COMPARATIVE STUDY OF 25 µg INTRAVAGINAL MISOPROSTOL AND 0.5 mg INTRACERVICAL DINOPROSTONE FOR INDUCTION OF LABOUR

By

Dr. VISHNU PRIYA KESANI MBBS

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DR. MUNIKRISHNA. M. MD, DGO

PROFESSOR

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

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Date :
Place : Kolar

SIGNATURE OF THE GIUDE
Dr. MUNIKRISHNA.M. **MD DGO**
Professor
Department Of OBG
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR-563101

ENDORSEMENT BY THE HEAD OF THE DEPARTMENT, PRINCIPAL / HEAD OF THE INSTITUTION

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Dr. SHEELA S.R
Professor & HOD
Department Of OBG
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Dr. HARENDRA KUMAR M.L
Principal,
Sri Devaraj Urs Medical College
Tamaka, Kolar

SRI DEVARAJ URS MEDICAL COLLEGE
TAMAKA, KOLAR-563101

ETHICS COMMITTEE CERTIFICATE

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DR. VISHNU PRIYA KESANI

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LIST OF ABBREVIATIONS USED

ACOG	: The American College of Obstetricians and Gynecologists
APGAR	: Activity, pulse, Grimace, Appearance, Respiration
DTA	: Deep Transverse Arrest
FDA	: U.S. Food & Drug Administration
FHR	: Fetal Heart Rate
IAI	: Induction to active phase interval
IDI	: Induction to delivery interval
IL	: Interleukin
MCP	: Monocyte Chemotactic protein.
MPA	: Misoprostol acid
NICU	: Neonatal Intensive Care Unit
NST	: Non stress test
PGE1	: Prostaglandin E1
PGE2	: Prostaglandin E2
RCOG	: The Royal College of Obstetricians and Gynaecologists
RCT	: Randomized controlled trial
WHO	: World Health Organization

ABSTRACT

COMPARATIVE STUDY OF 25 µg INTRAVAGINAL MISOPROSTOL AND 0.5 mg INTRACERVICAL DINOPROSTONE FOR INDUCTION OF LABOUR

INTRODUCTION

Induction of labour is an artificial initiation of uterine contractions prior to their spontaneous onset leading to progressive effacement and dilatation of cervix and delivery of the baby. It is one of the most commonly practised obstetric interventions. Labour induction is indicated in conditions in which prompt delivery is necessitated to reduce the risk of maternal and neonatal mortality and morbidity.

The chances of a successful vaginal delivery are less likely in the presence of an unfavourable cervix. Prostaglandins are drugs that have been routinely employed for cervical ripening and induction of labour. Prostaglandins in addition, to causing cervical changes, also initiate effective myometrial contractions which lead to achieving shorter induction to delivery intervals.

The most commonly employed prostaglandin analogs, for induction of labour include Prostaglandin E1 (misoprostol) and prostaglandin E2 (dinoprostone). A potential drawback with the use of misoprostol is excessive uterine contractility that can cause hyperstimulation of uterus and tachysystole, and this is more apparent with doses higher doses of misoprostol. ACOG recommends the use of low dose misoprostol (25 µg) for induction of labour. Dinoprostone causes normal physiological cervical ripening and studies have suggested lower rates of uterine hyperstimulation in comparison to misoprostol.

Lierature suggests need for further studies to ascertain a safe and efficaceous drug for labour induction. Hence, need for the present study is an attempt to compare the efficacy and safety of low dose misoprostol and dinoprostone for induction of labour.

OBJECTIVES

- To determine the safety & efficacy of 25 µg intravaginal misoprostol for Induction of labour.
- To determine the safety & efficacy of 0.5 mg intracervical dinoprostone for induction of labour.
- To compare the maternal & fetal outcomes between the two groups.

STUDY DESIGN

It is a randomized interventional study conducted in the Department of Obstetrics and Gynaecology from December 2016 to March 2018 at R L Jalappa Hospital and Research Center, Tamaka, Kolar.

MATERIALS AND METHODS

260 pregnant women included in the study. They were randomized to receive either 25 µg intravaginal misoprostol or 0.5 mg intracervical dinoprostone. Misoprostol was administered at 4^{th} hourly intervals up to a maximum of 6 doses, while dinoprostone was administered 8^{th} hourly up to a maximum of 3 doses. Subjects were induced till adequate uterine contractions (3 contractions in 10 minutes) were initiated or modified Bishop's score was >6 or cervical dilatation ≥3cms. If they did not respond to the above protocol it was considered as failed induction. In such cases, either patient was considered for augmentation with oxytocin or decision for caesarean section was taken. The progress of labour was monitored with a

partogram and all cases were monitored by electronic fetal monitoring. Total dose of induction, induction to delivery interval, mode of delivery, maternal and fetal outcome were recorded. The collected data was analysed using Independent sample t-test, Mann Whitney u test and Chi square test.

RESULTS

The mean induction to active phase interval was significantly shorter in the misoprostol group than in the dinoprostone group (9.60 ± 3.13 versus 10.83 ± 3.61 hours, P value 0.011). The mean induction to delivery interval was significantly shorter in the misoprostol group when compared to dinoprostone group (14.49 ± 3.93 versus 16.08 ± 4.54 hours, P value 0.011. Percentage of cases requiring oxytocin augmentation were similar in both dinoprostone and misoprostol group (54.2% versus 56.1 %, P = 0.784). The rate of achieving vaginal delivery was 72.3% and 73.84% in dinoprostone and misoprostol group respectively. And, 27.7% and 26.2% delivered by caesarean section in the dinoprostone and misoprostol group respectively. This difference was not statistically significant (P value 0.994). The most common indication in both the groups was fetal distress. The occurrence of meconium stained liquor was higher with misoprostol than with dinoprostone (23.8% versus 18.47%). However, this difference was not statistically significant. Rate of neonatal admission to NICU was 12.3% in the misoprostol group and 10% in the dinoprostone group and this was not statistically different. In the present study maternal complications were 9.2% in the dinoprostone and 12.3% in the misoprostol group and this was not statistically significant. Non-reassuring fetal heart tracing was more frequently observed in the misoprostol (20.77% versus 18.46%), however this difference was not statistically significant (P value 0.639).

CONCLUSION

Low dose misoprostol as a method of induction of labour is more efficacious than dinoprostone in terms of shorter induction to delivery interval, although both the drugs demonstrated similar outcomes with regard to maternal and fetal safety profiles. The stability of low dose misoprostol at room temperature and ease of storage in comparison to dinoprostone make misoprostol a more favoured drug for induction especially in developing countries with low resource settings.

Key words: induction of labour, low dose misoprostol, dinoprostone.

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INTRODUCTION

INTRODUCTION

Induction of labour is an intervention that artificially initiates uterine contractions leading to progressive dilatation and effacement of cervix and expulsion of fetus prior to spontaneous onset of labour**.**

Over the past several decades, the incidence of labour induction for shortening the duration of pregnancy has continued to rise. In developed countries, the proportion of infants delivered at term following induction of labour can be as high as one in four deliveries. Also, an increasing trend towards elective induction of labour and induction at maternal request has been observed.

Induction may be indicated to minimize maternal morbidity and fetal or neonatal morbidity and mortality by a timely intervention for termination of pregnancy.

For a successful induction, three aims have to be fulfilled:

1. The induction should initiate adequate uterine contractions leading to progressive dilatation of the cervix.
2. The labour should culminate in a vaginal delivery.
3. Maternal and fetal outcomes have to be favorable.

Achievement of the above goals is dependent on favourability of the cervix. Cervical priming methods to optimize the cervical score improve the chances of a successful induction.

Induction of labour in the presence of an unfavourable cervix was associated with high incidences of prolonged labour, instrumental delivery and caesarean section in the pre-prostaglandin era. Prostaglandin analogs are pharmacologic agents commonly used for both cervical ripening and induction of labour. Varying preparations of two commonly used cervical-ripening agents, dinoprostone (prostaglandin E2) and

misoprostol (prostaglandin E1), are commercially available. Existing data are limited, and further investigation is warranted to clarify the optimal agent, route of administration and dosing protocol for the induction of labour.

Although 50 µg of vaginal misoprostol may be more efficacious, safety concerns make the 25µg dose preferable. Safety profile was noted in terms of decreased rates of tachysystole, hyper stimulation, caesarean deliveries for non-reassuring FHR (fetal heart rate), NICU (neonatal intensive care unit) admissions, and meconium passage.

Literature suggests that Dinoprostone has lower rates of uterine tachysystole and hyperstimulation with or without fetal heart rate changes in comparison to Misoprostol. The trend is to attempt to lower the rates of tachysystole and uterine hyperstimulation.

Thus, the need for the present study is an attempt to establish a safe and efficacious drug for labour induction by comparing low dose misoprostol and dinoprostone based on appropriately conducted outcomes-based research.

OBJECTIVES

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REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY OF INDUCTION OF LABOUR

The history of induction of labour dates back to Hippocrates descriptions of mammary stimulation and mechanical dilation of the cervical canal.

In the early 100's, Soranus of Ephese described rupture of membranes, administration of an enema containing oil, water, andhoney, and pouring egg whites into the vagina to soften and relax the cervix along with mechanical dilation of the cervix.[1]

Moshion described manual dilation of the cervix, and Casis invented several instruments for cervical dilation. From, the 2nd through the 17th centuries, mechanical methods to induce labour came into more common practice. In 1756, at a meeting held in London, physicians discussed the efficacy and ethics of early delivery by rupturing the membranes to induce labor.[2]

In 1810, James was the first in the United States to use amniotomy to induce labour. Amniotomy and other mechanical methods remained the most commonly employed methods for induction of labour until the 20th century.[3] In 1856, Scanzoni used hot carbolic acid douche for induction of labour.[4]

In the late 1800s, several balloon devices were described. In 1862, Tarnier described a balloon device for stretching of the cervix and uterus through introduction of the device into the lower uterine segment.[1]

In 1906, Sir Henry Dale observed that extracts from the infundibular lobe of the pituitary gland caused myometrial contractions.[5] Three years later, Bell reported the experience with use of a pituitary extract for labour induction.[6] With the introduction of pituitary extract as a hormonal method of labour induction in 1913, the use of this method gained acceptance among obstetricians. However, due to the use of large doses and the impurity of the extract,

numerous adverse effects were reported. Gradually, the number of reported cases of uterine rupture increased with the use of pituitary extract thus discrediting its use. Initially, oxytocin (pituitary extract) was administered via intramuscular or subcutaneous routes. In 1943, Page suggested that the pituitary extract oxytocin be given in the form of an intravenous infusion,[7] and in 1949, Theobald reported his initial results with this form of administration.[8] Fourteen years later in 1953, the structural formula of oxytocin was discovered, and synthetic oxytocin has been in use since 1955.

In the 1930s, Raphael Kurzoak and Charles C Lieb discovered prostaglandins, when they found that fresh semen applied to myometrium specimens made the muscles contract & sometimes relax. Euler in 1935 named prostaglandins as he extracted them from seminal vesicles and prostate glands.[9]

In 1968, Karim et al were the first to report the use of prostaglandins for induction of labour with an intravenous prostaglandin F2α.[10]

REVIEW

ACOG asserts that elective induction of labour could be opted for logistic considerations or psychosocial causes but not before 39 weeks of gestation. Older meta-analysis of randomized studies that compare elective induction with expectant management showed a 20 % reduction in caesarean deliveries with elective induction compared with expectant management. A randomized control trail conducted at a military tertiary care center by Miller et al, involving 916 patients between march 2010 and February 2014 to ascertain the merits of elective induction versus expectant management, concluded that the caesarean section rate was not statistically different in either groups. The total length of hospital stay was 10 hours longer in the induced arm of the study, nonetheless, the postpartum length of stay and indications for caesarean section were not statistically different between the groups.[11]

In 2017, Little et al suggested that elective induction prior to 39 weeks was not recommended as elective delivery prior to 39 weeks of gestation was associated with increased risk of neonatal morbidity. The study also observed that labour induction was associated with significantly reduced odds of caesarean section compared to expectant management.[12]

In a systematic review and meta-analysis conducted by Chen et al in 2016, comparing the use of Foley catheter, Dinoprostone, and Misoprostol for induction of labour it was concluded that vaginal misoprostol followed by vaginal dinoprostone were the most effective methods for induction of labour, though these methods were associated with increased rates of hyperstimulation of uterus along with risk of fetal distress. Intracervical dinoprostone and induction with Foley's catheter were least effective methods, nonetheless these techniques had the lowest chances of uterine hyperstimulation and fetal distress. Also, the authors suggested requirement of further data to evaluate the risk of increased infection with use of mechanical methods of induction.[13]

Studies have concluded that low dose misoprostol and dinoprostone appeared to have similar efficacy and safety profile for cervical ripening and labour induction. There were few

incidences of maternal haemorrhage in misoprostol group and none in dinoprostone group. The additional benefits of misoprostol were, its stability at room temperature, the cost was significantly less per dose. Due to these benefits, they concluded that misoprostol was comparable or even superior to dinoprostone for induction of labour especially in developing and tropical countries like India.[14]

Literature has also suggested that the mean time taken for onset of labour & the duration from induction to delivery were both less in the misoprostol group than in the dinoprostone group. Hyperstimulation of the uterus & meconium stained liquor was more in the misoprostol group than in the dinoprostone group but it did not have any neonatal outcome.[15]

Few studies have shown that though oxytocin requirement was significantly less in the misoprostol group versus dinoprostone group there was no significant difference in the perinatal outcome and in the mean induction to delivery interval in both the groups. The limitation of these studies was their small sample size directing to potential for bias.[16]

According to a multicenter study conducted in UK in 2008, it was seen that a greater proportion of women who received dinoprostone had vaginal deliveries within 12 hours of induction compared with misoprostol recipients. The rates of vaginal deliveries achieved within 24 hours were similar between the misoprostol & dinoprostone recipients. The maternal and fetal adverse events were similarly distributed across the misoprostol and dinoprostone groups. This study concluded, that the efficacy between low-dose misoprostol (25 µg) and dinoprostone in terms of cervical ripening and labour induction and fetal and maternal safety profile were equivocal.[17]

In a meta-analysis study conducted in 2014, it was concluded that there was an increased incidence of uterine hyperstimulation & tachysystole in the misoprostol protocol in comparison to the Dinoprostone protocol. They also suggested that higher dosing of vaginal misoprostol (50 µg) resulted in increased chances of uterine hyperstimulation & FHR (fetal heart rate) decelerations when compared to lower doses of misoprostol. It was found that

dinoprostone was safer than misoprostol. They further directed that more studies were necessary to demonstrate the above viewpoint. In conclusion the study opined that intravaginal misoprostol though more efficacious than intracervical dinoprostone, dinoprostone was a safer drug due to its lower rates of uterine hyperstimulation & tachysystoles.[18]

In a study conducted at West Bengal, India in 2016, it was observed that low dose misoprostol (25 mcg) in comparison to dinoprostone shortened the induction delivery interval and also achieved lower caesarean section rates though the latter was not statistically significant. The occurrence of meconium stained amniotic fluid and hyperstimulation were greater than with dinoprostone. Also, in terms of neonatal safety profile, APAR scores of <7 at 5 minutes and admissions to the neonatal Intensive care unit though higher with misoprostol were not statistically significant. The study concluded that vaginal misoprostol was an effective method of induction and adverse perinatal outcomes were not increased with appropriate surveillance and timely interventions.[19]

In a prospective study conducted at Gujarat, in 2015 the investigators observed that greater number of women delivered vaginally in the dinoprostone group as compared to the misoprostol group. However, in the proportion of women who delivered vaginally with misoprostol the induction to delivery interval was significantly shorter and the number of women delivering within 12 hours of induction was also greater. They further observed that induction with misoprostol was associated with more chances of fetal distress. With regards to cost effectiveness, misoprostol was cheaper and also more favourable in terms of storage of misoprostol at room temperature while dinoprostone gel had to be refrigerated. The study concluded, that though dinoprostone was relatively slower in comparison to misoprostol but its steady progress in labour made it a more favourable option.[20]

In a study conducted in Spain involving 500 women in 2017, it was observed that the misoprostol cohort achieved better rates of vaginal delivery in < 24 hours than the dinoprostone cohort. The interval between administration of the drug till the appearance of

regular uterine contractions and the induction to active phase interval was shorter with misoprostol. The study conclude that misoprostol was associated with earlier and more effective contractions of higher frequencies that was associated with greater excitability of uterine myometrial cells.[21]

A retrospective cohort study of 331 patients conducted at a single hospital in New York, USA in 2014, to determine the resource utilization, obstetrical and cost outcomes between misoprostol and dinoprostone suggested that use of misoprostol showed an approximate 73% in the total cost savings.[22]

In a prospective study conducted by Radhika et al in Puducherry in 2013, with 300 women it was observed that the commonest indication for induction in both groups was prolonged pregnancy. The mean duration of labour was shorter in the dinoprostone group. However, other parameters in consideration such as oxytocin augmentation, mode of delivery and perinatal outcome was similar in both the groups. The investigators concluded that both misoprostol and dinoprostone were equally efficacious for cervical ripening, however misoprostol was much more economical in comparison to dinoprostone.[23]

In a study conducted by on 212 women in Kolkata, it was observed that dinoprostone had a shorter induction to delivery interval in comparison to misoprostol though not statistically significant. The duration was active stage was shorter in the dinoprostone arm. With regards to mode of delivery, misoprostol group had a significantly higher number of operative vaginal deliveries. Number of babies born with APGAR < 7 were significantly higher in the misoprostol group. Although, significantly greater number of digital vaginal examinations were performed in the misoprostol arm, the maternal outcomes with regards to postpartum febrile, chorioamnionitis and postpartum analgesic use were similar in both groups.[24]

ANATOMY OF UTERUS & CERVIX

The uterus is a pear-shaped organ and consists of two major parts. The upper triangular portion—the body or corpus, and a lower cylindrical portion—the cervix, which projects into the vagina. The isthmus is the union site of the two parts. In nulligravidas, the fundus and cervix are approximately equal in length, but in multiparas, the cervix is only a little more than a third of the total length.[25]

The isthmus has special obstetrical significance because it forms the lower uterine segment during pregnancy. At the superolateral margin of the body is the uterine cornu, from which a fallopian tube emerges. Between the points of fallopian tube insertion is the convex upper uterine segment called the fundus.[25]

The bulk of the uterine body is muscle. The inner surfaces of the anterior and posterior walls lie almost in contact, and the cavity between these walls forms a mere slit. The nulligravid uterus measures 6 to 8 cm in length and measures about 9 to 10 cm in multiparous women. The uterus weighs 60 g and typically weighs more in parous women.[25]

Pregnancy stimulates remarkable growth of the uterus due to muscle fiber hypertrophy. In pregnancy, the uterine fundus becomes dome shaped from a previously flattened convexity between tubal insertions.[25]

The cervical portion of the uterus is fusiform and open at each end by small apertures—the internal and external cervical ora. Proximal boundary of the cervix is the internal os and the distal boundary is the external os. The upper cervical segment that lies above the the vagina's attachment of the cervix is the portio supravaginalis and he lower cervical portion that protrudes into the vagina is the portio vaginalis.[25]

The composition of cervical stroma mainly consists of collagen, elastin, and proteoglycans, and very little smooth muscle. Changes in the amount, composition, and orientation of these components lead to cervical ripening prior to labour onset.[25]

Type I and type III collagen form the major composition of the extracellular matrix (ECM). Significant degradation of the collagen and rapid acceleration in loss of tensile strength of the tissue during parturition causes increased cervical compliance and softening. This progressive remodelling of the cervix leads to effacement. Effacement allows the cervix to respond to uterine contractions with progressive dilatation of the cervix and the ultimate delivery of the fetus.[26]

In early pregnancy, Chadwick's sign is due to the ectocervical blue tint secondary to increased vascularity within the cervical stroma beneath the epithelium. Cervical edema leads to softening— Goodell sign, whereas isthmic softening is Hegar's sign.[25]

PHYSIOLOGY OF CERVICAL RIPENING

The transformation of the cervix from a rigid closed structure to one that softens and dilates sufficiently for birth is a dynamic process. Cervical remodelling is loosely divided into four distinct overlapping phases: softening, ripening, dilatation and postpartum repair. Softening is defined as a decrease in the tensile strength and tissue compliance as compared with a nonpregnant cervix. Cervical ripening is an accelerated phase which is characterized by greater loss of tissue integrity and compliance. With progressive increase in uterine contractions a ripened cervix undergoes dilatation and effacement as labour progresses. This is followed by phase of remodelling and repair of cervix with restoration of tissue integrity in the postpartum period.[27]

The cervix is predominantly composed of fibrous connective tissue, an extracellular matrix consisting mainly collagen (70% Type I and 30% Type III) along with elastin and proteoglycans, and a cellular portion consisting of smooth muscle, fibroblasts, epithelium, and blood vessels.[28]

During this transformation, the total amount and composition of proteoglycans and glycosaminoglycans within the matrix are altered. The diameter of the collagen fibril and

spacing between the fibrils is increased. These changes occur due to accumulation of poorly cross-linked collagen and reduced expression of matricellular proteins. Dispersion of collagen fibrils leads to a loss of tissue integrity and increased tissue compliance. A dynamic change in collagen structure rather than collagen content regulates remodelling.[25]

Increased production of glycosaminoglycan occurs in the cervix during ripening. Stromal invasion with inflammatory cells within the extracellular matrix occurs during cervical ripening. cervical chemoattractants attract inflammatory cells, which in turn release proteases that may aid degradation of collagen and other matrix components. Hence, it has been postulated that ripening of the cervix could also be an inflammatory process.[25]

The neutrophils are a rich source of collagenases and neutrophil elastases. Matrix metalloproteinase enzyme which play a crucial role in the breakdown of inflammatory mediators notably Interleukin-8 (IL-8) and Monocyte chemotactic protein-1(MCP-1). These chemokines are responsible for release of collagenolytic enzymes, hence facilitating degradation of cervical collagen and eventually ripening the cervix. Estrogen stimulates collagenase production in pregnant cervix and progesterone degrades hyaluronic acid thus keeping its level low until term. Progesterone also inhibits IL-8 production by cervical tissue. As the effect of progesterone decreases in late pregnancy, IL-8 levels increase with production of more hyaluronic acid.[4]

PHYSIOLOGY OF LABOUR

Labour is defined as the process by which the fetus is expelled from the uterus. Labour is characterized by regular and effective uterine contractions that lead to progressive dilation and effacement of the cervix.

Labour initiation is species-specific and the mechanism is unique in humans. In non-human mammals, the fetus has a central role in the initiation of term labour, whereas in humans, the role of the fetus is not completely understood.[29]

During the first 36 to 38 weeks of a normal gestation, the myometrium is in an unresponsive preparatory state. Parturition requires transformations in both uterine and cervical function and it is arbitrarily divided into four overlapping phases that correlate with the major physiological transitions of the myometrium and cervix during pregnancy. The phases of parturition include:

1. Phase 1 of Parturition: Uterine Quiescence and Cervical Softening
2. Phase 2 of Parturition: Preparation for Labour
3. Phase 3 of Parturition: Labour
4. Phase 4 of parturition: the puerperium

Phase 1 of Parturition: Uterine Quiescence and Cervical Softening

Comprising almost 95 percent of pregnancy it is characterized by uterine myometrial quiescence and maintenance of cervical structural integrity.[25]

The phase is mediated by the action of progesterone, prostacyclin, relaxin, nitric oxide, parathyroid hormone related peptide.[29]

Progesterone sustains the uterine quiescence by suppression of production of contraction associated proteins (CAPs) like gap junction protein connexion 43, by reduction in expression of prostaglandin F2α & oxytocin receptions, and by regulation of ion channels within the uterine myometrium[30]

Phase 2 of Parturition: Preparation for Labour

The phase of uterine awakening or activation- progressive uterine changes during the last 6-8 weeks of pregnancy. Myometrial changes include expression of contraction associated proteins (CAPs) which are oxytocin receptor, prostaglandin F receptor, and connexion 43. These receptors increase uterine responsiveness to uterotonins.

Formation of the lower uterine segment is another critical event. Extensive remodelling of the cervix occurs during phase eventually resulting in cervical ripening and dilatation upon initiation of uterine contractions. The process of cervical ripening involves connective tissue changes; total amount and composition of proteoglycans and glycosaminoglycans within the matrix are altered. Collagen fibril diameter is increased with increased spacing between fibrils resulting in accumulation of poorly cross-linked collagen and decreased expression of matricellular proteins which leads to increased tissue compliance.

Phase 3 of Parturition: Labour

Labour is defined as the process by which regular, effective uterine contractions lead to dilatation and effacement of the cervix which lead to expulsion of the fetus from the uterus.[25]

The ability of the fetus to successfully negotiate the pelvis during labour depends upon the interactions of: uterine activity, the fetus, and the maternal pelvis (power, passenger, passage).[29]

The transition from uterine quiescence to prelabour is a progressively achieved through phase 1 & 2; onset of labour in phase 3 occurs following rapid long-distance signalling, mechanical triggering and electrical activity coverage of the mechanically sensitive electrogenic pacemakers that are distributed throughout the uterine wall. This phenomenon is termed mechanotransduction.[31]

Phase 4 of parturition: The Puerperium

It includes the remodelling processes; uterine involution and cervical repair that restore these organs to the nonpregnant state. Early puerperium also involves initiation of lactation.[25]

TIMING OF INDUCTION OF LABOUR

Evaluation of optimal timing for induction of labour is crucial in minimizing the feto-maternal risks. The ACOG, Society for Maternal-Fetal Medicine (SMFM), March of Dimes have all discouraged induction of labour in late preterm and early term gestations without maternal or fetal indication.[32]

ACOG recommends that the gestational age of the fetus to be at least 39 weeks or that the fetal lung maturity be established prior to induction.

INDICATIONS FOR LABOUR INDUCTION[29]

Induction of labour has a merit as a therapeutic option when the benefits of expediting the delivery outweigh the risks of continuing the pregnancy and the benefits of induction of labour must be weighed against the potential maternal and fetal risks associated with this procedure.[33]

Induction may be advocated to reduce maternal morbidity in pre-existing medical disorders associated with pregnancy or to minimize fetal morbidity and mortality in cases of fetal compromise or for feto-maternal benefit.[34]

Absolute indications:

- Hypertensive disorders
  - Preeclampsia / eclampsia
- Maternal medical conditions
  - Diabetes mellitus
  - Renal disease
  - Chronic pulmonary disease
- Prelabour rupture of membranes
- Chorioamnionitis

- Fetal compromise
    - Fetal growth restriction
    - Isoimmunization
    - Oligohydramnios
- Fetal demise
- Post term pregnancy (> 42 weeks)

Relative indications:

- Hypertensive disorders
    - Chronic hypertension
- Maternal medical disorders
    - Systemic lupus erythematosus
    - Gestational diabetes
    - Hypercoagulable disorders
    - Cholestasis of pregnancy
- Polyhydramnios
- Fetal anomalies requiring specialized neonatal care
- Logistic factors
    - Risk of rapid labour
    - Distance from hospital
    - Psychological indications
- Previous stillbirth

CONTRAINDICATIONS FOR LABOUR INDUCTION[35]

Any contraindication to labour or vaginal delivery. Most common contraindications include:

- placenta or vasa previa or cord presentation

- abnormal fetal lie or presentation (e.g. transverse lie or footling breech)
- prior classical or inverted T uterine incision
- significant prior uterine surgery (e.g. full thickness myomectomy)
- active genital herpes
- pelvic structural deformities
- invasive cervical carcinoma
- previous uterine rupture
- previous surgery for repair of vesicovaginal fistula

EVALUATION PRIOR TO INDUCTION OF LABOUR

The approach to induction of labour should be tailored to the clinical scenario with due consideration given to gestational age, indication for termination of pregnancy, maternal status, fetal status, prior uterine surgery and the presence or absence of spontaneous contractions. Also, factors such as cost and availability of immediate emergency caesarean delivery to be considered. A paediatrician to be notified for the care of the neonate.

Induction of labour should include the individual needs and preferences, and allow women the opportunity to make an informed decision.[36]

Preinduction evaluation of maternal and fetal parameters are important determinants of outcome of induction of labour.

Maternal parameters:

- Confirm the indication for induction
- Review contraindications to labour and/or vaginal delivery
- Clinical pelvimetry to assess pelvic shape and adequacy of bony pelvis
- Assessment of cervical status (Modified Bishop's score)
- Review risks, benefits and alternatives of induction of labour with the patient

Fetal parameters:

- Confirm gestational age
- Document fetal lung maturity
- Estimated fetal weight (either by clinical or ultrasound assessment)
- Determine fetal lie and presentation
- Confirm fetal well being

CERVICAL SCORING SYSTEMS

BISHOP'S SCORE

In 1964, a cervical scoring system, referred to as the Bishop's score was developed to assess the cervical status prior to induction of labour. This method is used to assess the readiness for onset of labour. This system considered the position, consistency, effacement, and the dilatation of the cervix, also the station of the presenting part of the fetus was taken into account. A modified Bishop's score that replaces effacement with cervical length has been developed. In these scoring systems, each component is assigned a score from 0 to 3, with a total maximum score of 13.[36,37]

BISHOP'S SCORE

	Score			
Factor	0	1	2	3
Dilatation (cm)	0	1-2	3-4	5-6
Effacement (%)	0-30	40-50	60-70	80
Station	-3	-2	-1 or 0	+1 or +2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Mid	Anterior	▪

MODIFIED BISHOP'S SCORE [38]

	Score			
Factor	0	1	2	3
Dilatation (cm)	0	1-2	3-4	5-6
Length (cm)	>4	2-4	1-2	0
Station	-3	-2	-1 or 0	+1 or +2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Mid	Anterior	

A higher score reflects a "favourable" cervix for induction. Routinely, a score of ≤ 6 is classified as an "unfavourable" cervix, and that would benefit from cervical ripening agents during labour induction.[39]

Bishop's score is also used to predict the likelihood of vaginal delivery with induction of labour. A score of ≤ 6 is associated with a higher probability of failed induction, while a score of > 8 probability of a vaginal delivery is same for induced or spontaneous labour.[36]

Dilatation of the cervix at the initiation of induction is the best independent predictor of success of induction of labour.[29]

Studies have suggested that cervical dilatation is inversely proportional to cesarean delivery. In a primiparous woman, a closed cervix is associated with a 50% caesarean section rate, whereas at 4 cm dilatation the risk for caesarean section was < 10%.[39]

METHODS FOR INDUCTION OF LABOUR

The modern techniques for induction of labour can be divided into 2 broad categories depending upon the cervical status prior to induction:

- Cervical ripening agents for unfavourable cervix, which constitutes the administration of prostaglandins and/or mechanical methods, such as insertion of catheters or dilators directly into the cervix
- Induction methods for a favourable cervix, which constitute the administration of systemic oxytocin or mechanical methods such as amniotomy.[36]

Methods of labour induction is classified by RCOG (The Royal College of Obstetricians & Gynaecologists) as follows: [40]

- Non-pharmacological methods
    - Membrane sweeping
    - Herbal supplements/ Homeopathy
    - Acupuncture
    - Castor oil, hot baths and enema
    - Sexual intercourse
    - Breast stimulation

- Surgical methods
    - Amniotomy
    - Mechanical methods (intracervical Foley's catheter/ balloon catheter/ laminaria tents)

- Pharmacological methods
    - Prostaglandins
    - Oxytocin
    - Mifepristone

Methods for induction of labour is also classified as follows:[36]

- Methods for cervical ripening
    - Pharmacological methods
        - Prostaglandins: Prostaglandin E1 (Misoprostol), Prostaglandin E2 (Dinoprostone)
        - Oxytocin
    - Mechanical methods
        - Membrane stripping
        - Balloon catheter
    - Combination methods
        - Foley's catheter with simultaneous use of either prostaglandins or oxytocin.

- Induction techniques for the favorable cervix
    - Mechanical methods: amniotomy
    - Pharmacological methods: oxytocin

MEMBRANE STRIPPING

In 1810, James Hamilton of England used sweeping/stripping of the membranes at term as a method of labour induction.[41] The goal of sweeping of the membranes is to initiate labour through a cascade of physiological events, and thus to reduce induction of labour with pharmacological techniques.

The technique is by introducing the clinician finger into the cervical os during a per vaginal examination and by a circular movement of the examining finger the membranes are detached from the lower uterine segment.[42]

This causes a significant increase in the prostaglandin $F_{2\alpha}$ and phospholipase A_2 activity which increases the likelihood of spontaneous labour within 48 hours.[33]

AMNIOTOMY

Amniotomy is the deliberate artificial rupture of the membranes, first described in 1756 by Thomas Denman, an English obstetrician.[43]

Amniotomy promotes the release of prostaglandins and oxytocin which in turn, accelerate labour and expedite delivery. It is an effective method of labour induction in multiparous women with favourable cervices.[44]

BREAST STIMULATION

Breast stimulation releases endogenous oxytocin which cause uterine contractions. However, further research is required to quantify its effectiveness, timing and frequency. Few studies have reported that breast stimulation is associated with decreased postpartum haemorrhage.[40,33]

SEXUAL INTERCOURSE

The mechanism of stimulating labour by sexual intercourse remains unclear, but it has been attributed to the presence of prostaglandins in human semen, partly due to physical stimulation of the lower uterine segment, and perhaps due to release of endogenous release of oxytocin as a result of orgasm.[45]

RCOG recommends that sexual intercourse should not be used as a method of induction of labour.[40]

MECHANICAL METHODS

Mechanical ripening devices apply pressure on the internal os of the cervix, thus overstretching the lower uterine segment; thereby, indirectly increasing the localized secretion of prostaglandins.[37] Mechanical methods of induction include use of

Foley catheters, double balloon catheter, hydroscopic dilators, laminaria.[35]

Studies concluded that use of Foley's catheter for induction of labour was associated with lowest rates of hyperstimulation in comparison to pharmacological methods of induction. Also, in women with high risk for fetal hypoxemia in conditions such as post-term pregnancy, pregnancy induced hypertension, sickle cell disease, intrauterine growth retardation induction of labour with Foley's catheter led to a decrease in fetal acidosis.[13]

The advantages of induction with a Foley's catheter includes easy storage, low cost and less stringent monitoring of uterine contractions. However, the drawbacks are an associated probable increased risk of chorioamnionitis, though this is considered as limited evidence as this outcome was rarely reported in randomized controlled trials (RCTs).[13]

The WHO induction guidelines of 2011 recommend Foley catheter as one of the first line methods with an increasing trend of its use.[46]

PHARMACOLOGICAL METHODS

MISOPROSTOL

It is synthetic prostaglandin E_1 analogue. Misoprostol can be administered via vaginal, oral, sublingual, and buccal routes. It is an inexpensive drug easily available for use. It is usually administered in 25 mcg or 50 mcg doses for induction of labour.

DINOPROSTONE

It is a Prostaglandin E_2 analogue approved by the U.S. FDA for cervical ripening. It is available as an intracervical gel 0.5 mg dinoprostone and as a vaginal insert containing 10 mg dinoprostone. The intracervical gel is administered every 6-12 hours up to a maximum of 3 doses, while the intravaginal insert is designed to release approximately 0.3 mg/ hour drug

over a 12-hour period. The insert to be removed upon onset of labour or 12 hours after insertion. Maintenance of a cold chain and proper storage in a refrigerator is necessary with dinoprostone.

OXYTOCIN

It is a sterile, clear, colourless aqueous solution of synthetic oxytocin, for intravenous infusion or intramuscular injection.[47]

Intravenous oxytocin is an effective means of labour induction especially for a favourable cervix. It is a peptide hormone from the posterior hypothalamus that can bind to receptors in the uterine myometrium and cause uterine contractions.[48] Pharmacokinetics of oxytocin show an onset of action within 3 to 5 minutes and a half-life of 10 to 12 minutes.[49]

High-dose protocols have a starting dose of 6 milliunits/min, with an incremental increase of 1 to 6 milliunits/min every 15 to 40 minutes, and a maximum dose of 40 milliunits/min. Low-dose protocols have starting doses of 0.5 to 1 milliunits/min, with an incremental increase of 1 to 2 milliunits/min every 15 to 40 minutes, and a maximum dose 20 to 40 milliunits/min.[50]

In 2007, FDA published a notice suggesting that for oxytocin was not indicated for elective induction of labour.[39]

PROSTAGLANDINS

Eicosanoid is a collective term for straight-chain polyunsaturated fatty acids (PUFAs) of 20 carbon units in length that have been metabolized or otherwise converted to oxygen-containing products. Prostaglandins are a subfamily of eicosanoids with a wide spectrum of effects. All prostaglandins are made up of a basic 20 carbon skeleton – "prostanoic acid".

The first prostaglandin effects were discovered in 1930, during artificial insemination when semen that was injected into the uterine cavity was expelled. However, injection of ringer's lactate was retained. It was thus discovered that semen contained a powerful vasodilator that could stimulate the uterine muscular activity. This substance was named prostaglandin and it consisted of lipid soluble unsaturated hydroxy acids and it was named prostaglandin E.[51]

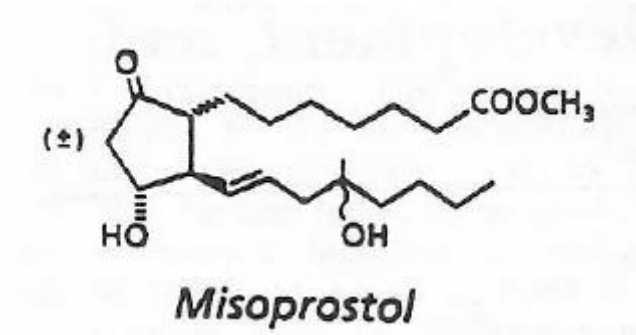
Synthetic prostaglandins mimic the cervical ripening action of endogenous prostaglandins. Synthetic prostaglandins have been designed to maintain a longer period of bioavailability. Prostaglandins most commonly used include misoprostol and dinoprostone.[52]

Prostaglandins play an important role in the ripening of the cervix by decreasing the concentration of collagen, and increasing the sulphated glycosaminoglycans and hyaluronic acid. Prostaglandin receptors are located in the myometrium and the cervix. PGE_2 has an affinity to all E series prostanoid (EP) receptors, while misoprostol is a selective EP2/EP3 receptor agonist. This selectivity to receptor binding causes different actions depending upon the type of receptor and dose of the prostaglandin.[53,54,55]

Synthetic prostaglandins mimic the cervical ripening action of endogenous prostaglandins. While, endogenous prostaglandins undergo rapid metabolism in the body, synthetic prostaglandins ensure longer periods of bioavailability.[52]

MISOPROSTOL

Misoprostol, owing to its wide range of uses in reproductive health, is on the World Health Organization Model List of Essential Medicines. Misoprostol (C22 H38 O5, M:W.= 382.5; (11, 13E,16-dihydroxy-16-methyl-9-oxoprost-13-en-1-oic acid methyl ester) is a synthetic prostaglandin E1 analogue that was developed in 1973 by Searle for the treatment and prevention of gastric ulcers.



Misoprostol

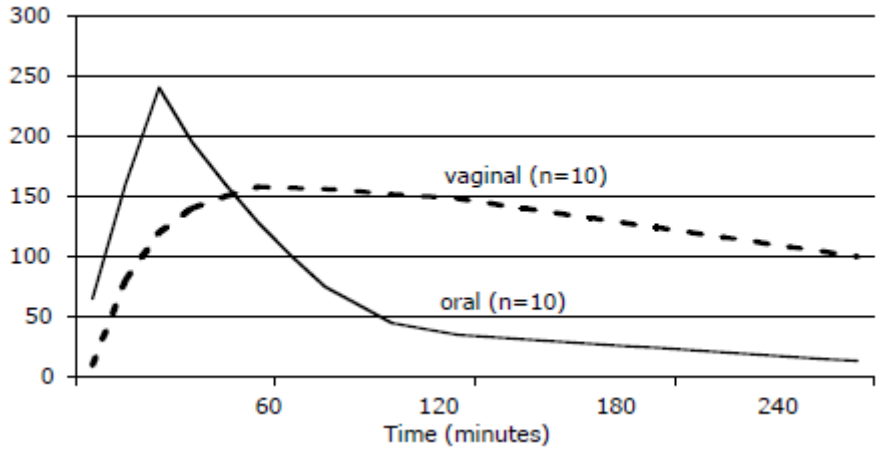
It differs structurally from prostaglandin E by of the presence of a methyl ester at C-1, a methyl group at C-16 and a hydroxyl group at C-16 rather than C-15. These structural changes confer an increase in the anti-secretory potency, duration of action of misoprostol, improved oral activity and the safety profile of the drug when compared with prostaglandin E. Chemical instability of the drug at room temperature was resolved through the dispersion of misoprostol in hydroxylpropylmethylcellulosa.[51]

Misoprostol has antisecretory and cytoprotective actions that can be administered orally, vaginally, sublingually, buccal and per rectally.[40]

Misoprostol is absorbed extensively and undergoes rapid de-esterification by the liver to form a free acid (misoprostol acid) (MPA) – pharmacologically active metabolite. The pharmacokinetic characteristics of misoprostol differ substantially according to the route of administration. Less than 1% of misoprostol's active metabolite is excreted in the urine.[56] The Tmax of misoprostol acid is 12 ± 3 minutes with a terminal half-life of 20 to 40 minutes after oral administration of misoprostol.[57]

Vaginal misoprostol is associated with slower absorption, lower peak plasma levels and slower clearance hence increasing the bioavailability, similar to an extended release preparation.[58]

However, the concentrations obtained by vaginal administration are more variable than after oral administration as they depend on the pH and quantity of the vaginal secretions, the existence of bleeding and the dissolution of the tablet. Misoprostol is stored at room temperature.[51]



Mean plasma concentrations of misoprostol acid over time with oral and vaginal administration modified from Zieman et al., 1997.

Effects of misoprostol on the uterus and the cervix

Misoprostol acts an effective myometrial stimulant of the gravid uterus by selective binding to EP-2/EP-3 prostaglandin receptors.[59]

Misoprostol, has uterotonic and cervical softening effects in the female genital tract. It causes an increase in uterine tonus. It causes disintegration and dissolution of the collagen in the cervix causing cervical softening.

Misoprostol has a cervical priming effect. Less force was required for mechanical dilatation of the cervix following use of misoprostol. Along with increasing uterine contractions misoprostol also has a direct softening effect on the cervix.[51]

Side effects of misoprostol

Toxic doses of misoprostol have not been determined; however, cumulative doses of up to 2200 μg administered over a period of 12 hours have been tolerated by pregnant women, with no serious adverse effects.[57]

Repeat dosing of misoprostol is not based on systemic plasma levels of misoprostol acid (MPA) but on cervical and uterine response. Misoprostol is a safe and well-tolerated drug. Diarrhoea, nausea and vomiting, fever with chills are the common self-limited side effects.[52]

Misoprostol administration is associated with uterine contractile abnormalities such as uterine tachysystole, uterine hypertonus or hypersystole and uterine hyperstimulation associated with fetal heart changes such as persistent decelerations, tachycardia and/or reduced beat to beat variability. The incidence of meconium stained amniotic fluid was also higher with misoprostol.[62] Incidence of rupture uterus especially when used in a scarred uterus was reported.

Misoprostol has no known drug interactions.[60]

First trimester exposure to misoprostol is associated with an increased likelihood of delivering babies with Mobius syndrome, other associated anomalies include fetal skull defects, cranial nerve palsies, facial malformations, and limb defects.[60,57] These effects were observed with misoprostol dosing of 400 to 1600 mcg (median dose 800 mcg) and it was estimated to effect < 1% of exposed fetuses.[61]

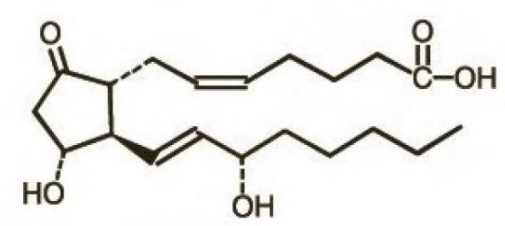
In 2002, the FDA approved a new label on the use of misoprostol during pregnancy for cervical ripening and induction of labour. ACOG recommends, that 25 mcg of misoprostol should be considered as the initial dose for cervical ripening and labour induction and the

frequency of administration should not be more than every 3-6 hours. ACOG further concluded that majority of adverse maternal and neonatal outcomes were associated with use of misoprostol doses >25 mcg.[33]

Low dose (25 mcg) misoprostol by either vaginal or oral route 6th hourly and 2nd hourly respectively are recommended for induction of labour by World Health Organization (WHO).[40]

DINOPROSTONE

Dinoprostone is a synthetic Prostaglandin E_2 (PGE_2) analogue. It is chemically designated as (5Z, 11a, 13E, 15S)-11,15-Dihydroxy-9-oxo-prosta-5,13-dien-1-oic acid. The molecular formula is $C_{20}H_{32}O_5$ and the molecular weight is 352.5. Dinoprostone is a white crystalline powder with a melting point in the range of 65˚ to 69˚C. [63]



Dinoprostone received FDA approval for cervical ripening in 1993, and is the first commercially available prostaglandin gel. Dinoprostone is available in two formulations – an intracervical gel and a vaginal insert. Systemic absorption of Dinoprostone occurs via vaginal route. Although, the cervical gel releases prostaglandins at a faster rate than vaginal insert, vaginal administration is associated with gradual increase in plasma levels hence achieving longer duration of action. [52]

The cervical gel must be refrigerated and thawed prior to use and the total maximum dose is 1.5 mg within a 24-hour period. Oxytocin augmentation should not be initiated until 6-12 hours after the final dose. [52]

10 mg Dinoprostone Vaginal Insert is the other formulation of dinoprostone. It is designed to release approximately 0.3 mg/hour drug over a period of 12 hours. The vaginal insert should be removed upon onset of active labour or after 12 hours of insertion.[64]

The biochemical changes caused by PGE_2 induced ripening are similar to the natural cervical ripening process and these changes occur independent of myometrial activity, however it is likely that endocervical administration PGE_2 causes effacement and softening of the cervix by a combination of contraction inducing and cervical ripening actions. These changes occur secondary to collagen degradation from collagenase secretion.

PGE_2 is completely metabolized in humans, extensively metabolized in lungs and further in liver and kidneys. Major route of elimination is its metabolism in the kidneys. The drug needs to be stored under continuous refrigeration (36° to 46°F; 2° to 8°C).[63]

A maximum cumulative dose of 1.5 mg of Dinoprostone within a 24-hour period can be administered with an interval of 6-12 hours between successive doses.[33]

Side effects of Dinoprostone

The most significant adverse effect of dinoprostone administration is uterine hyperstimulation. Studies have shown that rate of hyperstimulation of uterus with FHR changes is approximately 1% with intracervical gel and 5% with vaginal gel.[52]

Side effects such as nausea & vomiting, fever and diarrhea were reported in a few cases. ACOG recommends that caution to exercised when dinoprostone is used in patients with glaucoma, severe renal or hepatic dysfunction.[33]

MATERIALS &METHODS

MATERIAL AND METHODS

Study Design: It is a randomized interventional study (Single blinded study).

Source of Data: The study was conducted from December 2016 to March 2018 at R L Jalappa Hospital and Research Center, Tamaka, Kolar attached to Sri Devaraj Urs Medical College.

Sample Size: 260 cases (130 in misoprostol and 130 in dinoprostone group)

Was estimated based on the induction delivery interval between two groups (Misoprostol and Dinoprostone) as 20.08 ± 8.24 hours and 23.19 ± 9.59 hours respectively from the study by Monica Parmar et al. Considering these values at 5% alpha error and 80% power a sample size of 130 in each group was obtained from Open Epi software.

Sample Size for Comparing Two Means

Input Data

Confidence Interval (2-sided)	95%
Power	80%
Ratio of sample size (dinoprostone group/misoprostol group)	1

	Misoprostol Group	**Dinoprostone Group**	**Mean difference[1]**
Mean	20.08	23.19	-3.11
Standard deviation	8.24	9.59	
Variance	67.8976	91.9681	

Sample size of Misoprostol group	130
Sample size of Dinoprostone group	130
Total sample size	260

The sample size was calculated by the formula:

$$\text{Sample size} = \frac{2SD^2(Z_{\alpha/2}+Z_{\beta})^2}{d^2}$$

SD – Standard deviation = From previous studies or pilot study

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ (From Z table) at type 1 error of 5%

$Z_{\beta} = Z_{0.20} = 0.842$ (From Z table) at 80% power

d = effect size = difference between mean values

So now formula will be

$$\text{Sample size} = \frac{2SD^2(1.96+0.84)^2}{d^2}$$

Inclusion Criteria:

- Gestational age of 37 completed weeks or more
- Vertex presentation
- Singleton pregnancy
- Reactive Non stress test
- Modified Bishop score ≤ 5
- Intact membranes

Exclusion Criteria:

- Previous cesarean section, or any previous surgery of the uterus
- Parity greater than 5
- Any contraindication for vaginal delivery
- Modified Bishop score > 5
- Contraindication to the use of prostaglandins

Method of collection of data

Subjects: A total number of 260 pregnant women fulfilling the inclusion criteria were incorporated into the study after obtaining an informed consent.

Detailed history regarding age, parity, period of gestation, menstrual history, obstetric history, past history, and any complications in present pregnancy were taken. Indication for induction of labour was ascertained.

General clinical examination and complete obstetric examination was performed. Abdominal examination was done to determine the presentation, uterine tone and fetal heart rate. Per vaginal examination was done to assess the modified Bishop's score and to rule out cephalopelvic disproportion.

Necessary investigations along with a Non stress test (NST) and obstetric scan was done to ascertain fetal wellbeing.

Following exclusion of uterine contractions or a non reassuring NST and confirmation of modified Bishop's score ≤ 5, patients were randomized to receive either misoprostol or dinoprostone.

Route of drug intervention:

Subjects were randomized into two groups (Dinoprostone group & Misoprostol group).

Dinoprostone group (130 women) received 0.5 mg of dinoprostone gel intracervically under aseptic precautions, doses repeated every 8^{th} hourly up to a maximum of 3 doses till adequate uterine contractions (3 contractions in 10 minutes) were initiated or modified Bishop's score was >6 or cervical dilatation ≥3cms.

Misoprostol group (130 women) received 25µg of misoprostol in posterior fornix of vagina under aseptic precautions, doses repeated every 4^{th} hourly up to a maximum of

6 doses till adequate uterine contractions (3 contractions in 10 minutes) were initiated or modified Bishop's score was >6 or cervical dilatation ≥3cms.

Analysis of progression:

In both groups, progress of labour was monitored by a Partogram in active stage of labour. Labour was augmented with oxytocin if required. All cases were monitored by electronic fetal monitoring. If any fetal distress was present, operative intervention was undertaken.

If the Modified Bishop's Score remained unfavorable and/or no adequate uterine contractions were initiated even after 6 doses of misoprostol in the misoprostol group and 3 doses of dinoprostone in the dinoprostone group it was considered as failed induction. In such cases, either patient was considered for augmentation with oxytocin or decision for caesarean section was taken.

Total dose of induction, induction to active phase interval, induction to delivery interval, requirement of oxytocin augmentation, mode of delivery, meconium staining of liquor, fetal heart rate tracing abnormalities, maternal adverse effects and neonatal outcomes like APGAR score and requirement of Neonatal intensive care unit admission were recorded in both the groups.

Statistical analysis

- Data was entered in a Microsoft excel data sheet and was be analyzed using SPSS 22 version software.
- The primary outcomes are to determine the safety & efficacy of misoprostol and dinoprostone for Induction of labour. Study groups (Dinoprostone Versus Misoprostol) was considered as primary explanatory variable.

- Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.
- Data was represented using appropriate diagrams like bar diagram and box plots.
- For normally distributed Quantitative parameters the mean values were compared between study groups using **Independent sample t-test** (2 groups).
- For non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using **Mann Whitney u test** (2 groups).
- Categorical outcomes were compared between study groups using **Chi square test**.
- **P value** < 0.05 was considered statistically significant.
- **Statistical software**: IBM SPSS version 22 was used for statistical analysis. (Machines IB. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp Armonk, NY; 2013.)

RESULTS

RESULTS

A total 260 women were included in the analysis.

Table 1: Descriptive analysis of study groups in the study population

Study group	Number (N=260)	Percentage
Dinoprostone	130	50.00%
Misoprostol	130	50.00%

In the study, 130 (50%) women were in the Dinoprostone group and remaining 130 (50%) women were in the Misoprostol group. (Table 1)

Table 2: Comparison of mean age between the study groups

Parameter	Groups (N=260)		P value
	Dinoprostone (N=130)	Misoprostol (N=130)	
Age (Years) Mean± STD	23.05 ± 2.68	23.48 ± 3.71	0.292

The mean age was 23.05 ± 2.68 years in the Dinoprostone group and 23.48 ± 3.71 years in the misoprostol group. The difference between the two groups was statistically not significant (P value 0.292). (Table 2 & Graph 1)

Graph 1: Comparison of mean age between the study groups

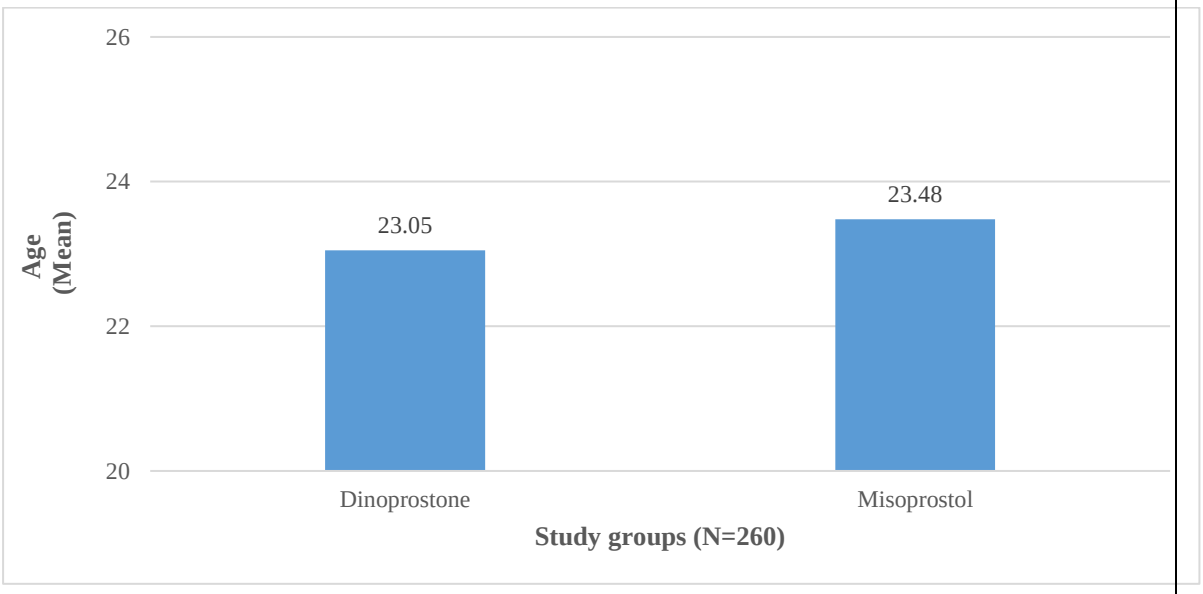


Table 3: Age distribution between the study groups

Age group	Groups (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
19-20 years	23 (17.7%)	29 (22.3%)	2.020	0.568
21-25 years	84 (64.6%)	77 (59.2%)		
26-30 years	22 (16.9%)	21 (16.2%)		
31-35 years	1 (0.8%)	3 (2.3%)		

Among the women in the Dinoprostone group, 23 (17.7%) were aged between 19 to 20 years, 84 (64.6%) were aged between 21 to 25 years, 22 (16.9%) were aged between 26 to 30 years and 1 (0.8%) was aged between 31 to 35 years. In the misoprostol group, 29 (22.3%) were aged between 19 to 20 years, 77 (59.2%) were aged between 21 to 25, 21 (16.2%) were aged between 26 to 30 years and 3 (2.3%) were aged between 31 to 35 years. The difference between study groups was statistically not significant (P value 0.568). (Table 3 & Graph 2)

Graph 2: Age distribution between the study groups

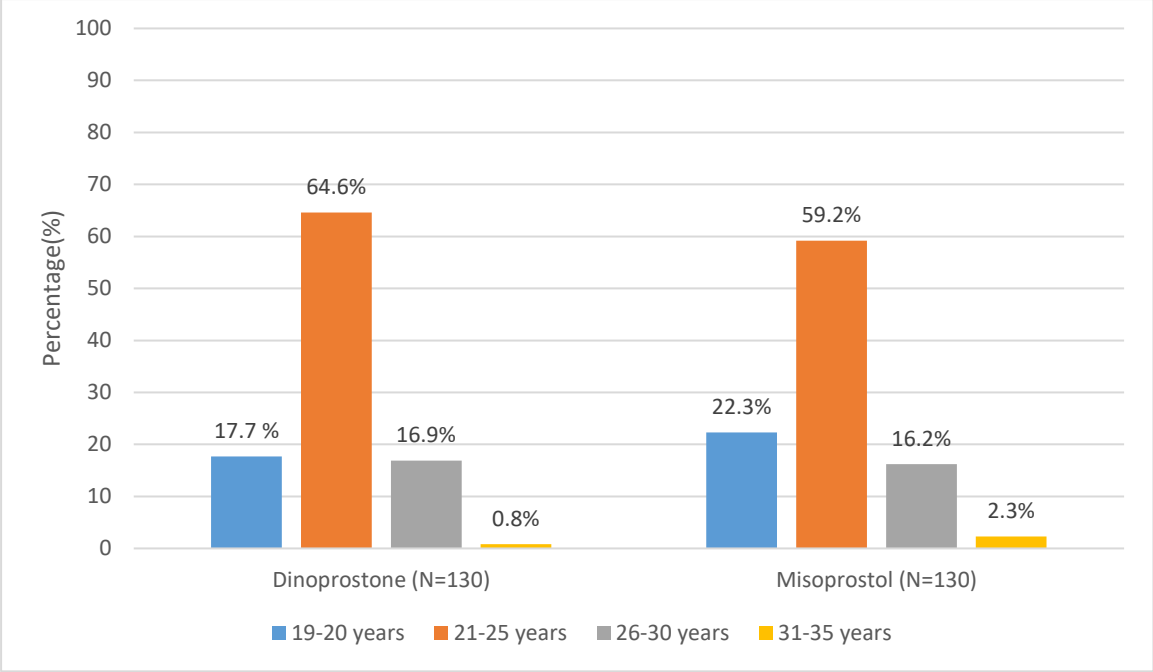


Table 4: Parity distribution between the study groups

Parity	Groups (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
Primigravida	82 (63.1%)	57 (43.8%)	9.662	0.002
Multigravida	48 (36.9%)	73 (56.2%)		

In the Dinoprostone group, 82 (63.1%) were primigravida and 48 (36.9%) were multigravida. While, in the misoprostol group, 57 (43.8%) were primigravida and 73 (56.2%) were multigravida. The difference in the distribution of parity between the groups was statistically significant (P value 0.002). (Table 4 & Graph 3)

Graph 3: Parity distribution between the study groups

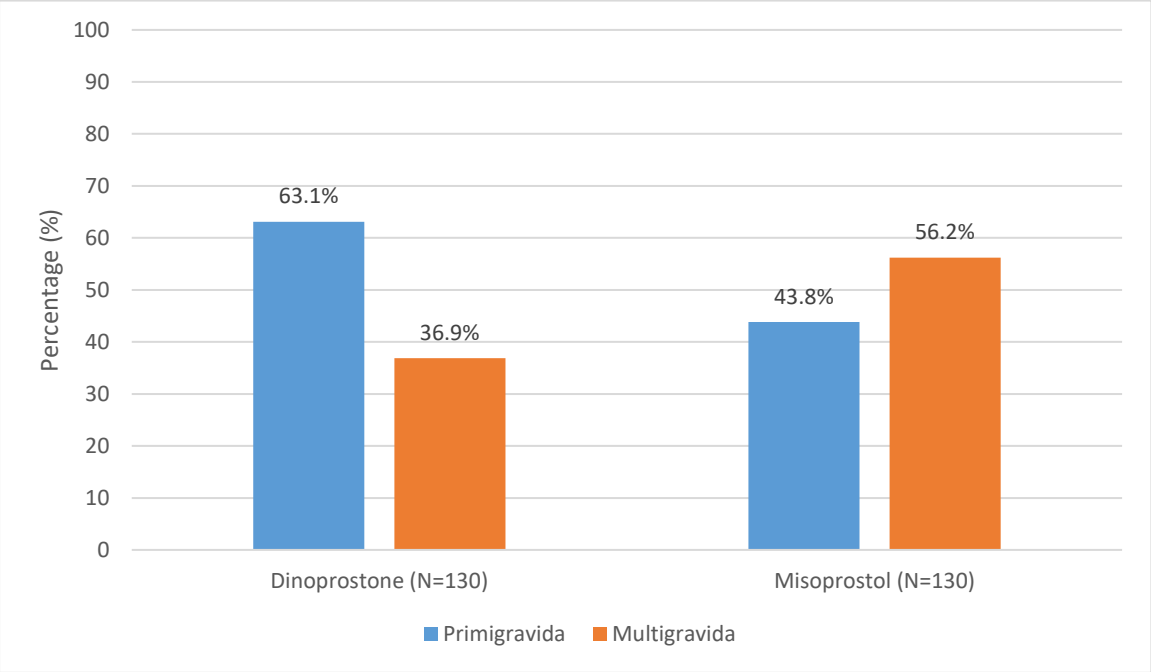


Table 5: Comparison of Period of Gestation between the study groups

Gestational age (weeks)	Groups (N=260)		P-value
	Dinoprostone (N=130)	Misoprostol (N=130)	
37 – 38+6	8 (6.2%)	10 (7.7%)	0.809
39– 39+6	13 (10%)	12 (9.2%)	
40 – 40+6	97 (74.6%)	92 (70.8%)	
41 – 41+6	12 (9.2%)	16 (12.3%)	

With regards to Period of gestation distribution between the study groups, in the dinoprostone group, 8 (6.2%) in 37 - 38+6 weeks, 13 (10%) in 39 - 39+6 weeks, 97 (74.6%) in 40 - 40+6 weeks and 12 (9.2%) in 41 - 41+6 weeks. In the misoprostol group, 10 (7.7%) in 37 - 38+6 weeks, 12 (9.2%) in 39- 39+6 weeks, 92 (70.8%) in 40 - 40+6 weeks, 16 (12.3%) in 41 - 41+6 weeks. The difference between the study groups with regards to period of gestation was not statistically significant (P value 0.809). (Table 5 & Graph 4)

Graph 4: Period of Gestation distribution between the study groups

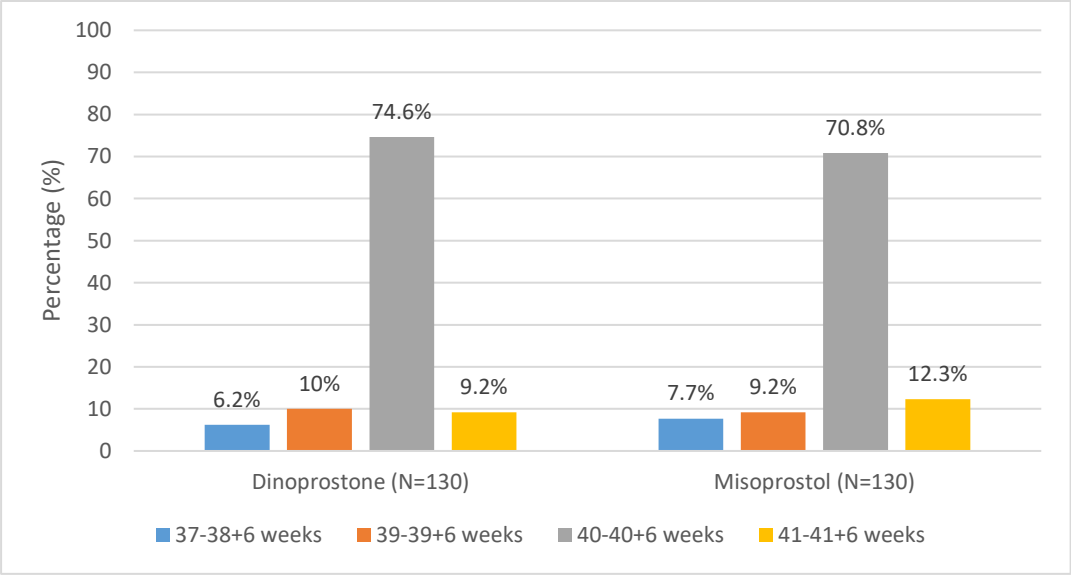


Table 6: Comparison of indication for induction between study groups

Indication for induction	Groups (N=260)		P value
	Dinoprostone (N=130)	Misoprostol (N=130)	
Post-dated pregnancy	109 (83.84%)	108 (83.07%)	0.349
Preeclampsia	14 (10.76%)	12 (9.23%)	
Oligohydramnios	7 (5.38%)	15 (11.53%)	
Rh Negative pregnancy	9 (6.92%)	7 (5.38%)	

The commonest indication for induction in both the groups was Post-dated pregnancy; 109 (83.84%) and 108 (83.07%) in the dinoprostone and misoprostol groups respectively. This was followed by preeclampsia in the dinoprostone group 14 (10.76%) and oligohydramnios in the misoprostol group 15 (11.53%). However, these differences were not statistically significant (P value 0.349). (Table 6 & Graph 5)

Graph 5: Comparison of Indication for Induction between the study groups

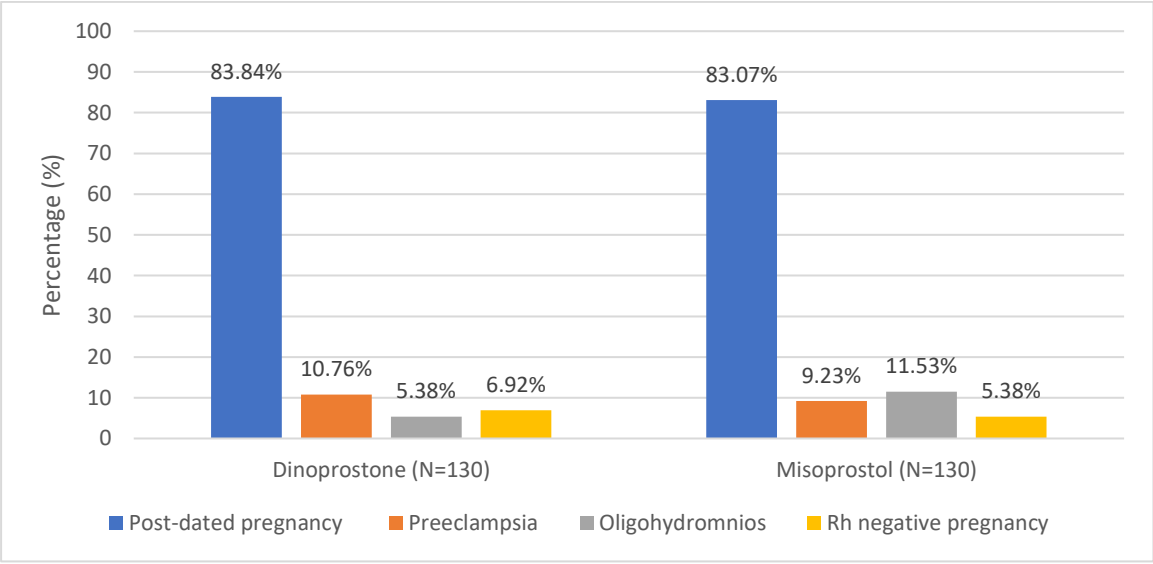


Table 7: Comparison of pre-induction Modified Bishop's Score between study groups

Pre-induction Modified Bishop's score	Group (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
2	37 (28.5%)	42 (32.3%)	5.32	0.069
3	44 (33.8%)	56 (43.1%)		
4	49 (37.7%)	32 (24.6%)		

In the dinoprostone group, 37 (28.5%) women had a pre-induction Modified Bishop's score of 2, 44 (33.8%) had a score of 3 and 49 (37.7%) had a score of 4. In the misoprostol group, 42 (32.3%) women had a pre-induction Bishop's score of 2, 56 (43.1%) had a score of 3 and 32 (24.6%) had a score of 4. The difference in the Modified Pre-induction Bishop's score between both the groups was not statistically significant (P value 0.069). (Table 7 & Graph 6)

Graph 6: Comparison of pre-induction Modified Bishop's Score between study groups

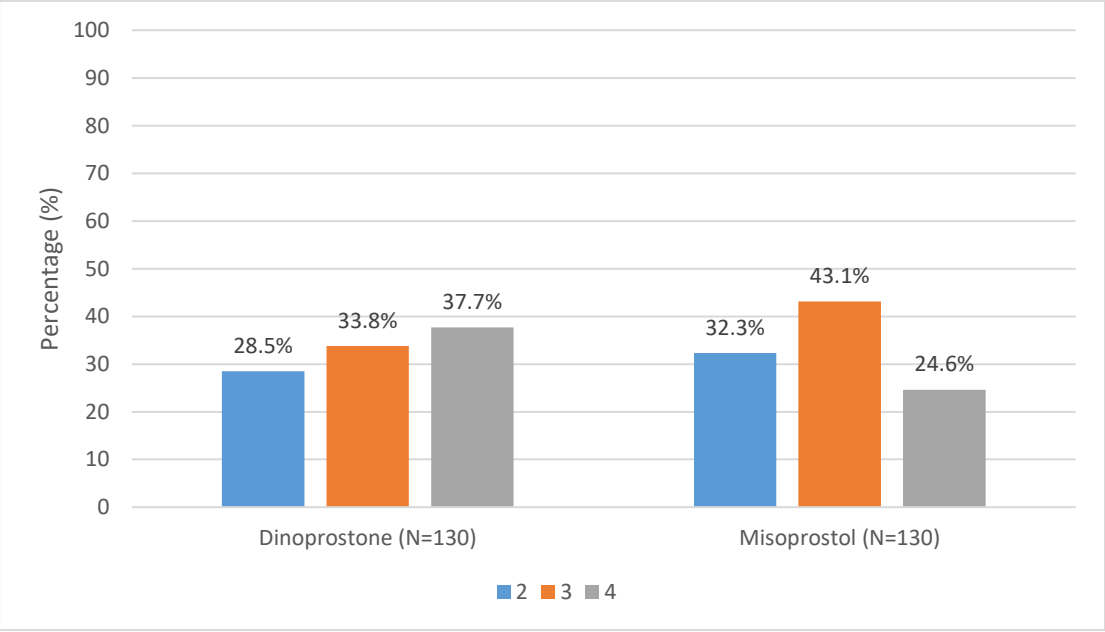


Table 8: Comparison of number of doses between study groups

Number of doses	Groups(N=260)		P-value
	Dinoprostone (N=130)	Misoprostol (N=130)	
1	72 (55.4%)	22 (16.9%)	*
2	41 (31.5%)	47 (36.2%)	
3	17 (13.1%)	18 (13.8%)	
4	0 (0%)	28 (21.5%)	
5	0 (0%)	7 (5.4%)	
6	0 (0%)	8 (6.2%)	

**No statistical test was applied- due to 0 subjects in the cells.*

In the dinoprostone group, 72 (55.4%) women required one dose, 41 (31.5%) women required 2 doses and 17 (13.1%) women required 3 doses. In the misoprostol group, 22 (16.9%) women required one dose, 47 (36.2%) women required 2 doses, 18 (13.8%) women required 3 doses, 28 (21.5%) women required 4 doses, 7 (5.4%) women required 5 doses and 8 (6.2%) women required 6 doses. (Table 8)

Table 9: Comparison of mean Induction to Active phase Interval between study groups

Parameter	Groups (N=197)		P value
	Dinoprostone (N=98)	Misoprostol (N=99)	
Induction to Active phase interval (in hours) Mean± STD	10.83 ± 3.61	9.60 ± 3.13	0.011

The mean duration of induction to active phase interval was 10.83 ± 3.61 hours in the dinoprostone group and it was 9.60 ± 3.13 hours in the misoprostol group. The difference between the two groups was statistically significant (P value 0.011). (Table 9 & Graph 7)

Graph 7: Comparison of mean Induction to Active phase Interval between the study groups

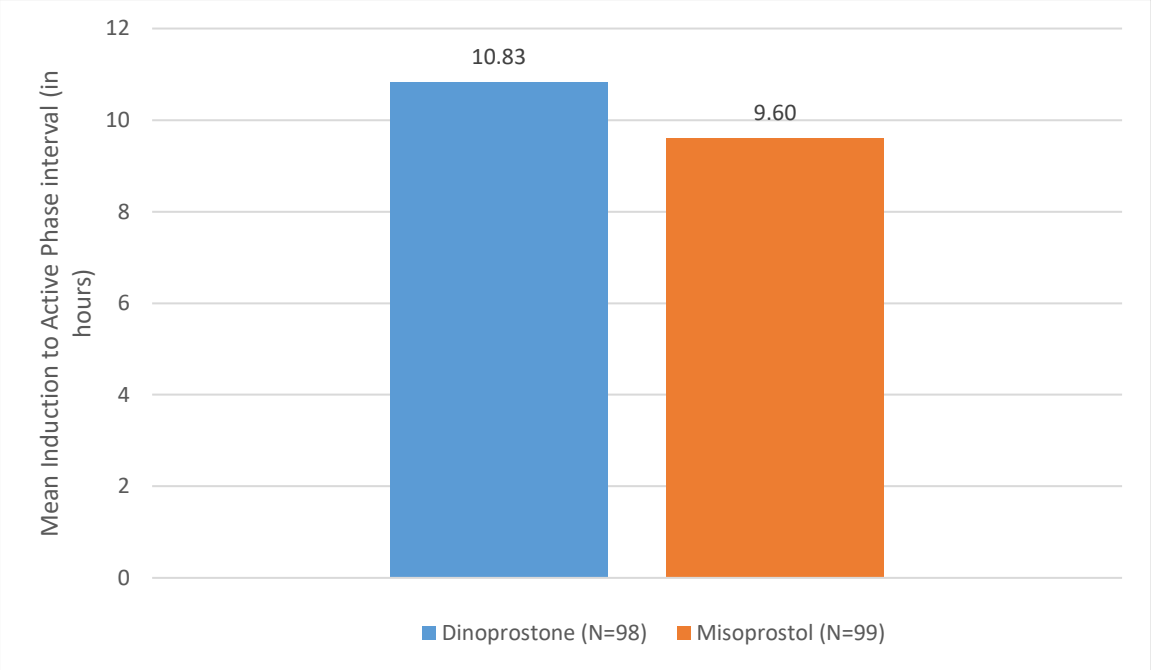


Table 10: Comparison of mean Induction to Delivery Interval between the study groups

Parameter	Groups (N= 190)		P value
	Dinoprostone (N= 94)	Misoprostol (N=96)	
Induction to delivery interval (in hours) Mean± STD	16.08 ± 4.54	14.49 ± 3.93	0.011

The mean duration of induction to delivery interval was 16.08 ± 4.54 hours in dinoprostone and it was 14.49 ± 3.93 hours in misoprostol. The difference between the two groups was statistically significant (P value 0.011). (Table 10 & Graph 8)

Graph 8: Comparison of mean Induction to Delivery Interval between the study groups

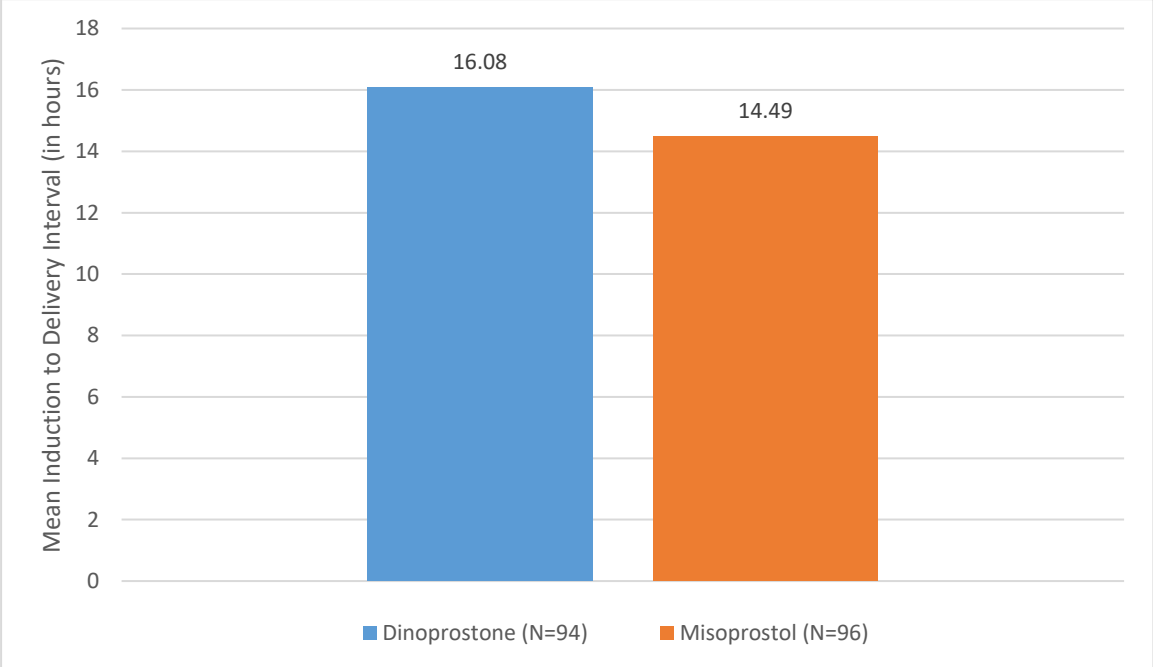


Table 11: Comparison of mode of delivery between the study groups

Mode of delivery	Groups (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
Vaginal delivery	87 (66.9%)	89 (68.5%)	0.080	0.994
Caesarean section	36 (27.7%)	34 (26.2%)		
Vacuum assisted vaginal delivery	5 (3.8%)	5 (3.8%)		
Forceps assisted vaginal delivery	2 (1.5%)	2 (1.5%)		

In the dinoprostone group, 87 (66.9%) women delivered vaginally, 36 (27.7%) women underwent caesarean delivery, 5 (3.8%) women delivered by vacuum assisted vaginal delivery and 5 (3.8%) women had forceps assisted vaginal delivery. In the misoprostol group, 89 (68.5%) women delivered vaginally, 34 (26.2%) women underwent caesarean section, 5 (3.8%) women delivered by vacuum assisted vaginal delivery and 2 (1.5%) women had forceps assisted vaginal delivery. The difference in the proportion of mode of delivery between study group was statistically not significant (P value 0.994). (Table 11 & Graph 9)

Graph 9: Comparison of mode of delivery between the study groups

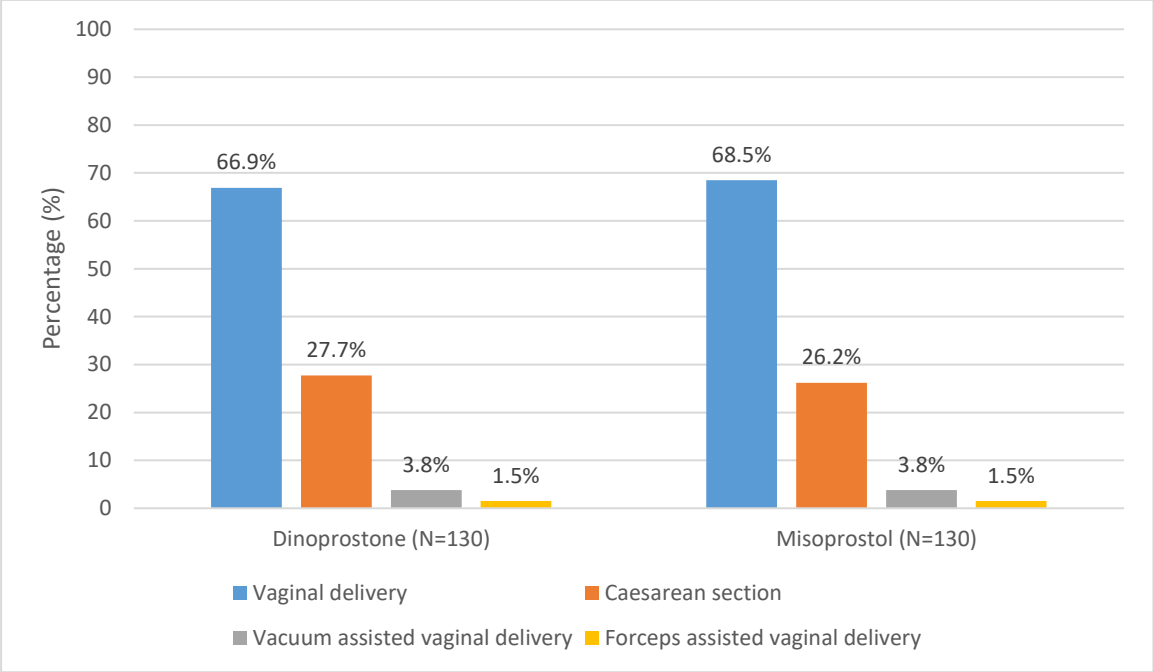


Table 12: Comparison of indication for caesarean section between the study groups

Indication for caesarean section	Groups (N=70)		Chi square	P-value
	Dinoprostone (N=36)	Misoprostol (N=34)		
Fetal distress	22 (61.1%)	25 (73.5%)	1.326	0.515
Failure of induction	13 (36.1%)	8 (23.5%)		
Deep Transverse Arrest	1 (2.8%)	1 (2.9%)		

In dinoprostone group, 22 (61.1%) women had fetal distress, failure of induction was seen in 13 (36.1%) women and 1 (2.8%) woman had Deep Transverse Arrest. In the misoprostol group, 25 (73.5%) women had fetal distress, failure of induction was seen in 8 (23.5%) women and 1 (2.9%) woman had Deep Transverse Arrest. The difference in the proportion of indication for caesarean between study group was statistically not significant (P value 0.515). (Table 12 & Graph 10)

Graph 10: Comparison of indication for Caesarean section between the study groups

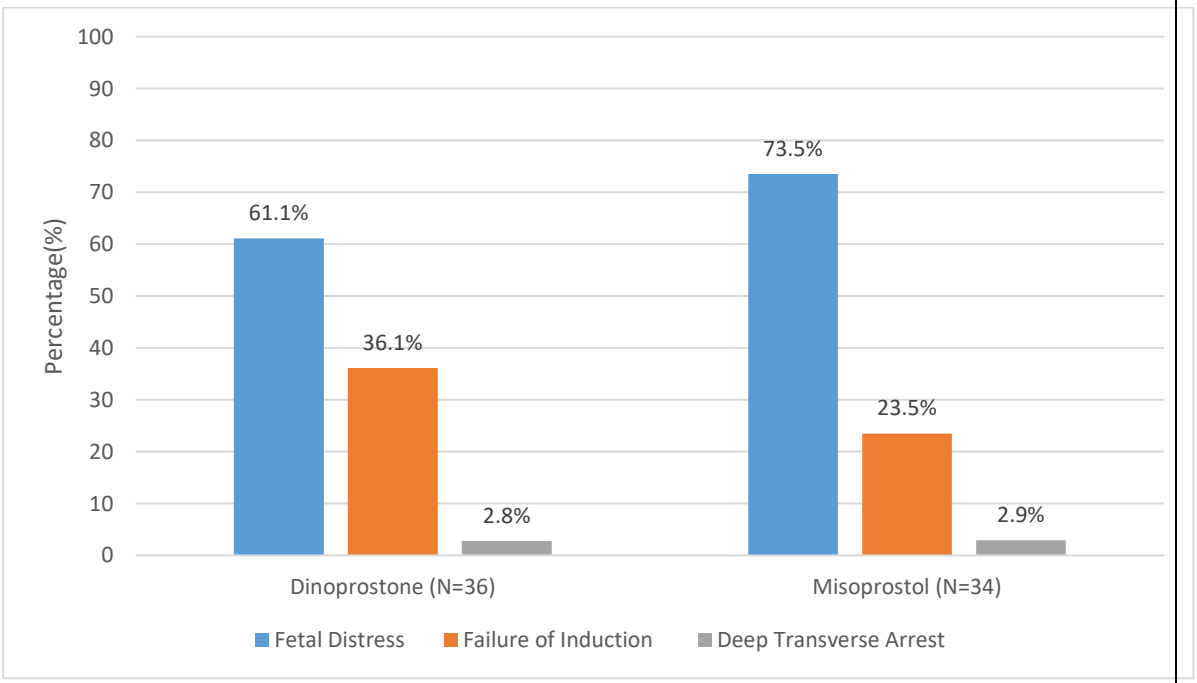


Table 13: Comparison of oxytocin augmentation requirement between the study groups

Oxytocin augmentation	Groups (N=194)		Chi square	P-value
	Dinoprostone (N=96)	Misoprostol (N=98)		
Not required	44 (45.8%)	43 (43.90%)	0.075	0.784
Required	52(54.2%)	55 (56.10%)		

In the dinoprostone group, 52(54.2%) women required oxytocin augmentation while in the Misoprostol group, 55 (56.10%) women required oxytocin augmentation. The difference in the proportion of oxytocin augmentation between study group was statistically not significant (P value 0.784). (Table 13 & Graph 11)

Graph 11: Comparison of oxytocin augmentation requirement between the study groups

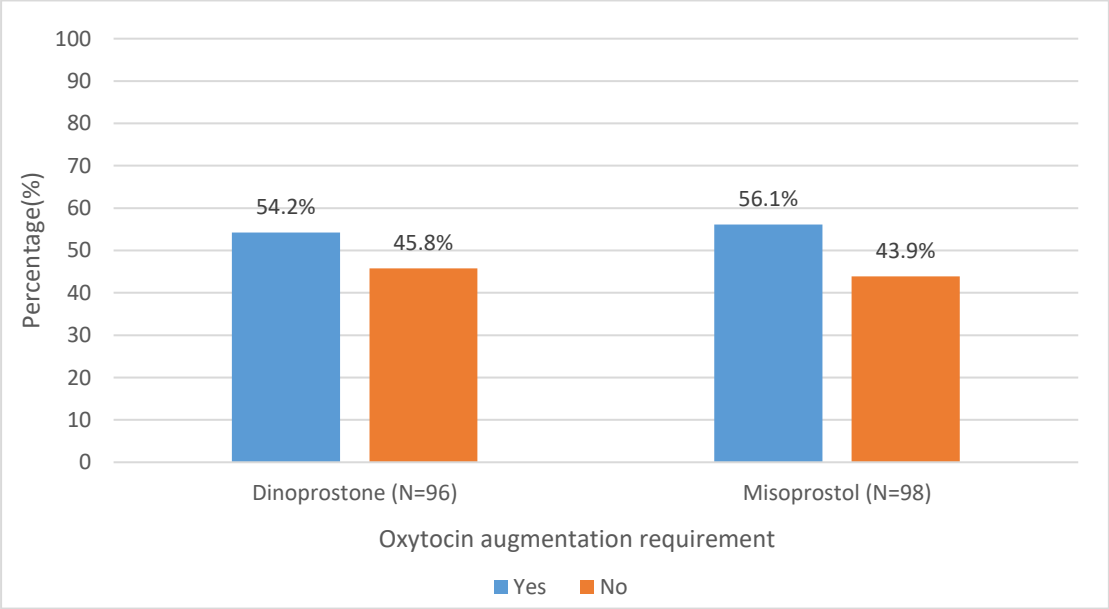


Table 14: Comparison of meconium staining of liquor between study groups

Liquor	Groups (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
Clear liquor	106 (81.53%)	99 (76.2%)	1.130	0.287
Meconium Stained liquor	24 (18.47%)	31 (23.8%)		

In the dinoprostone group, 106 (81.53%) women had clear liquor and 24 (18.47%) women had meconium stained liquor. In the misoprostol group, 99 (76.2%) women had clear liquor, 31 (23.8%) women had meconium stained liquor. The difference in the comparison of liquor between study group was statistically not significant (P value 0.287). (Table 14 & Graph 12)

Graph 12: Comparison of Meconium staining of liquor between the study groups

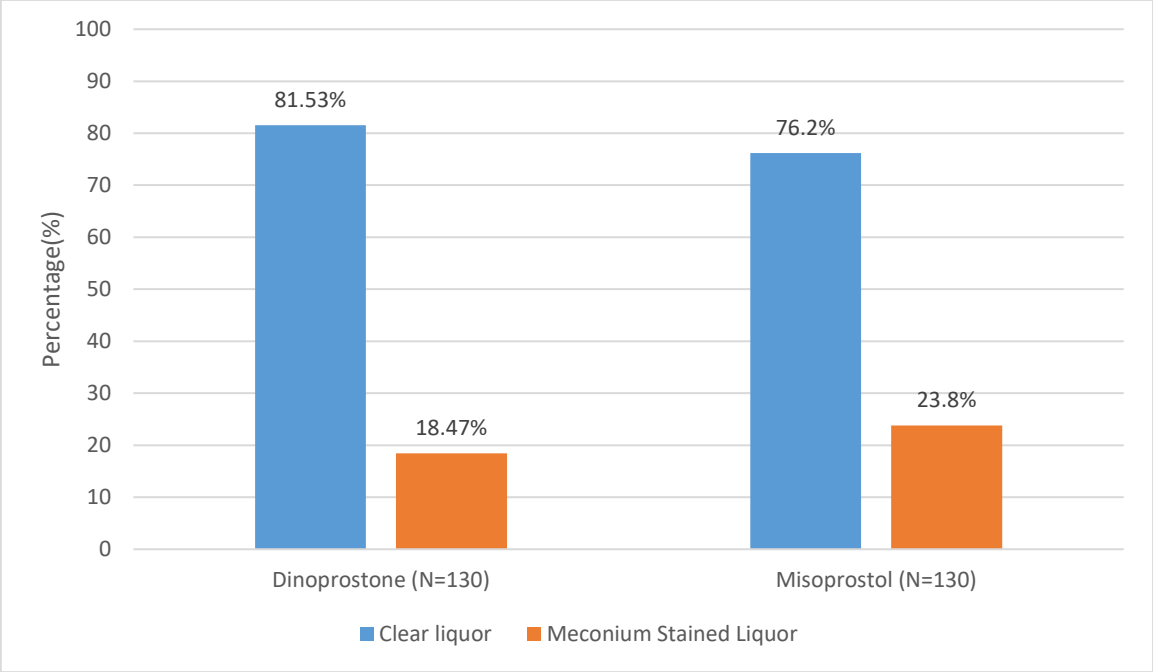


Table 15: Comparison of mean APGAR at 1 minute and 5 minutes between the study groups

Parameter	Groups (N=260)		P value
	Dinoprostone (N=130)	Misoprostol (N=130)	
APGAR at 1 minute Mean± STD	6.98 ± 0.17	6.93 ± 0.42	0.175
APGAR at 5 minutes Mean± STD	9 ± 0	8.95 ± 0.52	0.318

The mean APGAR score at 1 minute was 6.98 ± 0.17 in dinoprostone and 6.93 ± 0.42 in misoprostol. The difference between two groups was statistically not significant (P value 0.175). The mean APGAR score at 5 minutes was 9 ± 0 in dinoprostone and it was 8.95 ± 0.52 in misoprostol. The difference between two groups was statistically not significant (P value 0.318). (Table 15 & Graph 13)

Graph 13: Comparison of mean APGAR score at 1 minute & 5 minutes between the study groups

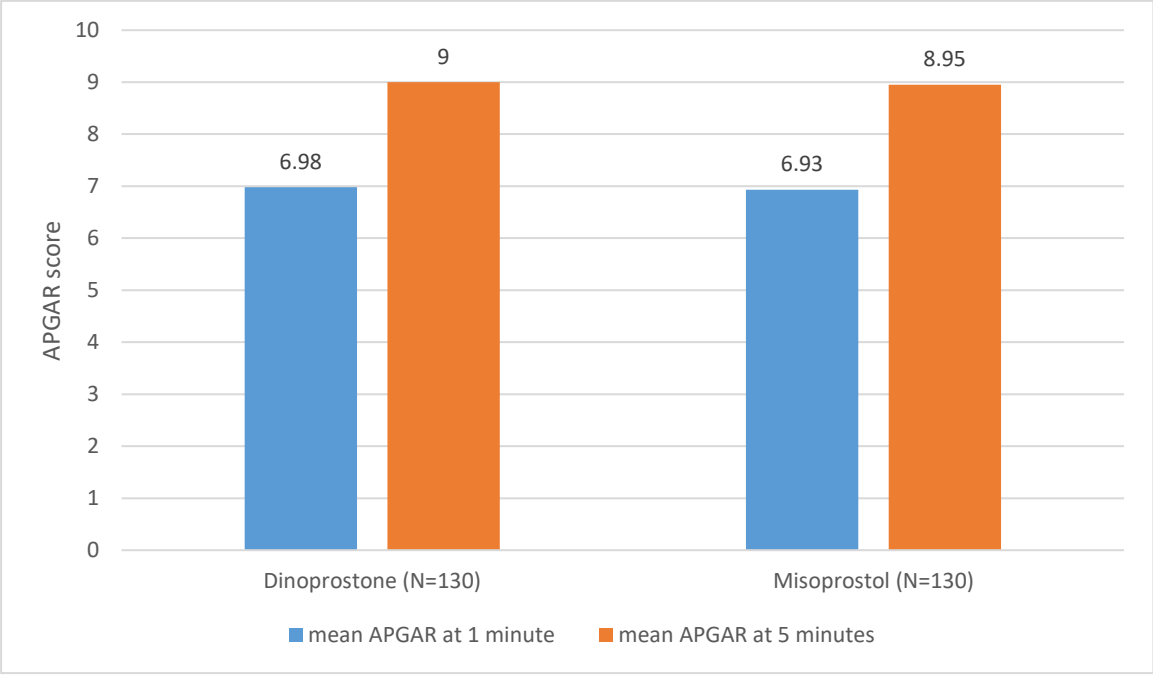


Table 16: Comparison of APGAR score at 1 minute between the study groups.

APGAR at 1 minute	Groups (N=260)		P value
	Dinoprostone (N=130)	Misoprostol (N=130)	
< 7	1 (0.77%)	5 (3.85%)	0.098
≥ 7	129 (99.23%)	125 (96.15%)	

3.85% in the misoprostol group and 0.77% in the dinoprostone group had an APGAR score of < 7 at 1 minute. This difference was not statistically significant (0.098). (Table 16)

Table 17: Comparison of NICU admission between the study groups

NICU admission	Groups (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
Yes	13(10%)	16 (12.3%)	0.349	0.555
No	117 (90%)	114 (87.7%)		

In the dinoprostone group, 13(10%) babies were admitted to the NICU. In the misoprostol group, 16 (12.3%) babies were admitted to the NICU. The difference in the proportion of NICU admission between study groups was statistically not significant (P value 0.555). (Table 17 & Graph 14)

Graph 14: Comparison of NICU admission between study groups

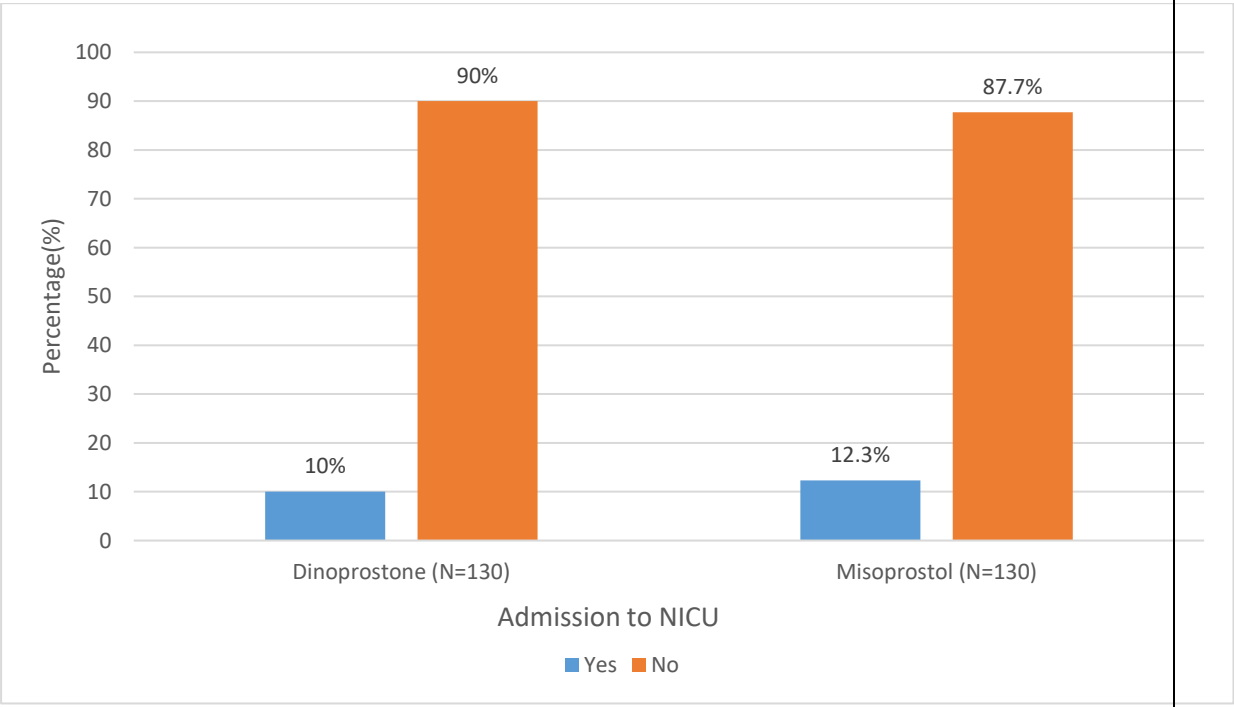


Table 18: Comparison of cause for NICU admission between study groups

Cause for NICU admission	Group (N=230)		P-value
	Dinoprostone (N=13)	Misoprostol (N=16)	
Post resuscitation care	1 (0.77%)	3 (2.31%)	0.635
Respiratory distress	11 (8.46%)	11 (8.46%)	
Secondary apnea	1 (0.77%)	1 (0.77%)	
Perinatal asphyxia	0 (0%)	1 (0.77%)	

In the dinoprostone group, 1 (0.77%) baby was admitted for post resuscitation care, 11 (8.46%) babies had respiratory distress and 1 (0.77%) baby had secondary apnea. In the misoprostol group, 3 (2.31%) babies were admitted for post resuscitation care, 11 (8.46%) babies had respiratory distress, 1 (0.77%) baby had secondary apnea and 1 (0.77%) baby had perinatal asphyxia and this caused perinatal mortality on day 1 of life. (Table 18 & Graph 15)

Graph 15: Comparison of groups with cause for NICU admission

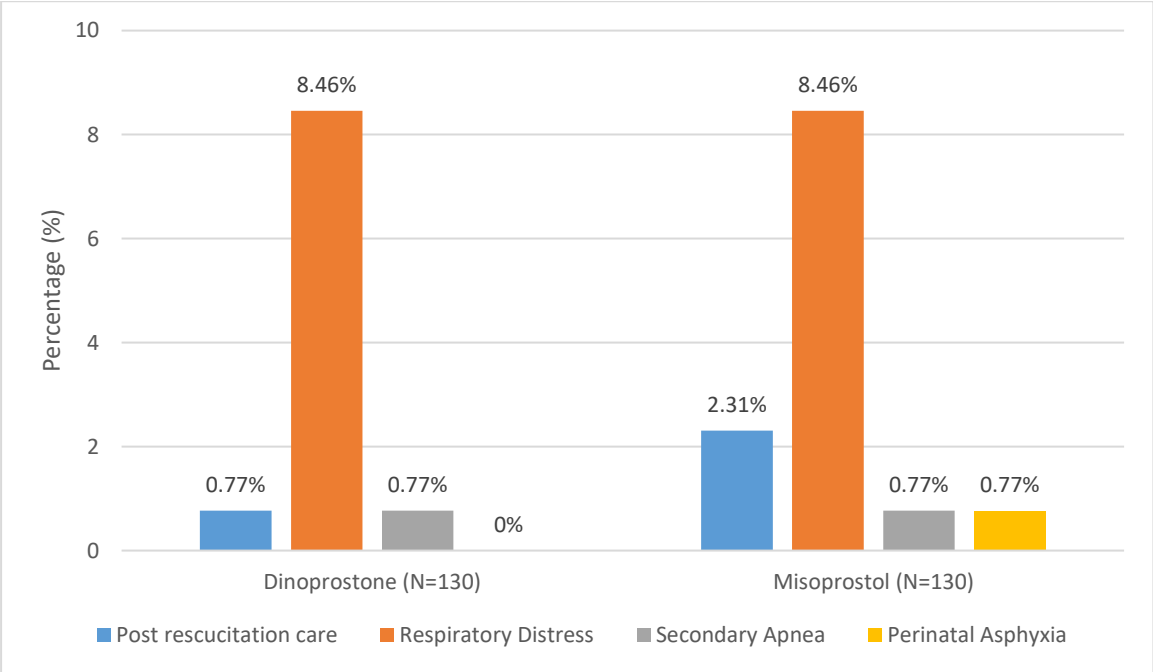


Table 19: Comparison of Maternal complications between the study groups

Maternal complications	Group (N=260)		Chi square	P-value
	Dinoprostone (N=130)	Misoprostol (N=130)		
Yes	12 (9.2%)	16 (12.3%)	3.467	0.424
No	118 (90.8%)	114 (87.8%)		

In the dinoprostone group, 12 (9.2%) women had maternal adverse effects. In the misoprostol group, 16 (12.3%) women had maternal adverse effects. The difference in the proportion of maternal adverse effects between study groups was statistically not significant (P value 0.424). (Table 19 & Graph 16)

Graph 16: Comparison of maternal complications between study groups

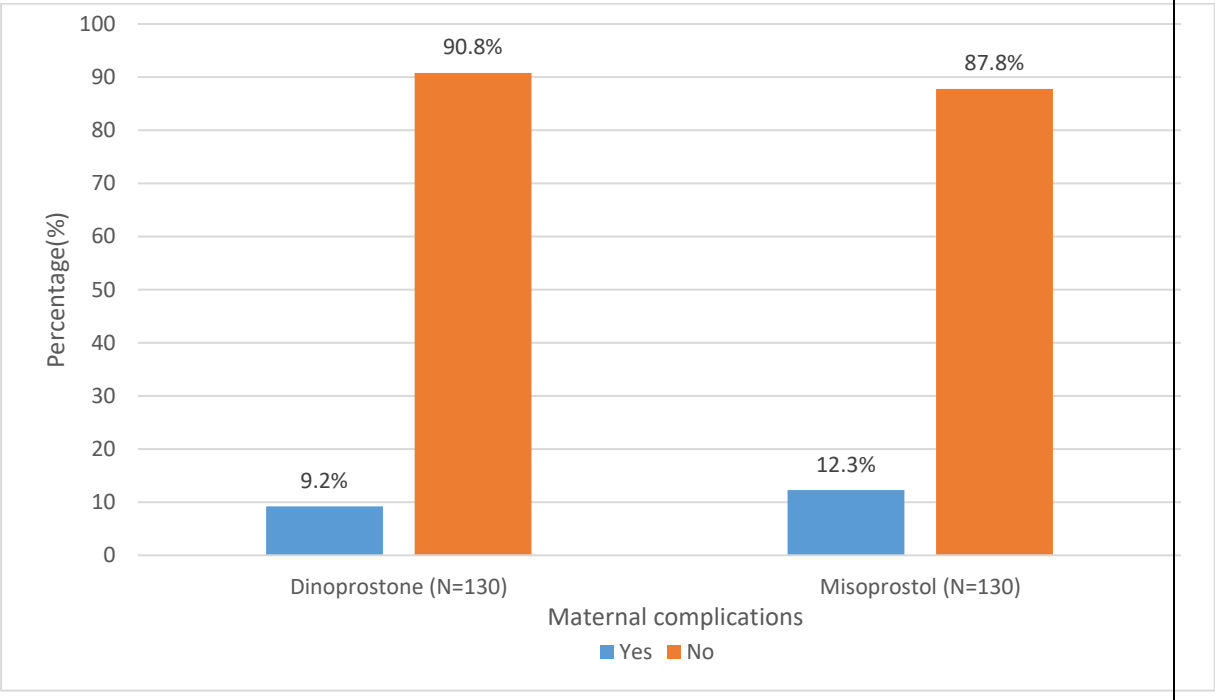


Table 20: Comparison of cause of maternal adverse effects between the study groups

Cause of maternal adverse effects	Groups (N=260)		P-value
	Dinoprostone (N=130)	Misoprostol (N=130)	
Diarrhea	1 (0.77%)	0 (0%)	*
Hyperstimulation of the uterus	3 (2.31%)	2 (1.53%)	0.651
Nausea & vomiting	3 (2.31%)	4 (3.08%)	0.701
PPH (atonic +traumatic)	3 (2.31%)	4 (3.08%)	0.701
Precipitate labour	1 (0.77%)	3 (2.31%)	0.313
Tachysystole	1 (0.77%)	1 (0.77%)	1.000
Fever	0 (0%)	2 (1.53%)	*

Cause of maternal complications were similar in both the groups, 9.2% in the dinoprostone and 12.3% in the misoprostol group with exception of maternal diarrhea which was seen in 0.77% with dinoprostone group and none with misoprostol and maternal fever which was seen in 1.53% of misoprostol and none in dinoprostone. Compared with dinoprostone, a relatively higher frequency of vomiting (3.08% versus 2.31%), Precipitate labour (2.31% versus 0.77%), postpartum haemorrhage (3.08% versus 2.31%) in the misoprostol group. Uterine hyperstimulation was more frequent with dinoprostone (2.31% versus 1.53%). No statistical significance was achieved for any of the above factors. No cases of uterine rupture or maternal death were reported in our study. (Table 20 & Graph 17)

Graph 17: Comparison of cause of maternal adverse effects between the study groups

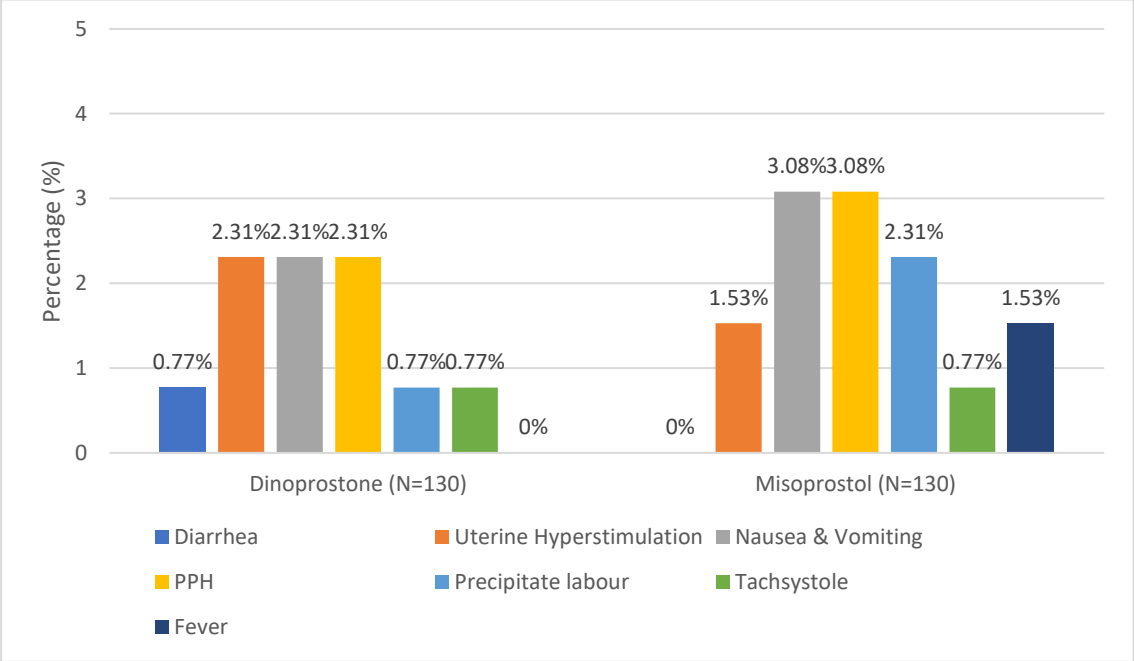


Table 21: Comparison of Fetal Heart Rate (FHR) tracing between the study groups

FHR tracing	Groups (N=260)		P-value
	Dinoprostone (N=130)	Misoprostol (N=130)	
Reactive FHR tracing	106(81.54%)	103 (79.23%)	0.639
Non-reassuring FHR tracing	24 (18.46%)	27 (20.77%)	

81.54% in the dinoprostone group and 79.23% in the misoprostol group had reactive FHR tracings. 18.46% in the dinoprostone and 20.77% in the misoprostol group had non-reassuring FHR tracings. This difference was not statistically significant (P value 0.639). (Table 21 & Graph 18)

Graph 18: Comparison of Fetal Heart Rate tracing between the study groups

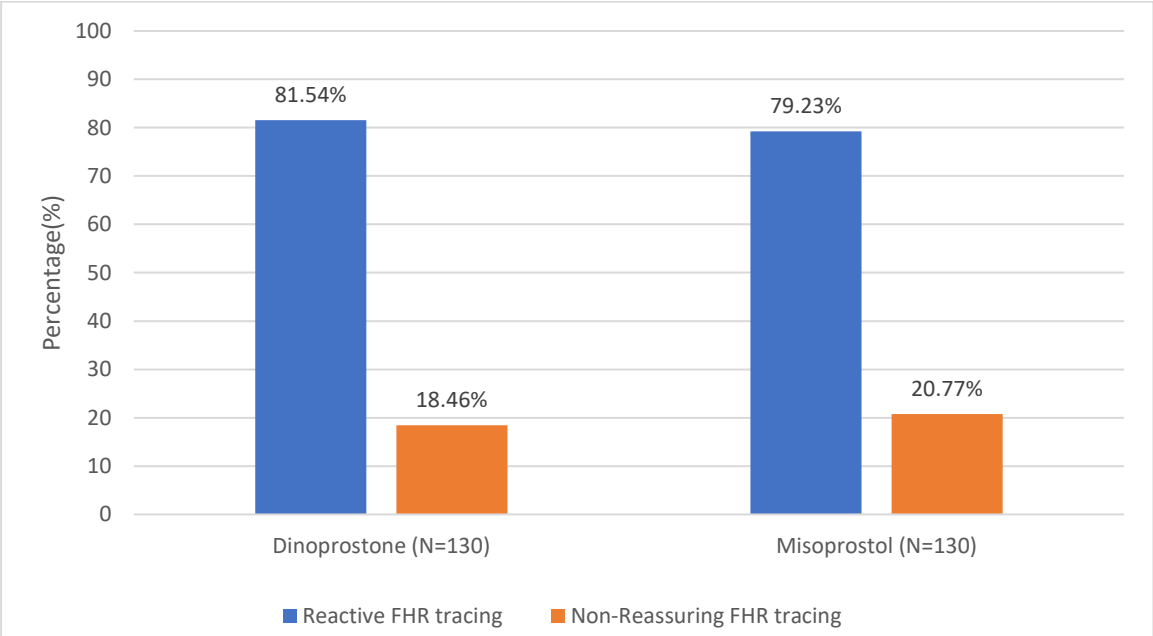
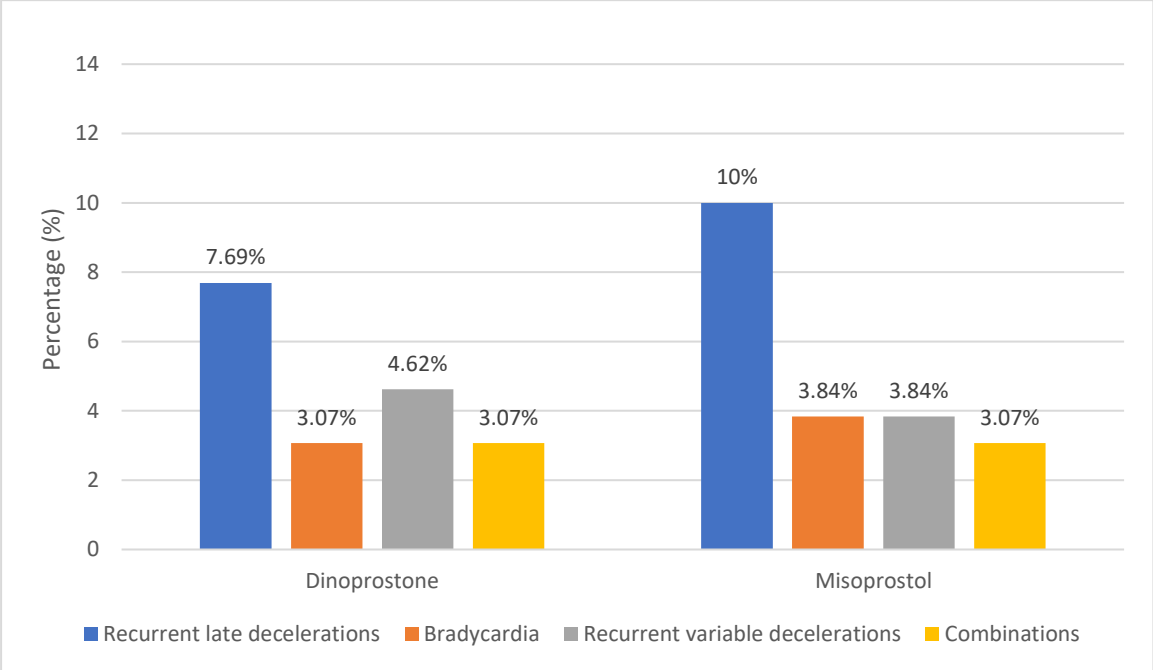


Table 22: Comparison of type of Non-Reassuring Fetal Heart Rate (FHR) tracing between the study groups

Type of non-reassuring FHR tracing	Groups (N=260)		P-value
	Dinoprostone (N=130)	Misoprostol (N=130)	
Recurrent late decelerations	10 (7.69%)	13 (10%)	0.936
Bradycardia	4 (3.07%)	5 (3.84%)	
Recurrent variable decelerations	6 (4.62%)	5 (3.84%)	
Combinations	4 (3.07%)	4 (3.07%)	

Recurrent late decelerations were seen in 10(7.69%) in the dinoprostone group and in 13(10%) of misoprostol group. Bradycardia was seen in 4(3.07%) and 5(3.84%) in the dinoprostone and misoprostol group respectively. Recurrent variable decelerations were seen in 6(4.62%) and 5(3.84%) in the dinoprostone and misoprostol group respectively. Combinations of various patterns of non-reassuring FHR tracings were seen in 4(3.07%) each of both the groups. The difference between both groups with respect to type of non-reassuring FHR tracing was not statistically significant (P value 0.936) (Table 22 & Graph 19)

Graph 19: Comparison of type of Non-Reassuring Fetal Heart Rate tracing between the study groups



DISCUSSION

DISCUSSION

This is a prospective study to determine the safety and efficacy of misoprostol for induction of labour and to compare the maternal and fetal outcomes between both the groups.

In the present study, maternal age, gestational age, and pre-induction Bishop's score were similar in both the groups.

Indications for induction of labour did not differ in either of the groups, and the most common being post-dated pregnancy. In the study by Parmar M et al, the indications were similar to the current study. However, according to the study by Radhika et al, the most common cause of induction in the misoprostol group was hypertensive disorders of pregnancy, while in the dinoprostone group it was premature rupture of membrane.[15,23]

In the present study, the pre-induction Bishop's Score distribution was similar in both the groups with a p value of 0.069.

NUMBER OF DOSES

In the present study, most women (55.4%) in the dinoprostone group achieved a favourable Bishop's score with one dose; while in the misoprostol group, most women (36.2 %) achieved a favourable Bishop's score with 2 doses of misoprostol. This was also reported by Malik et al, that the number doses required to achieve favourable Bishop's score was lesser in the dinoprostone group.[65] However, by Mandal A et al single dose of both misoprostol (63.73%) and dinoprostone (79.78%) resulted in a favourable score.[19]

INDUCTION TO ACTIVE PHASE INTERVAL

In the present study the mean induction to active phase interval in the misoprostol group was significantly shorter than in the dinoprostone group (9.60 ± 3.61 hours versus 10.83 ± 3.61 hours) with a p value of 0.011.

Similar results were obtained in a study by Lomte D et al, the induction to active phase was shorter in the misoprostol group than in the dinoprostone group (1 hour 57 minutes versus 4 hours 25 minutes) with a p value of 0.006. these results were also comparable to a study by Sharma P et al, interval from induction of labour to onset of active labour was significantly shorter in the Misoprostol group as compared to the Dinoprostone group (464.35 ± 253.61 minutes versus 617.57 ± 242.72 minutes, p<0.001)[66]

However, in a study by Chaudhuri S et al, the time to active labour was shorter in the in dinoprostone group than in the misoprostol group (4.59 ± 3.87 hours versus 5.36±4.54 hours) although the values did not reach statistical significance. (p=0.123)[24]

Various studies	Induction to Active stage interval		
	Dinoprostone	Misoprostol	P value
Lomte et al (2016)	4 hours 25 minutes	1 hour 57 minutes	0.006
Sharma P et al (2016)	464.3 ± 253.6 minutes	617.5 ± 242.7 minutes	<0.001
Chaudhuri S et al (2011)	4.59 ± 3.87 hours	5.36±4.54 hours	Not significant
Present study	10.83 hours	9.60 hours	0.011

INDUCTION TO DELIVERY INTERVAL

In the present study, the mean induction to delivery interval was significantly shorter in the misoprostol group in comparison to the dinoprostone group (14.49 ± 4.54 versus 16.08 ± 4.54, p = 0.011).

Similarly, Kalpana et al concluded that the mean induction to delivery interval in the misoprostol group was significantly shorter in the misoprostol group than in the dinoprostone group (11.68 ± 4.49 hours versus 14.85 ± 7.08 hours, P value 0.004).[69]

Though not statistically significant similar results were obtained in a study by Parmar et al., duration from induction to delivery interval was shorter (20.08 ± 8.24 hours versus 23.19 ± 9.59 hours, P >0.05) in the misoprostol than in the dinoprostone group.[15]

Wing e al (1995) concurred that the average the average interval from induction to vaginal delivery was significantly shorter in the misoprostol group (1323.0 ± 844.4 minutes) than in the dinoprostone group (1532.4 ± 706.5 minutes) (p < 0.05).[70]

Varaklis et al concluded that the women induced with misoprostol experienced a shorter mean induction to delivery time in comparison to the women induced with dinoprostone (16.0 ± 7.7 hours versus 22.4 ± 10.9 hours, P = 0.006).[68]

Nanda et al (2007) showed that, the mean Induction to delivery interval was shorter in the misoprostol group as compared with dinoprostone group (13.307 ± 8.74 hours versus 18.537 ± 11.33 hours, P 0.011).[67]

In the study by Sharma P et al (2016), it was concluded that the Induction to vaginal delivery interval was significantly lesser in the misoprostol versus the dinoprostone group (1165.60 ± 306.28 versus 1369.80 ± 286.37, P <0.001)[66]

The study by Radhika et al, showed no difference in mean induction delivery interval between the misoprostol and the dinoprostone group (18.67±10.22 versus 18.02±0.62, p=0.43).[23]

Various studies	Induction to Delivery Interval		
	Dinoprostone	Misoprostol	P value
Radhika et al (2013)	18.02±0.62 hours	18.67±10.22 hours	Not significant
Parmar et al (2014)	23.19 ± 9.59 hours	(20.08 ± 8.24 hours	> 0.05
Sharma P et al (2016)	1369.80 ± 286.37 minutes	1165.60 ± 306.28 minutes	< 0.001
Nanda et al (2007)	18.537 ± 11.33 hours	13.307 ± 8.74 hours	0.011
Kalpana et al (2017)	14.85 ± 7.08 hours	11.68 ± 4.49 hours	0.004
Wing et al (1995)	1532.4 ± 706.5 minutes	1323.0 ± 844.4 minutes	< 0.05
Varaklis et al (1995)	22.4 ± 10.9 hours	16.0 ± 7.7 hours	Not significant
Present study	16.08 ± 4.54 hours	14.49 ± 3.93 hours	0.011

OXYTOCIN AUGMENTATION

In the present study, percentage of cases requiring oxytocin augmentation was similar in both the groups (54.2 % versus 56.1%, P = 0.784).

A meta-analysis by Lui A et al (2014) concluded that there was no statistical significance in the requirement of oxytocin augmentation by both misoprostol and dinoprostone groups.[18]

In contrast, Saxena P et al (2011) concluded that requirement of oxytocin augmentation was significantly decreased in the misoprostol group in comparison to the dinoprostone group (21.4 % versus 30%, P < 0.01)[71]

Parmar et al (2014) concluded that need for Oxytocin augmentation was significantly less in misoprostol group as compared to dinoprostone group (16% versus 46%, P = 0.001).[15]

Varaklis et al (1995) concluded that women in the misoprostol group were much less likely to require oxytocin augmentation compared to the dinoprostone group (44.4% versus 87.9%, P < .001).[68]

	Requirement of oxytocin augmentation		
	Dinoprostone	Misoprostol	P value
Saxena P et al (2011)	30%	21.4%	< 0.01
Parmar et al (2014)	46%	16%	0.001
Varaklis et al (1995)	87.9%	44.4%	< 0.001
Present study	54.2%	56.1%	0.784

MODE OF DELIVERY

In the present study, rate of achieving vaginal delivery was 72.3% with dinoprostone and 73.84% with misoprostol induction. 27.7% and 26.2% underwent caesarean section with dinoprostone and misoprostol respectively. The incidence of vacuum assisted vaginal delivery was 3.8% each in both the groups. The incidence of forceps assisted vaginal delivery was 1.5% each in both the groups. The route of delivery did not differ significantly between the groups. (P value 0.994) Similar results were obtained by Radhika et al, Saxena Pet al and Wing et al., the mode of delivery was similar in both the misoprostol and dinoprostone groups.[23,71,70]

Meta-analysis by Lui et al also concluded similar rate of caesarean delivery with both groups.[18]

Various studies	Mode of Delivery		
	Dinoprostone	Misoprostol	P value
Radhika et al (2013)			
Vaginal delivery	84%	82.6%	Not significant
Caesarean section	7.79%	9%	Not significant
Vacuum assisted vaginal delivery	2.66%	4%	Not significant
Forceps assisted vaginal delivery	5.33%	5.33%	Not significant
Saxena P et al (2011)			
Vaginal delivery	85.4%	89.7%	Not significant
Caesarean section	31.4%	30%	Not significant
Wing e al (1995)			
Vaginal delivery	72.3%	79.7%	Not significant
Caesarean section	27.7%	20.3%	Not significant
Present study			
Vaginal delivery	66.9%	68.5%	Not significant
Caesarean section	27.7%	26.2%	Not significant
Vacuum assisted vaginal delivery	3.8%	3.8%	Not significant
Forceps assisted vaginal delivery	1.5%	1.5%	Not significant

INDICATIONS FOR CAESAREAN SECTION

The commonest indication for caesarean section in both the groups was fetal distress, though the absolute number of cases with fetal distress was greater in the misoprostol group 73.5% as compared to dinoprostone group 61.1%, this difference did not achieve statistical significance (P 0.515). Although the failure of induction rates was higher with dinoprostone (36.1%) compared to misoprostol (23.5%), the difference was not statistically significant.

Similar results were obtained in the study by Radhika et al, fetal distress followed by failure of induction were the commonest indications for caesarean section and there was no statistically significant difference between the groups.[23]

Wing et al concluded that, the cases undergoing caesarean section due to failure of induction was significantly higher in the dinoprostone group (71%) as compared to the misoprostol group (14.2%) ($P < 0.001$). Although commonest indication for caesarean section in the misoprostol group was fetal distress as compared to dinoprostone group, it did not amount to a statistically significant difference.[70]

MECONIUM STAINED LIQUOR

In the present study, incidence of meconium stained liquor though higher in the misoprostol group (23.8%) in comparison to the dinoprostone group (18.47%), the difference was not statistically significant ($P = 0.287$)

Wing et al observed that the rate of meconium passage was 17.4% in misoprostol group and 13.9% in the dinoprostone group, and the difference was not statistically significant.[70]

Malik N et al reported that the incidence of meconium stained liquor was higher in the misoprostol group than in the dinoprostone group (25% versus 12.5%), the difference was not statistically significant (P=0.152)[65]

Madaan M et al also noted similar results, meconium stained liquor with misoprostol versus dinoprostone (22% versus 12%) (P=0.092)[16]

Various studies	Meconium stained liquor		
	Dinoprostone	Misoprostol	P value
Madaan M et al (2014)	12%	22%	Not significant
Malik N et al (2017)	12.5%	25%	Not significant
Wing et al (1995)	13.9%	17.4%	Not significant
Present study	18.47%	23.8%	Not significant

MATERNAL ADVERSE EFFECTS

In the present study maternal complications were similar in both the groups, 9.2% in the dinoprostone and 12.3% in the misoprostol group with exception of maternal diarrhea which was seen in 0.77% with dinoprostone group and none with misoprostol and maternal fever which was seen in 1.53% of misoprostol and none in dinoprostone. Compared with dinoprostone, a relatively higher frequency of vomiting (3.08% versus 2.31%), Precipitate labour (2.31% versus 0.77%), postpartum haemorrhage (3.08% versus 2.31%) in the misoprostol group. Non-reassuring fetal heart tracing was more frequently observed in the misoprostol (20.77% versus

18.46%). Uterine hyperstimulation was more frequent with dinoprostone (2.31% versus 1.53%). No statistical significance was achieved for any of the above factors.

Radhika et al reported increased frequency of abnormal fetal heart tracing in the dinoprostone group (7.33% versus 4.66%), though the difference was not statistically significant. Other maternal complications were similar in both groups.[23]

Wing et al, reported increased frequency of abnormal fetal heart patterns in the dinoprostone group (32.1% versus 23.9%), and this difference was not statistically significant. Maternal side effects were minimal and were similar in both groups.[70]

Meta-analysis by Lui et al concluded that uterine hyperstimulation and tachysystole was more frequent with misoprostol, though not to the extent to achieve statistical significance.[18]

NEONATAL ADVERSE EFFECTS

In the present study, 12.3% in the misoprostol group and 10% babies in the dinoprostone group required neonatal intensive care unit (NICU) admission, not statistically significant (P=0.555). The mean APGAR score at 1 minute and 5 minutes was similar in both the groups. The commonest cause for neonatal NICU admission was respiratory distress in both the groups. There was one neonatal death in the misoprostol group secondary to perinatal asphyxia & meconium aspiration syndrome.

SUMMARY

SUMMARY

This is a prospective comparative study of 260 pregnant women who were randomized to receive either 25 µg intravaginal misoprostol or 0.5 mg of intracervical dinoprostone for induction of labour. This study was done over a period of 16 months from December 2016 to March 2018 at R L Jalappa Hospital and Research Center, Tamaka, Kolar.

- The mean maternal age was 23.05 ±2.68 years and 23.48 ±3.71 years in the dinoprostone and misoprostol group respectively.
- The maternal age distribution, gestational age and pre-induction modified Bishop's score were similar among the groups.
- The indications for induction of labour were similar between both the groups with post-dated pregnancy being the commonest indication.
- 55.4% women in the dinoprostone group responded to a single dose. However, 36.2% women in the misoprostol group required two doses.
- The mean induction to active phase interval was significantly shorter in the misoprostol group than in the dinoprostone group (9.60 ± 3.13 versus 10.83 ± 3.61 hours, P value 0.011)
- The mean induction to delivery interval was significantly shorter in the misoprostol group when compared to dinoprostone group (14.49 ± 3.93 versus 16.08 ± 4.54 hours , P value 0.011)
- Percentage of cases requiring oxytocin augmentation were similar in both dinoprostone and misoprostol group (54.2% versus 56.1 %, P = 0.784).
- The rate of achieving vaginal delivery was 72.3% and 73.84% in dinoprostone and misoprostol group respectively. And, 27.7% and 26.2%

delivered by caesarean section in the dinoprostone and misoprostol group respectively. This difference was not statistically significant (P value 0.994).

- 61.1% in the dinoprostone and 73.5% in the misoprostol group underwent caesarean section for fetal distress, this was the most common indication in both the groups.
- Failed induction was seen in 36.1% cases in the dinoprostone as compared to 23.5% in the misoprostol group, though it did not achieve statistical significance. (P value 0.515)
- The occurrence of meconium stained liquor was higher with misoprostol than with dinoprostone (23.8% versus 18.47%). However, this difference was not statistically significant.
- Mean 1 min APGAR score was 6.98 and 6.93 in the dinoprostone and misoprostol groups respectively. It's not statistically significant (P value 0.175). Mean 5 min APGAR score was 9 and 8.95 in the dinoprostone and misoprostol groups respectively, which is also not statistically significant. (P value 0.318)
- Rate of neonatal admission to NICU was 12.3% in the misoprostol group and 10% in the dinoprostone group.
- In the present study maternal complications were 9.2% in the dinoprostone and 12.3% in the misoprostol group. Maternal diarrhea was seen in 0.77% in the dinoprostone group and none in the misoprostol group. Maternal fever was seen in 1.53% in the misoprostol group and none in the dinoprostone group. Compared with dinoprostone, a relatively higher frequency of vomiting (3.08% versus 2.31%), Precipitate labour (2.31% versus 0.77%), postpartum hemorrhage (3.08% versus 2.31%) was seen in the misoprostol

group. Uterine hyperstimulation was more frequent with dinoprostone (2.31% versus 1.53%). No statistical significance was achieved for any of the above factors.

- Non-reassuring fetal heart tracing was more frequently observed in the misoprostol (20.77% versus 18.46%), however this difference was not statistically significant (P value 0.639).
- Recurrent late decelerations were observed in 7.69% in the dinoprostone group and 10% in the misoprostol group. This was followed by recurrent variable decelerations observed in 4.62% and 3.84% in the dinoprostone and misoprostol group respectively. Fetal bradycardia was seen in 3.07% in the dinoprostone group and 3.84% in the misoprostol group. A combination of two or more patterns of non-reassuring fetal heart tracings were seen in 3.07% each in both the groups. These differences were not statistically significant (P value 0.936).

CONCLUSION

CONCLUSION

Low dose misoprostol as a method of induction of labour is more efficacious than dinoprostone in terms of shorter induction to delivery interval; although, both the drugs demonstrated similar outcomes with regard to maternal and fetal safety profiles. The stability of low dose misoprostol at room temperature and ease of storage in comparison to dinoprostone make misoprostol a more favoured drug for induction especially in developing countries with low resource settings.

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ANNEXURES

PATIENT INFORMATION SHEET

Study title: **COMPARATIVE STUDY OF 25 µg INTRAVAGINAL MISOPROSTOL AND 0.5 mg INTRACERVICAL DINOPROSTONE FOR INDUCTION OF LABOUR.**

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Details-

In patients presenting beyond 37 weeks gestation, induction of labour will be done with either 25µg intravaginal misoprostol or 0.5 mg intracervical dinoprostone gel.

Patients in this study will have to undergo complete general physical examination, obstetric examination, routine blood investigations such as complete blood count, viral serology, urine routine and random blood sugar levels. To assess the fetal wellbeing a cardiotocograph and an obstetric ultrasound with biophysical profile will also be done.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study, we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The

care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

Dr. Vishnu Priya Kesani

Post graduate,

Department of obstetrics and gynecology,

Sri Devaraj Urs Medical College,

Kolar.

CASE PROFORMA

NAME: **IP NO:**

AGE: **DOA:**

OCCUPATION: **DOD:**

ADDRESS:

EDUCATION:

HUSBANDS OCCUPATION:

SOCIOECONOMIC STATUS:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

OBSTETRIC HISTORY:

Marital life: Consanguinity:

Gravida: Para: living: Abortion: Dead:

Details of previous pregnancy:

Details of present pregnancy:

MENSTRUAL HISTORY:

Last menstrual period: Age of menarche:

Expected delivery date:

Period of gestation:

Period of gestation according to early scan:

Past menstrual cycles:

PAST HISTORY:

Hypertension /Diabetes Mellitus/Bronchial Asthma/Tuberculosis /Blood Dyscrasias/ Epilepsy/ Thyroid Disorder/ Cardiac Disease/Allergy

H/O blood transfusions:

H/O Surgeries or hospitalization:

PERSONAL HISTORY:

Sleep and appetite:

Diet:

Bowel and bladder:

FAMILY HISTORY:

DRUG HISTORY:

GENERAL EXAMINATION:

General condition: Fair/ moderate/ Poor

Built: Nourishment:

Ht: cms Wt: kgs BMI:

Pallor: Icterus:

Cyanosis: Clubbing:

Lymphadenopathy: Edema:

VITALS:

Pulse rate: Respiratory rate:

Blood pressure : Temperature:

Breast : Spine : Thyroid :

SYSTEMIC EXAMINATION:

Cardiovascular system: Respiratory system: Central nervous system:

Per abdomen: Uterus size:

Relaxed / Irritable / Acting

Presentation: cephalic/ Breech/ other

FHS:

LOCAL EXAMINATION:

Per Speculum:

Per Vaginum: Effacement:

Dilatation:

Station:

Membranes:

Pelvis:

Modified Bishop Score:

DIAGNOSIS:

Total dose of induction:

Number of doses:

Induction to active stage interval:

Induction to delivery interval:

Mode of delivery:

Indication for cesarean section:

Need for oxytocin augmentation:

Maternal adverse effects:

APGAR score at 1 minute & 5 minutes:

Meconium stained liquor:

Fetal heart rate tracing (Non stress test and cardiotocograph findings) :

DETAILS OF THE NEONATE:

Sex: Date: Time:

Birth weight:

APGAR score: 1'- 5'-

Admission to NICU:

Neonatal resuscitation

Perinatal morbidity/mortality:

INVESTIGATIONS:

Blood group and Rh typing:

CBC: HB: HIV:

PCV: HbsAG:

RBC: VDRL:

WBC:

PLT: RBS:

Urine analysis: Albumin-

Sugar-

Microscopy-

OBSTETRICS SCAN:

SRI DEVARAJ URS MEDICAL COLLEGE & RESEARCH CENTRE, TAMAKA, KOLAR

Patient Consent Form

Case no:

I have read the foregoing information, or it has been read to me and has been explained to me in my own understanding language. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I have understood that I have the right to refuse consent or withdraw it at any time during the study and this will not affect my treatment in any way. I consent voluntarily to participate in this study

"COMPARATIVE STUDY OF 25 µg INTRAVAGINAL MISOPROSTOL AND 0.5 mg INTRACERVICAL DINOPROSTONE FOR INDUCTION OF LABOUR"

Name of Participant_____

Signature/ thumb print of Participant _____

Date _____

R.L Jalappa Hospital

Tamaka, Kolar.

ತಿಳುವಳಿಕೆಯ ಒಪ್ಪಿಗೆ ಪತ್ರ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ:– "COMPARATIVE STUDY OF INTRAVAGINAL 25µg MISOPROSTOL AND 0.5 mg INTRACERVICAL DINOPROSTONE GEL FOR INDUCTION OF LABOUR."

ಶ್ರೀ/ಶ್ರೀಮತಿ ಆದ ನಾನು ಈ ಮೇಲಿನ ಸಂಶೋಧನ ವಿಷಯದ ಬಗ್ಗೆ ನನಗೆ ಅರ್ಥವಾಗುವ ರೀತಿಯಲ್ಲಿ ನನ್ನದೇ ಭಾಷೆಯಲ್ಲಿ ತಿಳಿಸಿರುತ್ತಾರೆ. ಈ ಸಂಶೋಧನಾ ವಿಷಯದಲ್ಲಿ ನಾನು ಒಬ್ಬ ವಿಷಯಿಯಾಗಿ ಭಾಗವಹಿಸಲು ನನ್ನ ಸಂಪೂರ್ಣವಾಗಿ ಒಪ್ಪಿಗೆ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ಉದ್ದೇಶವನ್ನು ಪೂರ್ಣವಾಗಿ ಅರಿತಿರುತ್ತೇನೆ. ಈ ಸಂಶೋಧನೆಗೆ ನನ್ನಿಂದ ಯಾವುದೇ ಆರ್ಥಿಕತೆಯ ಅವಶ್ಯಕತೆ ಇರುವುದಿಲ್ಲ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಸಹಕಾರವನ್ನು ಹಿಂಪಡೆದು ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಹೋಗುವ ಹಕ್ಕನ್ನು ಹೊಂದಿರುತ್ತೇನೆ. ಇದರಿಂದ ನನ್ನ ಚಿಕಿತ್ಸೆಗೆ ಯಾವುದೇ ರೀತಿಯ ತೊಂದರೆಯಾಗುವುದಿಲ್ಲ. ಮುಖ್ಯವಾಗಿ ನನ್ನಿಂದ ಪಡೆದ ಈ ಮಾಹಿತಿಯು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಸೀಮಿತವಾಗಿರುತ್ತದೆ. ಮತ್ತು ಈ ಮಾಹಿತಿಯು ಎಲ್ಲೂ ಸೋರಿಕೆಯಾಗದಂತೆ ಎಚ್ಚರಿಕೆ ವಹಿಸುವುದಾಗಿ ತಿಳಿವಳಿಕೆ ನೀಡಿರುತ್ತಾರೆಂದು ನಾನು ದೃಢಪಡಿಸಿಕೊಂಡು ಒಪ್ಪಿಗೆ ನೀಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ/ ಸಾಕ್ಷಿ ಸಹಿ. ಸಂಶೋದಕನ ಸಹಿ

ಬೆರಳಚ್ಚು.

KEY TO MASTER CHART

- IP.No : In-patient hospital number
- Study group :
  - 1 : Misoprostol study group
  - 2 : Dinoprostone study group
- Obstetric score
  - 1 : Primigravida
  - 2 : Multigravida
- POG : Period of gestation
- Indication for induction
  - 1 : Postdated
  - 2 : Preeclampsia
  - 3 : Oligohydramnios
  - 4 : Rh Negative Pregnancy
- IAI : Induction To Active Phase Interval (in hours)
- IDI : Induction To Delivery Interval (in hours)
- Mode of delivery
  - 1 : Vaginal Delivery
  - 2 : Caesarean Section

- 3 : Vacuum Assisted Vaginal Delivery
- 4 : Forceps Assisted Vaginal Delivery

- Indication for Caesarean Section
  - 1 : Fetal Distress
  - 2 : Failure Of Induction
  - 3 : Deep Transverse Arrest

- Oxytocin augmentation requirement
  - 1 : Not required
  - 2 : Required

- Liquor
  - 1 : Clear liquor
  - 2 : Meconium stained liquor

- Resuscitation Measures
  - 1 : Baby Cried Immediately After Birth
  - 2 : Baby Cried After Stimulation
  - 3 : Cried After Bag And Mask Ventilation
  - 4 : Baby Intubated

- Cause for NICU Admission
  - 1 : Post Resuscitation Care
  - 2 : Respiratory Distress
  - 3 : Secondary Apnea
  - 4 : Perinatal Asphyxia
  - 5 : Perinatal Mortality

- Cause of Maternal Adverse Effects
  - 1 : Diarrhea
  - 2 : Hyperstimulation of the uterus
  - 3 : Nausea & vomiting
  - 4 : PPH (atonic +traumatic)
  - 5 : Precipitate labour
  - 6 : Tachysystole
  - 7 : Fever

- FHR tracing
  - 1 : Reactive FHR tracing
  - 2 : Non-reassuring FHR tracing

- Type of Non-Reassuring FHR Tracing
  - 1 : Recurrent late decelerations
  - 2 : Bradycardia
  - 3 : Recurrent variable decelerations
  - 4 : Combinations

Sl.No	IP.No	Study group	Age	Obstetric score	POG	Indication for Induction	pre induction Modified Bishop's score	Number of doses	(IAI HOURS)	IDI (HOURS)	mode of delivery	indication for cesarean section	oxytocin augmentation	baby weight	liquor	Resuscitation measures	APGAR 1'	APGAR 5'	NICU admission	cause for NICU admission	maternal adverse effects	cause of maternal adverse effects	FHR tracing	Type of non reasurring FHR tracing
1	441581	1	23	2	39+4	3	4	1	8.00	12.93	1		1	3.57	1	1	7	9	no		yes	3	1	
2	494202	2	21	1	40+5	1	2	1	8.00	11.08	1		1	3.02	1	1	7	9	no		no		1	
3	442163	1	24	2	40	1	4	2	18.00	21.38	1		1	2.7	1	1	7	9	no		no		1	
4	445459	2	24	1	40+3	1	2	2	18.00	24.75	1		2	3.19	1	1	7	9	no		no		1	
5	356095	1	24	2	40+4	1	4	1	8.00	9.35	1		2	2.9	1	1	7	9	no		no		1	
6	452677	2	19	1	40+2	1,2	2	1	8.00	9.17	1		1	2.6	1	1	7	9	no		yes	2	1	
7	420763	1	22	2	40+4	1	3	2	8.00	12.50	1		1	2.53	1	1	7	9	no		no		1	
8	498601	2	24	1	40	1	4	1	8.00	11.57	1		1	3	1	1	7	9	no		no		1	
9	442266	1	26	2	38+5	3	3	2	7.00	12.33	1		1	2.6	1	1	7	9	no		yes	5	1	
10	469063	2	21	2	41+1	1	3	1	8.00	10.00	1		1	3.7	1	1	7	9	no		no		1	
11	442153	1	20	1	39+2	2	3	2			2	1		3.52	2	1	7	9	yes	3	no		2	1
12	500600	2	24	1	40	1	2	2	10.00	22.00	1		1	3.2	1	1	7	9	no		no		1	
13	425988	1	24	2	41+5	1,2	2	6			2	2		3.06	1	1	7	9	no		no		1	
14	500692	2	24	2	41+3	1	2	1	6.00		2	3	2	3.34	2	3	5	9	yes	1	no		1	
15	444938	1	23	1	40	1	3	3	6.00	13.92	1		2	2.74	1	1	7	9	no		no		1	
16	449470	2	20	1	39+6	3	3	1	6.00	10.58	1		2	2.69	1	1	7	9	no		no		1	
17	445415	1	23	1	41+2	1	3	4	12.00	20.00	1		2	3.06	1	1	7	9	no		no		1	
18	491098	2	23	1	39 +3	2	3	2	12.00	19.33	1		2	3.1	1	1	7	9	no		no		1	
19	445917	1	19	1	38+5	4	3	2	10.00	15.00	1		2	2.5	1	1	7	9	no		no		1	
20	497201	2	19	1	40 weeks	1,4	3	1	10.00	15.00	1		1	3.1	1	1	7	9	no		no		1	
21	447475	1	24	2	39+1	2	2	5	8.00	12.63	4		2	3.5	1	2	6	9	yes	1	yes	4	1	
22	467867	2	23	2	40+1	1	4	1	18.00	23.83	1		1	2.62	1	1	7	9	no		no		1	
23	500584	1	20	1	38+4	2	3	2	15.00		2	1		2.8	2	1	7	9	no		no		2	1
24	357094	2	22	1	40+5	1	3	4	10.00	16.17	1		2	3.3	1	1	7	9	no		no		1	
25	443569	1	20	2	40+1	1	4	2	9.00	14.17	1		1	2.8	1	1	7	9	no		yes	5	1	
26	450895	2	22	1	40	1	3	1	11.00	14.17	4		2	3.2	2	1	7	9	yes	2	no		2	3
27	436965	1	22	2	41	1	4	1	9.00	13.25	1		1	2.9	1	1	7	9	no		no		1	
28	407222	2	19	1	40	1,4	3	1	9.00	13.25	3		2	3.4	2	1	7	9	no		no		1	
29	416132	1	21	2	38+3	3,4	3	2	10.00	13.75	1		2	2.7	2	1	7	9	yes	2	no		1	
30	502151	2	27	2	40+2	1	4	1	10.00	16.42	1		1	2.9	1	1	7	9	no		no		1	
31	446708	1	22	2	40+4	1	3	4	8.00	19.72	1		2	2.53	1	1	7	9	no		no		1	
32	505984	2	22	2	40+2	1	3	3			2	2		3.2	1	1	7	9	no		no		1	
33	447731	1	26	2	39+1	3	3	2	12.00	18.97	1		2	2.8	1	1	7	9	no		no		1	
34	501462	2	19	1	40+1	1	4	1	12.00	15.23	1		2	2.84	1	1	7	9	no		no		1	
35	447776	1	21	1	41+2	1	2	4			2	1		2.83	2	1	7	9	yes	2	yes	6	2	2

36	511390	2	22	1	38+1	2	3	2	13.67	17.33	1		2	2.6	2	1	7	9	yes	2	yes	4	1	
37	445057	1	20	1	40+3	1	3	2	10.00	16.20	1		2	2.75	1	1	7	9	no		no		1	
38	519082	2	22	2	39+2	3	3	1	10.00	16.58	1		1	2.62	1	1	7	9	no		no		1	
39	377286	1	28	2	38+3	2	4	2	20.00	26.00	3		2	2.6	2	1	7	9	no		no		1	
40	520000	2	20	1	40+2	1	2	3	20.00	20.87	1		2	2.74	1	1	7	9	no		no		1	
41	448413	1	23	1	40+1	1	3	5	8.00	12.03	1		2	3.4	1	1	7	9	no		yes	3	1	
42	470012	2	25	2	40	1	4	1	8.00	15.60	1		1	3.2	1	1	7	9	no		no		1	
43	443729	1	23	2	40+1	1	3	2	13.00	14.40	1		2	3	1	1	7	9	no		no		1	
44	430896	2	23	1	41	1	4	2	13.00	15.37	4		2	2.9	2	1	7	9	yes	2	no		1	
45	364380	1	29	2	40	1	2	4	10.00	13.73	1		2	2.9	1	1	7	9	no		no		1	
46	523802	2	28	1	40	1	3	1	10.00	21.18	1		1	2.54	1	1	7	9	no		no		1	
47	438254	1	24	2	41	1	3	1	6.00	12.20	1		1	2.8	1	1	7	9	no		no		1	
48	521691	2	21	2	39+2	3	3	1			2	1		2.84	2	1	7	9	no		no		2	2
49	376073	1	24	2	40	1	3	1	10.00	12.17	1		1	2.6	1	1	7	9	no		no		1	
50	521608	2	20	2	40	1	4	1	10.00	8.58	1		1	3.38	1	1	7	9	no		no		1	
51	368164	1	25	1	40+2	1	3	2			2	1		2.74	2	2	6	9	yes	1	yes	2	2	1
52	423588	2	20	1	40+3	1	3	3			2	2		3.6	1	1	7	9	no		no		1	
53	450340	1	26	2	40	1	4	3	10.00	16.27	1		2	3.2	1	1	7	9	no		no		1	
54	147138	2	24	2	40+2	1,4	4	1	12.00	17.00	1		1	2.9	1	1	7	9	no		no		1	
55	450303	1	22	1	40	1	2	1			2	1		2.7	2	1	7	9	no		no		2	2
56	514990	2	29	2	39+4	2	4	1	10.00	12.18	1		2	3	1	1	7	9	no		no		1	
57	450751	1	30	2	40	1	3	1	6.00	12.57	1		1	3.5	1	1	7	9	no		yes	4	1	
58	526696	2	22	1	40	1	4	1	8.00	10.77	1		2	3	1	1	7	9	no		no		1	
59	448019	1	28	2	40+2	1	4	1	12.00	16.18	1		1	3.2	1	1	7	9	no		no		1	
60	531138	2	24	1	40+1	1	3	2	12.00	12.08	1		2	2.92	1	1	7	9	no		no		1	
61	447525	1	22	2	40+1	1,4	2	2	8.00	10.33	1		1	3.56	2	1	7	9	yes	2	yes	2	1	
62	504480	2	24	2	39	2	4	1	9.00	12.33	1		1	2.9	1	1	7	9	no		no		1	
63	452257	1	22	1	40+2	1	2	4			2	1		2.65	2	1	7	9	yes	2	no		2	1
64	505054	2	28	2	40	1	4	1	6.00	15.33	1		1	2.75	1	1	7	9	no		yes	3	1	
65	452152	1	33	2	40	1	4	1	11.00	16.07	1		1	2.5	1	1	7	9	no		no		1	
66	480288	2	21	1	40+5	1	2	2	11.00	10.00	1		2	2.78	1	1	7	9	no		no		1	
67	447144	1	23	2	40+4	1	4	1	7.00	11.67	1		2	2.54	1	1	7	9	no		no		1	
68	505130	2	22	1	40+6	1	3	1	8.00	12.13	1		1	3	2	1	7	9	no		no		1	
69	377457	1	22	2	41+2	1	4	3			2	1		3.08	2	1	7	9	yes	2	no		2	1
70	506358	2	21	2	39+1	2	4	1			2	1		2.8	2	1	7	9	no		no		2	1
71	448220	1	20	1	40	1,4	2	4	8.00	11.58	1		2	3	1	1	7	9	no		no		1	
72	506502	2	24	1	40+1	1	4	1			2	1		3.12	2	1	7	9	yes	3	no		2	2
73	448012	1	22	2	40+5	1	4	2	12.00	15.33	1		2	2.8	1	1	7	9	no		no		1	
74	141379	2	24	1	40+2	1	2	3			2	2		3.28	1	1	7	9	no		no		1	
75	443770	1	24	1	40	1	4	2	8.00		2	1		2.6	2	1	7	9	no		no		2	2
76	488166	2	19	1	41	1	3	1	10.00	21.08	1		2	3	1	1	7	9	no		no		1	

77	454216	1	20	1	41	1	2	4	20.00	27.50	1		2	2.6	1	1	7	9	no		no		1	
78	511761	2	22	2	40+6	1	4	3	20.00	22.75	1		2	2.97	1	1	7	9	no		no		1	
79	455516	1	24	2	40+1	1	4	1	10.00	13.75	1		1	3.6	1	1	7	9	no		no		1	
80	511755	2	22	1	40+3	1	4	1			2	1		2.5	2	1	7	9	yes	2	no		2	1
81	455178	1	22	1	41+1	1	2	4	6.00	8.05	1		2	3.6	2	1	7	9	no		yes	3	1	
82	462496	2	28	2	41+3	1	4	1	6.00	20.87	1		1	2.8	1	1	7	9	no		yes	4	1	
83	385947	1	20	1	40+2	1	2	4	12.00	16.08	3		2	3	2	1	7	9	no		no		2	1
84	516159	2	24	1	40+1	1	3	2	16.00	20.70	3		2	3	1	1	7	9	yes	2	no		1	
85	448416	1	23	1	40+6	1	3	3	4.00	8.50	1		1	2.9	1	1	7	9	no		no		1	
86	143921	2	26	2	40+4	1	4	1	4.00	18.83	1		1	2.9	1	1	7	9	no		yes	2	1	
87	452533	1	20	1	40+2	1	2	4			2	1		3.2	2	1	7	9	no		no		2	1
88	513159	2	20	1	38+4	2	2	2			2	1		2.4	1	1	7	9	no		no		2	1
89	456082	1	21	1	40+3	1	2	3	10.00	14.68	1		1	2.7	1	1	7	9	no		no		1	
90	509111	2	22	1	40+1	1	4	1	9.00	15.20	1		2	2.84	1	1	7	9	no		no		1	
91	451181	1	22	2	40+1	1	3	2	8.00	10.33	1		1	3.12	1	1	7	9	no		no		1	
92	509012	2	21	1	41+4	1	2	1			2	1		2.86	1	1	7	9	no		yes	6	2	3
93	448256	1	24	2	40+1	1	4	2			2	1		2.9	2	1	7	9	no		no		2	1
94	520491	2	27	2	40+3	1	4	1	8.33	12.75	1		1	2.56	1	1	7	9	no		no		1	
95	416815	1	22	1	40+2	1	2	3	10.00	12.82	1		1	2.8	1	1	7	9	no		no		1	
96	515693	2	25	2	40	1	4	1	12.33	18.27	1		2	2.98	1	1	7	9	no		no		1	
97	458373	1	27	2	40+2	1	3	2	10.00	16.30	1		1	2.87	1	1	7	9	no		no		1	
98	435621	2	19	1	40+1	1,4	3	3			2	2		3	1	1	7	9	no		no		1	
99	457407	1	20	1	41	1	2	6			2	2		2.7	1	1	7	9	no		no		1	
100	506388	2	27	1	40+1	1	3	2			2	1		3.86	2	1	7	9	no		no		2	1
101	407302	1	20	2	39+6	3	3	3	10.00	18.68	1		2	2.92	1	1	7	9	no		no		1	
102	421089	2	30	1	38+5	3	2	2	12.00	17.87	1		2	2.4	2	1	7	9	no		no		1	
103	462357	1	25	1	40+4	1	3	2			2	1		2.86	1	1	7	9	no		no		2	1
104	521400	2	22	1	40+3	1	2	2	10.00	12.72	1		1	3.06	1	1	7	9	no		no		1	
105	460457	1	26	2	39+1	3	3	2	10.00	16.15	1		2	3.06	1	1	7	9	no		no		1	
106	521296	2	24	2	39+2	4	4	1	10.00	14.47	1		1	3.2	1	1	7	9	no		no		1	
107	386913	1	20	1	41+1	1	2	6			2	2		2.89	1	1	7	9	no		no		1	
108	521990	2	24	1	40+3	1	2	1			2	1		2.7	1	1	7	9	yes	2	no		2	4
109	448234	1	22	2	40	1	4	2	8.00	13.50	1		1	2.6	1	1	7	9	no		no		1	
110	508933	2	22	1	40 weeks	1	2	3			2	2		2.8	1	1	7	9	no		no		1	
111	427701	1	23	1	40	1	3	3	10.00	13.20	1		2	2.81	1	1	7	9	no		no		1	
112	520850	2	26	2	40+6	1	3	2	10.00	15.87	1		1	2.9	2	1	7	9	yes	2	no		1	
113	461273	1	25	2	38	2	2	4	12.00	16.33	1		1	2.7	1	1	7	9	no		no		1	
114	522191	2	24	1	40+1	1	3	2	14.00	18.08	1		2	2.6	1	1	7	9	no		no		1	
115	464101	1	24	1	40+1	1	3	4	6.00	7.03	1		1	2.7	1	1	7	9	no		no		1	
116	515887	2	27	2	40+5	1	4	1	20.67	28.92	1		1	2.9	1	1	7	9	no		yes	4	1	
117	461797	1	24	2	40	1	3	1	10.00	15.77	1		2	3.34	1	1	7	9	no		no		1	

118	522450	2	24	2	40+2	1	4	1	10.00	10.43	1		2	2.9	1	1	7	9	no		no		1	
119	129167	1	20	1	38+5	3,4	2	2			2	1		2.6	2	1	7	9	yes	2	no		2	3
120	522922	2	25	1	40+5	1	2	3			2	2		3.1	1	1	7	9	no		no		1	
121	462887	1	19	1	38+1	3	2	2			2	1		2.74	2	1	7	9	no		no		2	2
122	522535	2	22	1	40+2	1	3	1	10.00	14.50	1		2	3.3	1	1	7	9	no		no		1	
123	379225	1	20	2	38+3	2	4	4	12.00	17.87	1		2	2.78	2	1	7	9	no		no		1	
124	522545	2	21	1	40+2	1	3	2	14.00	19.53	1		2	3.09	1	1	7	9	no		no		1	
125	464706	1	22	2	38+5	2,3	3	3			2	1		2.6	2	1	7	9	no		no		2	3
126	519431	2	22	2	40+2	1	2	2	9.00	12.70	1		1	3.39	1	1	7	9	no		no		1	
127	465197	1	21	1	39+2	4	2	5	16.00	26.60	1		1	2.9	1	1	7	9	no		no		1	
128	515026	2	26	2	40+2	1	4	1	6.00	22.23	1		1	2.9	1	1	7	9	no		no		1	
129	466146	1	19	1	38+5	3	2	3			2	1		2.9	2	1	7	9	no		no		2	1
130	522995	2	25	2	40+2	1	2	1	10.00	19.72	3		2	2.72	1	1	7	9	yes	2	no		1	
131	467213	1	19	1	39+5	2,3	3	3	12.00	16.98	1		2	2.7	1	1	7	9	no		no		1	
132	481911	2	25	2	40+3	1	2	2	14.33	17.72	1		2	2.8	1	1	7	9	no		no		1	
133	451169	1	21	2	39+3	2	4	2	9.00	16.17	1		2	3.11	1	1	7	9	no		no		1	
134	517848	2	20	1	40	1	3	1			2	1		2.92	1	1	7	9	no		no		2	1
135	454028	1	22	2	39+4	3	3	2	10.00	15.60	1		2	3.03	1	1	7	9	no		no		1	
136	517560	2	30	2	38	2	4	2	10.00	13.27	1		2	3.11	1	1	7	9	no		no		1	
137	470726	1	22	1	40+3	1	2	4	10.00	16.53	1		2	2.9	1	1	7	9	no		no		1	
138	475740	2	19	1	40	1	2	3			2	2		2.8	1	1	7	9	no		no		1	
139	388683	1	20	2	40+2	1,2	3	2			2	1		3.14	1	3	5	9	yes	1	no		2	3
140	390445	2	24	1	40+3	1	4	2	10.00	16.07	1		2	3.2	1	1	7	9	no		no		1	
141	469215	1	19	1	40+1	1	2	5	10.00	16.53	1		2	2.6	1	1	7	9	no		no		1	
142	449468	2	23	1	40+3	1	4	2	15.00	18.78	1		2	3.2	1	1	7	9	no		no		1	
143	471857	1	20	1	40+3	1	3	3	10.00	16.30	1		2	3.02	1	1	7	9	no		no		1	
144	428040	2	22	1	40+2	1	3	1	10.00	15.57	1		2	3.3	1	1	7	9	no		no		1	
145	467075	1	20	1	40+4	1	2	2	12.00	17.87	1		2	2.88	1	1	7	9	no		no		1	
146	406229	2	21	1	40+2	1	3	2	12.00	14.37	1		2	3.09	1	1	7	9	no		no		1	
147	521619	1	22	2	40+2	1	3	2	10.00	16.98	1		1	2.72	1	1	7	9	no		no		1	
148	455773	2	22	1	40 weeks	1	2	3			2	2		2.8	1	1	7	9	no		no		1	
149	527278	1	22	2	40+4	1	3	2	8.00	12.50	1		1	3.23	1	1	7	9	no		no		1	
150	479247	2	24	1	40	1	4	1	8.00	8.75	1		1	3	1	1	7	9	no		no		1	
151	521390	1	21	2	40+3	1,3	3	3	20.00	27.50	1		2	2.9	2	1	7	9	yes	2	no		1	
152	479330	2	22	2	40+6	1	4	3	20.00	26.48	1		2	2.97	1	1	7	9	no		no		1	
153	523888	1	22	1	40+3	1	2	6			2	2		2.8	1	1	7	9	no		no		1	
154	479829	2	24	1	40	1	2	2	9.00	11.00	1		1	3.2	1	1	7	9	no		no		1	
155	471285	1	19	2	40+3	1	3	2	10.00	16.00	1		1	2.7	1	1	7	9	no		no		1	
156	503041	2	25	2	40+2	1	2	1	10.00	12.27	3		2	2.72	1	1	7	9	no		no		1	
157	528473	1	21	1	40+1	1	2	6			2	2		3.8	1	1	7	9	no		no		1	
158	480265	2	25	2	40+3	1	2	2	12.00	15.93	1		2	2.8	1	1	7	9	no		no		1	

159	528930	1	20	1	40+2	1	3	2			2	1		2.9	2	1	7	9	yes	2	no		2	3
160	445479	2	20	1	40	1	3	1			2	1		2.92	1	1	7	9	no		no		2	1
161	516674	1	20	2	40+4	1	2	3	12.00	16.17	1		2	2.78	1	1	7	9	no		no		1	
162	474984	2	19	1	40	1	2	3			2	2		2.8	1	1	7	9	no		no		1	
163	500624	1	23	2	40+5	1	4	2	10.00	16.53	1		2	3.7	1	1	7	9	no		no		1	
164	470836	2	24	1	40+3	1	4	2	7.00	12.60	1		2	3.2	1	1	7	9	no		no		1	
165	451742	1	24	2	40+4	1	4	1			2	1		3	2	1	6	9	yes	2	no		2	1
166	481578	2	22	1	40+3	1	4	1			2	1		2.5	2	1	7	9	no		no		2	4
167	530001	1	25	1	40+3	1	2	2			2	1		2.86	2	1	7	9	no		no		2	1
168	400905	2	21	1	41+4	1	2	1			2	1		2.86	1	1	7	9	no		no		2	2
169	529334	1	26	2	40+2	1	4	1	7.00	12.33	1		1	3.5	1	1	7	9	no		no		1	
170	477200	2	21	2	41+1	1	3	1	7.00	10.83	1		1	3.7	1	1	7	9	no		no		1	
171	524528	1	27	1	40+3	1	2	3			2	1		3.1	2	1	7	9	yes	2	no		2	1
172	406004	2	24	1	40	1	2	2	13.33	19.50	1		1	3.2	1	1	7	9	no		no		1	
173	147187	1	23	1	40+4	1,2	2	4	6.00	13.33	1		1	2.9	1	1	7	9	no		no		1	
174	475699	2	24	2	41+3	1	2	1	6.00		2	1	2	3.34	2	1	7	9	no		no		2	1
175	147105	1	24	2	40+6	1	3	3	6.00	13.92	4		2	3.1	2	1	7	9	no		yes	4	2	4
176	479657	2	20	1	39+6	3	3	1	10.00	16.23	1		2	2.69	1	1	7	9	no		no		1	
177	530545	1	28	2	39	3	3	2	7.00		2	1	1	2.9	1	4	3	3	yes	4,5	yes	4	2	1
178	479854	2	23	1	39 +3	2	3	2	15.33	22.03	1		2	3.1	1	1	7	9	no		no		1	
179	531383	1	25	2	40+3	1	3	4	10.00	13.33	1		2	2.6	1	1	7	9	no		no		1	
180	469347	2	19	1	40 weeks	1,4	3	1	12.33	19.87	1		1	3.1	1	1	7	9	no		no		1	
181	531695	1	23	1	40+2	1	2	4	10.00	16.05	3		2	3.3	1	1	7	9	no		no		1	
182	428001	2	20	1	38+4	2	2	2			2	1		2.4	1	1	7	9	no		no		2	1
183	533188	1	24	2	40+1	1	3	2	8.00	10.63	1		1	3.1	1	1	7	9	no		no		1	
184	478487	2	22	1	40+1	1	4	1	9.00	12.30	1		2	2.84	1	1	7	9	no		no		1	
185	527157	1	24	1	40+3	1,2	2	4			2	3	1	2.9	1	1	7	9	no		no		1	
186	327547	2	21	1	41+4	1	2	1			2	1		2.86	1	1	7	9	no		no		2	3
187	511555	1	29	1	40+4	1	2	4			2	1		3.2	1	1	7	9	no		no		2	4
188	412937	2	27	2	40+3	1	4	1	8.00	11.68	1		1	2.56	1	1	7	9	no		no		1	
189	537420	1	28	2	40+3	1	3	2	8.00	10.87	1		1	3.4	1	1	7	9	no		no		1	
190	483655	2	25	2	40	1	4	1	8.67	10.87	1		2	2.98	1	1	7	9	no		no		1	
191	533996	1	28	2	40+1	1	3	5	18.00	20.83	1		2	2.6	1	1	7	9	no		no		1	
192	478084	2	19	1	40+1	1,4	3	3			2	2		3	1	1	7	9	no		no		1	
193	478317	1	27	2	40+2	1	4	1	6.00	7.03	1		1	2.8	1	1	7	9	no		no		1	
194	405933	2	27	1	40+1	1	3	2			2	1		3.86	2	1	7	9	no		no		2	4
195	534149	1	26	2	40+6	1	3	2	10.00	13.00	1		2	2.6	1	1	7	9	no		no		1	
196	485014	2	30	1	38+5	3	2	2	13.33	12.93	1		2	2.4	2	1	7	9	no		no		1	
197	534823	1	24	1	40+5	1	2	~~5~~	10.00	17.28	3		2	3.1	1	1	7	9	no		no		1	
198	483564	2	22	1	40+3	1	2	2	10.00	24.40	1		1	3.06	1	1	7	9	no		no		1	
199	478317	1	34	2	40+2	1	4	1	10.00	14.48	1		1	3.1	1	1	7	9	no		no		1	

200	485014	2	24	2	39+2	4	4	1	10.00	10.35	1		1	3.2	1	1	7	9	no		no		1	
201	467847	1	27	2	40	1	4	1	8.00	12.90	1		1	2.7	1	1	7	9	yes	2	no		1	
202	485624	2	24	1	40+3	1	2	1			2	1		2.7	1	1	7	9	yes	2	no		2	2
203	504990	1	26	2	40+1	1	4	1	6.00	9.33	1		1	2.9	1	1	7	9	no		yes	3	1	
204	442498	2	22	1	40 weeks	1	2	3			2	2		2.8	1	1	7	9	no		no		1	
205	522454	1	32	2	40+4	1	4	2	7.00	13.20	1		1	2.6	1	1	7	9	no		no		1	
206	478622	2	26	2	40+6	1	3	2	10.00	13.90	1		1	2.9	2	1	7	9	yes	2	yes	2	1	
207	500164	1	24	1	40+2	1	2	4	12.00	16.33	3		2	3.3	1	1	7	9	no		no		1	
208	486247	2	24	1	40+1	1	3	2	14.00	20.67	1		2	2.6	1	1	7	9	no		no		1	
209	547938	1	21	1	41+2	1	2	4			2	1		2.83	2	1	7	9	no		no		2	3
210	478622	2	27	2	40+5	1	4	1	6.00	8.62	1		1	2.9	1	1	7	9	no		yes	3	1	
211	548390	1	20	1	40+3	1	3	2	10.00	13.83	1		2	2.75	1	1	7	9	no		no		1	
212	479683	2	31	2	40+2	1	4	1	10.00	16.58	1		2	2.9	1	1	7	9	no		no		1	
213	548372	1	28	2	39+3	3	4	2	11.00	14.30	1		2	2.6	2	1	7	9	no		yes	7	1	
214	478783	2	25	1	40+5	1	2	3			2	2		3.1	1	1	7	9	no		no		1	
215	361519	1	22	1	40+1	1	3	5	10.00	13.65	1		2	3.4	1	1	7	9	no		no		1	
216	488171	2	22	1	40+2	1	3	1	10.00	27.53	1		2	3.3	1	1	7	9	no		no		1	
217	425005	1	23	2	40+1	1	3	2	10.00	13.70	1		2	3	1	1	7	9	no		no		1	
218	478783	2	21	1	40+2	1	3	2	13.67	17.03	1		2	3.09	1	1	7	9	no		no		1	
219	549102	1	29	2	40	1	2	4	9.00	12.82	1		2	2.9	1	1	7	9	no		no		1	
220	445479	2	22	2	40+2	1	2	2	16.33	21.18	1		1	3.39	1	1	7	9	no		no		1	
221	562034	1	24	2	41	1	3	1	6.00	9.97	1		1	2.8	1	1	7	9	no		no		1	
222	489059	2	26	2	40+2	1	4	1	6.00	12.18	1		1	2.9	1	1	7	9	no		no		1	
223	551317	1	24	2	40	1	4	1	4.00	8.33	1		1	2.6	1	1	7	9	no		no		1	
224	378764	2	21	1	40+2	1	3	2	12.00	15.25	1		2	3.09	1	1	7	9	no		no		1	
225	544611	1	20	1	40	1	3	2			2	1		3.52	2	1	7	9	no		no		2	4
226	484501	2	28	2	40	1	4	1	6.00	11.42	1		1	2.75	1	1	7	9	no		yes	1	1	
227	240106	1	24	2	41+5	1	2	6			2	2		3.06	1	1	7	9	no		no		1	
228	490332	2	21	1	40+5	1	2	2	12.00	21.00	1		2	2.78	1	1	7	9	no		no		1	
229	553935	1	23	1	40	1	3	3	7.00	11.72	1		2	2.74	1	1	7	9	no		no		1	
230	490158	2	22	1	40+6	1	3	1	15.00	19.00	1		1	3	2	1	7	9	no		no		1	
231	475797	1	23	1	41+2	1	3	4	10.00	15.00	1		2	3.06	1	1	7	9	no		no		1	
232	426486	2	21	2	39+1	2	4	1			2	1		2.8	2	1	7	9	no		no		2	4
233	520324	1	25	2	40+4	1	2	4	10.00	16.67	1		1	2.7	1	1	7	9	no		no		1	
234	490803	2	24	1	40+1	1	4	2			2	1		3.12	2	1	7	9	no		no		2	1
235	472141	1	24	1	41+1	1	3	4	13.00	15.17	1		1	2.7	1	1	7	9	no		no		1	
236	394008	2	19	1	40 weeks	1,4	3	1	14.00	17.50	1		1	3.1	1	1	7	9	no		no		1	
237	562000	1	24	2	40	1	4	1	5.00	8.77	1		2	3.34	1	1	7	9	no		no		1	
238	247513	2	23	2	40+1	1	4	1	8.00	14.63	1		1	2.62	1	1	7	9	no		no		1	
239	155738	1	21	2	40+3	1	3	3	11.00	12.97	1		2	2.9	2	1	7	9	no		no		1	
240	401502	2	20	1	38+4	2	3	2	12.00		2	1		2.8	2	1	7	9	no		no		2	3

241	562522	1	22	1	40+3	1	2	6			2	2		2.8	1	1	7	9	no		no		1	
242	450150	2	24	1	40+2	1	2	3			2	2		3.28	1	1	7	9	no		no		1	
243	558133	1	19	2	40+3	1	3	2	8.00	12.15	1		1	2.7	1	1	7	9	no		no		1	
244	327458	2	19	1	41	1	3	1	8.00	12.27	1		2	3	1	1	7	9	no		no		1	
245	564507	1	21	2	40+1	1	2	6			2	2		3.8	1	1	7	9	no		no		1	
246	483564	2	22	2	40+6	1	4	3	20.00	22.12	1		2	2.97	1	1	7	9	no		no		1	
247	556515	1	20	1	40+2	1	3	2			2	1		2.9	2	1	7	9	no		yes	7	2	4
248	487876	2	22	1	40+3	1	4	1			2	1		2.5	2	1	7	9	yes	2	no		2	3
249	558414	1	20	1	40	1,4	2	4	6.00	8.08	1		2	3	1	1	7	9	no		no		1	
250	494263	2	28	2	41+3	1,3	4	1	13.67	17.75	1		1	2.8	1	1	7	9	no		yes	5	1	
251	566648	1	22	2	40+5	1	4	2	12.00	15.08	1		2	2.8	1	1	7	9	no		no		1	
252	524216	2	24	1	40+1	1	3	2	12.00	15.33	3		2	3	1	1	7	9	no		no		2	3
253	566994	1	24	1	40	1	4	2	4.00		2	1		2.6	2	1	7	9	no		no		2	2
254	496989	2	26	2	40+4	1	4	1	4.00	15.60	1		1	2.9	1	1	7	9	no		yes	3	1	
255	560974	1	22	1	40+5	1	3	4	8.00	11.55	1		2	3.3	1	1	7	9	no		no		1	
256	524534	2	22	1	40	1	4	1	8.00	17.00	1		2	3	1	1	7	9	no		no		1	
257	573134	1	20	2	40+1	1	4	2	11.00	13.50	1		1	2.8	1	1	7	9	no		yes	5	1	
258	525546	2	24	1	40+1	1	3	2	12.00	18.00	1		2	2.92	1	1	7	9	no		no		1	
259	574833	1	22	2	41	1	3	1	8.00	11.33	1		1	2.9	1	1	7	9	no		no		1	
260	520311	2	24	2	39	2	4	1	8.00	11.58	1		1	2.9	1	1	7	9	no		no		1	