Sublingual Versus Vaginal Misoprostol For Induction Of Labour At Term

Dr. Ahmed Taha Abdelfattah, Prof. Dr. Abdelfattah Mohammed Elsenity, Dr. Ahmed Osama Abdelmotaal, Ahmed Mohammed Abdelaziz Selim

Department of Obstetrics and Gynecology, Faculty of Medicine, Al – Azhar University, Cairo, Egypt
a_selim4004@yahoo.com

Abstract: Introduction: Induction of labor implies the artificial initiation of uterine activity to affect labor and delivery. The indications for induction have been steadily widened in recent years. The aim of successful induction is to achieve vaginal delivery with a safe maternal and perinatal outcome and to eliminate any anticipated adverse outcome associated with continuation of pregnancy. It should bring about adequate uterine activity sufficient for cervical changes and fetal descent to occur without causing hyperstimulation or fetal compromise. The objective of pharmacological induction is to mimic the natural process as closely as possible. **Aim of the work:** The aim of this study is to assess the effectiveness and safety of sublingual Misoprostol (25 microgram), compared with the same dose administered vaginally every 4 hours for cervical ripening and labour induction in women with a viable term pregnancy. **Patients and methods:** This randomized controlled study was conducted on 100 women who were admitted at Department of Obstetrics and Gynecology, Matareya Teaching Hospital (MTH) in Cairo, in the period between January 2018 to August 2018. All these cases were admitted for induction of labor by Misoprostol either sublingually or vaginally. These cases were randomized into Group A and Group B. Group A included sublingual group. Group B included vaginal group. **Results:** In group A, there were 36 cases delivered vaginally, versus 34 cases in group B. The difference between the two groups was statistically non significant. The number of cases delivered by C.S. was 14 cases in group A and 16 cases in group B, with no statistically significant difference between both groups. The mean misoprostol dose was higher in group B in comparison to group A with statistically significant difference between both groups. (P=0.015). There was statistically significant difference between two groups as regards induction-delivery interval and which was shorter in group A in comparison to group B. (P=0.045). In group A, 8 cases delivered by C.S. because of fetal distress, 4 cases were due to failed progress of labor, 2 cases were due to failed induction. In group B, there were 9 cases due to fetal distress, 6 cases due to failed progress of labor, 1 case due to failed induction. There was no statistically significant difference between two groups as regards the indication of delivery by C.S. There was no statistically significant difference between two groups as regards 1 and 5 minutes Apgar Score and NICU admission. There was no statistically significant difference between two groups as regards misoprostol side effects.

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1. Introduction

Induction of labor implies the artificial initiation of uterine activity to affect labor and delivery. The indications for induction have been steadily widened in recent years. The aim of successful induction is to achieve vaginal delivery with a safe maternal and perinatal outcome and to eliminate any anticipated adverse outcome associated with continuation of pregnancy. It should bring about adequate uterine activity sufficient for cervical changes and fetal descent to occur without causing hyperstimulation or fetal compromise. The objective of pharmacological induction is to mimic the natural process as closely as possible. **(Souza et al., 2008).**

Labor induction is one of the common techniques in obstetrics, reaching 20 % of deliveries worldwide. The increasing rate of labor induction has probably played a role in the increased rate of caesarean delivery observed in the United States during the past few decades. The increased rate of induction of labor is due to many factors including a desire for a suitable time for her family and the healthcare provider and the availability of a several agents and methods to induce labor. **(Guerra et al., 2009).**

In the presence of an unfavorable cervix, cervical ripening is recommended to increase the likelihood of successful induction and decrease the risk of a Cesarean delivery. The search for the ideal agent, timing, and dosage interval to convert an unfavorable cervix to one receptive to delivery is an ongoing process. Attention has been focused on prostaglandins as effective pharmacological adjuncts to induction. **(El Kattan et al., 2013).**

Methods for labor induction include both mechanical and pharmacological options. Although oxytocin is an effective drug for the augmentation of labor in patients with favorable cervices, in patients with an unfavorable cervix, a ripening agent may be used. **(ACOG, 2009).**

Misoprostol is a synthetic prostaglandin E1 analogue. Actually, it is more frequently used for cervical ripening and labor induction than natural prostaglandin, particularly in developing countries regarding its low cost. The most favorable method for the administration and the optimal dose of Misoprostol has not yet been established. Several studies indicate that oral Misoprostol is less effective and results in more side effects than intravaginal doses because of systemic diffusion and digestive passage. **(Fakhir et al., 2013).**

Sublingual Misoprostol is another route of administration that may perhaps be compared with vaginal administration, as both require mucosal uptake of the drug. Since the pharmacokinetics is different for sublingual and vaginal Misoprostol, differences in efficacy and side effects need to be compared. **(Fakhir et al., 2013).**

Misoprostol is inexpensive and effective and can be stored at room temperature. The Food and Drug Administration (FDA) has not approved Misoprostol for labor induction or cervical ripening yet, but this medication has been used successfully in several clinical trials. The ideal dose and routes of the administration of Misoprostol for the induction of labor at full term are still a matter of controversy. **(Jahromi et al., 2016).**

The National Institute for Health and Clinical Excellence (NICE) released a clinical guideline in 2008 and restricted the use of Misoprostol only to clinical trials and termination of pregnancies with a dead fetus. However, the American College of Obstetricians and Gynecologists (ACOG) supported its usage in 2009 for women who did not have a previous Cesarean delivery or a major uterine surgery. **(Jahromi et al., 2016).**

Vaginal and sublingual Misoprostol have a rapid onset action, due to their prolonged activity and bioavailability. A sublingual dose of 25 µg every 4 hours in most of cases, induce vaginal delivery within 24 hours and compared to an equivalent oral dose, less oxytocin augmentation is required. **(Ayati et al., 2014).**

However, the previous studies found few significant differences among the effectiveness of different doses of the Misoprostol, oral, vaginal or sublingual. So this study is performed to compare the efficacy and safety of vaginal versus sublingual Misoprostol with four hours interval for maximum of six doses for cervical ripening and induction of labor. **(Ayati et al., 2014).**

Aim of the work

The aim of this study is to assess the effectiveness and safety of sublingual Misoprostol (25 microgram), compared with the same dose administered vaginally every 4 hours for cervical ripening and labour induction in women with a viable term pregnancy.

2. Patients and Methods

Study design:

This randomized controlled study was conducted on 100 women who were admitted at Department of Obstetrics and Gynecology, Matareya Teaching Hospital (MTH) in Cairo in the period between January 2018 to August 2018. All these cases were admitted for induction of labour by Misoprostol either by sublingual route or vaginal route. These cases were randomized into Group A and Group B. Group A included women received 25 µg Misoprostol sublingually. Group B included women received 25 µg Misoprostol vaginally in the posterior fornix.

Inclusion criteria:

- Singleton viable pregnancy at gestational age of completed 37 weeks or more.
- Obstetrical indication for induction.
- Vertex presentation.
- Unfavorable cervix (Bishop 6 or less).
- No cephalopelvic disproportion.
- No history of bronchial asthma, glaucoma, serious cardiovascular disorders, renal diseases, metabolic or endocrinal disorders or allergy to Misoprostol.
- Nulliparous and multiparous women (parity < 5).
- Reassuring fetal heart tracing (since admission).
- Estimated fetal weight < 4000 grams.

Exclusion criteria:

- High parity (Para > 5).
- Multiple pregnancies.
- Malpresentation.
- Antepartum Hemorrhage.
- Previous uterine scar / Any other uterine surgery.
- Severe oligohydramnios (AFI < 5), or polyhydramnios (AFI > 25cm).
- Non reassuring fetal heart rate pattern.
- Intrauterine growth restriction (I.U.G.R.).
- Cephalopelvic disproportion.
- Renal and hepatic disease.
- Hypersensitivity to prostaglandins.
- Chorioamnionitis or Hyperthermia > 38°c.

- Intrauterine fetal death (I.U.F.D.).

The dose was repeated every 4 hours for a maximum of six doses (24 hours).

The primary outcome measure was the frequency of successful induction, defined as a vaginal delivery within 24 hours from the start of induction.

The secondary outcomes included the rate of C.S due to fetal distress, failed induction or failure to progress, the induction to delivery interval, the number of Misoprostol doses needed, the need for oxytocin augmentation, and the uterine hyperstimulation rates. The neonatal outcomes including: intrapartum meconium passage, an Apgar score at 1 and 5 minutes, and the need for NICU admission.

3. Results

One hundred women were enrolled in the study. They were divided into two equal groups; (Group A & Group B) each of 50 cases. In group A misoprostol was given sublingualy, in group B misoprostol was given vaginally.

The primary outcome measure was the frequency of successful induction, defined as a vaginal delivery within 24 hours from the start of induction.

The secondary outcomes included the rate of C.S due to fetal distress, failed induction or failure to progress, the induction to delivery interval, the number of Misoprostol doses needed, the need for oxytocin augmentation, and the uterine hyperstimulation rates. The neonatal outcomes including: intrapartum meconium passage, an Apgar score at 1 and 5 minutes, and the need for NICU admission.

There was no statistically significant difference between the two groups as regards mother age, gestational age, parity and Bishop`s score.

There was no statistically significant difference between two groups as regards indications for induction of labor.

In group A (Sublingual), there were 36 cases delivered vaginally, versus 34 cases in group B (Vaginal). The difference between the two groups was statistically non significant. The number of cases delivered by C.S. was 14 cases in group A and 16 cases in group B, with no statistically significant difference between both groups.

The mean misoprostol dose was higher in group B (Vaginal) in comparison to group A (Sublingual) with statistically significant difference between both groups.

There was statistically significant difference between two groups as regards induction-delivery interval, which was shorter in group A (Sublingual) in comparison to group B (Vaginal).

In group A (Sublingual), 8 cases delivered by C.S. because of fetal distress, 4 cases were due to failed progress of labor, 2 cases were due to failed induction. In group B (Vaginal), there were 9 cases delivered by C.S. due to fetal distress, 6 cases due to failed progress of labor, 1 case due to failed induction. There was no statistically significant difference between two groups as regards the indication for delivery by C.S.

There was no statistically significant difference between two groups as regards 1 and 5 minutes Apgar Score and the need for NICU admission.

There was no statistically significant difference between two groups as regards misoprostol side effects (Diarrhea, Fever, Vomiting and Uterine Hyperstimulation).

Table (1): Maternal basic characteristics of both groups.

	Group A (Sublingual) (N=50)	Group B (Vaginal) (N=50)	P value
Age (Y)	24.28 ± 4.031	24.00 ± 3.995	0.728 (> 0.05)N.S
Gest. Age (Wk)	40.74 ± 1.562	41.02 ± 1.421	0.351 (> 0.05)N.S
Bishop Score	3.84 ± 1.405	4.00 ± 1.443	0.576 (> 0.05)N.S

The table shows that mean age in group A was 24.28 ± 4.031 while in group B was 24. ± 3.995, the mean gestational age was 40.74 ± 1.562 in group A while in group B was 41.02 ± 1.421 and the mean of preinduction Bishop Score in group A was 3.84 ± 1.405 while in group B was 4. ± 1.443. There was no statistically significant difference between the two groups.

Table (2): Distribution of primigravida and multipara in each group.

Variable	Group A (Sublingual)		Group B (Vaginal)		P value
	No	%	No	%	
Primigravida (No = 62)	32	64	30	60	0.837 (> 0.05) N.S
Multipara (No = 38)	18	36	20	40	

The table shows that number of PG cases in group A was 32 cases while in group B was 30 cases and the number of multiparous women in group A was 18 cases and was 20 cases in group B. There was no statistically significant difference in the two groups as regards parity.

Table (3): Indication for induction of labor in each group.

Variable	Group A (Sublingual)	Group B (Vaginal)	P value
Postdate	28	32	0.636 (> 0.05) N.S
PROM	15	11	
HTN	2	4	
Preeclampsia	2	2	
D.M	3	1	

The table show that indction of labor was performed in group A among 28 cases postdate, 15 cases PROM, 2 cases hypertensive, 2 cases with preeclampsia and 3 cases with diabetes milletus, while was performed in group B among 32 cases postdate, 11 cases PROM, 4 cases hypertensive, 2 cases preeclamptic and only one case with diabetes milletus. There was no statistically significant difference in both groups as regards indications for induction of labor.

Table (4): Mode of delivery in each group. (primary outcome measures).

Mode of delivery	Group A (Sublingual)		Group B (Vaginal)		P value
	No	%	No	%	
Vaginal delivery No = 70	36	72	34	68	0.828 (> 0.05) N.S
Cesarean sections No = 30	14	28	16	32	

The table shows that 36 cases delivered vaginally in group A and 34 cases in group B, while cases delivered by C.S were 14 cases in group A and 16 cases in group B. The difference in mode of delivery between the two groups was not.

Table (5): Events during induction in both groups.

Variable	Group A (Sublingual)	Group B (Vaginal)	P value
Induction-delivery interval (h)	7.42 ± 5.489	10.08 ± 7.483	0.045 (< 0.05) Sig.
Need for oxytocin augmentation	17 (34%)	19 (38%)	0.835 (> 0.05) N.S
Meconium stained liqour	9 (18%)	8 (16%)	1 (> 0.05) N.S

The table shows that the mean of induction-delivery interval was 7.42 ± 5.489 hours in group A, while in group B it was 10.08 ± 7.483 hours (shorter in sublingual group than vaginal group). The difference between both groups was statistically significant (P = 0.045).

The number of cases which needed augmentation of labor with oxytocin was 17 cases in group A, while in group B it was 19 cases. Meconium stained liquor occurred in 9 cases of group A and 8 cases in group B.

There was no statistically significant difference between both groups as regards the need for augmentation of labor with oxytocin and the meconium staining of liquor during induction.

Table (6): Number of misoprostol doses given in both groups.

Dose	Group A (Sublingual)	Group B (Vaginal)	P value
One dose: 25 µg	22 (44%)	6 (12%)	0.015 (< 0.05) Sig.
Two doses: 50 µg	13 (26%)	19 (38%)	
Three doses: 75 µg	7 (14%)	8 (16%)	
Four doses: 100 µg	4 (8%)	15 (30%)	
Five doses: 125 µg	2 (4%)	1 (2%)	
Six doses: 150 µg	2 (4%)	1 (2%)	
Mean ± SD	2.14 ± 1.385	2.78 ± 1.183	

The table shows that the mean misoprostol dose in group A was 2.14 ± 1.385, while in group B it was 2.78 ± 1.183 (lower in sublingual group than vaginal group). The difference between the two groups regarding the number of misoprostol doses was statistically significant. (P = 0.015).

Table (7): Indications for cesarean sections in both groups.

Indication for C.S.	Group A (Sublingual)		Group B (Vaginal)		P value
	No	%	No	%	
Fetal distress (No = 17)	8	16	9	18	1 (> 0.05) N.S
Failed progress (No = 10)	4	8	6	12	0.318 (> 0.05) N.S
Failed induction (No = 3)	2	4	1	2	1 (> 0.05) N.S
Total (No = 30)	14	28	16	16	0.393 (> 0.05) N.S

The table shows that cases delivered by C.S in group A were 8 cases due to fetal distress, 4 cases due to failed progress of labor and 3 cases due to failed induction while in group B they were 9 cases due to fetal distress, 6 cases due to failed progress of labor and one case due to failed induction of labor. There was no statistically significant difference in both groups as regards the indications of delivery by cesarean section.

Table (8): Neonatal outcome in both groups.

Variable	Group A (Sublingual)	Group B (Vaginal)	P value
Apgar Score at 1 minute	8.18 ± 0.691	8.40 ± 0.606	0.094 (> 0.05) N.S
Apgar Score at 5 minutes	8.32 ± 1.039	8.50 ± 1.055	0.392 (> 0.05) N.S
NICU admission	5 (10%)	4 (8%)	0.727 (> 0.05) N.S

The table shows that the mean for neonatal Apgar Score at 1 minute was 8.18 ± 0.691 in group A while in group B it was 8.4 ± 0.606.

The mean for neonatal Apgar Score at 5 minute was 8.32 ± 1.039 in group A while in group B it was 8.5 ± 1.055.

Number of neonates needed NICU admission was 5 cases in group A while in group B it was 4 cases.

There was no statistically significant difference in both groups as regards neonatal outcomes (Apgar score at 1 & 5 minutes and NICU admission).

Table (9): Side effects of misoprostol in both groups.

Variable	Group A (Sublingual)		Group B (Vaginal)		P value
	No	%	No	%	
Vomiting (No = 10)	6	12	4	8	0.741 (> 0.05) N.S
Diarrhea (No = 4)	1	2	3	6	0.617 (> 0.05) N.S
Fever (No = 4)	2	4	2	4	1 (> 0.05) N.S
Hyperstimulation (No = 6)	2	4	4	8	0.678 (> 0.05) N.S
Total (No = 24)	11	22	13	26	0.591 (> 0.05) N.S

The table shows that there was no statistically significant difference between two groups as regards misoprostol side effects as the number of cases developed vomiting was 6 cases in group A while in group B were 4 cases, diarrhea occurred in only 1 cases in group A and 3 cases in group B, fever occurred in 2 cases in both groups and uterine hyperstimulation occurred in 2 cases in group A and 4 cases in group B.

4. Discussion

Induction of labor implies the artificial initiation of uterine activity to affect labor and delivery. The indications for induction have been steadily widened in recent years. The aim of successful induction is to achieve vaginal delivery with a safe maternal and perinatal outcome and to eliminate any anticipated adverse outcome associated with continuation of pregnancy. It should bring about adequate uterine activity sufficient for cervical changes and fetal descent to occur without causing hyperstimulation or fetal compromise. The objective of pharmacological induction is to mimic the natural process as closely as possible. **(Souza et al., 2008).**

In the presence of an unfavorable cervix, cervical ripening is recommended to increase the likelihood of successful induction and decrease the risk of a Cesarean delivery. The search for the ideal agent, timing, and dosage interval to convert an unfavorable cervix to one receptive to delivery is an ongoing process. Attention has been focused on prostaglandins as effective pharmacological adjuncts to induction **(El Kattan et al., 2013).**

Misoprostol is a synthetic prostaglandin E1 analogue. Actually, it is more frequently used for cervical ripening and labor induction than natural prostaglandin, particularly in developing countries regarding its low cost. The most favorable method for the administration and the optimal dose of Misoprostol has not yet been established. Several studies indicate that oral Misoprostol is less effective and results in more side effects than intravaginal doses because of systemic diffusion and digestive passage.

Sublingual Misoprostol is another route of administration that may perhaps be compared with vaginal administration, as both require mucosal uptake of the drug. Since the pharmacokinetics is different for sublingual and vaginal Misoprostol, differences in efficacy and side effects need to be compared **(Fakhir et al., 2013).**

The aim of this study is to compare the efficacy and safety of sublingual and vaginal misoprostol for impelling of labor.

During induction the following data were recorded

Induction-to-delivery (ID) time, the number of misoprostol doses given and total dose, the need for oxytocin augmentation, mode of delivery, the need for and indication of cesarean deliveries and neonatal outcomes, Apgar Score at 1 and 5 minutes, need for and indication of admission at NICU, and side effects of misoprostol.

This study comprised one hundred pregnant women, they were divided randomely into two equal groups. In group A every patient received 25 ug misoprostol placed under the tongue till completely dissolved. In group B every patient received 25 ug misoprostol inserted digitally in the posterior fornix of the vagina The doses were repeated at 4 hours interval till efficient uterine contractions is reached three or more over 10 minutes each last for 45 seconds, the maximum number of doses was 6 doses.

In the study it was highly considered to recruit parturients of almost similar conditions. The mean age of women included in the study was 24.14 ± 3.995 (range: 19-33 years). The mean gestational age of women included in the study was 40.88 ± 1.439 (range: 38-42 weeks). The mean pre-induction Bishop score was 3.92 ± 1.419 (range: 2-6). We selected only women with Bishop score 6 or less, considering the fact that the main goal for using medication for induction of labor was the ripening of an unfavorable cervix. There was no statistically significant difference between both groups as regards initial basic characteristics.

As regards parity in the included women, 62 cases were PG while multiparous women were 38 cases.

Indications for induction of labor were 60 cases postdate, 26 cases PROM, 6 cases hypertension, 4 cases preeclampsia and 4 cases diabetes milletus.

Regarding mode of delivery in this study, there were 36 cases delivered vaginally in group A versus 34 cases in group B. The difference between the two groups was statistically non significant, the rates of C.S in group A was 14 cases and 16 cases in group B with no statistically significant difference between the two groups.

Chirag et al., (2016), study done on 100 women, randomely divided into 50 patients in sublingual group and 50 patients in vaginal group, received 25 microgramms, and dose repeated at interval of four hours with maximum of six doses, their results came with agreement with the results of our study regarding mode of delivery in sublingual versus in vaginal group. The majority of cases in both groups delivered vaginally. Also the induction to delivery interval was shorter in sublingual group compared to vaginal group, which was like our study.

Hangaraga, U. S. (2017): study done on 100 women, randomely divided into 50 patients in sublingual group and 50 patients in vaginal group, received 25 microgramms, and dose repeated at interval of four hours with maximum of six doses, their results came in agreement with our study regarding mode of delivery, as the majority of women in both groups delivered vaginally. Also the induction delivery interval was shorter in sublingual group compared to the vaginal group and the mean number of misoprostol doses were less in sublingual group which is like our study.

Jahromi et al., (2016): study done on 200 primiparous women, randomely divided into 100 patients in sublingual group and 100 patients in vaginal group, 100 received sublingual misoprostol and vaginal placebo, while the others took vaginal misoprostol and sublingual placebo, and the dose repeated at interval of four hours with maximum of six doses, the results showed that number of women needed C.S was higher in sublingual group but with no statistically significant difference.

Saihood, S. T. (2012), study done on 416 women, randomely divided into 208 patients in sublingual group and 208 patients in vaginal group, received 25 microgramms, and dose repeated at interval of three hours with maximum of three doses, results showed that there was significant difference between the number of C.S in vaginal group (34.6%) and sublingual group (19.7%) which was unlike our result as the statistical difference was insignificant.

Ayati, et al. (2014), study done on 140 women, randomely divided into 90 patients in sublingual group and 50 patients in vaginal group, received 25 microgramms, and dose repeated at interval of four hours with maximum of six doses, the results came with agreement with our study regarding mode of delivery in both groups.

In our study the number of cases delivered by C.S in group A (Sublingual) were 14 cases, 8 cases due to fetal distress, 4 cases due to failed progress of labor and 2 cases due to failed induction. While number of cases delivered by C.S in group B were 16 cases, 9 cases due to fetal distress, 6 cases due to failed progress of labor and one case due to failed induction. As noted the majority of cases were due to fetal distress which was higher in the vaginal group, which may be attributed to the higher rate of uterine hyperstimulation that occurred in vaginal group.

In our study regarding the number of misoprostol doses required in either groups, in group A, the mean dose of misoprostol required was found to be less as compared to the group B, with statistically significant difference between both groups. (P=0.015).

This result came with agreement with **Chirag et al., (2016), Hangaraga, U. S. (2017), Jahromi et al., (2016), Saihood, S. T. (2012).**

However the only study which oppesed this result was **Ayati, et al. (2014),** which showed that there was no statistically significant difference between both groups although it was less in the sublingual group, this may be attributed to the significant difference in the Bishop score in the sublingual group.

Our study showed that there was statistically significant difference in both groups as regards induction-delivery interval as it was less in sublingual group than the vaginal grpup, (P=0.045).

This may be due to systemic bioavailability of sublingual administration of misoprostol and avoidance of first pass metabolism, also vaginal secretions decrease local effects of vaginal route.

This result came with agreement with **Chirag et al., (2016), Hangaraga, U. S. (2017), Saihood, S. T. (2012).**

Jahromi et al., (2016), results showed that induction-delivery interval was less in sublingual group compared to vaginal group but without statistically significant difference.

Ayati, et al. (2014), results showed no difference between both groups as regards induction-delivery interval.

In our study there was no statistically significant difference in both groups as regards the need for oxytocin augmentation, in group A were 17 cases (34%) while in group B were 19 cases (38%), (P=0.773).

This result came with agreement with **Chirag et al., (2016), Hangaraga, U. S. (2017), Saihood, S. T. (2012).**

Jahromi et al., (2016), results showed that no need for oxytocin augmentation at all in both groups.

In our study there was no statistically important difference among the two groups as regards neonatal outcomes, (Apgar score at 1 & 5 minutes, meconium staining of liqour and need for NICU admission).

Meconium stained liqour occurred in 9 cases in group A and 8 cases in group B, (P=0.773).

Mean Apgar score in 1 minute was 8.18 in group A and 8.40 in group B, (P=0.094).

Mean Apgar score in 5 minute was 8.32 in group A and 8.50 in group B, (P=0.392).

Number of cases needed NICU admission were 5 cases in group A and 4 cases in group B, (P=0.727).

These results came with agreement with **Chirag et al., (2016), Hangaraga, U. S. (2017), Saihood, Ayati, et al. (2014), S. T. (2012).**

Jahromi et al., (2016), results showed that meconium staining of liqour was 3 times more frequent in sublingual group than in vaginal group, (P=0.003), this may be attributed to the higher rate of uterine hyperstimulation which occurred more in the sublingual group.

In our study there was no statistically significant difference in both groups as regards side effects of misoprostol, (diarrhea, fever, vomiting and hyperstimulation).

Vomiting occurred in 6 cases in group A and 4 cases in group B, diarrhea occurred in 1 case in group A and 3 cases in group B, fever occurred in 2 cases in both groups, hyperstimulation occurred in 2 cases in group A and 4 cases in group B, (P=0.591).

These results came with agreement with **Chirag et al., (2016), Hangaraga, U. S. (2017), Saihood, S. T. (2012), Ayati, et al. (2014), Jahromi et al., (2016).**

Given the diarrhea as one of the adverse effects of misoprostol as it occurs in more than 10% of the persons who take the drug in high oral doses, we wonder whether misoprostol induces meconium passage via a direct effect on the bowel smooth muscles or it is a real sign of fetal distress and hypoxia.

There are two published studies comparing 25 and 50 micrograms of vaginal and sublingual misoprostol every 6 hours, both reported equal effectiveness and safety. **(Zahran, K.M et al., 2009), (Moraes Filho et al., 2005).**

Misoprostol with minimum doses of 25 micrograms administered orally, vaginally, sublingually, or buccally was compared to prostaglandins E2 in a systematic review, which concluded that misoprostol, compared to prostaglandin E2, was associated with increased risks of hyperstimulation and tachysystole, high rates of of vaginal deliveries within 24 hours, low rates of oxytocin use and increased meconium staining. **(Crane et al., 2001).**

Two studies copared patient satisfaction between sublingual and vaginal misoprostol and concluded that the sublingual method was associated with higher patient satisfaction. **(Zahran, K.M et al., 2009), (Nassar et al., 2007).**

Conclusion

- Misoprostol is effective in induction of labor both with sublingual and vaginal routes.
- Sublingual route has significantly less time of induction-delivery interval.
- Number of doses required in sublingual group was lesser compared to vaginal group.
- Only few patients had minor side effects in both groups. No major side effects were reported.
- Administration by sublingual group avoids repeated vaginal examination.
- Sublingual route seems to have better efficacy than vaginal Misoprostol, seems to be acceptable to patients and is an option to be considered to induce labor at term.

Recommendations

- Further studies are needed to delineate the proper dosing regimen to avoid the misuse of improper dose. A large trials adequately powered to detect significant differences in uterine hyperstimulation, operative deliveries and neonatal outcomes, is required.
- There was a growing need for misoprostol and this suggests a necessary recommendation for the pharmaceutical companies to produce special sublingual form.

References

1. ACOG Committee on Practice Bulletins -- Obstetrics (2009): ACOG Practice Bulletin No. 107: Induction of labor. Obstet Gynecol.; 114 (2 Pt 1): 386-397.
2. Ayati, S., Vahidroodsari, F., Farshidi, F., Shahabian, M., and Aghaee, M. A. (2014). Vaginal versus sublingual misoprostol for labor induction at term and post term: a randomized prospective study. Iranian journal of pharmaceutical research: IJPR, 13(1), 299.
3. Chirag M, Patel, P.A. Yadav, and R.C.V yas (2016). The Study of Coparison of Sublingual Versus Vaginal 25 Micro Gram of Misoprostol in the Induction of Labour at Term. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). PP 25-28.
4. Crane, J. M., Young, D. C., Butt, K. D., Bennett, K. A., and Hutchens, D. (2001). Excessive uterine activity accompanying induced labor. Obstetrics & Gynecology, 97(6), 926-931.
5. El Kattan, Eman A., Ghada A. Abdel Moety, and Abd El Rahman A. Abd El Razek. (2013): "Sublingual versus vaginal misoprostol for induction of labor in term primigravidas: a randomized study." Journal of Evidence-Based Women's Health Journal Society 3.3 111-114.
6. Fakhir B, Aboulfalah A, Asmouli H, and Soummani A (2013): Sublingual versus vaginal misopristol for labor induction at term: a prospective randomized trial. Science Postprint 1: e00003.
7. Guerra, G. V., Cecatti, J. G., Souza, J. P., Faundes, A., Morais, S. S., Gülmezoglu, A. M.,... and Carroli, G. (2009). Factors and outcomes associated with the induction of labour in Latin America. BJOG: An International Journal of Obstetrics & Gynaecology, 116(13), 1762-1772.
8. Hangaraga, U. S. (2017): Comparison of sublingual versus vaginal routes of misoprostol in induction of labor. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 6(7), 3062-3066.
9. Jahromi, B. N., Poorgholam, F., Yousefi, G., and Salarian, L. (2016): Sublingual versus vaginal misoprostol for the induction of labor at term: a randomized, triple-blind, placebo-controlled clinical trial. Iranian journal of medical sciences, 41(2), 79.
10. Moraes Filho, O. B. D., Albuquerque, R. M. D., Pacheco, Á. J. C., Ribeiro, R. H., Cecatti, J. G.,

and Welkovic, S. (2005). Sublingual versus vaginal misoprostol for labor induction of term pregnancies. Revista Brasileira de Ginecologia e Obstetrícia, 27(1), 24-31.

11. Nassar, A. H., Awwad, J., Khalil, A. M., Abu‐Musa, A., Mehio, G., Usta, and I. M. (2007). A randomised comparison of patient satisfaction with vaginal and sublingual misoprostol for induction of labour at term. BJOG: An International Journal of Obstetrics & Gynaecology, 114(10), 1215-1221.
12. Saihood, S. T. (2012): Role of Misoprostol in Induction of Labor: Sublingual versus Vaginal in Tikrit City. Tikret Journal of Pharmaceutical Sciences, 8(2), 165-171.
13. Souza AS, Amorim MM, and Feitosa FE (2008): Comparison of sublingual versus vaginal misoprostol for the induction of labour: a systematic review. BJOG. An International Journal of Obstetrics and Gynaecology; 115(11): 1340-1349.
14. Zahran, K. M., Shahin, A. Y., Abdellah, M. S., and Elsayh, K. I. (2009). Sublingual versus vaginal misoprostol for induction of labor at term: A randomized prospective placebo‐controlled study. Journal of Obstetrics and Gynaecology Research, 35(6), 1054-1060.

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