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A Comparative Study of Misoprostol and Dinoprostone Gel for Induction of Labor at a Tertiary Care Teaching Hospital

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Abstract: ***Objective****: The present study was conducted to compare induction of labor by using Misoprostol and Dinoprostone gel in a tertiary care hospital.*

Materials and Methods: *A prospective cross-sectional study was conducted in tertiary care hospital, Kadapa, A.P., and India for six months and utilized 80 women's with single live fetus, cephalic presentation, reactive fetal heart rate, gestational age > 36weeks. for the study. They were randomized and prescribed with 0.25 mcg of misoprostol tablet and 0.5 mg of dinoprostone tablet and combination of both drugs. To assess the efficacy of drug, the induction – initiation interval, induction to delivery interval, mode of delivery were recorded. The maternal and fetal outcome were measured with bishops scoring system, Apgar scoring system and maternal and fetal side effects.*

Result: *The mean time period between application of drug and establishment of satisfactory and regular uterine contractions in misoprostol group was 4.34, dinoprostone was 8.8 and combination of both drugs 4.45. By observing the mode ofdelivery, by administering misoprostol 92.3% women were delivered through vaginal 7.69% women by LSCS. B y administering dinoprostone 58.06% women by vaginal, 35.48% of women by LSCS and 6.45% women by forceps. 52.17% women delivered by vaginal, 8.69% women by foreceps,39.13% women by LSCS by administering the combination of both drugs. Maternal side effects were minimal with misoprostol when compared to dinoprostone and combination of both drugs.*

Conclusion: *Misoprostol is a better , effective and safe alternative drug for induction of labour than the dinoprostone gel.*

Keywords: *LMP- Last menstrual period, EDD- Expected date of delivery, IOL- Induction of labor.*

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I. Introduction

The term safe motherhood is now used to suggest measures to safe guard the health of pregnant women and her baby, ideally care for a women's health should be a concern right from her infant. Associated morbidity in postterm births includes an increased risk of fetal distress , shoulder dystocia , labor dysfunction , and obstetric trauma and an increase in perinatal complications, such as meconium aspiration , asphyxia, bone fracture, peripheral nerve injury, pneumonia and septicaemia. In India 67% of women have their births attended by a skilled medical professionals only 8% of births resulted in cesarean section.48%of women went to their postnatal visits two days after their birth. The total fertility rate per women in India is 2.2. Misoprostol has relative selectivity for the EP3 receptor but also binds to EP2 and stimulates the release of endogenous PGE2, resulting in cervical ripening and increasing uterine contractility. Dinoprostone targets all four EP receptors , activating EP1 and EP3 to increase intra cellular calcium, while EP2 and EP4 stimulate cyclic adenosine monophosphate (cAMP) production. Cervical ripening with Dinoprostone is therefore theoretically similar to endogenous cervical ripening prior to spontaneous labor.

II. Material And Methods

This prospective comparative study was carried out on subjects of Department of Obstetrics & Gynecology at tertiary care hospital, Kadapa, A.P., and India for six months and utilized 80 subjects.

Study Design: A prospective observational study.

Study Location: This was a tertiary care teaching hospital based study done in Department of Obstetrics & Gynecology, at Kadapa, Andhra Pradesh, India.

Study Duration: 6 months

Sample size: 80 patients.

Inclusion criteria:

- Pregnant women who are willing to participate in the study:
- Pregnant women with single live fetus and vaginal delivery indication of cephalic presentation, LSCS (lower Segment Cesarean Section).
- Pregnant women with reactive fetal heart rate, previous one LSCS, post maturity [41 weeks – 42 weeks].
- Pregnant women with hypertension (pre-eclampsia), eclampsia and gestational diabetes.

Exclusion criteria:

- Pregnant women who are not willing to participate in the study:
- Pregnant women with multiple pregnancies.
- Pregnant women with abnormal presentations [other than cephalic] and gestational age <36weeks.
- Pregnant women with previous uterine bleeding, malpresentation.
- Pregnant women with co-morbidities.

Materials of the study:

- Patient demographic data collection forms.
- Patient informed consent forms.
- Bishops scoring system (It's method to rate the readiness of the cervix for induction of labour)
- Apgar scoring system (To measure the physical condition of the new born infant.)
- Leaf let

Procedure methodology

A regular ward round participation was carried out in the departments of gynaecology and Obstetrics. All the information's of patients was recorded. During data collection patients were informed about the study using patient information format and obtained their written consent either from the patients or their caregivers. After enrolling the patient details, Physical Examination of Patient and laboratory parameters like haemoglobin, blood group, lymphocytes, platelets, leukocytes (eosinophils, basophils, monocytes) blood pressure, ECG etc., collected during their regular clinical visits.

Statistical analysis Paired T test is based on the differences between the values of each pair, that is one subtracted from the other. In the formula for a paired t-test, this difference is notated as d. Formula of the paired t test is the ratio of the sum of the differences of each pair to the square root of n times the sum of the differences squared minus the sum of the squared differences, all over n - 1.

III. Result

A sample of 80 patients were recruited in our study based on inclusion and exclusion criteria out of which, subjects prescribed with Misoprostol 0.25mcg, Dinoprostone gel 0.5mg were considered in our study to compare the safety, efficacy and outcome of labour in short duration with minimal time period. Results are recorded as follows with different categorisation.

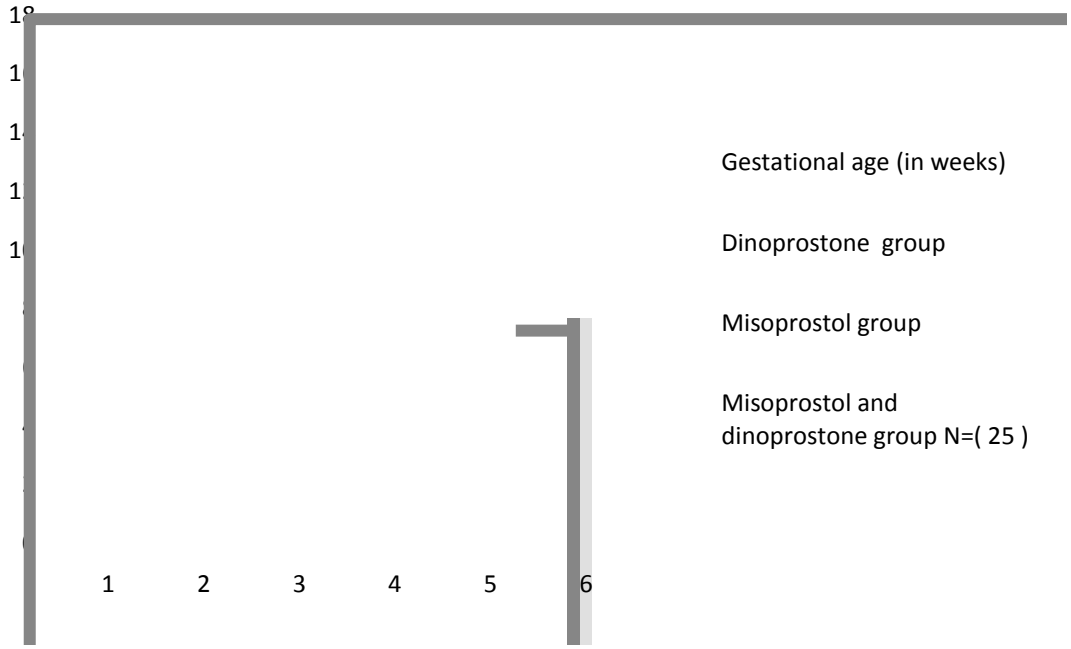
1. Gestational age of the study population:

The age of all subjects were observed and calculated average of age. Among 80 patients recruited in the study based on gestational age i.e. **36-38weeks, 39-40 weeks, and > 40 weeks** which were grouped under different gestational period respectively. Out of 80 patients, 26 patients had labour induction with dinoprostone gel, 29 had induction of labour with misoprostol tablet and 25 had labour induction with combination of drugs. Based on above consideration, 9, 18, 15 patients had IOL under 36-38 weeks of gestational age,;10, 5, 7 had IOL under 39-40 weeks of gestational age and 7, 6, 3 had IOL under >40 weeks of gestational age respectively.

Table no : 1

Gestational age (in weeks)	Dinoprostone Group N=26	Misoprostol Group N=29	Misoprostol and Dinoprostone Group N=25
36 -38	9	18	15
39 - 40	10	5	7
>40	7	6	3

Graph no: 1



2. Comparison of Drugs Based on Gestational Age:

Among 80 patients recruited in the study, based on age 18-22 years, 23 – 28 years, 29-33 years, 34-38 years of age respectively. Out of 80 patients, 26patients had labour induction with dinoprostone gel, 31 patients had IOL with misoprostol tablet and 23 patients had IOL with combination of drugs. 6, 11, 8 had IOL under age of 18-22 years;15, 17, 13 had IOL under age of 23-28 years; 2, 3, 1 had IOL under age of 29-33 years of age and 3,0,1 had IOL under age of age.

Table no : 2

Age Years	Dinoprostone group N =26	%	Misoprostol group N=31	%	Misoprostol and dinoprostone group N=23	%
18-22	6	23.0	11	35.4	8	34.7
23-28	15	57.6	17	54.8	13	56.5
29-33	2	7.6	3	9.6	1	4.3
34-38	3	11.5	0	0	1	4.3

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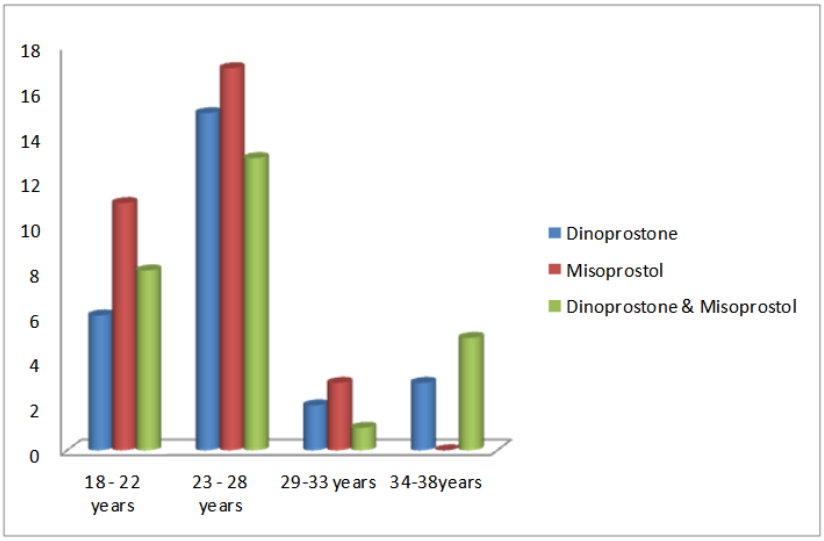
Graph no: 2



3. Distribution of Patients Based on Gravida:

Among 80 patients recruited in the study based on gravid .Out of which 31 patients had IOL with misoprostol, 26 patients had IOL with dinoprostone gel and 23 patients had IOL with combination of drugs. Based on above consideration 21, 18, 17 had IOL under primigravida and 10, 8, 17 had IOL under multigravida.

Table no : 3

Gravida	Misoprostol N=31	%	Dinoprostone N=26	%	Misoprostol & Dinoprostone N=23	%
Primigravida	21	67.7	18	69.2	17	73.90
Multigravida	10	32.2	8	30.7	6	26.08

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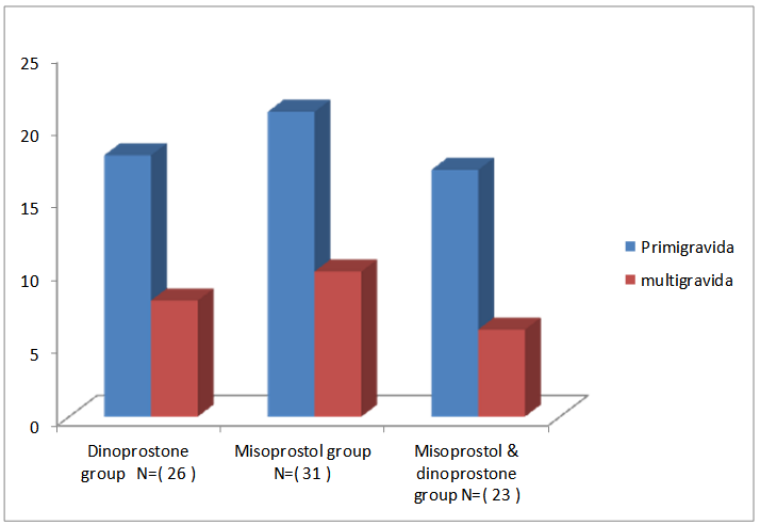
Graph no: 3



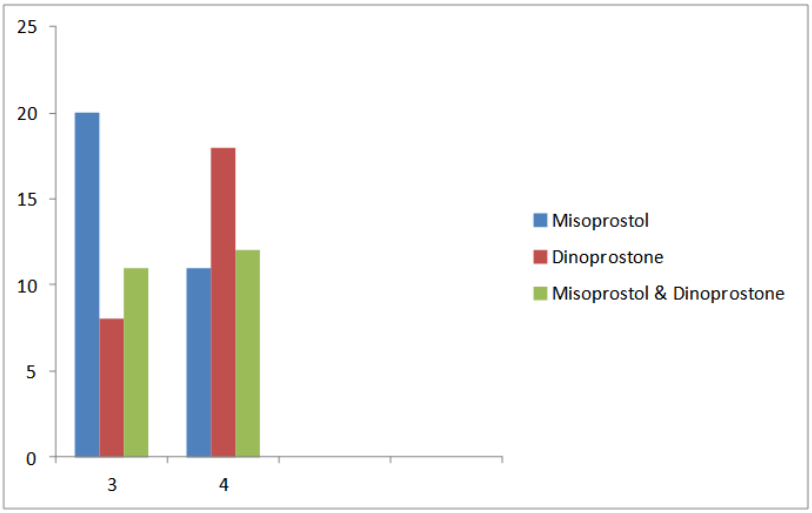
4. Bishops Scoring System

Among 80 patients recruited in the study based on bishops scoring system. Out of which 31 patients were treated with misoprostol tablet, 26 patients were treated with dinoprostone gel and 23 patients were treated with combination of drugs. Based on above consideration, 20, 8, 11 patients had bishops score 3 and 11, 18, 12 patients had bishops score 4 respectively.

Table no : 4

Bishops score	Misoprostol N=31		Dinoprostone N=26		Misoprostol & Dinoprostone N=23		P value
3	20	64.5	8	30.7	11	47.8	< 0.03
4	11	35.4	18	69.2	12	52.1	< 0.03

Graph no: 4



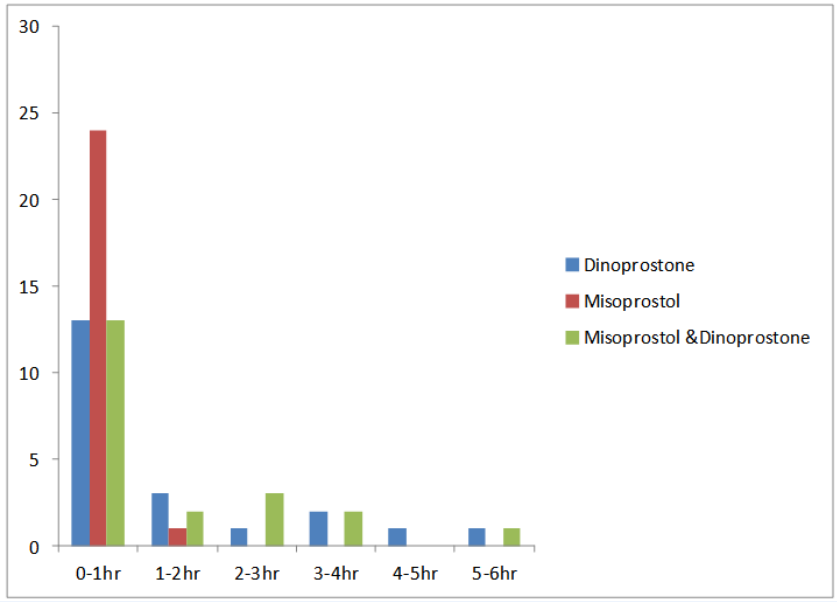
5. Distribution of Patients According to Induction Initiation Labour Interval

Among 80 patients recruited in the study based on induction initiation labour interval. Out of which 26 patients had IOL with dinoprostone gel, 30 patients had IOL with misoprostol tablet, and 24 patients had IOL with combination of drugs. Based on above consideration, 13, 24, 13 had induction initiation interval within 0-1 hour; 3, 1, 2 patients had induction initiation interval within 1-2 hours; 1, 0, 3 patients had induction initiation interval within 2-3 hours; 2, 0, 2 patients had induction imitation interval within 3-4 hours; 1, 0, 0 patients had induction initiation interval within 4-5 hours; 1, 0, 1 patients had induction initiation interval within 5-6 hours; and 5, 5, 3 patients had induction initiation interval >6 hours

Table no: 5

Time (Hour)	Dinoprostone group N=26)	%	Misoprostol Group N=30	%	Misoprostol & dinoprostone group N=24	%
0-1	13	50%	24	92.3%	13	54.1%
1-2	3	11.5%	1	3.3%	2	8.3%
2-3	1	3.8%	0	0%	3	11.5%
3-4	2	7.6%	0	0%	2	8.3%
4-5	1	3.8%	0	0%	0	0%
5-6	1	3.8%	0	0%	1	4.1%
>6	5	19.2%	5	16.5%	3	11.5%
Std dev	4.34		8.88		4.35	
P value	<0.05					

Graph no: 5



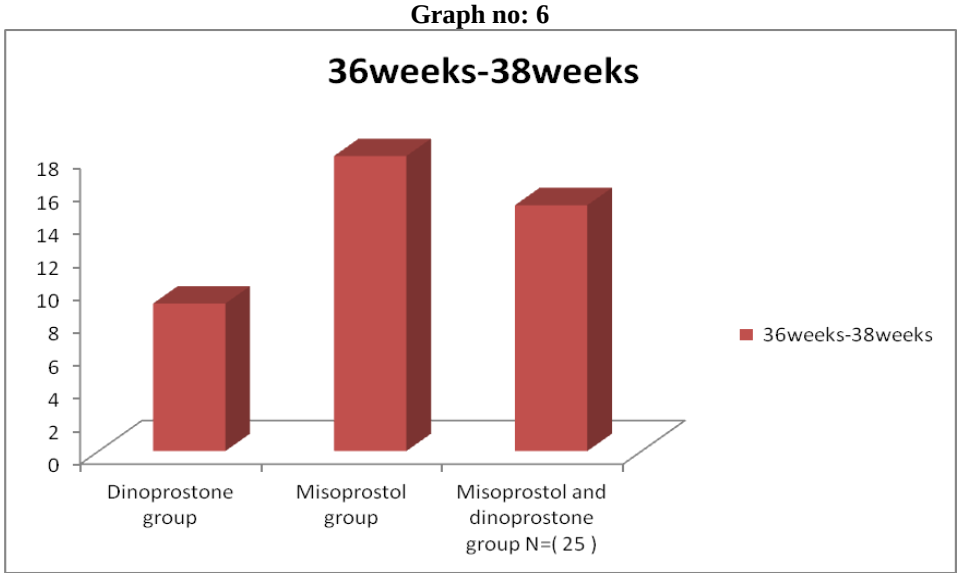
6. Induction to delivery interval:

Among 80 patients recruited in the study based on induction to delivery interval, among them 26 patients had IOL with dinoprostone gel, 31 patients had IOL with misoprostol tablet and 23 patients had IOL with combination of drugs. Based on above consideration 24, 28, 18 patients had IOL within 12 hours and 2, 3, 5 patients had IOL within 24 hours.

Table no : 6

Time	Dinoprostone group N=26	%	Misoprostol group N= 31	%	Misoprostol and Dinoprostone group N=23)	%	Std dev	P value
Delivery in 12 hours	24	92.3%	28	90	18	78.2	5.03	<0.05
Delivery n in 24hrs	2	7.69%	3	9.6	5	21.7	1.52	

Graph no: 6



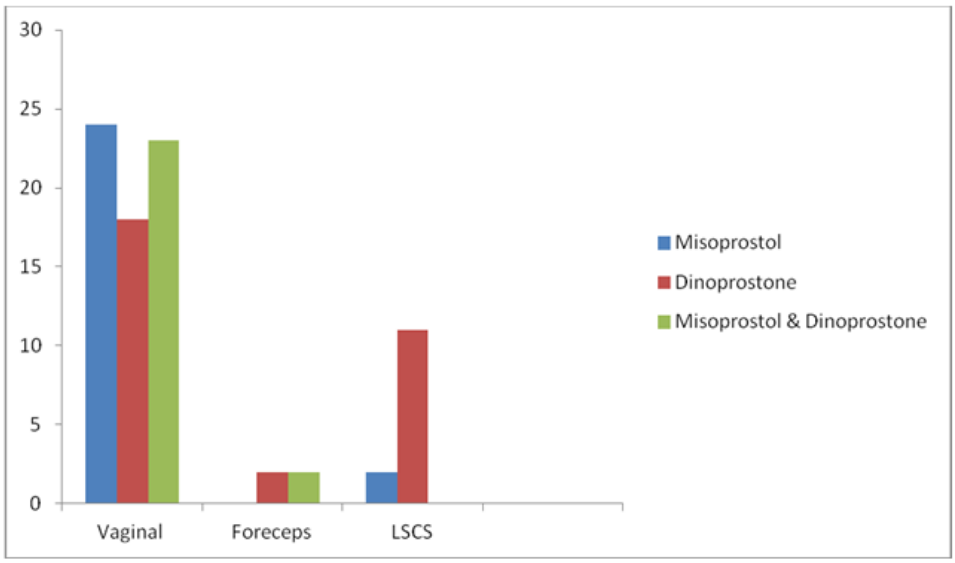
7. Mode of Delivery

Among 80 patients recruited in the study based on mode of delivery. Out of 80 patients, 26 patients had IOL with misoprostol, 31 patients had IOL with dinoprostone gel, and 23 patients had IOL with combination of drugs. Based on above consideration 24, 18, 23 had vaginal delivery. 2, 2 patients had IOL with forceps and 2, 11, 9 patients had IOL by LSCS.

Table no : 7

Mode of delivery	Misoprostol group N=26	%	Dinoprostone group N=31	%	Misoprostol & dinoprostone group N=23	%
Vaginal	24	92.3%	18	58.06%	12	52.17%
-Forcep	0	0%	2	6.45%	2	8.69%
Caesarean induction	2	7.69%	11	35.48%	9	39.13%

Graph no: 7



8. Side Effects:

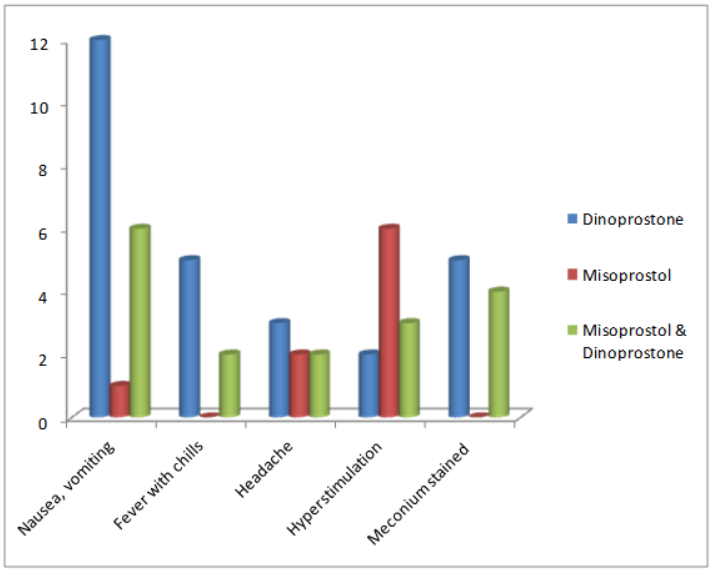
Among 80 patients recruited in the study based on the side effects affected by individual women. Out of which 19 patients had developed side effects who were treated with dinoprostone gel. 7 patients had developed side effects who were treated with misoprostol tablet and 10 patients had developing side effects with the treatment of combination of drugs. Based on above consideration, 8, 1, 3 patients had nausea & vomiting; 3,

0, 2 patients had developed fever with chills; 3, 2, 5 patients had developed headache: 1, 4, 1 patients had developed hyper stimulation; and 4, 0, 2 patients had meconium stained liquor respectively.

Table no : 8

Side Effects	Dinoprostone group N=19	%	Misoprostol group N=7	%	Misoprostol & dinoprostone group N= 10	%	Std Dev	P value
Nausea, Vomiting	8	42.1	1	14.2	3	30	5.05	<0.05
Fever with chills	3	15.7	0	0	2	20	2.51	
Headache	3	15.7	2	28.5	2	20	0.57	
Hyper stimulation	1	5.2	4	57.4	1	10	2.08	
Meconium stained liquor	4	21.5	0	0	2	20	0.00	

Graph no: 8



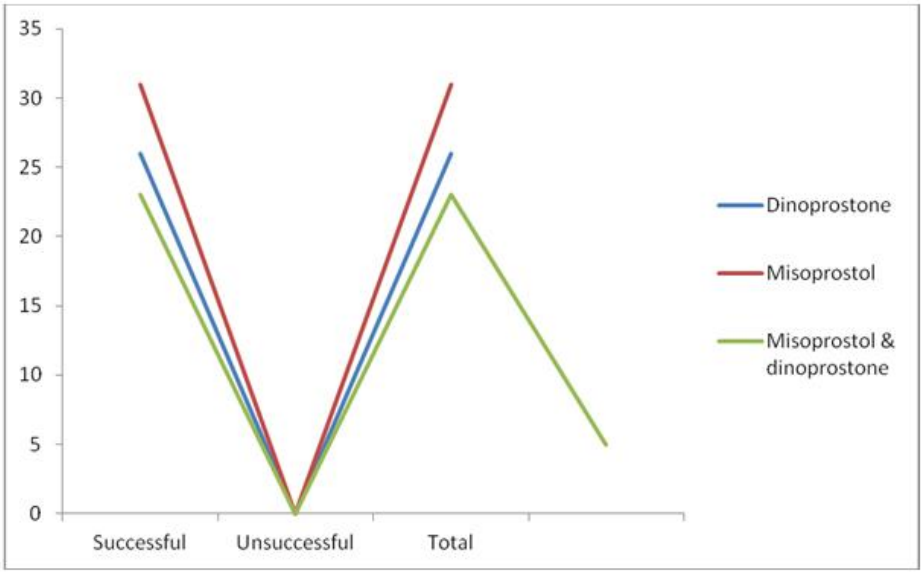
9. Outcome of Induction of Labour:

Among 80patients recruited in the study based on outcome of the delivery. Out of which 26 patients had successful IOL with dinoprostone gel, 31 patients had IOL with misoprostol tablet and 23 patients had IOL with combination of drugs.

Table no: 9

Outcome	Dinoprostone group N=26	Misoprostol group N=31	Misoprostol and Dinoprostone group N=23	Std dev	P value
Successful	26	31	23	0.69	
Unsuccessful	0	0	0	0.00	>0.05
Total	26	31	23	0.69	

Graph no: 9



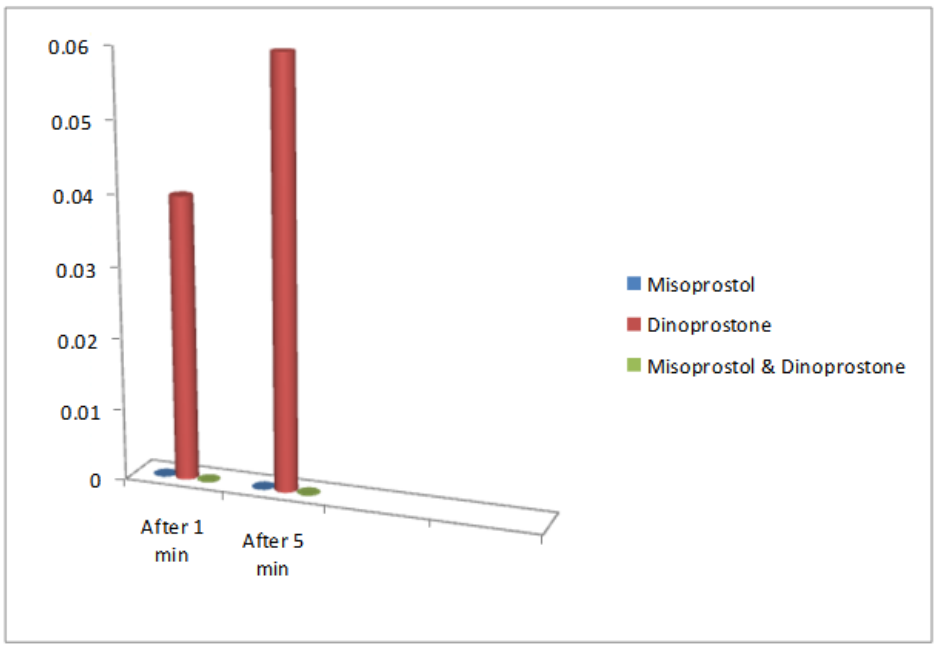
10. Neonatal Outcome :

In this study we found the neonatal outcome by using APGAR scoring system. Out of 80 patients 31 patients are administered with misoprostol and their neonatal outcome is >7. 26 patients had treated with dinoprostone gel and their neonatal outcome is 6% & 4% after 1 & 5 minute respectively. 23 patients had treated with combination of drugs and neonatal outcome is 1% after 5 minutes.

Table no : 10

APGAR SCORE <7	Misoprostol group N=31	Dinoprostone group N=26	Misoprostol & Dinoprostone N=23
After 1 min	-	6%	-
After 5 min	-	4%	1%

Graph no: 10



IV. Discussion

Induction of labour indicates the artificial initiation of uterine contractions after the period of viability by medical and/or surgical method for the purpose of vaginal delivery [4].Induction of labour is a common procedure in obstetrics. WHO defines IOL as the initiation of labour by artificial means prior to its spontaneous onset at a viable gestational age, with the aim of achieving of vaginal delivery in pregnant women with intact membranes[20].

Induction primarily refers to attempt to produce regular uterine contractions along with cervical changes to begin the active phase of labour. Cervical ripening is an essential prerequisite for induction and is assessed with bishop scoring system[4]. Induction of labour has become a common intervention with induction rate ranging from 16% to 44%.[25].

Prostaglandins have evolved as the most popular and frequently used pharmacological agents for induction of labour, owing to their dual action of cervical ripening and uterine contraction inducing effect[20].

Misoprostol[MSP],the synthetic analogue of PGE1, commonly used as a gastric cytoprotective agent.It has several potential advantages, it is stable at room temperature, it is relatively inexpensive and it has been shown to be effective and safe in stimulating uterine contractions[24].

Dinoprostone[PGE] is a synthetic preparation of naturally occurring prostaglandin E2[15].It requires an intra cervical application, needs refrigeration and is expensive[8].PGE2 gel is available in 2.5ml syringe for an intracervical application of 0.5mg dinoprostone[15].

The present study was undertaken to assess the efficacy and safety of misoprostol as compared to the intracervical dinoprostone for induction of labour and to assess maternal and foetal outcome. The present study, we observed that the mean time period between application of drug and establishment of regular uterine contractions in misoprostol group and dinoprostone group.

A total of 80 patients were chosen for this study, and they are treated with misoprostol tablet (0.5mg), dinoprostone (0.25mcg) and misoprostol & dinoprostone.

The present study, we observed that, the mean time period between application of drug and establishment of satisfactory and regular uterine contractions in misoprostol group was 4.34, dinoprostone group was 8.8 and combination of both groups it was 4.45. In this study the mean induction to delivery interval was less in the misoprostol group, which is statistically significant (p=<0.05). Similar results were seen in study in 2013 by Dr Pooja patil et al where it was 11.12, 14.61, and 13.9.

The p value related to modified bishops score in both the dinoprostone , mosoprostol and combination of both drugs is <0.03 and is statistically significant. 64.5% and 35.4% of patients had MBS of 3 and 4 respectively in misoprostol group. In dinoprostone group, 30.7% and 69.2% of patients had MBS as 3 and 4 respectively. Similar results were seen in Pooja patil et al.

By observing the mode of delivery 26 women were treated with misoprostol tablet , 31 women were treated with dinoprostone gel and 23 women were treated with combination of misoprostol and dinoprostone. By administering misoprostol ,92.3% (24) women were delivered through vaginal ,7.69% (2) women were delivered by CS; By administering dinoprostone gel 58.06% (18) women were delivered through vaginal delivery ,6.45% (2) deliveries by forceps, 35.48% (11) of women were undergone to caesarean section; By administering combination of both drugs 52.17%(12) women delivered through vaginal delivery, 8.69% (2) women were delivered foreceps, 39.13%(9) women delivered by LSCS. By observing the mode of delivery, it was found that misoprostol was able to increase the incidence of spontaneous labour and delivery. It was favoured by the studies of 2010 Hemaannasaheb et al showed that induction delivery interval was significantly shorter in misoprostol group. In our study CS was significantly less in misoprostol group, this is similar to the study done by S. Kulshreshtha et al(2007).

Maternal side effects were minimal in misoprostol group when compared to dinoprostone group and combination of both drugs. In misoprostol group 4 (57.4%) patients under went to hyper stimulation of uterus, 2(28.5%) patients were having headache and 1 (14.2%)patient have a nausea & vomiting. In dinoprostone group 8(42.1%) women were underwent to nausea & vomiting, 3(15.7%) women with fever, chills, 3 (15.7%)women have headache, 4 (21.5%) women have meconium stained liquor. In combination of both drugs 3 (30%) women have nausea & vomiting, 2(20%) women have fever, 2(20%) women have headache, 2(20%) women have meconium stained liquor. Maternal side effects were minimal in misoprostol group. In 2013 Pooja patil notified that misoprostol have less side effects than dinoprostone and combination of both drugs.

By observing the study, we found that 31women who were treated with misoprostol tablet, 26 women were treated with dinoprostone and 23 women were treated with combination of misoprostol & dinoprostone had successful induction, the difference between the three groups being statistically significant (p=<0.05).

The neonatal outcome in both the groups was comparable. Apgar score <7 at 1min was seen in 3 cases of dinoprostone group out of which two had to be admitted to NICU. Pooja patil et al also had 6% newborns with Apgar <7 at one minute in the dinoprostone group which is consistent with our study.

V. Conclusion

The use of PG's providing an effective method for achieving the induction of labour. On the basis of our study, misoprostol appears to be an effective agent for the induction and augmentation of labour as compared to the dinoprostone. The results of labour outcome convincingly prove that in the patients treated with misoproatol, induction interval was shorter and the incidence of caesarean section were reduced. There was clearly a superior neonatal outcome in terms of Apgar score and perinatal outcome in misoprostol group, when compared to dinoprostone and combination of both dinoprostone gel & misoprostol tablet.

Therefore, misoprostol is cheaper than dinoprostone, easy to administer by vaginal route and does not require refrigeration, where as dinoprostone requires refrigeration for its storage and cost effective.
This indicates that misoprostol is a better, effective and safe alternative drug for induction of labour.

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