Original Article

Comparing the efficacy of sublingual and vaginal misoprostol for induction of labor at term live pregnancy

Omaima Zubair Khan, Muhammad Hamza Khan, Sara Batool, Rahat Akhtar

Department of Gynecology, Nishtar Hospital, Multan, Pakistan

Objective: To compare the efficacy of misoprostol oral and vaginal when administered for induction of labor at term live pregnancy.

Methodology: This randomized control trial was conducted in the department of obstetrics and gynecology, Nishtar hospital, Multan, Pakistan from February 22, 2017 to July 22, 2017. Chi square test was applied for effect modification or association of outcome variables with effect modifiers. Data were analyzed using SPSS version 23.

Results: A total of 272 pregnant women were included, divided into two equal groups, 136 in each i.e. sublingual group and Vaginal group. Time interval between starting misoprostol and delivery was 361.7±1.91 minutes in sublingual group and 396.08±1.41minutes in vaginal group (p=0.000). Strong association was found with time interval between starting misoprostol and delivery.

Conclusion: Sublingual misoprostol is more effective in induction of labor at term pregnancy with live fetus as compared to vaginal misoprostol in terms of time of interval between starting to delivery. It had minimum complications and easy to administered as compared to vaginal administration. (Rawal Med J 201;43:444-447).

Keywords: Misoprostol, term pregnancy, induction of labor.

INTRODUCTION

Termination of pregnancy through artificial induction method is necessary when maternal life is on risk due to pregnancy complications even full term live pregnancy.[1] There are many maternal and fetal indications for termination of full term pregnancy like preeclampsia, intrauterine fetal death, rupture of membrane, placenta previa, abruption, antiphospholipid syndrome and maternal diabetes.[2] Many techniques have been used for artificial induction of labor but there is still need to develop a consensus.[3]

Misoprostol is used for treatment of peptic ulcer; it is prostaglandin E1 methyl ester. It works by denaturing active misoprostol acid.[4] In uterus, misoprostol binds with EP2/EP3 prostanoid receptors and stimulates myometrium for contractions, which is helpful in termination process.[5] It was used for pregnancy termination in 1992 first time when fetus was live. It has no effects on vessels, lungs, asthma and can be stored at room temperature as compare to other prostaglandins.[6]

Misoprostol use in pregnancy can cause abortion.[7] As gestational age increases chances of uterine rupture after misoprostol administration also increases.[8] Sublingual misoprostol reaches at maximum peak concentrations in very shorter time period as compared to vaginal doses.[9,10] There was no significant difference in termination of pregnancy when misoprostol used sublingually or vaginaly.[6] Mean time of delivery in sublingual rout was 497.10±291.49 and 511.67± 308.46 through vaginal route. The aim of this study was to compare the efficacy of oral misoprostol to vaginal route for induction of labor at term live pregnancy.

METHODOLOGY

This randomized control trial was conducted in the department of obstetrics and gynecology, Nishtar hospital, Multan, Pakistan from February 22, 2017 to July 22, 2017. Non probability consecutive sampling technique was used and sample size of 272 patients was calculated from online statistical calculator by using following statistics; CI 95%, Power of study 80% and P1 fetal distress in sublingual misoprostol 13% and P2 fetal distress after vaginal misoprostol 7%. We divided 272 patients into two groups; (group S and group V). Women with third trimester of pregnancy with singleton pregnancy and gestational age 37 weeks, live fetus estimated weight more than 2.5 kg women were included in the study. Women with congenital fetal abnormality, allergy to prostaglandins,

previous uterine surgery, fetal growth restriction, abnormal heart rate and oligohydramnios were excluded from the study. Study was started after approval from ethical board of institution and informed consent was obtained from patients or their guardian.

Misoprostol 25 mgs tablets were wrapped in packages and labeled as "S" and "V". In "S" group misoprostol was given sublingually and in V group misoprostol given vaginaly. Same colored envelops were used for all packages and women were asked to choose one packages for randomization. Preparation for medication was same for all patients. Medication was applied after 4 hours until Bishop score was more than 8. Every time before giving next dose uterine contractions and Bishop score was noted. Maximum dose of 150 mcg was used (six doses). If after six doses contractions did not occurr than oxytocin was used after six hours. Maternal and fetal vitals were monitored.

Data were analyzed using SPSS version 23. Chi square test was applied for effect modification or association of outcome variables with effect modifiers. P<0.05 was considered as significant.

RESULTS

A total 272 women were included in the study. Mean age, gestational age, Bishop score and time interval between starting misoprostol and delivery of the women of sublingual group were 25.14±2.90 years, 39.44±1.13weeks, 5.02±1.27 and 361.7±1.91 minutes, respectively. Mean age, gestational age, Bishop score and time interval between starting misoprostol and delivery of the Vaginal group were 25.24±3.17 years, 39.39±1.18 weeks, 4.64±1.35 and 396.08±1.41 minutes, respectively (Table 1). No association was found between respiratory distress and groups ($\div^2$= 0.204 DF = 1, P value=0.652) (Table 2).

Apgar score after one minute less than 7 and after five minutes less than 7 noted as 18.4% (n=25) and 2.2% (n=3) respectively, in sublingual group (Table 3). No association was found between Apgar score and groups ($\div^2$= 1.497 DF = 2, P value=0.473) (Table 3). But a strong association was found with time interval between starting misoprostol and delivery with groups ($\div^2$= 2.72 DF = 1, P value=0.000) (Table 4).

Table 1. Baseline characteristics in randomized study of vertical laparotomy wound closure.

Variable	Sublingual (n=136)	Vaginal (n=136)
Age (years)	25.14±2.90 years	25.24±3.17 years
Gestational Age (weeks)	39.44±1.13weeks	39.39±1.18weeks
Bishop Score	5.02±1.27	4.64±1.35
Time interval between starting misoprostol and delivery	361.7±1.91 minutes	396.08±1.41 minutes
Respiratory distress	2.2%	1.5%
Apgar score after one minute less than 7	18.4%	22.1%
Apgar score after five minutes less than 7	2.2%	0.7%
More than 7	79.4%	77.2%

Table 2. Association of Respiratory Distress with groups, age, gestational age and Bishop Score.

Variable		Respiratory Distress		Total	P-value
		Yes	No		
Groups	Sublingual	3	133	136	0.652
	Vaginal	2	134	136	
Total		5	267	272	
Stratified Age	18-25 Years	2	150	152	0.740
	26-37 Years	3	117	120	
Total		5	267	272	
Gestational Age	37-39 Weeks	4	159	163	0.355
	40-42 Weeks	1	108	109	
Total		5	267	272	
Bishop Score	1-5 Score	5	184	189	0.135
	6-10 Score	0	83	83	
Total		5	267	272	

Table 3. Association of Apgar Score with groups, age, gestational age and Bishop Score.

Variable		Apgar Score			Total	P-value
		More than 7	After 1 Minute >7	After 5 Minute >7		
Groups	Sublingual	108	25	3	136	0.473
	Vaginal	105	30	1	136	
Total		213	55	4	272	
Stratified Age	18-25 Years	116	35	1	152	0.216
	26-37 Years	97	20	3	120	
Total		213	55	4	272	
Gestational Age	37-39 Weeks	132	29	2	163	0.423
	40-42 Weeks	81	26	2	109	
Total		213	55	4	272	
Bishop Score	1-5 Score	151	34	4	189	0.175
	6-10 Score	62	21	0	83	
Total		213	55	4	272	

Table 4. Association of time interval between starting misoprostol and delivery with groups, age, gestational age and Bishop Score

Variable		Time Interval		Total	P-value
		350-375 Minutes	376-400 Minutes		
Groups	Sublingual	136	0	136	0.000
	Vaginal	0	136	136	
Total		136	136	272	
Stratified age	18-25 Years	77	75	152	0.807
	26-37 Years	59	61	120	
Total		136	136	272	
Gestational age	37-39 Weeks	81	82	163	0.902
	40-42 Weeks	55	54	109	
Total		136	136	272	
Bishop Score	1-5 Score	87	102	189	0.048
	6-10 Score	49	34	83	
Total		136	136	272	

No association was found of respiratory distress with age (p=0.740), gestational age (p=0.355) and bishop score (p=0.135) (Table 2). No association was found of Apgar score with age (p=0.216), gestational age (p=0.423) and Bishop score (p=0.175) (Table 3). No association was found of time interval between starting misoprostol and delivery with age (p=0.807), gestational age (p=0.902) and association was found with Bishop score (p=0.048) (Table 4).

DISCUSSION

A study concluded that there was no makeable difference in both groups of misoprostol oral and vaginal when used at term for termination of pregnancy but sublingual misoprostol had advantage of easy administration.[11] Another study on this topic reported that misoprostol sublingual and vaginal showed similar efficacy for induction of labor when used for termination of pregnancies with full term live fetus, maternal and fetal outcomes were almost similar without any significant difference in both groups.[6]

Malik et al[12] conducted a similar study in 2010 and concluded that 50 mg sublingual misoprostol had equal safety and efficacy when compared with 100 mg oral misoprostol when used in primigravida. We also had primigravida in our study but our results goes in favor of oral misoprostol both safety and efficacy wise. Bartusevicius et al[13] compared sublingual with vaginal misoprostol and concluded that dose of 50 mg misoprostol sublingual 4 hourly was equally effective as 25 mg vaginal misoprostol when used in live fetal cases for induction of labor at term.

Souza et al[14] reported in his study that sublingual administration was equally effective vaginal administration when used in full term pregnancy induction. But adverse effects, perinatal outcome, safety and dose optimization of this route remain to be established, and it cannot be suggested for routine use in obstetric cases. Observation of our study about fetal distress and some other outcomes also showed similar results. Same results reported by Brusati et al.[15]

Tayyaba et al[16] reported that sublingual misoprostol with dose of 50 mg every four hours had no efficacy over vaginal misoprostol with dose of 25 mg. Time interval between starting misoprostol and delivery was 361.7±1.91 minutes and in vaginal group it was 396.08±1.41 minutes (p=0.000). Our results showed that oral misoprostol was more effective in induction of delivery time. Similar results also reported by Swamy et al.[17] Similar results were reported by Hissane et al,[18] Fakhir B[19] and Rasheed et al[20] in their studies that there was no significant difference in efficacy of misoprostol when administered orally of vaginaly. Our results are against to their results that there is a markable difference in both groups when observed about their time of induction and fetal and maternal complications and improvement.

CONCLUSION

Sublingual misoprostol was more effective in induction of labor at term pregnancy with live fetus as compared to vaginal misoprostol in terms of time of interval between starting to delivery. It had minimal complications and ease of administration as compared to vaginal route.

Author Contributions:
Conception and design: Omaima Zubair Khan
Collection and assembly of data: Sara Batool
Analysis and interpretation of the data: Muhammad Hamza Khan
Drafting of the article: Omaima Zubair Khan
Critical revision of the article for important intellectual content: Rahat Akhtar
Statistical expertise: Rahat Akhtar
Final approval and guarantor of the article: Rahat Akhtar
Corresponding author email: Rahat Akhtar: dr-rahat@hotmail.com
Conflict of Interest: None declared
Rec. Date: Sep 22, 2017 Revision Rec. Date: Apr 10, 2018 Accept Date: May 1, 2018

REFERENCES

1. Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, Cifkova R, Ferreira R, Foidart J-M, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J 2011;32:3147-97.
2. Reggia R, Bazzani C, Andreoli L, Motta M, Lojacono A, Zatti S, et al. The Efficacy and Safety of Cyclosporin A in Pregnant Patients with Systemic Autoimmune Diseases. Am J Reprod Immunol 2016;75:654-60.
3. Bernstein A. Common Law Fundamentals of the Right to Abortion. Buff L Rev 2015;63:1141.
4. Watkinson G, Akbar F. Misoprostol in peptic ulcer disease. Prostaglandins 1987;33:78-92.
5. Li J, Liang X, Wang Q, Breyer RM, McCullough L, Andreasson K. Misoprostol, an anti-ulcer agent and PGE 2 receptor agonist, protects against cerebral ischemia. Neurosci lett 2008;438:210-5.
6. Jahromi BN, Poorgholam F, Yousefi G, Salarian L. Sublingual versus vaginal misoprostol for the induction of labor at term: a randomized, triple-blind, placebo-controlled clinical trial. Iran J Med Sci 2016;41:79-85.
7. Chen W, Xue J, Peprah M, Wen S, Walker M, Gao Y, et al. A systematic review and network meta?analysis comparing the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in the induction of labour. BJOG 2016;123:346-54.
8. Nzewi C, Araklitis G, Narvekar N. The use of mifepristone and misoprostol in the management of late intrauterine fetal death. Obstetrician Gynaecologist 2014;16:233-8.
9. Milani F, Sharami SH, Arjmandi S. Comparison of sublingual and vaginal misoprostol for second-trimester pregnancy terminations. J Family Reprod Health 2014;8:41-4.
10. Jogi SR. Comparative study of sublingual and vaginal misoprostol in second trimester induced abortion. Int J Reprod Contracept Obstet Gynecol 2015;4:1453-9.
11. Ayati S, Vahidroodsari F, Farshidi F, Shahabian M, Aghaee MA. Vaginal versus sublingual misoprostol for labor induction at term and post term: a randomized prospective study. Iran J Pharm Res 2014;13:299-304.
12. Malik HZ, Khawaja NP, Zahid B, Rehman R. Sublingual versus oral misoprostol for induction of labour in prelabour rupture of membranes at term. J Coll Physicians Surg Pak 2010;20:242-5.
13. Bartusevicius A, Barcaite E, Krikstolaitis R, Gintautas V, Nadisauskiene R. Sublingual compared with vaginal misoprostol for labour induction at term: a randomised controlled trial. BJOG 2006;113:1431-7.
14. Souza A, Amorim M, Feitosa F. Comparison of sublingual versus vaginal misoprostol for the induction of labour: a systematic review. BJOG 2008;115:1340-9.
15. Brusati V, Brembilla G, Cirillo F, Mastricci L, Rossi S, Paganelli AM, et al. Efficacy of sublingual misoprostol for induction of labor at term and post term according to parity and membrane integrity: a prospective observational study. J Matern Fetal Neonatal Med 2017;30:508-513..
16. Tayyaba A, Mehreen N. Comparison between Sublingual and Vaginal Misoprostol for Labor Induction at Term. Pak J Med Health Sci 2013;7:1038-41.
17. Swamy MJ, U. S. Hangaraga. Comparison of sublingual versus vaginal routes of misoprostol in induction of labor. Int J Rep Contr Obs Gynecol 2017;6:3062-6.
18. Hissane EM, El Karroumi M, Mikou F, Ghazli M, Matar N. Misoprostol Sublingually Versus Vaginally for Labor Induction at Term: A Randomized Study. Res Obstet Gynecol 2012;1:27-9.
19. Fakhir B, Aboulfalah A, Asmouki H, Soummani A. Sublingual versus vaginal misoprostol for labor induction at term: a prospective randomized trial. Science Postprint. 2013;1(1):e00003. doi:10.14340/spp.2013.10C0003
20. Rasheed R, Alam AA, Younus S, Raza F. Oral versus vaginal misoprostol for labour induction. J Pak Med Assoc 2007;57:404-7.