RESEARCH PAPER | Home Science | Volume : 2 | Issue : 1 | October 2012 | ISSN - 2249-555X

Comparative Study of Misoprostol with Dinoprostone Intracervical Gel for Cervical Ripening and Induction of Labour

KEYWORDS: Misoprostol, Dinoprostone, cervical ripening, labour induction.

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ABSTRACT *The present study is aimed to compare the efficacy ,safety and cost effectiveness of Dinoprostone with oxytocin infusion and Misoprostol alone for ripening and induction of labour in women with unfavourable cervix.*
This prospective study was conducted for a period of 3 years in the Obstetrics and Gynaecology department at Bharati Medical College and Hospital Pune. 200 antenatal women, with single live pregnancy more than 34 weeks with vertex presentation and Bishop's score 6 or less who required induction of labour were included in the study. In conclusion a low dose of Misoprostol was as effective as Dinoprostone Gel for cervical ripening and labour induction. The induction to delivery time was significantly longer in the Misoprostol group (19.29+/-2.42 hours) but the foetal distress and cervical dystocia was similar in both the groups. The neonatal outcome was good and no drug related side effects were encountered in both the groups.

INTRODUCTION:
Induction of labour has become a common intervention with induction rate ranging from 16 %(Calder et al 1) to 44 % (Yeast et al 2).

For majority of women labour starts spontaneously and results in vaginal delivery. Many medical and obstetrical complication of pregnancy overweighs the risk of spontaneous delivery. Labour induction in presence of unfavourable cervix is often prolonged and may lead to induction failure 3.Hence ,Cervical ripening is required before induction of labour to achieve more successful outcome .The only medical method of proven efficacy for pre-induction cervical ripening and labour induction currently is combination of Dinoprostone Gel given intracervically and intravenous oxytocin infusion4,5.Dinoprostone Gel ,preparation has to be administers by intracervical route which is invasive. It has to be refrigerated during storage and a minimum time gap of six hours has to be elapsed after the dose for further management6.Misoprostol ,the synthetic analogue of PGE1 commonly used as gastric cytoprotective agent ,was first reported in 1987 for induction of labour, in case of intrauterine foetal death in third trimester7.

Recently, it has been shown to be an effective and safe agent for pre-induction in many clinical trials. The use of Misoprostol is non-invasive and convenient. The drug is stable at room temperature and cost-effective in comparison to inducing agent currently available8.A major adverse effect of the obstetrical use of Misoprostol is hyper stimulation of uterus and foetal distress, but it is usually seen in cases where Misoprostol is given in higher doses9.

The present study is aimed to compare the efficacy, safety and cost effectiveness of Dinoprostone with oxytocin infusion and Misoprostol alone for ripening and induction of labour in women with unfavourable cervix.

MATERIAL AND METHODS:
An institute based prospective study was carried out from August 2007 to April 2010involving antenatal women requiring induction of labour admitted in the antenatal ward of the Obstetrics and Gynaecology department of Bharati Medical College and Hospital, a tertiary care teaching institution in Pune.

Patient's eligibility criteria:
200 antenatal women who require induction of labour for different indications were included in this study. First a detailed history, thorough general, systemic and obstetric examination including per-vaginum examination in all patients who needed induction was done after informed consent. All antenatal women had singleton viable pregnancy more than 34 weeks with vertex presentation with Bishop's score 6 or less. All patients with previous lower segment caesarean section, cephalopelvic disproportion, antepartum haemorrhage, grand multipara (parity >4),malpresentation, multiple gestation, patient already in established labour, abnormal foetal heart rate, premature rupture of membranes, known hypersensitivity to prostaglandins, heart disease and bronchial asthma were excluded from this study.

The antenatal patients were divided into two groups group 'A' were given Tab Misoprostol (25µgm)was introduced vaginally hourly upto maximum of 8 doses (maximum dose of 200µgm).These patients were examined at four hourly interval to know the improvement in Bishop's score. In the Group 'B' intracervical Dinoprostone gel (0.5mg), if required was repeated after 6 hours followed by oxytocin infusion. The cases were reviewed 6 hours after first instillation. If the score was still poor reinstallation was done and they were examined four hours after the second instillation to judge the improvement in Bishop's score .Once the Bishop's score was more than 8, oxytocin drip was started. Progress of labour was monitored with the help of partogram in both groups. Record of induction delivery time, complications (tachysystole ,foetal distress etc) and requirement of any operative intervention was maintained. Non stress test was done on all patients before induction. Amniotomy was done in active phase of labour, no sedatives, analgesics and no dilators (Hyoscine , Drotavarine) were used.

OBSERVATION:
AGE DISTRIBUTION :
Both the groups were statistically similar vis a vis age. Majority of the patients (96% in the Misoprostol and 88% in the Dinoprostone group were in the age group 17 to 24 years.

GRAVIDITY:
Bothe the study groups were similar in terms of gravidity. Maximum number of patients (54% in the Misoprostol group and 65% in the Dinoprostone group) were primigravidas.

GESTATIONAL AGE:
Both the groups were similar in terms of gestational age

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.Maximum number of patients(57% in the Misoprostol group and 55% in the Dinoprostone group) were of the gestational age between 40-41 weeks. The age group 38 to 40 weeks formed the next largest group(30% in the misoprostol and 27% in the Dinoprostone group).

INDUCTION DELIVERY TIME(As per Gravida):
Primigravidas had a longer mean induction to delivery time within each group but it failed to achieve a statistical significance (p-value 0.757 in Misoprostol Vs 0.563 in Dinoprostone).

Mean induction delivery time in the Misoprostol group (19.59, standard deviation – 2.42) and in the Dinoprostone group (17.98, standard deviation – 2.09) with the P value being 0.001.The induction delivery time in the Misoprostol group is significantly more than the Dinoprostone group.

Chart 1: Induction Delivery Time . just about here.
INDUCTION DELIVERY TIME (as per BISHOP'S SCORE):
Table 1 : Induction delivery time (as per BISHOPS SCORE) Misoprostol group .just about here.

This table shows that 60% of patients had induction delivery time in between 16 to 20 hours with Bishop's score less than or equal to 6. 50% of the patients had a Bishop's score of 4 before induction.

Table 2 :Induction delivery time (as per BISHOPS SCORE) Dinoprostone group. just about here.
This table shows that maximum patients (72%) with Bishop's score 5 or less had induction delivery time of 16 to 20 hours.

Induction delivery time as per time distribution showed that the majority of patients (60% in the Misoprostol and 72% in Dinoprostone group) had delivered in 16 to 20 hours.

NUMBER OF DOSES OF MISOPROSTOL:
Majority of patients(57%) undergoing induction were of gestational age 40 to 41 weeks and 61 %(34 primigravida and 27 multigravida) of the patients required 4 doses of Misoprostol with a Bishop's score less than or equal to 6.While 28%(14 primigravida and 14 multigravida) required 5 tablets of Misoprostol.

NUMBER OF DINOPROSTONE GEL INSTILLATON REQUIRED:
98% patients required a single instillation of Dinoprostone gel irrespective of the Bishop's score (54.1% in gestation age 40-41 weeks) while 2% patients in the same gestation age required a second instillation of Dinoprostone gel with the Bishop's score less than or equal to 3 before induction. All multigravidas(35%) required just one instillation of Dinoprostone gel while 2% of the primigravida's required a second instillation of the gel.

MODE OF DELIVERY:
Both the groups were statistically similar in terms of mode of delivery. Majority of patients (91% in Misoprostol group and 87% in Dinoprostone group) had full term normal deliveries. Caesarean section was done in 8% of Misoprostol and 11% of the Dinoprostone group.

MEAN BLOOD LOSS:
This study shows that both the groups were statistically similar in terms of blood loss. Blood loss of more than 500 ml was seen in 9% of the Misoprostone group and 5 % of the Dinoprostone group.

COMPLICATIONS:
This study showed that both the groups were statistically similar in terms of complications(fetal distress 8% in misoprostone group and 11 % in Dinoprostone group(P value 0.469) and cervical dystocia was seen in 1 % in misoprostone group and 2 % in the Dinoprostone group(P value 0.561).No cases of Tachysystole and Uterine rupture were seen.

APGAR SCORE at1 minute:
An APGAR SCORE of 8 was seen in maximum percentage in both the groups. None of the Misoprostol group had a score of 9 while none of the Dinoprostone group had a score of 0.
APGAR SCORE at 5 minutes:

The APGAR SCORE of 9 was seen in 83% of Misoprostol group and 90% of the Dinoprostone group.None of the Misoprostol group had an APGAR SCORE of 7 while none in the Dinoprostone group had a zero score.

COST ANALYSIS:
Induction by Misoprostol is more than six times cost effective than induction by Dinoprostone gel.

DISCUSSION:
In the present study the maximum number of patients were in the age group 17 to 24 years which was attributed to early marriage and early obstetrical career in our country .These findings were similar to the findings in the study conducted by Kulshreshtha S et al10 .Whereas a study conducted by Kadanalli S et al11 noted that 58% patients belonged to the age group of 24 to 30 years. The reason for this was attributed to late marriages in the western countries.

In the study conducted by Peter Danielian12 a maximum number of patients were primigravida(54% in Misoprostol and 59% in Dinoprostone group).However ,statistically no significant difference was found as per parity in both the groups also the gestational age of the patients was 40 -41 weeks. In the present study also the results were similar with maximum patients being primigravida(54% in the Misoprostol group and 65% in the Dinoprostone group)the difference was not statistically significant .In our study too the maximum number of patients were in the gestational age 40-41 weeks(57% in the Misoprostol and 55 % in the Dinoprostone group).

The indication for induction of labour was studied by Germund N13 in the Misoprostol group where post –term pregnancy was most common, seen in 28% cases. In the Dinoprostone group hypertension and post –term pregnancy in 24% .In the study conducted by Ozkan14 ,the maximum percentage of patients, which was 28.6% ,were induced for hypertension in both the Misoprostol and Dinoprostone groups. . Pandis G15 conducted a study with similar results where postdatism as an indication of induction of labor was seen in 62.6% in the misoprostol group and 60 % in the Dinoprostone group.

The present study includes maximum cases of postdatism (69% of misoprostol and 71% of Dinoprostone gel) as an indication for labour induction.

The present study shows that primigravida patients had taken more induction delivery time than multigravida in both the Misoprostol and Dinoprostone group but failed to reach statistical significance. In contrast to our study Gregson S16 observed that majority of women who delivered in 24 hours were multiparous.

In the present study the Misoprostol group has taken the longer induction time than Dinoprostone group (p value -0.001). 60 % of the patients in the Misoprostol group and 72% in the Dinoprostone group have delivered in 16 to 20 hours irrespective of the Bishop's score before labour induction. The reason for this could be that oxytocin infusion has been used in the Dinoprostone gel group. Dallenbach P17 have noted a similar findings where the Misoprostol group took longer induction delivery time(21.25 hours).This delay in these studies may be related to the administration of Misoprostol in low doses and with longer interval(ie.25mcg over 4 to 6 hours interval) in comparison to Dinoprostone group (18hrs). Chuck FJ et al18 studied in 103 patients the safety and efficacy of intravaginal Misoprostol with Dinoprostone gel for labour induction. They found that the induction delivery time in Misoprostol was shorter than the Dinoprostone gel(11.4 Vs 18.9 hours).No significant difference was seen in the mode of delivery and maternal,foetal complications.

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However Szczesny W 19et al observed that 95% of the patients delivered vaginally within 24 hours when the Bishop's score was 3 and in 75% of those who had a Bishop's score <=3.

In contrast Sifakis S20 found a shorter delivery time(11.3 hours) in the Misoprostol group which could be explained with the higher doses (50 and 100mcg with a comparatively shorter time interval 2-4 hours).He also found no significant difference in the number of doses needed as per gestational age and parity though maximum number of patients were post dated.

In the present study 57% of patients who were in the gestational age 40 to 41 weeks required 4(61%patients) to 5(28%patients) doses of Misoprostol for induction. About 61% of patients with Bishop's score <6 needed only 4 doses of Misoprostol(25mcg 4 hourly,intravaginally) whereas 98% of patients with the same score required only one Dinoprostone gel instillation along with Oxytocin infusion explaining the shorter delivery time. It was observed that there was no significant difference in the number of doses required for the patient as per parity in both the groups(primigravida54 %,multigravida46%). Due to the low dose, the incidence of hyperstimulation and meconium stained amniotic fluid are found less frequently. Although the progess of labour is a little slower but a higher spontaneous birth rate and low Caesarean section rates were seen with less NICU admissions for the newborns.

Ozkan S ,Pandis G , Danielian P and Sifakis used a higher dose of Misoprostol .The induction time was definitely shorter but a higher incidence of Caesarean section for foetal distress ,increased rate of hyperstimulation, and an increased number of NICU admissions for birth asphyxia, meconium aspiration syndrome were increased.

The present study showed that maximum patients had delivered vaginally without the use of operative interventions irrespective of the method used(91 % in Misoprostol group and 87% in Dinoprostone group .However 8% of the patients underwent Cesarean section in the Misoprostol group and 11% in the Dinoprostone group. This could be due to low dose of Misoprostol and Dinoprostone used in our study and also due to the less number of high risk cases in our study group.

Similar results were seen by KadanaliS, Denguezli S21 and Ozkan S , Misoprostol being used in low doses with longer intervals. In contrast a higher Cesarean rate due to high risk cases was observed by Gemund N whereas higher doses of the drugs causing foetal distress and failure to progress was the reason in studies conducted by Pandis G.

In the present study complications like foetal distress was seen in 8% cases in Misoprostol group and 11 % cases in Dinoprostone group. Cervical dystocia was seen in 1% cases in Misoprostol group and 2% in the Dinoprostone group both were not statistically significant. There were no cases of hyperstimulation and uterine rupture in the present study in both the groups. This was attributed to low dosage of drugs, critical CTG monitoring and observation of the progress of labour with the help of the partogram.

High rates of foetal distress was observed by Denguezeli and Ozkan S , though it was statistically insignificant which was linked to the high doses of Misoprostol and Dinoprostone gel. There were no other studies where uterine rupture was observed except those done by Szczesny and Kjollesdal where 11 patients with previous ceasarean section were induced with Misoprostol and one patient had an uterine rupture.

In our study a mean blood loss of more than 500ml was seen in 14% of cases wherein 9% were seen in the Misoprostol group and 5% in the Dinoprostone group though there was no statistical significance. Gregson S , Danielian P and Ozkan have observed no statistical difference in both the Misoprostol and Dinoprostone group.

Present study showed an APGAR score of 7 or 8 at 1 minute and 9 at 5 minute after birth but the difference was not statistically significant in both the groups. Our study showed a good neonatal outcome and less Neonatal intensive care unit(NICU) admissions.. Gemund N observed adverse neonatal outcome like birth asphyxia, meconium aspiration, small for gestation age (21% in the Misoprostol and 23% in the Dinoprostone group) though it was not statistically significant.

In the present study maximum number of patients required 4 doses of Misoprostol (25mcg) and one dose of Dinoprostone gel (0.5mg). The total cost of Dinoprostone came to more than Rs 200 which was nearly 6 times the cost of the Misoprostol group(Rs 34). the cost of the Dinoprostone group will be higher due to the requirement of refrigeration, use of infusion sets, intravenous catheters, normal saline. The unavailability of the refrigeration facilities in remote corners of the country increases the fear of degeneration of the drug with a break in the cold chain thus making the use of Misoprostol a more cost effective and attractive option.

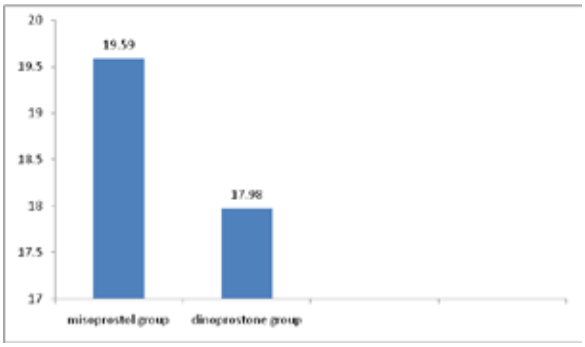
Despite numerous studies comparing Misoprostol and Dinoprostone in different dosages , none of the authors could conclusively prove the advantage of Misoprostol over Dinoprostone.

CONCLUSION:

In conclusion we can say that low dose Misoprostol was as effective as Dinoprostone gel for cervical ripening and induction of labour. Induction to delivery time was significantly longer in the Misoprostol group than in the Dinoprostone group. The total average cost of treatment in the Misoprostol group was cheaper than in the Dinoprostone group. Misoprostol as well as Dinoprostone group had similar incidences of foetal distress and cervical dystocia. Neonatal outcome was good and Neonatal intensive care unit(NICU) admissions were less and was similar in both the groups. No drug related side effects were encountered in both the study groups.

LEGENDS

Chart 1: Induction Delivery Time



Vertical axis: mean induction delivery time

Horizontal axis: misoprostol and dinoprostone group

Table 1:Induction delivery time (as per BISHOPS SCORE) Misoprostol group.

BISHOP'S SCORE

TIME(hrs)	2	3	4	5	6	Total
8-12	-	-	-	-	-	-
12-16	0	0	0	5	0	5
16-20	0	2	34	23	1	60
20-24	0	7	16	6	0	29
>24	4	2	0	0	0	6
Total	4	11	50	34	1	100

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Table 2:Induction delivery time (as per BISHOPS SCORE) Dinoprostone group.
BISHOP'S SCORE

TIME(hrs)	2	3	4	5	6	Total
8-12	0	1	0	1	0	2
12-16	1	2	6	8	1	18
16-20	3	7	42	20	0	72
20-24	0	1	2	5	0	8
>24	-	-	-	-	--	-
Total	4	11	50	34	1	100

This table shows that maximum patients (72%) with Bishop's score 5 or less had induction

CERTIFICATE

This is to certify that the Original article entitled , "**Comparative Study Of Misoprostol With Dinoprostone Intracervical Gel For Cervical Ripening and Induction Of Labour**" has been seen and approved by all of us. There is no conflict of interest among the authors. It has not been published elsewhere either in printed or electronic form and is not under consideration for publication elsewhere.

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REFERENCES

1.Calder AA. Review of prostaglandin in use in labour induaction.Br J Obstet Gynaecol.1997 Oct;104 suppl 15:2-7:20-5. | 2.Yeast JD, Jones A, Poskin M. Induction of labor and the relationship to cesarian delivery:A review of 7001 consecutive inductions.American Journal Of Obs Gynaec 1999 Mar;180(3 Pt 1):628-33. | 3.Brindley BA, Sokal RJ .Induction and management of labour. Basis and methods for current practise. Obstet gynecol Surv1988;43:730. | 4.Seitchik J, Amico J, Robinson AG, et al: Oxytocin augmentation of dysfunctional labor, 4. Oxytocin pharmacokinetics. Am J Obstet Gynecol 150:225, 1984. | 5.Bernstein P: Prostaglandin E2 gel for cervical ripening and labour induction: A multi-centre placebo-controlled trial. Can Med Assoc J 145:1249, 1991. | 6.Novakov A, Segedi D , Milasinovic L, Vejnovic T. Induction of labor by endocervical application of prostaglandins and intravenous infusion of oxytocin in post term pregnancy. Medl Pregl Curcic A 1998 Sept- Oct;51(9-10):419-26. | 7.Andrew weeks. Clarifying the role of Misoprostol in obstetrics. African health sciences editorial. Afr health sci.2001 dec;1(2):52-54. | 8.Wing DA,Rahall A,Jones MM,Goodwin TM,PaulRH.Misoprostol :an effective agent for cervical ripening and labor induction.Am J Obstet Gynecol.1995 june;172(6):1811-6. | 9.Hofmeyr GJ. GulmezogluAM, Alfirevic Z. Misoprostol for induction of labor : a systematic review.(adverse effects).Br J Obstet Gynaecol.1999 Aug;106(8):798-803. | 10.Kulshrestha S, Sharma P ,Mohan G, Singh S . Comparative study of Misoprostol Vs Dinoprostone for induction of labour. Indian J Physiol Pharmacol, 2007,51(1):55-61. | 11.Kadanali S,Kücüközkan T,Zor N,Kumtepe Y.Comparison of labor induction with Misoprostol Vs Oxytocin/Prostaglandin E2 in term pregnancy. Int J Gynaecol Obstet .1996 Nov;55(20:99-104. | 12.Danielian P,Belinda P.Misoprostol for induction of labour at term:a more effective agent than Dinoprostone vaginal gel.BJOG,Aug,1999 ;106:793-797. | 13.Van Gemund N, Scherjon S, LeCessie S, Van Leeuwen JH, Van Roosmalen J, Kanhai HH.a randomized trial comparing low dosevaginal Misoprostol and Dinoprostone for labour induction .BJOG.2004 Jan;111(1):42-9. | 14.Ozkan S,Caliskan E,Doger E et al.Comparative efficacy and safety of vaginal Misoprostol versud Dinoprostone vaginal insert in labor induction at term,a randomized trial. Arch Gynecol Obstet (2009).280:19-24. | 15.Pandis GK, Papageorghiou AT, Otigbah CM, Howard RJ, Nicolaides KH. Randomized study of vaginal Misoprostol(PGE1) and Dinorostone (PGE2) for induction of labor at term. Ultrasound Obstet Gynecol ,2001 Dec;1896):629. | 16.Gregson S,Waterstone M,Norman I,Murrells T.A randomised clinical trial comparing low dose vaginal misoprostol and dinoprostone vaginal gel for inducing labour at term. BJOG;112(4)2005:438-44. | 17.Dallenbach P,Boulvain M,Viardot C,Irion O.Oral Misoprostol or vaginal Dinoprostone for labor induction:a randomized controlled trial. Am J obstet Gynecol,2003,188(1):162-7. | 18.Chuck FJ, Huffaker BJ. Labor induction with intravaginal misoprostol versus intracervical prostaglandin E2 gel(Prepidil gel):randomized comparison .Am J of Obstet Gynecol, 1995 Oct;17394):1137-42. | 19.Szczesny W,Kjollesdal M,Karlsson B,Nielsen S.Bishop's score nad outcome of labour with Misoprostol.Acta Obstet Gynecol Scand 2006;85(5);579-82. | 20.Sifakis S,Angelakis E,Avgoustinakis E,Fragouli Y,mantas N.koukoura O,vardaki e,Koumantakis E.a randomized comparison between intravaginal misoprostol and prostaglandin E2 for labor induction.Arch Gynecol obstet,2006,275(4):263-7. | 21.Denguezli W ,Trimech A,Haddad A,Hajjaji A,Saidani Z,Faleh R,Sakouhi M.Efficacy and safety of six hourly vaginal misoprostol versus intracervical dinoprostone:a randomised controlled trial. Arch Gynecol Obstet 2007;276(2):119-24. |