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Current Practice and results of labour induction in teaching hospitals Khartoum

By

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(ونقر فى الأرحام ما نشاء إلى أجل مسمى ثم نخرجكم طفلا)

صدق الله العظيم

سورة طه

الآية (25-28)

Dedication

To the soul of my mother, asking the God to lay his mercifulness upon her.

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I am greatly indebted to my supervisor ***Prof. Abdel Salam Gerais****, Department of Obstetric and Gynaecology, Faculty of Medicine, University of Khartoum, for constructive criticism throughout this study.*

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List of Abbreviations

ARM	Artificial rupture of membranes
B.P.P	Biophysical profile
CTG	Cardiotocography
C/S	Caesarean section
FSB	Fresh stillbirth
Hb	Haemoglobin
IUFD	Intrauterine Foetal Death
MRNA	Messengers of Ribonucleic Acid
mg	Milligram
PGE2	ProstaglandinsE2
PPH	Postpartum Haemorrhage
PIH	Pregnancy Induced Hypertension
UK	United Kingdom
USA	Unites States of America
V.D	Vaginal Delivery
μg	Microgram

ABSTRACT

In this study 388 patients for induction of labour, 188 of favourable cervix induced by oxytocin, 200 patients of unfavourabl cervix induced by either intravaginal misoprostol of prostaglandins E2 (PGE2).

The commonest indication for induction was prolonged pregnancy (70.6%), followed by PIH (17%) and then DM (8.2%). The average doses were 6.5 units for oxytocin, 59 μg for misoprostol and 3 mg for PGE2.

The time of induction to delivery interval in the three methods misoprostol, oxytocin and PGE2 were 430 minutes, 499 minutes and 585 minutes, respectively. There were no significant differences between the three methods in the form of neonatal outcome or maternal complications. However, uterine hyperstimulation was more common in patients induced by misoprostol.

The rate of C/S was 16%, no significant difference between the three methods in the C/S.

Vaginal misoprostol was cheaper, stable at room temperature and more effective in labour induction than either PGE2 or oxytocin.

ملخص الأطروحة

أجـريت هذه الدراسة على 388 مريضة معدة لتحريض الولادة منها 188 عنق الرحم فيها مواتى للتحريض، إستعمل فيها عقار اكسوتوسين بينما مائتي حالة أخرى عنق الرحم فيها غير مواتى إستخدم فيها عقار- ميزوبرستول حبوب مهبلية أو بروستين حبوب مهبلية.

من الأسباب الرئيسية التىأدت إلى تحريض الولادة فى هذه العينة من المريضات كانت طول فترة الحمل عن الوقت المحدد لها، إرتفاع ضغط الدم أثناء الحمل، الإصابة بداء السكرى.

كان متوسط الجرعة فى عقار اكستوسين 6.5 وحدة بينما كان متوسط الجرعة فى عقار ميزوبرستول وبروستين 59 مايكروجرام، 3 ملجم على التوالى.

الفترة الزمنية التى استغرقها التحريض كانت كالآتى أقصرها فترة الميزوبرستول 430 دقيقة، تليها اكستوسين499 دقيقة وآخرها 585 دقيقة بواسطة بروستين.

لا فرق يذكر بين العقارات الثلاثة فى المضاعفات على الأم أو الجنين، ما عدا الزيادة فى إنقباضات الرحم التى لازمت التحريض بالمبزوبرستول (9.5%).

عقار ميزوبرستول يعتبر عقار وهيد الثمن ولا يتأثر بدرجة حرارة الغرفة وهو عقار فعال فى تحريض الولادة أكثر من عقاري بروستين واكسوتوسين.

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INTRODUCTION AND LITERATURE REVIEW

Definition:

The intentional initiation of uterine contractions and cervical dilatation from 24 weeks with the aim of delivering the fetus vaginally before the spontaneous offset of labour.

Incidence:

The role of labour induction has been gradually increasing in the last decade due to early detection of foetal Jeopardy, improve of neonatal therapy and the availability of cervical ripening agents.(1) The incidence of induction varies, but in the UK it is in the order of 15 – 25%.(2)

In the USA the incidence of induction is between 20-34%.(3) The Incidence of induction in the Sudan is unknown but in Soba University Hospital, the induction rate in the year 2000 was 4.3% and 6.67% in the year 2001.

Historical development of labour induction:

Accounts may be found in an ancient literature of techniques often extremely bizarre, whose purpose was to bring about the onset of labour. The first really effective intervention was artificial rupture of the

membranes or amniotomy, which was described in 1756 by Thomas Denman of the Middelsex Hospital, and came to be known as the (English method). Although it represented a major advance it was not without its complications, most notably if it did not lead to delivery within a relatively short space of time. The longer the interval between amniotomy and delivery the greater the likelihood of intrauterine infection. Because of this techniques were explored in the 9th and the early 20th century to avoid the need for amniotomy. Prominent among these was the use of various boogies or balloons, which were introduced through the cervix. Although the aim was to initiate uterine contractions, the biological impact was to provoke the release of endogenous prostaglandins although this has only been recognized within the last 30 years. Next in important was the discovery of oxytocin, which was widely accepted through the efforts of Turnbull and Anderson (1968) who advocated a policy of amniotomy followed by immediate intravenous titration of oxytocin. The later half of the 20th century has seen the biological role of prostaglandins.(4)

Indications of induction:

There are no absolute indications for induction of labour. However, termination of pregnancy is indicated when the fetus was in

greater danger in the uterus than it would be if delivered, or if the mother's life or health is endangered by the pregnancy continuing but, since the contributory factors are often multiple and rarely absolute, decisions are influenced by the nature and availability of resources in the delivery unit.[5] The spectrum of valid indications for induction of labour included emergency conditions, such as ruptured membranes with chorioaminitis or severe preeclampsia. There are also several relative indications. Indications of induction may be fetal or maternal.

Fetal factors:

Impaired placental function leads to fetal anoxia, the predisposing factors include preeclampsia and others hypertensive disorders, maternal diabetes and sickle cell disease, general factors such as duration of pregnancy, maternal age and nutrition.[5]

Prolonged pregnancy is a common indication of induction because the fetuses were noted to be at risk for hypoglycemia, thermal instability, and meconium aspiration. The small placentae lead to placental insufficiency, driving the fetus to use its own energy stores in the liver and adipose tissues. The result is a neonate with little subcutaneous fat and some degree of fetal weight restriction. Due to poor placental function, the amniotic fluid may be decreased, resulting

in increased risk of cord compression and passage of meconium. Uteroplacental insufficiency may result in non-reassuring foetal heart rate patterns even foetal death. So that induction of labour due to prolong pregnancy is undertaken 10-14 days after the expected date of delivery. Dates preferably confirmed by an early U/S will avoid unnecessary inductions for this indication.

Rhesus or other erythrocyte antibodies may indicate the need of induction depending on the effect of the fetus and antibody titers, the time of induction depends on the facilities.

Antepartum haemorrhage due to abruptio placentae commonly leads to induction of labour.[5]

Other foetal factors, like malpresentation may be an indication for induction in circumstances like unstable lie. To do stabilization and induction reduces the hazards to mother and her baby. Also congenital malformation for example (Anencephaly) is regard as an indication for induction. IUFD is a common indication.

Maternal factors:

The maternal factors are uncommon with pregnancy complications such as preeclampsia and abruptio placentae, but foetal Consideration are usually dominant; planned delivery is desirable when

maternal disorders require carefully planned therapy or when spontaneous labour would cause additional hazard, e.g., diabetes Mellitus, nephritis, respiratory disease, infections, malignancies and certain autoimmune disorders.[5]

Bist and colleagues (1999) in study of indications and obstetrics outcomes in tertiary referred hospitals found that the overall induction rate was 23%. The commonest indication is post-date (42%), diabetes mellitus (21%), PIH (12%), ruptured membranes (9%), foetal growth restriction (5%), and 4% due to chorioaminitis, the rest for non defined indications.[6]

Brennand and Greer (1997) at Queen Mother's Hospital, Glasgow, found that indications of induction is 61.9% due to post term, 11.4% due to PIH, 0.9% oligohydramonas, while 0.5% were due to diabetes mellitus and other conditions (12.4%).[7]

Contraindications to induction:

A number of uterine, fetal or maternal conditions present contraindication to labour induction. Most of these are similar to those that would preclude spontaneous labor and delivery. Uterine contraindications primarily relate to a prior disruption such as a classical incision of uterine surgery or hysterotomy or full thickness

myomectomy. Placenta praevia would also preclude labour. Foetal contraindications include macrosomia, some fetal anomalies such as hydrocephalus, mal-presentations, or non-reassuring foetal status. Maternal contraindications are related to contracted pelvis, and selected medical conditions such as active genital herpes pelvic tumor.[3]

Assessment of the patients for induction:

Before the beginning of induction we must assess the patient by gestational age, the menstrual dates and cycle should be checked together with any other available evidence, such as ultrasound, radiology and foetal lung maturity may be assessed by the amniotic fluid lecithin/sphingomyelin ratio to check is there any contraindication of induction.[5]

The condition or "favorability" of the cervix is important for labour induction, in many cases, the induction technique chosen depends upon the perceived ease of it's anticipated success.

Physical characteristics of the cervix and lower uterine segment are most important. The level of the presenting part or station is also important. One quantifiable method that is predictive of a successful labour induction is that described by Bishop (1964). Elements of the

Bishop score include dilatation, effacement, station, consistence, and position of the cervix (Table 1-1).

Table1-1: Bishop scoring system used for assessment of inducibility

Score	Dilatation (cm)	Effacement (%)	Station	Cervical consistency	Cervical position
0	Closed	0 - 30	-3	Firm	Posterior
1	1 -2	40 - 50	-2	Medium	Mid-position
2	3 – 4	60 – 70	-1	Soft	Anterior
3	≥ 5	≥ 80	+1, +2	—	—

Induction to active labour is usually successful with a score of 9 or greater and less successful with lower scores. Most practitioners would consider a women whose cervix is 2cm dilated, 80% effaced, soft and mid-position, and with the fetal occiput at -1 station as likely to have a successful labour induction. In these circumstances, initiation of labor with a dilute intravenous oxytocin solution is usually successful.

As the Bishop score decreases, with unripe cervix, these are an increasingly unsuccessful induction rate. This research has been directed toward various techniques to "ripen" the cervix prior to stimulation of uterine contractions.[8] The onset of human parturition does not fit into many of the animal models used. It is thought that the mechanism may depend on an interaction between the contiguous

tissues of the fetus and mother, namely the chorion (both membranes and placenta) and the decidua.

The action of prostaglandins in initiating labour is partly by stimulation contractions, but probably mainly by ripening and increasing the sensitivity of the cervix to oxytocin.[2]

Physiology of labour:

Labour is defined as the progressive dilatation of the cervix in association with repetitive, strong uterine contractions. The factors that initiate and promote labour are complex and not well understood. Oxytocin receptors in the uterus increase 100 fold by 32 week gestation and 300 fold at parturition. Although important for the actual labour process, this increased sensitivity to oxytocin only minimally predicts the duration of labour, which is more affected by parity and cervical status at the onset of labour. Cervical ripening (the softening, effacement and dilatation that occur before active labour is mediated by multiple factors (PGE2, PGF2-α) appear to be the final mediators in this process, although the exact mechanism is unknown.

Endogenous oxytocin is the main stimulator of uterine contractions. It also stimulate the production of PGE2 and PGF2-α and these may stimulate myometrial contractility.[9]

Methods of induction of labour:

These can be divided into medical (prostaglandins and oxytocin) and mechanical methods (amniotomy, membrane sweep, hygroscopic tents or dilators). Other medical and mechanical methods exist but are not commonly used, the choice depends on the state of the cervix as determined by Bishop score and the obstetric history. Amniotomy is the corner stone of any method of induction.[1]

Amniotomy:

Amniotomy or artificial rupture of the membranes, also referred to as surgical induction, is commonly used to induce or augment labour. The main disadvantage of amniotomy when used alone for induction is long interval to the onset of contractions. In randomized trial Bakos and Backstrom (1987) found that amniotomy alone or combined to oxytocin was superior to oxytocin alone, Mercer and colleagues (1995), found that early amniotomy at 1-2 cm dilatation was associated with significant shorter labour four hours but there was increased. Incidence of chorioaminitis and cord compression.[3]

Amniotomy and release of the amniotic fluid is the most efficient mechanical method of inducing labour. The way in which this is

mediated by separation of membranes results in prostaglandins release and this may encourage uterine activity.[10]

Low amniotomy:

A forewater rupture is easily performed by inserting the fingers and ruptured the membranes with a sharp pointed instrument (Goodwins Forceps, Amnihook) or with a Kocher forceps. Hind water rupture is achieved by introducing a specially designed (Drew-Smythe) catheter between the membranes and the uterine to a point above the presenting part, it is not used routinely in practice due to the hazard of trauma to the uterus, and separation of the placenta, Amniotomy alone results in delivery with 24 hours in about two-third of cases.[5]

Disruption of the chorioamnion likely results in arachidonic acid conversion by the cyclooxygenase pathway to PGE_2, resulting in increased uterine activity. In addition, reducing the intrauterine volume by allowing egress of amniotic fluid may allow an increase in contractile strength. It is a highly successful means when used in conjunction with the other methods of labour induction. The indications for amniotomy other than induction inability to monitor the foetal heart rate with external means, the need to evaluate the amniotic fluid, the need to administer an amnion infusion; the contraindications: placentae

praevia, vasapraevia abnormal foetal lie, prior classical caesarean incision, or active herpes simplex virus infection. In general amniotomy should be avoided in patients with an unengaged presenting part, this will increase the risk of umbilical cord prolapse.[11]

Oxytocin:

Oxytocin is a polypeptide hormone, which first became widely used for induction of labour in 1955. This was relatively impure and had varying degrees of vasopressor and antidiuretic activity as well as occasionally in pure form and produce for fewer secondary effects. Although oxytocin is not in itself responsible for the onset of spontaneous labour it is extremely effective in inducing uterine activity. It's mode of action is to depolarize cell membrane potential and other permeability to sodium. Osterogen and progesterone increase membrane potential and can therefore, inhibit the action of oxytocin. In late pregnancy oxytocin increases the frequency and amplitude of contractions, thus potentiating an already existing contraction pattern. Maximal sensitivity to oxytocin is achieved by 34-36 weeks gestation.[5]

Oxytocin should be used for induction following ARM of favourable cervix. It should only be started if the membranes have been ruptured. CTG monitoring is mandatory.[12]

Oxytocin is a hormone that contains eight amino acids and is produced by the posterior pituitary gland. In the circulation it has an effective half-life 5-10 minutes, pharmacological preparations are available for administration by buccal, intranasal, intramuscular or intravenous route. It acts by increasing free intracellular calcium and stimulate uterine contractions. The route of administration is by infusion because of the potential side effects of excessive uterine activity and systemic hypotension. The dose is 1-2 mU/min, with subsequent increases of 1-2 mU/min every 30 minutes until the desirable contractile pattern is reached. Although higher starting doses and more rapid increase in infusion rate have resulted in shorter duration of labour, however, it is associated with, high incidence of uterine hyperstimulations. There is still some debate about the optimal dosing regimen of oxytocin for maximal effectiveness and minimal untoward effects.

Kelly, et al (2001) in study of intravenous oxytocin and induction of labour found that, vaginal delivery is 89.6%, C/S (10.4%), using average dose (10 units), the time of induction to delivery 340 minutes.[13]Studies show a wide range of effective dosage and changes intervals, and no regimen has been shown to be clearly superior.[14]

Side effects:

The side effects of oxytocin can be extremely serious. Excessive doses can cause uterine hyper-stimulation, which may cause fetal hypoxia and uterine rupture. High doses of oxytocin may have an antidiuretic effect that results in significant fluid retention and overload with prolonged administration.[11]

Special supervision and precautions are required in multiparae who tend to be more sensitive to oxytocin; when the uterus is scarred from caesarean section, hystrotomy, myomectomy scar or following cone biopsy of the cervix; when dispropotion is suspected; or when fluid over load may be particularly hazardous as in cardiac disease.[5]

Oxytocin titration for induction of labour: the study show that, the oxytocin doses was" escalated every 15 min in the first group whilst for the second group the dose was increased every 30 min till optimal uterine activity was achieved, there was no significant difference in the mean maximum dose of oxytocin and length of labour in the two groups.[14]

For the induction of labour in women of high parity the infusion rate of oxytocin should be increased every 45 minutes rather than every 15 minutes until contractions occur three times in 10 minutes and

this infusion rate of oxytocin is maintained until delivery, this reduces the complications of labour and delivery but increase the time of induction by means 2 hours.[15]

Oxytocin receptor undergoes desensitization after prolonged or repeated stimulation. The concentration of myometrial oxytocin receptors and the steady state of its mRNA were measured in patients 477 (175-641) FMOL mg (-1) protein and decreased to 140(72-206) FMOL mg (-1) protein during prolonged oxytocin-augmented and oxytocin-induced labour, respectively. The corresponding oxytocin receptors mRNA concentrations decreased by 60-300 fold, respectively. The decrease in receptor binding and mRNA in women receiving oxytocin infusion indicates that homologous receptor desensitization occurs in vivo.[16]

Prostaglandins:

These are long-chain unsaturated fatty acids containing a five carbon ring along their length, derivatives of a hypothetical molecule, "prostanoic acid". They are found in most tissues and in especially high concentration in seminal vesicles. There are four major groups of naturally occurring prostaglandins, E, F, A and B. Some prostaglandins and a number of chemical derivatives have been synthesized. The

compounds of most importance in obstetric practice are prostaglandins E_1, E_2 and F_2-α. Other derivatives must be regarded as still under evaluation.[17]

Prostaglandins clearly play role in the initiation of the normal labour process in humans. One of the key processes linked to prostaglandins is an alteration in the collagen matrix and water content of the cervix. These changes result in softening and effacement, a process referred to as ripening. Artificial ripening of the cervix is a method used commonly in preparation for labour induction in parturients whose cervix has not yet undergone natural ripening. Success of labour induction is initiated with a ripened cervix in contrast to an unripened cervix. Artificial cervical ripening can be accomplished through the use of exogenous prostaglandin preparations applied to the cervix or by promoting local endogenous prostaglandins production by mechanically disrupting the interface between the foetal membranes and the upper cervix. Methods commonly used to increase local prostaglandin production include placement of mechanical dilators into cervical canal, digital sweeping of the membranes away from the cervix or placement of a Foley's catheter through the cervical canal and instilling crystalloid solution through the catheter to elevate the foetal

membrane away from the cervix and lower uterine segment. These methods cause release of arachidonic acid from the fetal membranes with subsequent endogenous prostaglandins production.

Exogenous PGE_2 preparation is commonly used for initiations of local cervical ripening and induction of labour.

Important prerequisites for the use of PGE_2 preparations are the ability to monitor uterine activity and foetal heart rate. After administration, the patient remains recumbent for 1 hour and remain under monitoring of uterine activity and fetal heartbeat for at least 2 hours.[11]

Route of administration and preparations of prostaglandins

Local application of prostaglandins of prostaglandin E_2 gel (Dinoprostone) is widely used with intracervical or intravaginal. The gel is available in a 2.5 ml syringe that contain 0.5 mg of dinoproston. The intracervical route offers the advantages of prompting less uterine activity and greater efficacy in women with a very unripe cervix.

Prostaglandins E_2 vaginal tabs various dosage of intracervical (0.3-0.5 mg) or intravaginal (3-5mg) high into posterior fornix with the second dose 6-8 hours if the labour not established. Maximum dose is 6 mg. A 10 mg dinoprostone vaginal insert (cervidil) also was approved

1995 for cervical ripening. The insert provides slower release of medication (0.3 mg/hr) than the gel. The advantage of the insert can be removed if hyperstimulation occur.[18]

Prostaglandin gel inserted into the posterior fornix, primigravida 2mg gel and multiparae 1 mg gel, if there is no uterine activity after 6 hours give further dose. The maximum quoted dose is 4 mg in primigravidae and 3 mg in multiparae.[12]

Prostaglandins increase the frequency and amplitude of uterine contractions, possibly by promoting oxytocin release from posterior pituitary but more likely by sensitizing myometrial cells to oxytocin. PGE2 is 5-10 times more effective in stimulating uterine activity than the other major oxytoxic $PGF_{2\text{-}\alpha}$.

Intravenous administration:

I.V. PGE_2 are very effective given at initial dosage of 0.25 μg/min, but have unpleasant side effects particularly gastrointestinal symptoms and local inflammatory reactions.

Oral tablets:

Oral tablets has advantage of convenience to patient, but the side effects usually prove to be unacceptable, before adequate therapeutic effect has been achieved, the side effect usually is less

than when PGE2 is used. The dose is 0.5 mg hourly initially rising up to 2 mg hourly.

Local administration:

Various modes of local administrations, including intraaminotic injection, extraaminotic infusion, gel and pessaries. For most obstetrical purpose local application of PG is preferred because of the effectiveness and minimal side effects.[5]

Side effects of PGE_2:

Hyperstimulation can occur, which cause fetal asphyxia and may lead to ruptured uterus. Gastrointestinal symptoms are 1% in local administration but more in systemic, and it may cause fever.[3]

Other side effects: nausea, vomiting, diarrhoea, muscle weakness, dizziness, dyspnoea, chest pain, mild pyrexia, headache and peripheral flushing due to vasodilatation are relatively uncommon with vaginal or intrauterine administration.

Special features:

The pessaries are easy to use; the gel allows flexibility of dose and provide more rapid absorption. Pessaries or gels should be stored at 4°C. Prostaglandins have no antidiuretic effect so can be used on

patient with cardiac disease or severe pre-eclampsia. They are active on the uterus at any stage of pregnancy if sufficient dose is used.[17]

The prostaglandins have been found to produce the best results for inducing labour when the cervix is unripe and are most effective when administered locally and most convenient when placed in the vagina as a viscous gel, wax pessary or slow release pessary. They are of benefit for labour induction in cases previously delivered by lower segment caesarean section, breech presentation and multiple pregnancies hyperstimulation and foetal distress may occur and this might be reduced with the use of the controlled release hydrogel pessary.[19]

Kelly, Kavanagh, et al (1999) in study of vaginal prostaglandins (PGE_2 and PGF_2-α) for induction of labour at term found that, achieved vaginal delivery with 24 hours by 82% versus 1% placebo or no treatment. The C/S were not different between groups, although the risk of uterine hyperstimulation with foetal heart changes is 4.6% and risk of oxytocin augmentation reduced (53.9%).[20]

Bahar and colleagues at Abha Maternity Hospital found that, the low dose regimen of 1.5 mg is as effective as the high dose regimen of 3 mg PGE_2 vaginal tablets in inducing labour. No difference

in induction-delivery interval, C/S rate and Apgar score. They found that C/S rate depends only on maternal age and Bishop score rather than on parity and gestational age.[21]

Misoprostol:

A new synthetic prostaglandin that is achieving wide acceptance for labour induction, it is a synthetic, methylated PGE_1 analog originally developed to treat gastrointestinal ulcers; misoprostol has been shown to have improved efficacy to that of PGE_2 in the aspects of safety, successful induction and side effect profile. It is currently administered intravaginally or orally. The intravaginal dose range from 25-100 μg every 4 - 5 hours. Misoprostol is a potent agent, and it is major side effects noted is an increase in the incidence of tachysystole, which is usually defined as the occurrence of more than six contractions in a 10 minute time period. It differs from uterine hyperstimulation in that it is not associated with fetal heart rate abnormalities and typically required no treatment. No significant differences between misoprostol and PGE_2 in the incidence of caesarean section, maternal side effects or neonatal outcome. The optimal dosage and dosing interval have yet to be completely determined.[11]

Route of administrative doses:

Vaginal misoprostol:

Initial studies suggested that misoprostol tablets placed into the vagina were either superior to or equivalent in efficacy compared with intracervical prostaglandins E_2 gel. The dose of intravaginal misoprostol in an approximate 25 μg, such usage is considered to decrease the need for oxytocin, achieve higher rates of vaginal delivery within 24 hours of induction, and significantly reduce induction-to-delivery intervals.[22] The 50μg dose result in significantly increased tachysystole, meconium passage and meconium aspiration compared with prostaglandin E_2 gel. This will also increase incidence of caesarean delivery due to uterine hyperstimulation when compared with dinoprostone. The 25 μg dose every 3 hours was associated with significantly fewer adverse effects than the 50μg dose.[23] In one report, Plaut and associates (1999) described uterine rupture in 5 of 89 (6%) women with a previous caesarean delivery who were induced with misoprostol compared only 1 of 423 such women not given misoprostol.[24]

Oral misoprostol:

Windrim and associates (1997) reported that orally administered misoprostol was of similar efficacy for cervical ripening and labour induction as intravaginal administration. Bennett and colleagues and Toppozada and co-workers (1997) found a shorter interval-to-delivery with the vaginal application, but more frequent foetal heart rate abnormalities. Adair and colleagues (1998) conclude that oral and vaginal applications were of similar efficacy but that an oral dosage of 200 μg was associated with more frequent abnormal uterine contractility. Wing and collaborators (1999) reported that 50 μg oral misoprostol was less effective than 25 μg administered vaginally for cervical ripening and labour induction. These investigators (Wind and colleagues, 2000) subsequently reported that a 100 μg oral dose was as effective as the 25 μg intravaginal dose.[22]

Advantages of misoprostol:

It is cheap in price one $ by one tablet, can be stable at room temperature no need for refrigeration. Misoprostol is useful in the management of elective medical and surgical abortion, miscarriage, and postpartum haemorrhage.[25]

Misoprostol is more effective drug in labour induction than dinoprostone. 200 μg of misoprostol intravaginal tablets compared with 3 mg of dinoprostone, the study show that in the misoprostol group labour was successfully established in 92% of cases compared with 64% in dinoprotone group. Maternal and neonatal complications, mode of delivery, the need for oxytocin and pethidine were quite similar statistically but polysystole is more frequent in misoprostol.[26]Fifty μg of sublingual misoprostol every four hours has the same efficacy and safety profile as compared with 100 μg orally, but the oral route might be preferred by women.[27]

Mjoko, Zeizawi (2002) in study of vaginal misoprostol for induction of labour found that, the need for augmentation with oxytocin is significantly in mode of delivery. There was a significantly reduced risk of C/S for failure of progress in the vaginal misoprostol, vaginal misoprostol significantly shortened time interval from induction to delivery, there were more admission to neonatal units in the misoprostol group.[28]

Sanches and others (1995) found that the use of misoprostol was associated with a higher incidence of tachysystolic but not

hyperstimulation, and the mean interval from "start of induction to delivery was 4.6 hours.[29]

Mechanical methods of induction of labour (Surgical):

Balloon Catheter:

Was first attributed to Barnes by Woodman (1863) for dilation of the cervix. Several variations of this method are used currently. One method includes the infusion of extra-amniotic normal saline and is referred to by some as EASI. Sherman and colleagues (1996) summarized the results of balloon catheter with or without saline infusion concluded that, the method resulted in rapid improvement of Bishop Scores and shorter labours.[30] Schreyer and colleagues (1989) found that extra-amniotic saline infusion resulted in greater increase in Bishop Score in less time than vaginal prostaglandins E_2.[31] Vengalil and colleagues (1998) reported similar outcomes with caesarean delivery rates and induction-to-delivery times with catheter infusion compared with 50μg misoprostol administered vaginally every 4 hours.[32] Hemlin and Moller (1998) reported that balloon catheter is effective in ripening of the cervix more than intracervical PGE_2.[3]

In randomized prospective study April 1992, the study was to compare the efficacy and to variability of three methods of cervical

ripening in patients at term for induction of labour with unfavourable cervix (Bishop Score less than 6). In the first group patient received an intracervical instillation of PGE_2. Second group, an intracervical Foley's catheter with it is balloon inflated to 50 cc of sterile water. The third group extraamniotic injection of PGE_2 via a Foley's catheter. These results show the superior efficacy of the catheter plus PGE compared with other two methods; as well as that intracervical catheter is equally effective in terms of success and failure as a catheter alone.[33]

Hygroscopic cervical dilators:

One or more hygroscopic dilators can be inserted into the cervix and produce softening and dilatation through expansion by absorbing fluid. Improvement of the Bishop Score takes from four to eight hours after insertion.[1] Cuinn and co-workers (2000) reported that cervical ripening with cervical dilators plus oxytocin induction were similar in efficacy to either catheter infusion or prostaglandin E_2, cervical gel. It is of some benefit for initiation of cervical dilation, the attraction of these dilators is their low cost, ease of placement, and their ability to be quickly removed.[34]

Sweeping the membranes:

Membrane sweeping or stripping is an old method of inducing labour that is still in common use. This intervention results in a local increase in prostaglandin production and to hasten the onset of labour. The intervention had no significant impact on mode of delivery or the incidence of maternal or neonatal infections but it is painful to the women.[35]

Other methods of induction of labour:

1. Electrical stimulation of the myometrium.
2. Administration of corticosteroid.

These techniques do not result in immediate onset of labour but may be of value in increasing myometrial sensitivity to oxytocin or may hasten the onset of labour in prolonged pregnancy.[5]

Comparative studies between different methods of labour induction:

Kadanali et al (2000) in their study to compare the efficacy and safety of intravaginal and oral misoprostol vs. oxytocin/PGE_2 for third trimester labour induction, the results, induction to active phase of labour was successfully achieved 85.7% in misoprostol group vs. 76.8% in the oxytocin /PGE_2 group, but the drug initiation delivery

interval was significantly shorter in the misoprostol (9.2 ± 2.4 hrs.) than in the oxytocin/ PGE2 group (15.2 ± 3.2 hrs.), the incidence of adverse intrapartum outcomes was similar for both methods. There was a higher prevalence of C/S for failed induction in the oxytocin/ PGE_2 group than in the misoprostol (13.4% vs. 6.3%) the neonatal outcome of both groups were also similar.[36]

In comparative study of misoprostol with oxytocin, they found that latent period per minutes and time of induction to vaginal delivery (hours). Misoprostol 252.9 min (latent period), interval from induction to delivery (10.6 hrs). Oxytocin 352.3 min (latent period), interval from induction to delivery (14.8 hrs).The dose of misoprostol is 25 μg, while the dose of oxytocin is maximum 20 mU/min. Vaginal delivery misoprostol 81%, 64% in oxytocin.[37]

Hazards of induction of labour:

Induction of labour while potentially of great benefit may also bring complications. Amniotomy exposes the fetus to the risk of intrauterine infection, especially if delivery is delayed and may also result in prolapse of the umbilical cord.[4] High dose of oxytocin infusion and diluted solutions may cause fluid retention, pulmonary oedema, electrolyte imbalance, coma and death. Hyperstimulation of the uterus

may lead to fetal distress or ruptured uterus. Placental abruption particularly following an uncontrolled amniotomy with polyhydramnios. Following prolonged induction may result in uterine exhaustion and atonia which cause postpartum haemorrhage.[1] It is also likely that the increase in caesarean deliveries associated with labour induction.[3]

Boulvai and others (2001) found that when evaluate the risks of maternal and perinatal morbidity associated with induction of labour, high risk of C/S, use of epidural analgesia was more frequent, resuscitation and admission to the intensive care unit were more frequent.[38]

Hofmeyer (2001) found that induction of labour using misoprostol overall C/S rates appear to be reduced, despite a relative increase in C/S for fetal heart rate abnormalities. Concern remains regarding increase rates of uterine hyperstimulation and meconium stained amniotic fluid, increase PPH, and isolated report of uterine rupture.[39]

OBJECTIVES

- To study the different methods used in practice of labour induction in teaching hospitals as their effectiveness and safety.

    1- Oxytocin plus artificial rupture of membranes.

    2- Prostaglandins:

        a. PGE2.

        b Misoprostol.

- Effectiveness to be assessed by:

    a. Duration of induction.

    b. Failure rate leading to caesarean section.

- Safety to be assessed by degree of maternal and foetal complications.

PATIENTS AND METHODS

Study design and duration:

A hospital-based prospective study conducted in June 2002 to July 2003.

Study area:

This study was conducted in the Omdurman Military Hospital, Omdurman Maternity Hospital, Suba University Hospital and Elsaudi Hospital.

Study population:

Patients planned, or for emergency induction attending the above mentioned hospitals.

Inclusion criteria:

The choice of the cases depends on the following: single pregnancy, viable, term, cephalic, no uterine scar before, no placenta praevia and the parity not more than four, estimated foetal weight not more than 4 kg. Reactive CTG and B.P.P to be accepted to whom the investigations was done.

Exclusion criteria:

Estimated foetal weight greater than 4,000 g or evidence of cephalopelvic disproportion; placenta praevia or any unexplained vaginal bleeding, foetal malformation, previous uterine scar, any situation when vaginal delivery was not indicated and any contraindication of use of prostaglandins or oxytocin (heart defect, glaucoma, increased intraocular pressure, bronchial (asthma).

Investigations:

General investigation e.g. Mb, urine general analysis and specific investigations, mainly for the foetal wellbeing cardiotocography and biophysical profile, but this had not been done in all patients, because of the lack of resources.

Questionnaire:

Information on age, parity, mode of previous deliveries, indication of induction and detailed about assessment obstetrical examination especially the favourability of the cervix, which determine the choice of the method of induction, the result of the induction to the mother and her baby.

Methods of induction:

The choice of the method depends on the condition of the cervix, favourable or not, in case of favoutable cervix infusion ocytocin was titrated and the starting dose varies according to the parity in primigravida, we start with 2 units and increase the rate and concentration until we reach the efficient contractions, however, if the patient is multipara the starting dose is one unit. Amniotomy was carried out when cervical dilatation is four centimeter or more. Monitoring of foetal heart rate every 15 minute using either Penard stethoscope or sonicaid for hearing the foetal heart and calculating the rate after the start of the contractions.

In case of an unfavourable cervix we use either misoprostol or prostin. For women receiving misoprostol 50 μg were administered in the posterior fornix of the vagina. If there are no contractions the dose was repeated after 4 - 6 hours until reach four doses maximum dose 200 μg. If the onset of contraction occurs but not three contractions or more per ten minutes, infusion oxytocin and amniotomy was to be done.

The other group of unfavourable cervix, which randomly selected 3 mg of prostin (PGE2) was inserted in the posterior fornix of

the vagina after four hours if there is no contraction another dose was to be repeated. If the contractions not efficient oxytocin and amniotomy to be done.

Close follow up specially by foetal heart monitoring, and intrapartum uterine activity was performed. If hyperstimulation of the uterus present, the following measures were taken:

- Prostaglandins preparation were washed out from the vagina.
- Oxytocin infusion was abandoned, because of unavailability of uterine relaxant if hyperstimulation dose not stopped the patient will be prepared for surgical intervention by caesarean section.

Data analysis:

For data analysis, the comparability of the groups was initially evaluated through the variable distributions.

RESULTS

Three hundred eighty-eight pregnant women were induced by different methods, 188 were allocated to use oxytocin, 168 to use misoprostol, and 32 used prostin. In order to demonstrate the randomization process for the groups, the results were presented.

Demographic characteristic of women in the study:

Age:

The age of the pregnant women in the study was between 17-40 years. However, the majority of women 354 (92%) were between 17-34 years. The distribution of study population according to age is shown in (**Fig.1**).

Origin and occupation:

The women in the study were from different areas in the capital Khartoum and ground it. The majority of women in the study (89.2%) were housewives and 10.8% were employee.

One hundred fifty-six of the patients (40%) were primigravida, 232 were multiparae (60%), most multiparae had smooth previous vaginal deliveries, and only 16 patients (6.7%) had been induced before (**Fig. 2a**). Prolonged pregnancy was the commonest indication of induction of labour followed by PIH, DM (**Fig. 2b**).

The majority of the primigravidae induced, because they had prolonged pregnancy, PIH and DM. However, in multiparae but in different percentage (**Table 1**).

The dose of misoprostol was 50 μg if there is no contractions another dose should be administered after four hours. The mean dose is 59ug. In inefficient contractions oxytocin should be given, 29(17.3%) of the pregnant women induced by misoprostol received oxytocin, 3 mg vaginal tablets were used of PGE_2 as a single dose, no added dose was administered, but 8(25%) of the women induced by PGE_2 needed additional acceleration by oxytocin to have efficient contractions. The average dose of oxytocin was 6.5 units (**Table 2**).

The average time of the onset of efficient contractions from the beginning of induction in the different methods (**Fig. 3**).

The first stage of labour in misoprostol, oxytocin, PGE_2 was 414 min, 456 min, 559 min respectively, the second stage was 12 min, 33 min, 19 min respectively, the third stage was 4 min, 10 min and 7 min respectively (**Fig. 4a, b**).

The duration of induction in the three methods (misoprostol, oxytocin and PGE2) were 430 min, 599 min, 585 min respectively (**Table 3**).

Mode of delivery: there was no significant different in mode of delivery of the three methods.

The overall failure rate of induction of labour in all the three methods end in C/S was 16%, instrumental delivery about 3% and 81% vaginal delivery (**Fig. 5**).

Table 4 shows the mode of delivery according to the different methods.

Indications of C/S in the different methods showed significant difference in uterine hyperstimulation, which was the commonest indications of C/S in misoprostol, however, failure of progress was the commonest in both PGE2 and oxytocin (**Table 5**).

Foetal assessment:

Foetal assessment before induction was essential, but lack of facilities prevent the assessment, so is the majority of the pregnant women in the study, no CTG done to 79.6% of women in the study population, all the cases of the study, which CTG had done to, had reactive CTG. Biophysical profile had been done to 23(5.9%), not done to 365(94.1%). The minimal score for induction in the study of B.P.P was 6/8, this should include adequate liquor (**Tables 6 and 7**).

Foetal outcome from the total study population (**Table 8**). Foetal outcome from three different methods show no significant difference of foetal outcome (**Table 9**).

The three different methods only differ on the complication of uterine hyperstimulation, which was 9.5% of the women induced by misoprostol and zero percent to other two groups of PGE_2 and oxytocin. In other complications there was no significant difference in the three methods of induction (**Table 10**).

Foetal weight:

The majority of the foetal weight (81.7%) were located between the range of 2.6 - 3.5 kg. The weight which was > 4 kg should not be included in the study, but this appeared due to wrong estimation of foetal weight, 4 cases (1%), they end in 50% C/S and 50% instrumental delivery. The weight, which was below normal (2-2.5 kg) were (3.3%) had result of 7.7% fresh stillbirth (**Fig. 6**).

There was no significant difference in mode of delivery and foetal outcome in the study group in relation to weight (**Tables 11 and 12**).

DISCUSSION

Post-maturity is the commonest indications of labour induction worldwide.[5] In this study the majority of pregnant women were induced due to prolonged pregnancy too (70.6%).

In other study[6] the percentage of post date is 44%, in this study is 70.6%, this difference may be due to the patient behaviour to the induction of labour in the other communities.

In previous studies the optimal dose of oxytocin was between 1-2 mU/min, this was calculated by automated machine. However, the dose in this study was almost always the same even it was calculated by drops and concentrations.

In the literature the oxytocin was titrated by increasing the rate in 15 min and 30 min in low parity[14] but in 45 min in women with high parity.[15] this study the titration of oxytocin by increasing the rate every 30 min, which is effective and of less complications.

Studies show a wide range of effective dosage and changes intervals, and no regimen has been shown to be clearly superior.[14]

In study of oxytocin dose found that the average dose was 10 units, in this study the average dose is 6.5 units.

The dose of misoprostol in the literature by vaginal route range between 25-100 μg every 4-6 hours.[11] In this study the mean optimal dose was 59 μg.

In comparison to literature the dose of PGE_2 by vaginal route was 3-5 mg/ with the second dose, 6-8 hours, maximum dose 6 mg.[3] ln this study the dose was 3 mg, no additional dose was given, however, oxytocin was used additionally to 25% of the patients who received PGE_2.

In comparative study of misoprostol with oxytocin, they found that, the time of induction to the vaginal delivery in hours 10.6 hours and 14.8 hours, in this study the time of induction to delivery was 7.15, 9.75 hours respectively, ^this shows decreases time of induction in this study.

The duration of induction of labour in the literature, in comparative analysis of the three methods, misoprostol, oxytocin and PGE2 was 9, 11 and 10 hours respectively,[37] In comparison and contrast to this study the duration of induction of labour by these methods were 7.15, 8.3 and 9.75 hours respectively. The different of comparative duration showed that, time of induction of PGE_2 was more

than oxytocin, in this study because we used PGE_2 in unfavourable cervix and oxytocin when only the cervix was favourable.

The vaginal delivery in this study using misoprostol, PGE_2, oxytocin is [83.1%, 75% and 81% respectively] in comparable with Literature[36] vaginal delivery was successfully achieved in 85.7%, 76.8%, 76.8% respectively, no significant difference between the three groups.

The C/S in misoprostol, PGE_2 and oxytocin is 17%, 16% and 15% in this study, however, in the previous study 13.4%, 16.3% and 8.2% respectively.[36] This different mainly due to 6 mg of PGE_2 used in the previous study.

In contrast to the literature, no significant difference following induction of labour by misoprostol, oxytocin and PGE_2, in uterine hyperstimulation, however, in this study, there was significant difference in uterine hyperstimulation following induction of labour by misoprostol (9.5%) compared to induction by either oxytocin or PGE_2 (0%) and (0%) respectively. This in comparison with the literature may be due to that, misoprostol was used in a dose of 25 μg,[3] where these studies were found to compare with used 50 μg in the hospitals, where the study had been carried. Uterine hyperstimulation may be over

diagnose because it may be just tachysystole (increase uterine contractions with normal fetal heart).

No significant difference in other maternal complications like, abruptio placentae, P.P.H, cord prolapse in this study compared to the literature.[1,5,33]

The comparison of the literature to this study in foetal outcome, alive, fresh stillbirth, well cried immediately, resuscitated or admitted to the nursery, there was no significant different in the three methods of induction in form of foetal outcome. Misoprostol, oxytocin and PGE_2 alive baby, well cried immediately (89.9%), 85%, 90%, in form of fresh stillbirth, 0.5%. 0.6%. 0% respectively.

In previous studied[3,11,27,33] concerning foetal outcome, there no significant difference with this study.

CONCLUSION

- Intra-vaginal misoprostol and dinoprostone are safe and effective medications for use in cervical ripening and labour induction, misoprostol results in a shorter interval from induction to delivery, cheap and stable at room temperature. However, C/S due to uterine hyperstimulation should be considered.
- Dinoprostone is expensive and needs refrigeration to maintain its potency.
- Oxytocin is a drug of choice in the patients with favourable cervix.
- There was no significant differences between misoprostol, PGE_2 and oxytocin in the rate of C/S and foetal outcome.

RECOMMENDATIONS

- Before starting induction of labour good assessment of the mother and her baby should be done.
- Induction of labour should be early in the morning to avoid night complications.
- Intrapartum foetal monitoring is the cornerstone in induction of labour.
- Any patient prepared for induction should be prepared for the possibility of an urgent C/S.
- The choice of the methods according to the cervix condition, oxytocin plus ARM in favourable cervix and misoprostol was a drug of choice in unfavourable cervix.
- Titration of oxytocin every 30 min in small dose in multiparae patients.
- Misoprostol intravaginally should be 25 μg every four hours to avoid uterine hyperstimulation.
- Protocols for induction of labour should be available in all hospitals.

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