Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(1A):9-14 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com DOI: 10.36347/sjams.2016.v04i01.003

Original Research Article

To compare the efficacy and safety of 25 µcg VS 50 µcg intravaginal misoprostol for induction of labour

Dr Singh Priyanka[1], Dr Agrawal Sunita (MS) [2]
[1]Senior resident, SMS Medical College, Jaipur, Rajasthan
[2]Senior Deputy Director, Department of Obstetrics & Gynaecology, Institute - JLN Hospital & Research Centre, Sector-9, Bhilai, Chhattisgarh

***Corresponding author**
Dr Priyanka Singh
Email: priyankadr@gmail.com

Abstract: To compare the efficacy and safety of two (25mcg/4hourly vs 50mcg/8hourly) regimens of intravaginal misoprostol for induction of labour. Settings & Design- It was a prospective comparative randomized study conducted at JLN Hospital & Research Centre, Bhilai, Chhattisgarh. Statically Analysis- Averaged data were reported as mean and standard deviation. Categorical variables were analyzed by chi square test or Fisher exact test and continuous variables by student t-test by using SSPS 14. Methods & Material- 200 eligible pregnant women, admitted for induction of labour were randomly assigned to receive either 25µcg intravaginal misoprostol 4 hourly (group A) or 50 µcg intravaginal misoprostol 8 hourly to a maximum up to 150 µcg and oxytocin augmentation, if needed. Result- Mean induction delivery interval was similar (9.676 hours in group A vs 9.2028 hours in group B). Although there were no difference in mode of delivery among two groups but caesarean for non assuring foetal heart rate and meconium is more in group B whereas it is more for failed induction and non progress of labour in group A. There is significantly more incidences of tachysystole and uterine hyper stimulation in group B (P value <0.039). In Conclusion-25 mcg intravaginal misoprostol 4 hourly is more prudent choice for induction of labour as 50 mcg intravaginal misoprostol 8 hourly is associated with more chances of uterine hyper stimulation and tachysystole without significant difference in mode of delivery, induction delivery interval and early neonatal outcome.
Keywords: intravaginal misoprostol, induction of labour

INTRODUCTION

Induction of labour is often essential when obstetrics or medical problems affect the maternal or foetal well being. Timely induction can reduce maternal morbidity and mortality as well as assure delivery of a healthy baby. Various methods are used for preinduction cervical ripening and labour induction. Among these misoprostol is promising in low resource settings.

Misoprostol is methyl analogue of PGE1 and is the first synthetic prostaglandin. In its native form, it is water insoluble, viscous and oily. Dispersion on hydroxy propyl methyl cellulose is much more stable and tablets of solid dispersion have shelf life of several years at room temperature. This drug is easily stored and transported and when these advantages are combined with its extremely low cost, it has a particular relevance for use in developing world. Misoprostol is a myometrial stimulant which acts by selectively binding to EP2/EP3 prostanoid receptors. Although other prostaglandins (prostaglandin E2 and prostaglandin F2α) can cause myocardial infarction and bronchospasm, misoprostol does not.

Its effects on the reproductive tract are increased and gastrointestinal adverse effects are decreased, if administered vaginally. After vaginal administration of misoprostol, there is a gradual rise in plasma concentration and reaches peak in 60-120 minutes. At 240 minutes, the level is still at 60% of peak level. Thus, vaginal administration results in slow increase and low peak plasma concentration of misoprostol than does oral administration, but overall exposure time to drug is increased.

Presently many regimens are in use but optimal dose of vaginally administered misoprostol is still to be determined. In present study higher dose (50mcg) of misoprostol was used at lower frequency (8 hourly) to see whether this regimen is able to decrease incidence of uterine hyper stimulation, tachysystole and passage of meconium with simultaneously maintaining high success in achieving delivery within

24 hours. We have compared the efficacy and safety of 25mcg versus 50 mcg of misoprostol given vaginally at different frequency for induction of labour at term, because

1. It is an effective inexpensive labour inducing agent thus very useful in low resource settings.
2. Vaginal route is more effective than other routes.

METHODOLOGY

This was a prospective randomized comparative study conducted over a period of one year from December 2011 to November 2012. The local ethics committee approved the study protocol. 200 women were enrolled in this study. None of them opted out, once recruited and there were no protocol violations.

An informed consent was taken from all the women who volunteered to participate in the study and who were fulfilling inclusion criteria. The inclusion criteria were Singleton pregnancy, Cephalic presentation, gestational age ≥ 37 weeks, reactive foetal heart pattern, bishop score of < 6 ,cervical dilatation < 3.Those with parity > 4, estimated foetal weight > 4.5kg or < 2kg, AFI ≤5cm, previous uterine scar, abnormal lie, history of allergy to prostaglandins, any contraindication to vaginal delivery, severe medical illness such as asthma, heart disease were excluded. Indications for induction were premature rupture of membrane, Hypertensive disorders of pregnancy, post dated pregnancy**,** cholestasis of pregnancy**,** gestational diabetes mellitus**,** oligohydroamnios, Foetal growth restriction**,** maternal medical illnesses requiring termination like DM, chronic hypertension.

Detailed clinical history of all women was taken. Period of gestation was ascertained by last menstrual period and the duration of previous menstrual cycles or by first trimester ultrasound scan, if not sure of date. General physical examination and obstetric examination was done. Routine antenatal investigations were done in all the cases. Special investigations were carried out in relevant cases. All the women enrolled were randomized into two groups - Group A **(**consist of cases induced with 25mcg of misoprostol/4 hourly) and Group B **(**consist of cases induced with 50mcg of misoprostol/8 hourly). Prior to administration of intravaginal misoprostol, per vaginal examination was performed by attending obstetrician to assess the cervix and pelvis and NST was routinely performed to evaluate foetal well-being. After confirmation of a reactive NST and a Bishop score of < 6, women received either 25mcg or 50mcg of intravaginal misoprostol placed in the posterior fornix. The dose was repeated in every 4 hours in Group A and in every 8 hours in Group B. Every 4 hours per vaginal examination was performed to assess the cervical score. Foetal heart rate monitoring was done by intermittent auscultation. The maximum permissible dose was 150mcg in both the groups. Subsequent dose was withheld in presence of regular uterine contractions with cervical dilatation > 3, adequate uterine contractions (at least three contractions in 10 minute each lasting for 40-45 seconds). In those conditions artificial rupture of membrane was done and oxytocin augmentation was started, if indicated. Progress of labour was monitored by maintaining partograph.

Observation were made and recorded and patients were managed accordingly. Both mother and baby were followed up for a week or until discharge. Labour induction was considered successful if a patient delivered within 24 hours of initiation of induction. Any deviation from normal was dealt with, as and when required accordingly. All cases were closely watched. Vento use or forceps was applied when indicated. If any obstetrical indication for caesarean occurred then the patient was immediately considered for caesarean section. Averaged data were reported as means and standard deviations and compared by using relevant statistical software (Statistical Package for the Social Sciences, SSPS, and version 14). Categorical variables were analyzed by either chi square test or the Fisher Exact test and student t-test was used to analyze continuous variables. $P < 0.05$ considered significant.

RESULTS

The baseline data of both groups were comparable (Table1). Indications for induction were similar in two groups. Most common was PROM followed by postdates and preeclampsia (Table2). In the two groups, there was no significant difference in caesarean section rate (p=0.071). Though the difference in instrumental delivery in between the two groups had not reached statistically significant level (p=0.054) however the trend was towards Group B. The subjects in Group A were more likely to deliver vaginally than Group B (P=0.009) (Table3). The need for oxytocin augmentation was not significant between the two groups (60.2% vs 52.9% in Group A and Group B) (Table 3). More subjects were delivered in Group A than Group B within 12 hours of start of induction (76.3% vs 74.1%) (Table 3). In Group A more subjects had caesarean section for failed induction (42.9% vs none) and non progress of labour (28.6% vs 6.7%) than Group B. Whereas meconium stained liquor in latent phase of labour (46.7%) and non assuring foetal heart rate (46.7%) formed most of the indications for caesarean section in Group B (Table 4). Uterine hyper stimulation (2% vs none) and tachysystole (5% vs none) were significantly more in Group B than Group A (Table 5). The difference was not significant in the rate of third stage complications in between the two groups (Table 5). Hyperbilirubinemia, meconium aspiration syndrome, birth asphyxia and respiratory distress were

found in 10% vs 12%, 1% vs 3%, 2% vs 4% and 1% each in Group A and Group B respectively (Table 5). There was one perinatal mortality in Group B due to severe hypoxic encephalopathy with multiple organ failure syndromes (Table 5). Passage of meconium was more in Group B than Group a (18% vs 7%) but not reached the significance level (Table 5).

Table-1: Baseline data

			Group A	Group B	Total	p Value
Ubooked/Booked	Unbooked		48	40	88	0.254
	Booked		52	60	112	
AGE	MEAN		25.21	25.38		0.720
	<20		7.0%	10.0%	8.5%	
	21-25		49.0%	40.0%	44.5%	
	26-30		37.0%	44.0%	40.5%	
	>30		7.0%	6.0%	6.5%	
B. M. I (Kg/m^2)	Mean		21.0023	21.5515		0.147
	<18		5.0%	2.0%	3.5%	0.444
	18-24.9		90.0%	91.0%	90.5%	
	>25		5.0%	7.0%	6.0%	
Parity	Multiparous		29.0%	25.0%	27.0%	0.524
	Nulliparous		71.0%	75.0%	73.0%	
Gestational age	Mean		276.0200	274.1500		0.105
Bishop Score	Mean		3.55	3.48		0.703
Urban/Rural	Urban		86.0%	92.0%	89%	0.175
	Rural		14.0%	8.0%	11%	

Table -2: Indication for Induction of Labour

Indication	Group A	**Group B**	Total	p Value
PROM	46.0%	47.0%	46.5%	0.827
Post Dated	33.0%	28.0%	30.5%	
Pre-Eclampsia	16.0%	19.0%	17.5%	
Diabetes Mellitus-II	0%	1.0%	0.5%	
Foetal Growth Restriction	3.0%	4.0%	3.5%	
Oligohydroamnios	2.0%	1.0%	1.5%	

Table -3: Labour Outcome

Mode of delivery		Group A	Group B	Total	p Value
	FTND	92.0%	79.0%	85.5%	0.009
	LSCS	7.0%	15.0%	11.0%	0.071
	FORCEPS	1.0%	3.0%	2.0%	0.054
	VACUUM	0%	3.0%	1.5%	
Induction delivery	MEAN	9.676	9.2028		0.472
	<12hours	76.3%	74.1%	75.3%	0.731
Need for oxytocin		60.2%	52.9%	56.7%	0.328

Table -4: Indication of Caesarean Section

Indication Of Caesarean Section	Group A	Group B	Total	P value
Failed Induction	42.9%	0%	13.6%	0.013
MSL In Latent Phase Of Labour	14.3%	46.7%	36.4%	
Non Progress Of Labour	28.6%	6.7%	13.6%	
Non Assuring Foetal Heart Rate	14.3%	46.7%	36.4%	

Table -5: Others outcomes

	Group A	Group B	Total	p Value
Fever	2.0%	0%	1.0%	0.039
Vomiting	1.0%	0%	0.5%	
Hyper stimulation	0%	2.0%	1.0%	
Tachysystole	0%	5.0%	2.5%	
Hyperbilirubinemia	10.0%	12.0%	11.0%	0.651
Meconium Aspiration Syndrome	1.0%	3.0%	2.0%	0.312
Perinatal Asphyxia	2.0%	4.0%	3.0%	0.407
Respiratory Distress	1.0%	1.0%	1.0%	1.00
Septicaemia	1.0%	0%	0.5%	0.316
Meconium Passage	7%	18%	12.5%	0.019
LBW(2-2.5kg)	7%	4%	5.5%	0.756
Neonatal Death	0%	1%	0.5%	0.316

DISCUSSION

The mean gestational age in days was 276.02±7.74 in Group A and 274.15±8.45 in Group B, which was 288±1.5 in Group A and 289±2 in Group B in M. M. Meydanli *et al.;*[1] study and 275.52±7.42 vs 275.94±7.21 in Group A and Group B in Shivarudraiah Girija *et al.;*[2] study. The mean pre induction Bishop score was 3.55±1.431 in Group A and 3.48±1.150 in Group B, which was similar to Shivarudraiah Girija *et al.;*[2] study ((3.18±1.17 vs 3±1.49). It was less (2.3±0.6 in Group A vs 2.1±0.7 in Group B) in M. M. Meydanli *et al.;* [1] study might be because of population variation or observational bias.

In both the groups, indication for induction was almost similar and there was no difference found (p= 0.827). In M. T. EL-Sherbiny *et al.;* [3] study of 185 subjects; post-dated pregnancy was indication in 27.97% of Group A and 27.17% of Group B subjects. This was similar to our finding (33% vs 28%) but in Shivarudraiah Girija *et al.;* [2] study of 100 subjects; post-dated pregnancy was indication for induction in 70% of Group A and 74% of Group B subjects. It was just double than our result. These differences could be due to the institutional protocol.

In the study of Sherbiny *et al.;* [3]. Pre - eclampsia was Indication for induction in almost similar number of subjects (26.88% vs 28.26% in Group A and Group B respectively). While in Shivarudraiah Girija *et al.;* [2] study it was 2% vs 6%. The difference is quite large and our finding laid in between (16% vs 19%) them. These differences could be because of institutional protocol or population differences of the studies.

Foetal growth restriction was also indicated in almost similar number of subjects in Sherbiny *et al.* [3] study (9.67% vs 8.70% in Group A and Group B respectively) but none of the patient was induced due to foetal growth restriction in Shivarudraiah Girija *et al.;* [2] study. It was 3% vs 4% in our study. Higher incidence of foetal growth restriction in Sherbiny *et al.;* [3] studies could be due to more pre-eclampsia in that study as compared to our.

In Shivarudraiah Girija *et al.;* [2] study premature rupture of membrane was indication in 26% of Group A and 20% of Group B subjects. It was more (46% vs 47%) in our study, the reason is unknown. Sherbiny *et al.;* [3] had excluded PROM from their study. In Group A 56 (60.2%) and in Group B 45 (52.9%) subjects needed oxytocin augmentation, which was similar to Elhassan E. M. *et al.;* [4] study (61.5% in Group A vs 56.3% in Group B). Although the need for oxytocin augmentation was less in the studies of M.T. EL-Sherbiny *et al.;* [3] (37.63% vs 26.08%) and Bounyasong Suntit [5] (12.05% vs 20.48%) than our study, they also reported no difference in the need for oxytocin augmentation in between the two groups. There was less requirement of oxytocin augmentation in these studies probably because they had good mean pre induction Bishop score than our study [in our study it was 3.55±1.4 vs 3.48±1.15 while in M.T. EL-Sherbiny *et al.;* [53] study 4.11±2.21 vs 4.01±2.18 and Bounyasong Suntit (2000) [5] study 5.12 vs 4.93 in Group A and Group B respectively]. Despite of less pre induction Bishop score (2.3±0.6 vs 2.1±0.7) in M. M. Meydanli [1] study the need for oxytocin augmentation was very less (6.7% vs 11.6%) than our study, might be because of more average number of dose of misoprostol used by them. But again the difference in the oxytocin requirement in between the two groups was not significant. On comparison of mean induction delivery interval between the two groups no significant difference was found (p 0.472), which was consistent with M. M. Meydanli *et al.;* [1] and Shivarudraiah Girija *et al.;* [2] studies. The mean induction delivery interval was 9.67±4.52 hours and 9.20±4.19 hours in Group A and Group B respectively, which was high in M. M. Meydanli *et al.;* [1] study (11.41±3.3 hours vs 10.45±2.95 hours) than our study, probably due to less

pre induction Bishop score in their study as compared to our. In Shivarudraiah Girija *et al.;* [2] study despite of comparable Bishop score to our study induction-delivery interval was longer (14.42±13.2 hours in Group A vs 18.58±13.73 hours in Group B), probably because of different dosing interval (25mcg/6 hour vs 50mcg stat) than our study.

Out of 200 subjects 171(85.5%) had normal vaginal delivery. In Group A 92% and in Group B 79% subjects had normal vaginal delivery with significant difference (p value 0.009). It was 81.6% vs 78.3% in M.M. Meydanli *et al.;* [1] study and 73.33% vs 70% in Shivarudraiah Girija *et al.;*[2] study. In our study more Groups A subjects had normal vaginal delivery as compare to Group B subjects.

Instrumental delivery was needed in 1% of Group A and 6 % of Group B subjects which was 3.3% vs 5% in M.M. Meydanli *et al.;*[1] study and 6.7% vs 3.3% in Shivarudraiah Girija *et al.;*[2] study. We had 5% more Instrumental vaginal delivery in group B that could be because of higher incidences of passage of meconium and non assurance of foetal heart rate in that group.

Caesarean section was done for 22 (11%) subjects out of which 7 (7%) were in Group A and 15 (15%) were in Group B. In M.M. Meydanli *et al.;* study [1] it was 18.3% in Group A and 21.6% in Group B. It was 20% vs 26.7% in Shivarudraiah Girija *et al.;* [2] study and 17.20% vs 14.13% in Sherbiny EL-MT[3] study. On comparing with the above mentioned studies the rate of caesarean section was less in Group A as well as in Group B in our study.

There was significant difference in indication for caesarean section between the two groups (p 0.013). Out of 22 caesarean sections, 8 (36.4%) were done for non assuring foetal heart rate. Meconium stained liquor in latent phase of labour was indication for another 8 (36.4%) subjects. Non progress of labour and failed induction were indicated in equal number of subjects 3 (13.6%) each. Failed induction , non assuring foetal heart rate, meconium in latent phase of labour and non progress of labour were indication for caesarean section in 3 (42.9%), 1 (14.3%), 1 (14.3%) and 2 (28.6%) subjects of Group A respectively.

Whereas in Group B, 1 (6.7%) subject had caesarean for non progress of labour and 7 (46.7%) each had caesarean for non assuring foetal heart rate and meconium in latent phase of labour. In M.M. Meydanli *et al.;* study [1] who included only post-dated pregnancy in their study, non assuring foetal heart rate was indication in 13.3% vs 15% subjects of Group A and Group B respectively.

Meconium in latent phase of labour was indication in more subjects of Group B than Group A (46.7% vs 4.3%). Failed induction was indication in 42.9%of Group A subjects and none of the Group B. In Sherbiny ET-MT *et al.;* [3] study more caesarean was done for failed induction in Group A, which was consistent with our study.

Fever and vomiting were associated with 2 (2%) and 1 (1%) of subjects in Group A (could be due to associated PROM and gastritis) and was not found in Group B, whereas uterine hyper stimulation and tachysystole were present in 2 (2%) and 5 (5%) subjects of Group B and was not found in Group A. In our study significantly more uterine hyper stimulation and tachysystole found in Group B than Group A.

In Sherbiny EL-MT *et al.;*[3] study the incidence of tachysystole was 7.53% in Group A and 21.15% in Group B which was higher than our finding (none vs 5%), might be due to population variation and that of hyper stimulation it was none in Group A and 6.52% in Group B which was same as our finding in Group A (0%) but more than our finding in Group B (2%) might be due to more frequent dosing in their study as compared to our study (4 hour vs 8 hour). Though the overall incidence of uterine hyper stimulation and tachysystole was higher than our finding, the difference was significant between the two groups in that study also.

The difference in the incidence of tachysystole between the two groups was not significant in studies M. M. Meydanli *et al.;* [1] (1.7% vs 3.3%) and Shivarudraiah Girija *et al.;* [2] (2% vs 10%) which was not consistent with our finding.

The difference in the third stage complications between the two groups was not statistically significant (p=0.40). In Shivarudraiah Girija *et al.;*[2] study postpartum haemorrhage occurred in 4% vs 6% subjects of Group A and Group B respectively. Though it was than our study but there was no significant difference in the incidence of postpartum haemorrhage among the two groups in this study also.

There was no significant difference in incidences of hyperbilirubinemia and meconium aspiration syndrome in between the two groups in our study as well as Sherbiny EL-MT *et al.;*[3] study.

CONCLUSION

The present study concludes that, 25 mcg/4 hours per vaginum misoprostol dose regimen is more prudent choice from the perspective of safety for induction of labour. Although there were more chances of caesarean section for failed induction and non progress of labour, there were significantly less

incidences of uterine hyper stimulation, tachysystole, passage of meconium and non assuring foetal heart rate in 25mcg/4 hour per vaginum misoprostol regimen.

Even after decreasing frequency of higher dose of misoprostol than previous studies (50mcg/4 hour to 50 mcg/8 hour) the incidence of uterine hyper stimulation, tachysystole and passage of meconium was more as compared to 25mcg/4hour regimen. We, therefore, recommend the 25mcg misoprostol per vaginum every 4 hourly as a safe and effective method for induction of labour.

REFERENCES

1. Meydanli MM, Caliskan E, Burak F, Narin MA, Atmaca R; Labour induction post-term with 25mcg vs 50mcg intravaginal misoprostol. International Journal of Gynaecology and Obstetrics 2003; 81(3): 249-55.
2. Shivarudraiah Ginja, Manjunath Palaksha Attibele: Turkish-German gynaecological association 2009; 10: 220-25.
3. Sherbiny EL, El-Gharieb IH, Gewely HA; International Journal of Gynaecology and Obstetrics 2001; 72(1): 25-30.
4. Elhassan EM, Mirghani OA, Adam I; cervical ripening and labour induction with 25mcg vs 50mcg of intravaginal misoprostol. International Journal of Gynaecology and Obstetrics 2005; 90: 234-35.
5. Bounyasong Suntit; A randomized comparison between 25 mcg misoprostol gel and 50 mcg misoprostol vaginal tablet for induction of labour. Thai Journal of Obst. And Gynae. 2000; 12; 21-5.