maternal and fetal condition is satisfactory, expectant management should be continued to 37-38 weeks gestation. Deferring delivery beyond this gestation confers no benefit to the infant while increasing the risk of deterioration in the maternal and / fetal condition (Dewhurst). In chronic hypertension cases however, delivery

should be allowed to continue until the onset of labour, or until 41 weeks in the absence of superimposed pre eclampsia (O'Connor).

INDUCTION OF LABOUR

The rate of induction is on the rise and elective induction is more frequently performed. However data concerning an induction of labour on the high-risk groups (who had medical and obstetric problems) were limited. Induction of labour had been shown to be effective and safe in normal, low risk pregnant woman and does not increase caesarean delivery unless certain risk factors were present. (Macer et al)

However Yudkin et al found that induction of labour was associated with a higher incidence of operative delivery and more need for neonatal resuscitation by intubations.

Maternal complication such as postpartum haemorrhage, pyrexia, urinary tract injuries, and endometritis were similar in-group, induction and spontaneous labour (Smith et al).

Induction of labour in high-risk patients has been associated with a higher rate of caesarean delivery, instrumental delivery, maternal and foetal adverse outcome (Robson et al).

The condition of the cervix is now accepted as an important determinant of successful labour induction, thus knowledge on the anatomy, physiology and the process that involved in the cervical ripeness is important before one pursue to induce labour.

3.3 ANATOMY AND PHYSIOLOGY OF THE UTERINE CERVIX

The human uterine is a complex organ that undergoes extensive changes throughout pregnancy. During pregnancy it must maintain the tissue integrity to ensure that the fetus is retained and fully developed, and at the other hand it must change it's tissue

composition to allow a safe passage for the fetus to be expelled from the uterus at parturition.

The cervix is dominated by fibrous connective tissue. It is composed of extracellular matrix consisting predominantly of collagen with elastin and proteoglycans, and cellular component consisting of smooth muscle and fibroblast, epithelium, and blood vessels.

CERVICAL STRUCTURE:

EXTRACELLULAR MATRIX

Collagen is the predominant component and it is consisted of type I (70%) and type III (30%). Another important molecule involved in collagen structure is decorin (small molecular weight proteoglycan). Cervical cells secrete decorin in human pregnancy and the level is increased in late pregnancy and in labour. When it's ratio to collagen increases will result in dispersal of collagen fibrils and disorganisation.

As the pregnancy progresses the level of collagen decreases as the fibres being dispersed and remodelled into fine fibers. As a result the level of hyaluronic acid increases together with the water content (80%) in late pregnancy. This further decrease in collagen concentration is clinically evident as 'softer cervix'.

ELASTIC COMPONENT

This is another important component. Elastin is organized parallel to and between the collagen fibers. In its closed state, this allows the uterus to retain the fetus and in mechanical stress it can be stretch to allow the cervix to dilate during labour

ELEMENT AFFECTING CERVICAL RIPENING

Various elements had been implicated which include decorin, hyaluronic acid, hormones, cytokines and protease. Overall, these factors are responsible for increasing the water content in the cervix, decreasing the collagen concentration and collagen restructure. Decorin causes dispersion and disorganization of the collagen fibrils

The other mechanism that allows the cervical dilatation is the enzymatic degradation of the extracellular matrix. The level of both collagenase and elastase are elevated at term.

Cytokines such as interleukin –1 and interleukin-8 enhance the activity of collagenases and their levels are increased during term pregnancy. Hyaluronic acid has also been shown to stimulate the synthesis of proteolytic enzymes by cervical fibroblast. The level is increased with cervical ripening and increase dramatically with the onset of labour. It increases the water content of the cervix at term, which leads to a loosening and dispersal of the fibres.

Hormonal manipulation may, in an as –yet unknown mechanism, also has a role in cervical ripening. At term, there is down regulation of both estrogen and progesterone receptors. Estrogen and its precursors have been shown to stimulate collagenase production in the pregnant human cervix. Progesterone may maintain high level of enzymes that degrade hyaluronic acid, thereby keeping its level in the cervix low until term when progesterone and progesterone receptor level decrease. Progesterone also inhibits the production of interleukin-8 from the cervix. Thus as the progesterone diminishes the level of hyaluronic acid and interleukin –8 will be elevated.

3.4 HISTORIC PERSPECTIVES OF LABOUR INDUCTION

Technique of labour induction had been available for more than 400 years ago. Native American practices a various chemical methods for labour induction, such as rattlesnake's rattle, teas from the blossoms of Indian corn, berries of ground cedar bushes and infusion of the inner bark of pine trees.

Hippo crates recommended two methods. One was nipple stimulation, which would lead to uterine contractions and initiation of labour. The other method was called Hippocratic succussion whereby the patient was placed onto a tree branch and was tossed.

Soranus of Ephesus described the need of inducing labour in a small pelvis patient before the full growth of the fetus. He recommended emptying of the bladder, administering an enema containing oil, water and honey, pouring the whites of several eggs into the vagina to soften and relax the cervix and rupturing the membranes with his finger or scalpel.

In 16th century the French obstetrician Ambrois Pare devised an instrument for mechanically dilating the woman's cervix.

First convention on labour induction in 1756 concluded that rupturing the membrane of woman with small pelvis could induce labour.

Thomas James (1776-1835) suggested that premature labour could be induced by venesection (blood-letting), administration of enemas and rupturing the amniotic membranes.

In 1810, Professor James Hamilton suggested digital separation of the membranes from the lower uterine segment and then rupturing the membranes above the foetal head (high rupture).

In 1846, Dr Kiwisch proposed using a stream of tepid water into the vagina and against the cervix so that the water can separate the foetal membrane to the uterine wall. However this procedure resulted in uterine rupture and severe maternal mortality rates and was abandoned.

In early 20th century, ergot, quinine and pituitary extract became the primary medication for induction of labour. American Obstetrician, John Stern in 1807, had described ergot. He administered ergot orally every 20 min until uterine contraction ensued. However ergot is associated with high rates of foetal morbidity.

Mullan (1885) discovered that 4 grains of quinine cause muscle contraction and initiated labour.

In 1909, William Blair started using pituitary extract to induce and initiate labour. In 1928, Vincent du Vigneaud identified the posterior pituitary hormone. Oliver Kamm and his associates identified that there were two different posterior pituitary hormones, oxytocin and vasopressin.

In 1949, the first modern inducing agent, oxytocin was developed by Vincent du Vigneaud who isolated pure oxytocin from the neurohypophysis and described its molecular structure. In 1953 he had synthesised oxytocin and showed that it is identical to the natural oxytocin.

In 1969, chemist at Upjohn Pharmaceuticals and Elias J. Corey with his colleagues at Harvard were able to synthesise prostaglandins and start the era of the use of prostaglandin in labour induction.

3.5 PREINDUCTION CERVICAL ASSESSMENT

HISTORY

Calkins proposed a dichotomous system for assessing cervical factors.' Effacement was considered present or absent, engagement of the presenting part when at or below the ischial spines and consistency of the cervix was called 2 if its soft or softer than one' lip and it was 3 if its similar to or firmer than the nasal ala. He noted that the patient had a shorter labour times when demonstrated a favourable features.

In 1955,Cocks describes cervices into 5 types. Type 1 cervix was soft, effaced and admit a finger into the internal os. Type 2 cervix was soft, admitted 1 finger into the internal os but uneffaced. Type 3 if uneffaced and type 4 if somewhat uneffaced and anomalous cervix was type 5.

In 1960, Garret categorized cervix as ripe when it's dilated enough to admit 3 fingers or 2 fingers but well effaced and unripe cervix. Successful labour induction was noted in 96% of favourable cervix and 63% of unfavourable cervix.

Friedman et al (1962) noted that an initial cervical dilation greater than 2cm associated with a shorter latent phase.

The scoring system that has become prevalent is the Bishop score. It consists of 5 component, dilation, effacement, consistency and position of the cervix in addition to the station of the presenting part. Many have evaluated and confirmed the validity of the Bishop score . The score had a range of 0-13,the higher score indicating a very ripe cervix. Bishop score of 8-10 indicate that labour will follow within a few days, and score of 0-3

indicate that labour may be delayed for up to several weeks and associated with high incidence of caesarean section, maternal and foetal complications.

In 1974, Calder had modified the Bishop score, which was easier to apply in practice.

USE OF ULTRASOUND IMAGING

Lim et al in 1992 evaluated the correlation of transvaginal ultrasound and digital examination for assessing cervical length and dilation. They found that ultrasound underestimated the cervical dilation. In 1996, Watson et al found that the cervical dilation was the only predictive factor of the duration of the latent phase of labour.

3.6 METHODS OF CERVICAL RIPENING AND LABOUR INDUCTION

There were various methods and agents have been described in obstetric literature.

They can be divided into:

- a) Mechanical dilatation (Balloon catheters, Laminaria japonica, Synthetic osmotic dilators.)
- b) Amniotomy
- c) Pharmacological hormonal preparation (Prostaglandin E2, Oxytocin, Misoprostol (PGE1 analogue), Mifepristone, Relaxin and Nitric oxide)
- d) Non pharmacological method (Herbal, sexual intercourse and breast stimulation)

The most common methods are surgical method (amniotomy) and medical methods include oxytocin and prostaglandin.

NON-PHARMACOLOGIC METHODS

HERBAL SUPPLEMENT

Commonly used agent includes evening primrose oil, blue and black cohosh and raspberry leaves. Primrose oil used as an adjunct to promote cervical ripening during a long period of time i.e., more than 1 week. It was administered as 3 capsules per day for one week, either given all at once or on an interval basis of every 8 hours. This regime is re-evaluated after 1 week and if no cervical improvement, the dose may be repeated for as many as 3 more administrations.

Black cohosh is administered orally (10 drops under the tongue hourly) until cervical change occurs.

SEXUAL INTERCOURSE

Not well studied as a method of cervical priming. Sexual intercourse usually involves breast stimulation, which may promote the release of oxytocin and subsequent occurrence of uterine contraction. Uterine contractility has been described in association with sexual intercourse and female orgasm. However there is currently no evidence that sexual intercourse can shorten the duration of pregnancy, despite the high prostaglandin content of seminal plasma (Keirse 1993)

BREAST STIMULATION

Breast stimulation as a mechanical means to induce the release of oxytocin. Elliot and Flaherly had found that in 81 patient who had breast stimulation by a gentle massage

with a warm, moist cloth for 1 hour, 3 times a day, 45% of patient went into labour spontaneously whereas only 6% of the control group.

MEMBRANE STRIPPING

It has been used clinically for many years but has not been well studied. The procedure requires minimal cervical dilation that allows the practitioner to insert the examining finger through the cervical os and vigorously “scratch” or ream the membranes in a circular motion. It allows the release of endogenous prostaglandins and its precursor enzymes. It was a safe procedure and associated with earlier delivery and decreased the incidence of post term pregnancy.

AMNIOTOMY

Refers to the practice of artificial rupture of membranes that most likely result in endogenous prostaglandin release and subsequent cervical ripening and uterine contraction. In women with a ripe cervix and a high Bishop score, amniotomy has been reported to 88% successful in inducing labour (UK Amniotomy group). Ideally it is performed when the cervix is favourable. The technique has been associated with a shorter labour duration, less labour dystocia and less oxytocin used (Fraser et al). The advantages of this method are, high success rate, enable to observe the amniotic fluid for meconium or blood, easy access to secure intrauterine pressure catheter, fetal scalp electrode and for scalp blood sampling. The associated risks are cord prolapsed, placental trauma and infectious morbidity.

MECHANICAL MODALITIES

HYGROSCOPIC DILATORS

The use of hygroscopic dilator relies on the osmotic properties of either natural or synthetic rods that are inserted through the cervical os and left stationary for a defined period.

The natural osmotic dilator are derived from the seaweed *Laminaria Japonicum*. It has the ability to double the size from 2mm to 6mm within 6 to 12 hours. *Laminaria* has been shown to be safe and effective in improving Bishop score, successful induction and shorter the delivery interval. However the use of *Laminaria* has been associated with significant increase in maternal morbidity (endometritis), neonatal morbidity and mortality. (Kazzi et al).

Synthetic osmotic dilators have the advantages, foremost, rigid production standard, and fewer dilators required and faster osmotic action. Commercially available but not in Malaysia are Lamicel (Cabot medical corp, Langhorne, PA) and Dilapan (Gynotech, Middlesex, NJ). The technique for insertion involves using a sterile speculum examination under aseptic technique. The dilators are inserted using the direct visualisation with the tail allowed to fall in the vagina. The numbers inserted depends on the amount readily introduced into the endocervix

BALLON DEVICES

Foley or designer balloon devices have been used for cervical priming. The device inserted in the presence of either intact or ruptured membranes. Once properly placed the balloon reservoir is inflated with normal saline and retracted into the cervical os to

facilitate the balloon resting on the internal os. Spontaneous passage of the catheter usually correlates with a cervical dilation of 2 cm to 3 cm.

Non-pharmacological methods are effective, safe and less costly than the pharmacological counterpart. However there have been limited researches to precisely determine the overall usefulness and the effectiveness of this method.

PHARMACOLOGICAL METHOD

OXYTOCIN

HISTORICAL BACKGROUND

In 1906, British scientist Sir Henry Dale showed that the intravenous injection of extracts of ox posterior gland caused uterine contraction in the gravid cat. William Blair Bell used the extract of posterior pituitary at caesarean section to cause uterine contraction in human uterus. Hofbauer used it to treat delayed labour and to induce labour.

Then in 1953, Vincent du Vigneaud and associates proposed the structure and synthesised a product indistinguishable from the naturally occurring hormone.

PHYSIOLOGY AND PHARMACOLOGY

Oxytocin is synthesised in the paraventricular and supraoptic nuclei and stored in the neurohypophysis. It's a short neuropeptide consisting of nine amino acids residues with a disulfide bridge between two cysteine residues in position 1 and 6. It circulates in an unbound form and is cleared from the maternal circulation by the kidney and liver at the rate of 20 to 29ml/kg. Oxytocin is released in a pulsatile manner and the half-life is in a range of 2 to 7 minutes.

Oxytocin stimulates myometrial contractility by increasing the intracellular concentration of calcium achieved either by release of calcium from the endoplasmic reticulum or enhanced entry of extra cellular calcium.

Oxytocin activity is mediated through specific membrane receptors that are coupled to transducer and effector proteins that carry the information inside the cell. The oxytocin receptor -G protein complex stimulates phospholipase C (PLC) through which will selectively hydrolyse phosphatidylinositol 4,5-bisphosphate (PIP₂) to generate inositol 1,4,5-trisphosphate (IP₃) and 1,2-diacylglycerol. IP₃ causes release of calcium from the endoplasmic reticulum which leads to an increase in concentration of cytoplasmic calcium.

There has been a positive interaction between oxytocin and prostaglandin in addition to their independent uterotonic action, and it is possible that prostaglandin release by oxytocin is necessary for the uterine contraction to become fully efficient during labour. Myometrial responsiveness to oxytocin begins at about 20 weeks and increases steadily until a marked rate of increase at 30 weeks, reaching a maximum at full term in spontaneous labour.

It has been shown that after intravenous infusion of oxytocin, uterine response occurs within 3 to 5 minutes and steady plasma concentration is reached within 40 minutes. The dosage of oxytocin varies; some prefer low-dose (2 to 4 mu/min) and the other high dose (6 mu/min), however both methods are equally successful in establishing adequate labour. Maximum dose should not exceed 40 mu/min.

A prospective randomised study on patients with a valid obstetric indication for induction of labour received either 3 mg prostaglandin E₂ vaginal pessaries immediately prior to oxytocin or oxytocin alone were performed by Lange et al (1984). There were no

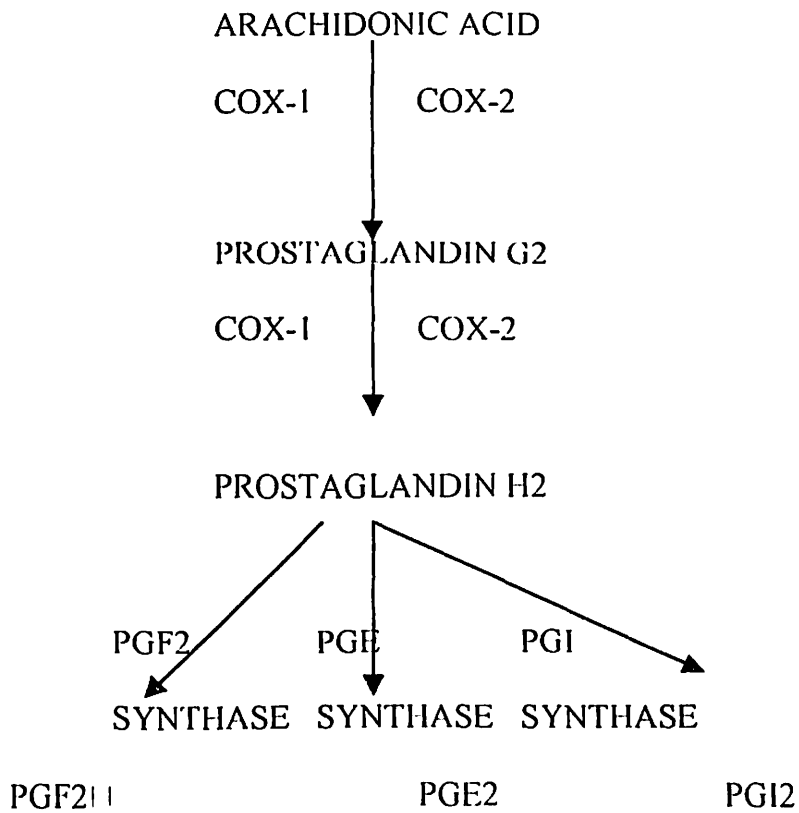
difference in the incidence of caesarean section between patients in whom prostaglandin was used for the induction of labour and those in whom only oxytocin was used. Caesarean section performed for failure of induction is lower in prostaglandin group (2%) as compared to 5% in the oxytocin group, however these results were not significant. They defined failure of induction when the cervical dilatation was 2cm or less and absent of regular uterine contraction. Uterine hyper tonus was recorded in 6% of the patients of the prostaglandin group who required oxytocin, and not in prostaglandin group only. But it was higher in the oxytocin group only (13%), which was statistically significant ($p < 0.005$). There were no apparent perinatal complications and the incidence of fetal distress in labour and the 1 and 5 minutes Apgar scores were also similar in the both groups.

Oxytocin should only be used once the Bishop score is favourable. It has been reported that induction of labour with an intravenous oxytocin in patient with unfavourable score resulting in a high incidence of caesarean section (16.5%) and a high failure rate (7%)(Arulkumaran et al, 1985)

PROSTAGLANDIN

The prostaglandins are a series of 20-carbon unsaturated fatty acids containing cyclopentane ring. The term prostaglandin was first coined by von Euler in 1936 after he had isolated a substance from the accessory glands of the male genital tract. Prostaglandins have been used successfully for cervical ripening and subsequent labour induction in the clinical environment since the early 1970s.

BIOSYNTHESIS OF PROSTAGLANDIN



Their biosynthesis is limited by the activity of the enzyme arachidonic acid cyclo-oxygenase that catalyses the transformation of arachidonic acid to the prostaglandin G2 and the subsequent reduction of the prostaglandin G2 to prostaglandin H2. COX-1 is a gene product that's expressed under normal physiologic condition. COX-2 is an inducible enzyme that appears after stimulation of the cells by extracellular signals.

MECHANISM OF ACTION IN CERVICAL RIPENING

Three mechanisms responsible in cervical ripening:

- a) Softening the cervix by altering the extra cellular ground substance. PGE₂ increases the activity of collagenase and elastase and increased the level of glycosaminoglycan, dermatan sulphate and hyaluronic acid. (Rath et al) and Norman et al.
- b) Relaxes the cervical smooth muscle thus facilitating the cervical dilation (Bryman et al)
- c) Facilitation of the formation of gap junction that is necessary for a coordinated uterine contraction. This also enhances the sensitisation of the uterus to oxytocin

Prostaglandin agents have been used intravenously, oral, intravaginal and intracervical routes to induce labour, all of which are effective. Intravenous and oral preparation was introduced in 1970 whereas transvaginal route was popular in 1980.

EFFECTIVENESS

Intravaginal PGE₂ suppositories to ripen the cervix were first proposed by Shepherd et al. He and his colleagues in a series of unselected woman where labour was induced by PGE₂ proved that the method was safe, simple and efficient and successfully softened and ripened the unfavourable cervix. The overall rate of failed induction resulting in caesarean section has fallen from 42 to 2.5%. (Shepherd et al).

Prostaglandin vaginal pessaries (3mgPGE2) significantly reduces the caesarean section rate in nulliparous with poor cervical score (23.7% vs. 43.5%)when compared to induction using oxytocin and amniotomy (Kurup et al)

In extensive metaanalysis Keirse (1993) showed PGE2 to be a successful cervical ripener:

- 1) Significantly improve the Bishop score.
- 2) Reduced the number of failed induction
- 3) Increased the number of patient in labour while undergoing cervical ripening
- 4) Increased the number of patient delivered while undergoing cervical ripening
- 5) Increased the number of patient delivering less than 24 hours.

OPTIMAL DOSING AND ROUTE OF ADMINISTRATION

Oral and parenteral routes of administration were investigated and were found to be associated with an unacceptability high rate of gastrointestinal side effects (20-25%). On the other hand, local methods of prostaglandin application including extra amniotic gels, endocervical gels and vaginal tablets, gels and suppositories have all been reported to be safe, and effective for cervical with reduced side effects.

Gordon –Wright and colleague analysed in a prospective randomised study, the effectiveness of PGE2 tablet administered intravaginally using increasing dose of 1 to 5 mg to induce labour. With progressively increasing dose, more patients were induced successfully.