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Comparison of Maternal and Foetal Outcome in Induction of Labour by Oral and Vaginal Misoprostol

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ABSTRACT

Objective: *To study the efficacy of oral misoprostol in comparison to vaginal misoprostol for induction of labour.*

Methods: *Hundred Pregnant women with a singleton cephalic presentation at ≥ 37 weeks' gestation, with an indication for induction of labour were divided in oral and vaginal groups alternately. In oral group a tablet of 200 mcg was dissolved in 200 ml tap water in a bottle.. Twenty ml of solution every 2 hours was given until adequate uterine contractions were achieved (subject to maximum of 12 doses). Women in vaginal group were given 25 mcg vaginal misoprostol tablet every 4 hours (subject to maximum of 6 doses). Main outcome measures numbers of women delivered vaginally within 12 hours of the first dose of misoprostol, interval from the start of induction to vaginal delivery, rate of caesarean section, maternal complications and neonatal outcome.*

Results: *100 women were alternately allotted to two groups, 50 to the oral misoprostol group and 50 to the vaginal misoprostol group. There were no significant differences between the two treatment groups in the primary outcomes: The mean induction to delivery interval was 13.34±6.83 hours in oral group and 11.98±5.93 hours in vaginal group, vaginal birth achieved in 12 hours (oral 27/50 (54.0%) v vaginal 29/50 (58%); P = 0.8403), caesarean section (7/50 (14%) v 6/50 (12%); P = 0.296). There were no significant differences in adverse maternal or neonatal outcomes.*

Conclusions: *It can be concluded from the present study that both oral and vaginal route are effective agents for preinduction cervical ripening which substantially improve the Bishops score and increase the chances of successful labor induction.*

KEYWORDS :Misoprostol, oral solution, induction, labor

Introduction

Induction of labour (IOL) may be defined as "intervention designed to initiate uterine contractions artificially leading to progressive effacement and dilatation of cervix and birth of the baby.[1]Induction of labour is a common obstetric intervention, performed when the perceived risk to the mother or fetus associated continuation of the pregnancy are greater than those associated with birth.[2]Labour may be induced for medical or obstetrics indications (such as hypertensive conditions, impaired glucose tolerance, prolonged pregnancy, intrauterine growth restriction) or for the convenience of mother or obstetrician (so called "social" indications). The greatest maternal risk of induction of labour is the risk of morbidity associated with CS for failed induction and for other obstetric indications like non-progress of labour and fetal distress. Prolonged Induction delivery interval may result in pyrexia, poor neonatal outcome and others. IOL in presence of an unripe cervix results in a longer labour and a higher incidence of CS and birth asphyxia[3]

Induction of labour can be achieved through various non pharmacological (mechanical) and pharmacological methods. Pharmacological methods include the use of oxytocin and prostaglandins mainly.Misoprostol (PGE_1) is licensed for use in the treatment of gastric ulcer disease, and does not have a product license for use in pregnancy, but has been widely used for induction of labour. [4] But it has become an important drug in obstetrical and gynaecologic practice because of its uterotonic and cervical ripening actions. Misoprostol is useful for elective medical abortion, cervical ripening before surgical abortion, evacuation of the uterus in cases of embryonic or fetal death and induction of labour. The drug may also be used to treat and even prevent post partum hemorrhage. Misoprostol appears to be more effective than conventional methods of cervical ripening and labour induction.[5]

The pharmacokinetics of misoprostol suggestthat it is more bioavailable when administered vaginally as compared with orally. Plasma concentrations of its metabolite, misoprostol acid, peak one to two hours after vaginal application as compared with the peak seen 30 minutes

following oral administration, and although peak levels are lower with the vaginal route, they are sustained longer and overall exposure to the drug is increased. This may be an explanation for its greater efficacy vaginally, along with its possible direct effects on the cervix[6] it has lower rates of uterine hyperstimulation because the total systemic bioavailability of orally administered misoprostol is three times lesser than that of vaginally administered misoprostol.13 In order to avoid uterinehyperstimulation, current suggestions are in favor of oral misoprostol given in small, frequent doses, titrated according to uterine response.[7]

Although the efficacy of misoprostol has been proven by various randomized trials, the search for an ideal route of administration is still ongoing. So, the study was planned to evaluate the efficacy and suitability of oral misoprostol for induction of labour when compared with an low dose given vaginally.

Study Population

It was a comparative prospective study involving 100 antenatal women requiring induction of labor with an unfavorable (≤7) Bishop's score cervix admitted in obstetrics ward requiring induction of labor with an unfavorable bishop score of cervix which was taken as ≤7in Department of Obstetrics and Gynaecology,PGIMS Rohtak from jan 2014 to june 2015. Women with period of gestation ≥37 weeks, singleton fetus,cephalic presentation and Bishop score ≤7 with an indication of induction of labour were included in study. While women with previous uterine scar, any active or purulent

infection of lower genital tract, abnormal preinduction FHR, multifoetal gestation, foetalmacrosomia, malpresentation, placenta praevi,cephalopelvic disproportion and known hypersensitivity to prostaglandins were excluded.

METHODOLOGY

In patients admitted in obstetric ward for induction of labor, case history will be taken and general physical, obstetric, systematic and per vaginal examination will be carried out. After the rationale for induction was reviewed and approved and cervical examination confirmed a Bishop

score of less than 7 consent was obtained. The pregnant women will be allocated to two groups alternately.

Group-I: (Oral misoprostol) 50 women. For thisgroup, a tablet of 200 ug will be dissolved in 200 ml tap water in a bottle. The misoprostol solution will be used within 24 hr after preparation. Twenty ml of solution every 2 hours will be given until adequate uterine contractions will be achieved (subject to maximum of 12 doses). The subsequent dose of medication will be withheld in presence of any of the following: atleast three regular uterine contractionsin 10 minutes lasting more than 40 seconds, active phase of labour(defined as regular uterine contractions with cervical dilatation more than or equal to 4 cm) and cervix favourable for amniotomy(Bishop score >8). If needed, oxytocin will be admistered 2 hrs after the last dose.

Group-Ii: (Vaginal misoprostol) 50 women Women in this group were given 25 mcg vaginal misoprostol tablet every 4 hours until attaining a more favourable cervix(Bishop score greater than or equal to 7) or adequate uterine activity(greater than or equal to three contractions in 10 minutes) or entering active labour(subject to maximum of 6 doses). If needed, oxytocin will be administered 4 hrs after the last dose.

As soon as foetal head was engaged and cervical dilatation permits, amniotomy was performed followed by oxytocin augmentation if contractions are inadequate. If the women did not pass into labour or has poor Bishop'sscore(<6) cesarean section was offered after an interval of 24 hrs following the first dose of misoprostol. Continuous foetal monitoring was done throughout the study. Progress of labour following the administration of misoprostol was assessed and noted on partogram.

The **primary outcomes** in both the groups was observed by the number of women delivered vaginally within 24 hours of the first dose of misoprostol, interval from the start of induction to vaginal delivery, the number of misoprostol doses and the need for oxytocin augmentation.The**secondary outcomes** included the number of women who underwent caesarean section, maternal adverse effects like nausea, vomiting, diarrhea and hyperthermia, uterine hyperstimulation, rupture, postpartum haemorrhage and other maternal complications. Neonatal outcome including Apgar score (1 minute & 5 minute), incidence of meconium stained amniotic fluid, neonatal jaundice, NICU admissions and perinatal death will be noted.

RESULTS

Demographic and clinical characteristics of patients are shown in the Table 1. There was no significant difference between the groups regarding any of the studied parameters including age, nulliparity, gestational age, Bishop's score. Mostly women induced for postdated pregnancy and preterm rupture of membranes.

Table 1.Demographic and clinical characteristics of patients

	Oral group(n==50)	Vaginal group(n=50)	p-value
Age	24.32	23.68	0.524
Nulliparity	30(60%)	39978%)	0.158
Gestational age	39.7±1.374	39.1±0.192	0.337
Bishop's score on admission	4.02±1.237	3.92±0.203	0.710
Indications of induction Postdatism PROM Medical or obs.	60% 26% 14%	28% 48% 24%	0.038

Labour characteristics and delivery outcome data Both values of mean time from induction to active phase and induction to delivery were similar in both the groups (9.86±5.97 and 13.34±6.83 versus 9.21±5.44 and 11.98±5.93 hours respectively, both p-values were >0.05). The rate of vaginal deliveries within the first 12 hours was comparable between both groups.Labour characteristics and delivery outcomes data is summarized in Table2.

Table 2.Delivery outcome data

	Oral group(n==50)	Vaginal group(n=50)	p-value
Induction to active phase	9.86±5.97	9.2±5.441	0.594
Induction to delivery interval	13.34±6.83	11.98±5.93	0.2896
Vaginal delivery <12 hours	54%	58%	0.8403
Mode of delivery Spontaneous Vaginal instrumental LSCS	82% 4% 14%	82% 6% 12%	0.664
Indication of LSCS NPOL NRFH Failed induction Others	14%	2% 10%	0.296
Oxytocin use	3.5±1.927	1.429±0.7868	0.0201

Maternal complications Except for the gastrointestinal symptoms, there were no statistically significant differences between the oxytocin and misoprostol patients groups in terms of other maternal complications (Table 3).

Table 3 Comparison of adverse effects of different routes of drug administration in two groups

Adverse effects	Group I (n=18)	Group II (n=23)	p-value
Hyperthermia	2(4%)	4(8%)	p=0.363 (>0.05 N.S.)
Vomiting	7(14%)	13(26%)	
Meconium stained liquor	8(16%)	6(12%)	
PPH	1(2%)	0	
Total	18(36%)	23(46%)	

Neonatal outcomes As shown in Table 4, the 1 and 5-Minute Apgar scores and birth weight were similar between the groups.The mean birth weight in group I was2.88±0.410 kg and 2.73±0.496 kg in group II. There was admission of 3 babies in group I and 5 babies in group II and all of them discharged in good health after observation. No maternal and neonatal deaths occurred in either group.

Table 4 Comparison of fetal wellbeing by Apgar scoring at 1min and 5 min in two groups

Fetal Apgar	Group I (n=50)	Group II (n=50)	Statistical significance
Apgar 1 min (mean)	6.580	6.780	P = 0.1150,
Apgar 5 min (mean)	8.66	8.84	P = 0.0601,
NICU admission	3(6%)	5(10%)	0.4610

DISCUSSION

Induced labor is one in which pregnancy is terminated artificially, anytime after fetal viability is attained, by a method that aims to secure vaginal delivery. Induction of labor is indicated when the benefits to either mother or fetus outweigh those of continuing the pregnancy.

The success of induction depends upon various factors like-Cervical factor: cervical status/favorability at time of induction; Maternal factors: parity, age, BMI; Fetal factors: fetal weight, gestational age.[8] Consistency, compliance and configuration of cervix is the major determinant for successful induction of labor which is assessed by various cervical scoring systems, the commonly used one is the Bishops score which takes into consideration five factors: dilatation, effacement, position, consistency of cervix, and station of the presenting part. A score less than 6 is labeled unfavorable and ≥ 6 as favorable for a successful labor induction. Labor induction in unfavorable cervical conditions is a difficult and lengthy procedure, extenuating for both mother and obstetrician.[9] Many times it may fail and this outcome can be frustrating for both increasing the likelihood of prolonged labor and an increased incidence of chorioamnionitis and caesarean delivery. Since cervix plays an important role in induction of labor, a simple and effective method of preinduction ripening of cervix is therefore clearly of use.

Misoprostol given vaginally or orally is used for inducing cervical ripening before induction of labour with or without oxytocin. Interest in oral misoprostol for induction of labour is increasing because of lower incidence of hyper stimulation and lower rate of fetal distress as compared to vaginal misoprostol. The present study compared the two routes of misoprostol for labour induction to indentify the efficacy and safety of oral misoprostol regimes with the intravaginal regimes.

Previous studies on the efficacy of oral misoprostol have used different dosing regimens with varying degrees of effectiveness.Mostauthors have reported that vaginally administered misoprostolwas more effective then oral misoprostol when usedat same doses, presumably because of the previouslymentioned ''first-pass effect''[10]

We found that giving 20ml solution of 1ug per 1ml of misoprostol solution every 2 hours was as effective and safe as vaginal administration of 25ug doses every 4 hours, with respectto our primary outcome, the induction to delivery interval inthose delivering vaginally. This finding correlates with others study as shown in Table 5.

TABLE 5 INDUCTION DELIVERY INTERVAL (I-D-I) IN DIFFERENT STUDIES

Mean I-D-I (in hours)	Oral misoprostol	Vaginal misoprostl
Komala et al(2013)[11]	12.92	14.04
Hall et al(2002)[12]	15.5	17.5
Ayaz et al(2009)[13]	10.4	12
Cheng et al(2008)[14]	8.2	17.6
Sreelatha et al(2014)[15]	11.86	12.94
Present study	13.34	11.98

In our study, majority women delivered vaginally in both the groups. Out of these 2 patients in oral and 3 patients in the vaginal group required instrumentation indication being fetal distress and prolonged second stage of labour. Seven patients (14%) in oral groups and six women(12%) in vaginal group required cesarean section. Table 6 compares the rates of caesarean section in different studies.

TABLE 6 RATES OF CAESSAREAN SECTIONS IN DIFFERENT STUDIES

	Oral misoprostol	Vaginal misoprostol
Sreelatha et al(2014)[15]	4%	12%
Hall et al(2002)[12]	15%	17%
Komala et al(2013)[11]	6%	14%
Ashalatha et al(2000)[10]	24.6%	22.8%
Fischer et al(2001)[16]	19.4%	22.8%
Present study	14%	12%

In our study, we found with no significant difference in maternal side effects and neonatal outcomes. This has been noted by others.[12,14,16]Cheng et al reviewed 220 women between 24 and 42 wks of gestation for induction of labour. They gave titrated oral misoprostol 20ug every hr for maximum of 4 doses then 40ug every hr for maximum of 4 doses then 60ug for maximum of 4 doses and in vaginal group 25ug every 4 hrs for 3 doses until 3 contractions occur in every 10 minutes or Bishop score 7 or more. The incidence of uterine hyper stimulations was 0.0% in the titrated oral group compared with 11.3% in vaginal group.

Our findings indicate that, in a closely supervised hospital-setting with adequate monitoring, oral misoprostolhas the potential to induce labor as safely and effectively as its vaginal analogue. Twenty microgram misoprostol with an interval of 2 h seems to be the idealprotocol for oral use of misoprostol for inducing labor. Asoral use of the drug is easier for both, the patient and thedoctor, oral misoprostol may be preferred instead of thevaginal route for labor induction.

CONCLUSION

The results tend to confirm that the oral route represents a valid alternative to vaginal route for induction of labour. According to studies the oral route appears to have the advantage of a greater acceptance by women than the vaginal route. It is understandable that it is more comfortable to give medicine by the mouth than by the vagina. Till date, the safety, adverse effects dose, maternal and perinatal outcome related to this route of administration were uncertain, it was not recommended for routine use in obstetric practice and its use was reserved for clinical research protocols only.

But in our study, oral administration of misoprostol is found to be equally effective and safe but more acceptable to the patient and has better ease of use in comparison to vaginal route, it may be concluded that the oral application is a better alternative to vaginal route. Given the proven feasibility of using the oral route and the preference of women, similar trials with a larger sample size should be carried out in near future.

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