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COMPARISON OF ORAL AND VAGINAL ADMINISTRATION OF MISOPROSTOL FOR INDUCTION OF LABOR IN SOUTH INDIAN WOMAN- A HOSPITAL BASED EXPERIMENTAL STUDY

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Abstract:

Background: In modern obstetrics, around 30% of cases require induction of labour for various reasons. Misoprostol is gaining popularity as pharmacological inducing agent, though the route and dosage of administration are not standardised.

Objective: To compare the safety and efficacy of the oral (50 mcg 4th hourly) and vaginal (25 mcg 4th hourly) routes of misoprostol administration for induction of labour at term.

Methods: 180 women at full term and post term gestation were selected in two equal groups. One group provided with oral and another group provided with vaginal administration of misoprostol drug for the labor induction.

Results: Study demonstrated that 50 mcg oral misoprostol was more effective at induction of labor at 38- 40 week pregnancy than vaginal misoprostol. However, occurrence of lesser incidence of meconium-stained liquor and NICU admissions and fewer caesareans with better neonatal outcome in women induced with oral misoprostol outweighs its advantages over the vaginal misoprostol.

Conclusion: Orally administered 50 mcg misoprostol is highly effective cervical ripener and labor inducing agent than vaginal misoprostol, but its use demands close monitoring for uterine contractile abnormalities.

Keywords: Induction Of Labor, Oral Misoprostol, Prostaglandin, Vaginal Misoprostol, dinoprostone

Introduction:

Induction of labor at term with unfavourable cervix is associated with increased risk of failed induction and cesarean sections. Conventional methods for cervical ripening (oxytocin, Foley's catheter) are being used since ages but have their own merits and demerits, hence there is a need for more efficient inducing agent with less limitations. Till today no ideal agent has been found. Prostaglandin is new drug of interest in this field. Out of all prostaglandins PGE1 and PGE2 have been tried for induction of labor.1-3 PGE2 is being used as gel and tablet, has the advantage of being used intracervical orvaginally but is expensive and needs refrigeration. PGE1's synthetic analogue, misoprostol, originally used as gastroprotective agent,4 its use as cervical ripener and labor inducer is upcoming5 and is being tried enthusiastically by obstetricians worldwide. With time it has crossed the legal hurdles in western as well as developing countries including India. It has advantage of being cheap, stable at room temperature and easy to be administered by various routes i.e. vaginal, oral, sublingual or rectal.6Misoprostol, sold under the brandname Cytotec among others, is a medication used to prevent and treat stomach ulcers, induction of labor, cause an abortion, and treat atonic postpartum

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haemorrage1,2 For labor induction or abortion, it is taken either in the cheek, under the tongue, or placed in the vagina.3,5

Labor induction; Misoprostol is commonly used for labor induction. It causes uterine contractions and the ripening (effacement or thinning) of the cervix.6 It can be less expensive than the other commonly used ripening agent, dinoprostone.7

Oxytocin has long been used as the standard agent for labor induction, but does not work well when the cervix is not yet ripe. Misoprostol also may be used in conjunction with oxytocin.8

Between 2002 and 2012, a misoprostol vaginal insert was studied, and was approved in the EU.[14][15] It was not approved for use in the USA, and the US FDA still considers cervical ripening and labor induction to be outside of the approved uses for misoprostol.9

Abortion: Misoprostol is used either alone or in conjunction with another medication (mifepristone or methotrexate) for medical abortions as an alternative to surgical abortion.10 Medical abortion has the advantage of being less invasive, and more autonomous, self-directed, and discrete. The World Health Organization provides clear guidelines on the use, benefit and risks of misoprostol for abortions.13

Absorption by oral route is erratic at the same time it is more rapid than vaginally administered misoprostol reaching peak serum concentrations within 30 min compared to one hour with vaginal route. Oral misoprostol is eliminated rapidly (2–3 h)15 than vaginal (C4 h).16 Hence, vaginal route seems to be more efficacious than oral and should result in shorter induction–delivery interval and reduced need for oxytocin augmentation17 but at the cost of little more complications. We have taken up this study to compare vaginal and oral routes of 50 mcg misoprostol for cervical ripening and induction of labor.

Indications for induction include-9,10

- Postterm pregnancy, i.e. if the pregnancy has gone past the end of the 40 week.
- Mothers with pre eclampsia with intra uterine growth retardation .
- Premature rupture of the membranes (PROM); this is when the membranes have ruptured, but labor does not start within a specific amount of time.
- Premature termination of the pregnancy (abortion).
- Fetal death in utero and previous history of stillbirth.
- Twin pregnancy continuing beyond 38 weeks.
- Previous health conditions that puts risk on the woman and/or her child such as diabetes, high blood pressure.
- High BMI Induction of labor in those who are either at or after term improves outcomes for the baby and decreases the number of C-sections performed.
- The aim of this study was to study the efficacy and the side effects of 50 mcg misoprostol by oral and vaginal route of administration for induction of labor in 38 weeks to postterm pregnancy.

MATERIALS AND METHODS

This is a hospital based comparative study of 50 mcg misoprostol oral and 25 mcg vaginal route, conducted on 180 pregnant women. The study

was carried out from January 2018 to February 2019, in the Department of Gynecology and Obstetrics, All women with term gestation who were admitted in labor room of Mallareddy Institute of Medical Sciences, Hyderabad, Telangana. The study included

180 pregnant women of between 20-30 years age group. An ethical clearance was obtained from the institutional committee prior to the study. An informed consent was taken from the patient herself or from her close relative.

Inclusion and exclusion criteria: patient with Bishop score of five or less were taken. Nulli and multigravida women were included in both groups.

patients with post dated pregnancy , pregnancy induced hypertension, premature rupture of membranes , selected cases if oligohydramnios and intrauterine growth retardation(with normal doppler study) were included in both groups.Total 180 women were studied.

Patients with malpresentations and multiple gestations were excluded from the study.

Any evidence of acute fetal distress was considered as contraindication for induction.

Patient with previous uterine scar(caesarean section, myomectomy) abnormal vaginal bleeding, abruption placenta, placenta previa and significant maternal diaease(cardiac , renal, haepatic) are excluded.

Any evidence of acute fetal distress was considered as contraindication

Women with Bishop score>4, Cephalopelvic disproportion, placenta praevia or unexplained vaginal bleeding, previous caesarian section/or other uterine surgery, active herpes simplex, carcinoma cervix, chorio-amnionitis and any contraindication to use of prostaglandins e.g. hypersensitivity, asthma, acute PID etc. were excluded.

Zitotec 50 mcg tablet (Sun Pharma Laboratories Ltd) was used for the study.

Group A: n=90 (Oral misoprostol): The patients were given 50 µg (self administered) orally, which was repeated 4th hrly for a maximum of 4 doses.

Group B: n=90 (vaginal misoprostol): 25 µg of misoprostol (soaked in saline) was placed in posterior fornix of the vagina and the dose was repeated 4th hrly for maximum 4 doses.

Progress of labor was monitored especially for uterine contractions its frequency, intensity and duration, fetal heart rate and other fetal and maternal complications like nausea, vomiting, diarrhea, distress etc. Complications were managed symptomatically with anti-emetics, I/V fluid etc. Woman was said to be in 'active labor' if she had three uterine contractions per 10 min, lasting for 60seconds and of good intensity which was judged subjectively. Both oral and vaginal tablet were repeated every 4 hourly till either she went into active labor or maximum dose six tablets have been consumed. Once she went into active labor no further tablet was given orally or vaginally. Induction was said to be a ''failure'' if woman did not go into active labor four hours after 6th dose.

Note was made especially for mode of delivery, intrapartum and postpartum maternal and fetal complications. After delivery both mother and the neonate were observed throughout the hospital stay for any complication especially nursery admission. The main measure of efficacy was successful induction i.e. number of women who achieved active labor within 24 hour of induction and their induction delivery interval. Other measures were number of deliveries within 24 hour, total dose of misoprostol required for delivery and mode of delivery. The measures of safety included the uterine tachysystole, uterine hypertonus, abnormal fetal heart tracings, incidence of meconium passage and the neonatal outcome. Baseline data included maternal age, socioeconomic status, parity, gestation, indication for induction and pre-induction cervical score.

Statistical Analysis: Both groups were analyzed statistically by applying Student's unpaired t-test using statistical SPSS Software version 21.0. F- value, degree of freedom, and P<0.05 were considered statistically significant. The chi-square test was applied wherever applicable.

RESULTS

The Epidemiological and obstetric profile of study population was compared in Table 1. Maternal demographic characteristics and indications for induction were comparable in both the groups.

There was very less difference in the mean age of both group candidates, so that the p=06 which is not significant. The difference between gravid and parity was significant. Gravida showed more frequency than parity which was statistically significant.

Single dose was effective in 25 subjects of oral administration group (27.77%) and 2 doses were found to be more effective in vaginal administered group (26.66%). Very few subjects required 5 in group A and 7 in Group B six doses. The study revealed gradual decrease of doses in both groups. Table 2 showed numbers of doses required for Induction of labor in pre as well as postterm pregnancy. Commonest indication for induction of labor was hypertensive disorders in both vaginal and oral groups.

Table 3 gives the side effects observed in the two groups. Among the 180 participants, the symptom questionnaire was completed by all women. Severe abdominal pain was found in 3 pregnant women in group B and 2 subjects in Group A. which was statistically nonsignificant. Tolerable abdominal pain was found to be in 49 candidates of both the groups the difference was not statistically significant. Similarly nausea in 51 pregnant women from both the groups found to be in similar frequency. Vomiting was seen higher (27 subjects) in oral group than (16) in vaginal group, this finding was statistically significant. Diarrhea and dizziness were less frequently found in both groups. All the side effects were manageable and were comparable in the two groups. No hospitalization or blood transfusion was needed for excessive bleeding.

Table 1: Epidemiological and obstetric profile of study patients

Parameters	Group A	Group B	p-value
Age of patient	27.45±5.0	26.21±5.2	0.06
Gravid	2.5±1.8	2.2±1.5	0.171
Parity	1.8±1.2	1.1±1.0	0.021

Table 2: Number of Doses Required

Doses	Group A (n=90)		Group B (n=90)	
	No	%	No	%
1	25	27.77	21	23.33
2	22	24.44	24	26.66
3	16	17.77	18	20.00
4	13	14.44	11	12.22
5	9	10.00	9	10.00
6	5	5.55	7	7.77

Table 3: Adverse effects in both the groups.

Parameters	Group A	Group B	p-value
Abdominal pain requiring analgesia	2 (3.2)	3 (4.9)	0.51
Tolerable abdominal pain	23 (37.1)	26 (42.6)	0.51
Nausea	24 (38.7)	27 (44.3)	0.51
Vomiting	27 (45.6)	16 (26.2)	0.04
Diarrhea	3 (4.8)	5 (8.2)	0.34
Dizziness	0 (0)	2 (3.3)	-

DISCUSSION

The oral rather than vaginal administration of misoprostol may extend the use of medical abortion up to 9 weeks. The complete abortion rate in this study is in agreement with that reported by El Rafaey et al.24 In their study, 95% aborted with the vaginally administered misoprostol and 87% aborted with oral misoprostol. Ashok et al25 reported the complete abortion rate after mifepristone administration alone as 2%. Two of our 128 women aborted with mifepristone alone.Kant and Taneja26 administered misoprostol orally in the outpatient department in doctor's presence. Our study also demonstrated that misoprostol can be self administered at home without sacrificing safety. Pymar and Creinin27 provided evidence that vaginal misoprostol is more effective than the oral form in achieving complete abortion between 7 and 9 weeks gestation. The limitation of our study is that only28 women requested for medical abortion just after seven weeks gestation. So we could not demonstrate a better outcome with vaginal administration in this gestational age group.Misoprostol is a wonderful drug in the armamentarium of obstetricians for induction of labor. Vaginal misoprostol is an effective cervical ripener and labor inducing agent.21 In our study successful induction with 50 mcg oral misoprostol was higher (90.38 vs. 74.51%, RR 2.6, 95% CI 0. 78–4.42). This was in accordance with the study conducted by Shetty et al.5 who reported lower failure (2.4 vs. 6.76%, RR 2.7,95% CI 0. 7–10.0) with 25 mcg vaginal misoprostol as compared to oral and at the same time reported shorter induction delivery interval by 10.1 h.5 In the study by Latika et al1 observed 100% success rate with 25 mcg vaginal misoprostol1 and 50 mcg oral misoprostol.8 In our study also induction delivery interval was shorter by 5.28 h with 50 mcg oral misoprostol (9.79 h vs. 16.47 h, RR 0.79, 95% CI, 0.27–1.31).While comparing 25 mcg vaginal misoprostol with Foley's catheter/ oxytocin successfulinduction was 90.61 vs. 78.44% and induction delivery interval shorter by 7.87 h in vaginal misoprostol group.9 As vaginal misoprostol is absorbed rapidly and eliminated slowly from body making it available to act for a longer time as compare to oral4 resulting in rapid progression of labor leading to greater number of women delivering within 24 h of induction (69.5 vs. 56.4%).5 In our study more women delivered within 24 h in vaginal group. Main fear with this drug is excessive uterine contractions and uterine rupture in both scarred and unscarred uterus. These complications are dose related higher the dose; more is uterine stimulation but shorter is the induction delivery interval.6 With 25 mcg vaginal misoprostol incidence of uterine contractile abnormalities have been reported to be 4.9%,5 9%,9 12%,1 and 26.92% in our study Evert et al10 observed these complications incidence as 3, 6.25, 10% with 25,100 and 200 mcg controlled release vaginal inserts of misoprostol. While with 50 and 100 mcg oral misoprostol uterine hyper stimulation incidence of 0.8%,5 6.4%,11 respectively are reported. Oxytocin which has been considered safer than misoprostol9 is also not devoid of uterine abnormalities incidence being 19.2%. Apart from this PGE2 also had lesser complications (12%)12 than misoprostol. One uterine rupture was reported in scarred9 and one in unscarred13 uterus with vaginal misoprostol and one with dinoprostone.2 In our observation despite of high incidence of uterine contractile abnormalities with vaginal route it does not increase in cesarean section rate rather LSCS rate in our oral group was significantly more 25.49 vs. 9.62%, which is consistent with Shetty et al5 (24.6 vs. 22.8%) and

How et al(33 vs. 17%).6 Severe abdominal pain was found in 3 pregnant women in group B and 2 subjects in Group A. which was statistically non-significant. This finding was similarly found in the study by Shetty et al and Evert et al.5,10 Tolerable abdominal pain was found to be in 49 candidates of both the groups the difference was not statistically significant. This was in accordance with study conducted by Shetty et al and Evert et al This finding was found to be similarly nausea in 51 pregnant women from both the groups found to be in similar frequency. Vomiting was seen higher (27 subjects) in oral group than (16 subjects) in vaginal group, this finding was statistically significant. Diarrhea and dizziness were less frequently found in both groups. The different results were found in the study conducted by Latika et al1 who stated that misoprostol by vaginal route was more effective than oral administration.Commonest indication for cesarean section in our study was fetal distress irrespective of route used for misoprostol where as fetal distress contributed 2.4% with oral and 13% with vaginal use.5 Misoprostol and its use by vaginal and oral route does not adversely affect neonatal and maternal outcome.5,6,9 This finding was similar to the previously conducted study by Latika et al and Shetty et al.5,10 El Rafaey et al24 reported that the incidence of gastrointestinal side effects was higher when misoprostol was given orally than when it was administered vaginally. They reported that one woman in the vaginal group bled heavily and required a blood transfusion. Although this complication is uncommon, the possibility of hemorrhage with medical abortion highlights the need for vigilance and ready access to medical help.

CONCLUSION

Orally administered 50 mcg misoprostol is highly effective cervical ripener and labor inducing agent than vaginal misoprostol, but its use demands close monitoring for uterine contractile abnormalities. The advantage of evacuation by Misoprostol is that it includes no surgery and hence no anaesthesia. Misoprostol tablet has advantage of low cost, long shelf life, lack of need for refrigeration and its easy availability. Thus, it may be advocated to be used in outpatient setting in the treatment of early pregnancy failure even at the primary care level. However, the dose schedule should be adhered to. According to the route, these should be altered.

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