USEFULLNESS OF 100 MICROGRAM MISOPROSTOL IN TERM GRAVID PATIENTS REGARDING LABOUR, FETAL AND MATERNAL OUTCOME

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ABSTRACT

Objective: *To determine the effect of 100 microgram misoprostol for induction of labour in term gravid patients regarding, labour, fetal, and maternal outcome.*

Material and Methods: *This descriptive study was carried out in the Gyne "A" Unit of PGMI/Lady Reading Hospital Peshawar, from June 2005 to February 2006. A total of 100 admitted patients were selected for the study in whom 100 microgram Misoprostol was administered orally. Labour was induced in selected patients and post delivery complications were recorded.*

Results: *The age range of patients was from 15-39 years. Out of 100 gravid patients, primigravida were 63%. In 83% of patients pre-induction cervical scoring was <4 while 4-7 in 17% patients. Indications for induction of labour were; raised blood pressure 40%, post dates 35%, intrauterine fetal death 11%, I.U.G.R.10% and diabetes mellitus 4% cases. Misoprostol 100 microgram was given as one dose to 37% women, 2 doses to 44% women, 3 doses to 13% women, while 4 doses were given to 6% women. Normal vaginal delivery was done in 68% cases. Instrumental delivery was done in 30% cases, while cesarean section was done in 2% cases due to fetal distress. Majority of patients (69%) delivered within 24 hours. Stay in the hospital was 2 days in 42%, 3-4days in 48%, and 5-6 days in 10% of cases. Maternal complications included nausea/vomiting in 61% cases and postpartum hemorrhage in 1%. Fetal low APGAR score was observed in 6% cases.*

Conclusion: *Oral misoprostol is an attractive alternative for induction of labour in patients with full term pregnancy.*

Key Words: *Oral Misoprostol, Labor Induction, Maternal Outcome, Fetal Outcome.*

INTRODUCTION

Labour induction is undertaken when the advantage for the mother and/or baby is considered to out weigh the disadvantage. When uterine cervix is unfavourable, oxytocin with or without amniotomy is frequently ineffective, vaginal prostaglandin E2 is most commonly used if it is affordable.[1] Recently Misoprostol, a prostaglandin E1 analogue, has been used for induction of labour.[2,3] First it was introduced as a treatment for peptic ulcer but was later use as an abortifacient in the first and second trimester of pregnancy. It is cheep and stable at room temperature. It is licensed only for oral use but it is also available for vaginal use in almost 87 countries. It is commonly used in black market in places where the abortion is illegal. In North America misoprostol is popular in the streets as the star pill (due to the five corners of the tablet) and is available as a street drug in urban centers.[2-6] It costs 150.00 Pakistani Rupees as compared to 1800.00 Pakistani Rupees for prostaglandins E2. A study conducted in the University of Texas Southeastern Medical Centre at Dallas shows that oral misoprostol reduced the use of oxytocin stimulation from 90% to 37% ($P < .001$) and was associated with approximately a 7 hour shorter elapsed time in labour unit.[7] However uterine stimulations occur in 25% of women in oral misoprostol group. The side effects most commonly related to misoprostol are lower abdominal pain, nausea, vomiting, diarrhea and hyperstimulation of uterus and fetal distress. Many studies have shown less nausea/vomiting and diarrhea with vaginal misoprostol than with oral use.[8-10] A pharmacokinetic study has shown that peak concentration level of misoprostol is achieved in a shorter time with oral and sublingual use than

with vaginal route.[11]

The purpose of this study was to assess the use of oral misoprostol 100 microgram in term induction regarding maternal and fetal outcome in gravid women.

MATERIAL AND METHODS

This study was conducted in the Gynae "A" unit of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar from June 2005 to February 2006. A total of 100 admitted patients were selected for the study in whom 100 microgram Misoprostol was administered orally. All those patients who presented with the history of previous cesarean section, known hypersensitivity to drugs, grand multipara and eclampsia were excluded from the study. While Primigravida, multigravidas, postdate patient, intrauterine foetal death, hypertensive, diabetic with term pregnancy and intra uterine growth restricted patient were included in study. All the selected women were admitted in the Gyne "A" unit. After taking informed consent from them. All investigations were carried out on in-patient basis. All patients were given 100 microgram of oral misoprostol at four hourly intervals up to a maximum of five doses or until labour was established. The parameters analyzed included parity, gestational age, maternal age, mode of delivery, contractility pattern, fetal well-being, labour and delivery complications, neonatal and maternal morbidity, period of hospitalization, and cervical ripening according to the Bishop score. The primary outcome measure was the interval from start of induction (administration of first dose) to delivery, other outcome measures included caesarean delivery, hypertonus (prolonged uterine contraction lasting more than two minutes). Tachystole (contraction pattern of more than six contractions in ten minutes), hyperstimulation (hypertonus or tachystole in the context of an abnormal fetal heart rate requiring intervention) and failed induction. Neonatal outcome measures included infant Apgar score, need for neonatal resuscitation and neonatal asphyxia. Resuscitation was defined as the need for positive pressure ventilation or intubation. Neonatal asphyxia has been defined as the presence of acidosis and five minutes Apgar score of 0-3 and neonatal neurologic sequelae. All the studied variables i.e. age, gravity, gestational age, cervical scoring, indications for induction, maternal outcome, fetal outcome, number of doses given, mode of delivery, indication for cesarean section, time interval between start of induction till delivery, hospital stay, were analyzed for descriptive statistics. The frequencies and percentages were calculated for all qualitative variables and mean, ± standard deviations were determined for quantitative variables. Data interpretation, calculations, tabulations and various other analytical procedures were done by SPSS for windows version 11.

GESTATIONAL AGE OF PATIENTS

Gestational Age	No. of Patients (n=100)	%age
37-40 weeks	65	65%
41 and above	35	35%

Table 1

RESULTS

During the period from June 2005 to February 2006 a total of 100 admitted patients were selected for the study in whom misoprostol was administered.

In this study majority of the patients, 62% were in the age range of 20-35 years, while 24% were in the age range of 15-19 years and 14% were in age range of above 35 years. Minimum age was 15 years while maximum age was 39 years. Mean age was 25.94 (SD +/- 7.10) years in all age groups.

Among these 100 gravid patients, primigravida were 63 (63%) and multigravida were 37%. Sixty-five (65%) women presented with gestational age range of 37-40 weeks and 35 (35%) presented with range of 41 and above weeks

PRE-INDUCTION CERVICAL SCORING AND INDICATION FOR INDUCT ION IN PATIENTS

Variables		No. of Patients (n=100)	Percentage
CERVICAL SCORE	< 4	83	83%
	> 4 - < 7	17	17%
INDICATIONS FOR INDUCT ION	Raised blood pressure	40	40%
	Postdates	35	35%
	Intrauterine fetal death	11	11%
	I.U.G.R.	10	10%
	Diabetes mellitus	04	04%

Table 2

MATERNAL AND FETAL OUTCOME (n=100)

Maternal Complications	No. of Patients	Percentage
Nausea/vomiting	61	61 %
Postpartum hemorrhage	01	01 %
Neonatal Outcome		
Weight of the Baby	**No. of Patients**	**Percentage**
2.5 - 3.5 kg	87	87%
3.6 - 4 kg	11	11%
Above 4 kg	02	02%
Apgar score 8/10 - 10/10	94	94%
Apgar score 6/10-8/10	04	4%
4/10-6/10	02	2%
Neonatal Unit Admission		
Neonatal unit admission	10	10%
Indication for Neonatal admission		
a. Low apgar score	06	6%
b. Infant of diabetic mother (for observation)	04	4%

Table 3

gestation (Table No.1). In majority of patients (83%) pre-induction cervical scoring was < 4, while > 4 - < 7 was in 17 (17%) patients. While indications for induction of labour were, raised blood pressure in 40 (40%) cases, post dates in 35 (35%) cases, intrauterine fetal death in 11 (11%) cases, I.U.G.R. in 10 (10%) cases, and diabetes mellitus was in 4 (4%) cases (Table No. 2). Maternal complications such as nausea/vomiting was observed in 61 (61%) women, postpartum hemorrhage was observed in 1 (1%) case. Majority of babies i:e 87 (87%) were in the weight range of 2.5 - 3.5 kg, 11 (11%) were in 3.6 - 4 kg range, and 2 (2%) were above 4 kg. Neonatal admission due to some fetal complications was (10%) who were stable after treatment in neonatal Intensive care unit (Table No. 3). Misoprostol 100 microgram was given as one dose to 37% women, two doses given to 44 (44%) women, three doses given to 13% women, while four doses were given to 6 (6%) women.

Artificial rupture of membrane were done in 56 patients with no oxytocin because of excessive (more than 6 per 10 minutes) or normal uterine contraction (3 contraction per 10 minutes) while 44 patients received oxytocin. In this study, normal vaginal delivery was the most common mode of delivery with the frequency of 68% cases; instrumental delivery was done in 30 (30%) cases, while cesarean section was done in 2 (2%) cases. Indication for cesarean section was fetal distress in 2 (2%) cases. Time interval from start of induction till delivery was noted and majority of patients 69 (69%) delivered within 24 hours, 24-48 hours was noted in 31 (31%) patients. During the study period majority of patients i.e 48 (48%) stayed in the hospital within the range of 73-96 hours, 42 (42%) stayed within the range of 28-72 hours, and 10 (10%) stayed within the range of 97-120 hours (Table No. 4).

DISCUSSION

The process of cervical ripening depends on cytokines, leukotriene, adhesive molecules and prostaglandins. Amniotomy and oxytocin infusions are the routine methods most commonly applied to induce labour. These methods are not effective when the cervix is unripe. Prostaglandin may accelerate the process of cervical repining independently of stimulation of uterine contraction. Prostaglandins have been used for induction of labour since 1960'. Initial work focussed on prostaglandin F2a as E2 was considered unsuitable for a number of reasons. With the development of alternative routes of administration comparison were made between various formulations of prostaglandin.[12-14] Misoprostol which is prostaglandin E1 analogue is nowadays used for induction of labour. Misoprostol is widely used in the United States and other countries for cervix ripening and labour induction. Its use for these indications is not yet approved by FDA. In 1987 it was used for the first time in labour induction. It is only approved for the prevention and treatment of gastric ulcer resulting from non-steroidal anti-inflammatory drug use. Many trials have been conducted and proved that misoprostol in a low dose is effective for induction of labour. The use of oxytocin is also reducing in those cases where misoprostol is used as inducing agent. It has also

OUTCOME IN LABOUR (n=100)

Doses of Misoprostol		
Doses	**No. of Patients**	**Percentage**
One dose	37	37%
Two doses	44	44%
Three doses	13	13%
Four doses	06	06%
Oxytocin Given To Patients		
ARM done No Oxytocin	56	56%
ARM followed by Oxytocin	44	44%
Excessive uterine contraction (more than 6 per 10 m)	10	10%
Mode of Delivery		
Normal vaginal delivery	68	68%
Instrumental delivery	30	30%
Cesarean section	02	02%
Indication For Cesarean Section		
Fetal distress	02	02%
Time interval for start of induction till delivery		
Within 24 hours	69	69%
Within 24-48 hours	31	31%
Hospital Stay in Patients		
28 -72 hours	42	42%
73 - 96 hours	48	48%
97 - 120 hours	10	10%

Table 4

the added benefit of temperature stability at room temperature which is unlike other prostaglandin preparations and low cost. The proper timing of cervical ripening with adequate uterine contraction enables a normal and uncomplicated course of delivery.[15-17]

The result of our study showed that misoprostol in term induction is and effective regarding maternal and fetal outcome, and hospital stay. A study done by Hussan AA at Humdard University compared the oral misoprostol with vaginal prostaglandin E2.[18] He found that oral misoprostol is more efficient and cost effective than PGE2 vaginal pessary. There was 93% successful induction. In our study the success rate was 98% which is comparable to the above result. Most of the trials fail to demonstrate a significant change in the cesarean delivery rate with the use of misoprostol.[18] The data is still not sufficient to support the wide use of misoprostol for cervical ripening and induction. Overall cesarean section rate appears to be reduced despite a relative increase in caesarean section for fetal distress. In our study two caesarean sections were done for fetal heart rate abnormality. Concern remains regarding increase rate of uterine contraction and meconium fluid liquor. In our study there were 2 cases (02%) of fetal distress and 10 neonates were admitted in neonatal intensive care unit from where they were discharged in good health.

Cochrane database also suggest that oral misoprostol is an effective method for labour induction in the 3rd trimester. However the data on optimal regimens and safety is lacking. It is possible that effective oral regimens may have an unacceptably high incidence of complications such as uterine hyperstimulation and possibly uterine rupture.[19] The chances of post-partum haemorrhage and rupture uterus with or without previous cesarean section are high in some trials. However by using low dose regimens and careful monitoring the adverse outcomes may be reduced.[1,20]

A study conducted by Shetty et al at Aberdeen Maternity hospital, compared the same dose of oral misoprostol with same dose vaginally. They concluded that although the labour induction takes short time and induces efficiently in cases of vaginal route but the uterine hyperstimulation and fetal distress are lower in oral route. So the

preferred route of administration is oral but still there is a need for right oral dosage that combines efficacy with safety.[2]

CONCLUSION

Its ideal dose, route and frequency of administration are still under investigation.

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REFERENCES

1. Justus Hofmeyr G. Induction of labour with an unfavourable cervix. Best Pract Res Clin Obstet Gynaecol 2003;17: 777-94.
2. Shetty A, Livingstone I, Acharya S, Rice P, Danielian P, Templeton A. A randomised comparison of oral misoprostol and vaginal prostaglandin E2 tablets in labour induction at term. Br J Obstet Gynaecol 2004; 111: 436-40.
3. Dadi H, Putwardan SC, Alkami A, Ojuliku D. Self induction of labour using misoprostol: an unusual case of uterus hyperstimulation. Br J Obstet Gynaecol 2004; 111: 1018-9.
4. Royal College of Obstetricians and Gynaecologists. Induction of labour. In: RCOG evidence based clinical guideline. London: Royal College of Obstetricians and Gynaecologists, 2001; 9.
5. Alexander JM, McIntire DD, Leveno KJ. Prolonged pregnancy: Induction of labour and cesarean birth. Obstet Gynaecol 2001; 97: 911-5.
6. Shetty A, Martin R, Danielian P, Templeton A. A comparison of two dosage regimens of oral misoprostol for labor induction at term. Acta Obstet Gynecol Scand 2002; 81: 337-42.
7. Lo JY, Alexander JM, McIntire DD, Leveno KJ. Ruptured membranes at term: Randomized, double-blind trial of oral misoprostol for labor induction. Obstet Gynecol 2003; 101: 685-9.
8. Ngai SW, Chan YM, Lam SW, Lao TT. Labour characteristics and uterine activity: Misoprostol compared with oxytocin in women at term with prelabour rupture of the membranes. Br J Obstet Gynaecol 2000; 107: 222-7.
9. Mathews JE, Mathai M, George A. Uterine rupture in a multiparous woman during labor induction with oral misoprostol. Int J Gynaecol Obstet 2000; 68: 43-4.
10. Day L, Tailor A, Howard R, Burrell S. Misoprostol for induction of labour at term. Br J Obstet Gynaecol 2000; 107: 576-7.
11. Andolina KL, Tolosa JE, Monzo JM, Roberts NS, Daly S. Oral misoprostol is rapidly absorbed in women at term. J Matern Fetal Neonatal Med 2003; 14: 229-32.
12. Leszczynska-Gorzelak B, Laskowska M, Oleszczuk J. Comparative analysis of the effectiveness of misoprostol and prostaglandin E(2) in the preinduction and induction of labor. Med Sci Monit 2001; 7: 1023-8.
13. Papanikolaou EG, Plachouras N, Drougia A, Andronikou S, Vlachou C, Stefos T, et al. Comparison of Misoprostol and Dinoprostone for elective induction of labour in nulliparous women at full term: A randomized prospective study. Reprod Biol Endocrinol 2004; 2: 70.
14. Kwon JS, Davies GA, Mackenzie VP. A comparison of oral and vaginal misoprostol for induction of labour at term: A randomised trial. Br J Obstet Gynaecol 2001; 108: 23-6.
15. Hofmeyr GJ. Induction of labour with misoprostol. Curr Opin Obstet Gynecol 2001; 13: 577-81.
16. Ghidini A, Spong CY, Korker V, Mariani E. Randomized controlled trial of 50 and 100 mcg of misoprostol for induction of labor at term. Arch Gynecol Obstet 2001; 265: 128-30.
17. Crane JM, Young DC, Butt KD, Bennett KA, Hutchens D. Excessive uterine activity accompanying induced labor. Obstet Gynecol 2001; 97: 926-31.
18. Hassan A. A comparison of oral misoprostol tablet and vaginal prostoglandin E2 pessary in induction of labour at term. J Coll Physicians Surg Pak 2005; 15: 284-7.
19. Alfirevic Z. Oral misoprostol for induction of labour. Cochrane Database Syst Rev 2001;(2): CD001338.
20. Paungmora N, Herabutya Y, O-Prasertsawat P, Punyavachira P. Comparison of oral and vaginal misoprostol for induction of labor at term: A randomized controlled trial. J Obstet Gynaecol Res 2004; 30: 358-62.

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