ORIGINAL ARTICLE

THE EFFICACY AND SAFETY OF SUBLINGUAL VS ORAL MISOPROSTOL FOR INDUCTION OF LABOUR IN LOW-RISK PREGNANCIES AT TERM

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Abstract

Objective: Various methods of induction of labor are being used by doctors to achieve vaginal birth. Globally, 25% of births involve induction of labor. Misoprostol has gained attention recently in settings with limited resources due to its affordability, easy administration, and stability at room temperature. The study aims to evaluate the safety and effectiveness of sublingual misoprostol with oral misoprostol for the induction of labor in low-risk pregnancies at term.
Method: A randomized controlled, prospective study was carried out in the Obstetrics and Gynecology Unit III, Jinnah Hospital, Lahore for a period of 3 months.
Results: Eighty-four women were divided into two groups and given misoprostol for induction of labor via the sublingual or oral route, respectively. Both groups had comparable side effects and fetal outcomes. Delivery outcomes were similar with slightly lower cesarean section rates and reduced interval of induction-to-delivery in the sublingual group.
Conclusion: Sublingual route of misoprostol for the induction of labor acts faster and reduces time from induction to delivery as compared to the oral route, with similar safety.

Key words: Induction of labor (IOL), Misoprostol, Low-risk pregnancy.

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INTRODUCTION

The decision of inducing labor has a pivotal role in obstetrics for timely intervention in order to avoid unwanted consequences. Several studies showed the effectiveness of current protocols utilizing intravenous oxytocin and prostaglandin for labor induction.[1] Induction of labor refers to a medical procedure that involves pharmacological or non-pharmacological methods to initiate uterine contractions. The purpose of this intervention is to aid pregnant women in achieving a vaginal delivery.[2]

In developed nations, approximately 25% of all births involve delivery by labor induction. However, in the developing world, the rates of induction vary. An international survey on maternal and perinatal health conducted by the WHO in two countries found that labor induction accounted for 9.6% of total deliveries. Additionally, the study identified a significant rise in the frequency for the need of labor induction.[3]

Among cervical softening techniques, commonly used methods are either pharmacological or mechanical methods. Prostaglandins are the predominant type of drugs used when the cervix is unfavorable. These medications serve the purpose of cervical softening as well as initiate uterine contractility.[4]

Prostaglandin E1 renders several benefits, such as its efficacy at low doses, low cost, easy administration with less gastric irritation, and, in particular, it does not require cold chain storage. It has been used orally, sublingually, and vaginally since the 1980s for cervical softening and labor induction.[5] Pergialiotis V showed in his study that sublingual misoprostol, when compared to vaginal

misoprostol, had better results in reducing the interval between induction and delivery. (MD - 1.11 h, 95% CI- 2.06, - 0.17). Contrarily, intracervical dose showed less beneficial results when compared to the vaginal misoprostol in terms of interval between induction and delivery (MD 3.45 h, 95% CI 1.85, 5.06). The morbidity of mother and neonate remains unaffected by method or dosage of prostaglandin E1.[6]

A randomized, triple-blind, placebo-controlled clinical trial showed that in sublingual and vaginal groups, the mean interval between start of dose and delivery was 497.10±291.49 and 511.67±08.46 minutes, correspondingly.[7] A local study conducted by Khan OZ, found that sublingual method of misoprostol was more effective than vaginal method in terms of the interval from initiation of labor till delivery and had fewer complications and was more easily administered when compared to vaginal route.[8] A local study at Ganga Ram Hospital was conducted in the primigravida with pre-labor rupture of membranes at term and found that 50 µg sublingual misoprostol was equally effective as 100 µg oral misoprostol for labor induction.[9, 10, 11]

Swatch & Doke concluded in their study that both oral and sublingual route are effective and safer techniques for inducing labor with an unripe cervix at term, and a lower dose of 25ug is as effective as higher doses mentioned in the literature.[12]

Our study suggests that the oral route of misoprostol dosage outlined in the study is a safe and beneficial approach that decreases perinatal and maternal morbidity making it suitable for application in settings with limited resources. It is also a cheap and stable option at room temperature when compared to oxytocin and prostaglandin E2. The widespread use of oral misoprostol and its simplicity in administration will increase the rate of successful labor inductions in underdeveloped countries, which will subsequently improve the alarmingly high maternal and perinatal mortality statistics in such areas.[13]

J. Shetty concludes in a study published in 2023 in JSAFOG that both 25 µg oral solution of misoprostol and 25 µg of sublingual misoprostol routes are safe and well-established methods for inducing labor in the case of an unripe cervix, and the drinkable solution of misoprostol was more beneficial than the sublingual method in regards to the time of induction of labor to delivery and rate of vaginal delivery.[14]

The current study was aimed to compare the efficacy and safety of sublingual versus oral misoprostol for inducing labor at term.

METHODS

A Randomized controlled, prospective study was carried out in Obstetrics and Gynecology unit III, Jinnah Hospital, Lahore, for a period of 3 months.

The calculation of sample size was done by sample size calculator (select statistics), taking a 95% (CI) confidence interval and 80% power. n=84 women were admitted through the emergency labor ward, n=42 for each group, sublingual misoprostol (group A) vs. oral misoprostol group.

Inclusion criteria: All women admitted in the labor ward for a plan of induction of labor, aged 18-40 years, having low-risk singleton pregnancies at term with vertex presentation and a bishop score of ≤6 were included in the study.

Exclusion criteria: Para 5 or more, women having scarred uterus, high-risk pregnancy, having known hypersensitivity to misoprostol, and those who refused to give consent were excluded.

Patients were randomized by the lottery method into two groups. Each group was given 25µg misoprostol by sublingual or oral route, respectively. Every woman was evaluated for the need of another dose after every 4 hours. Induction was done in the early morning in the presence of specialists ensuring the availability of an emergency theater for prompt intervention if required. All anticipated side effects were addressed immediately and treated accordingly. Each woman was monitored till delivery, and various parameters were noted and compared in both study groups in terms of efficacy of the drug and maternal and fetal safety. All women were monitored till delivery, and various parameters were noted and compared in both study groups in terms of the efficacy of drug and feto-maternal safety.

After approval from the Ethical review board, the research team collected data from labor room using a consecutive random sampling technique. All cases fulfilling inclusion criteria were selected. Data of these variables was entered on an excel sheet designed by investigators. Data analysis was done using SSPS 28. Quantitative variables were analyzed using mean ± Standard deviation. Difference of proportions was assessed using Chi-Squared test and t-test was used for comparing difference of means.

Complications	Management
Fever	I/V paracetamol
Nausea, vomiting	Antiemetic
Uterine hyper stimulation	S/C tocolytics
PPH	Third stage of labor actively managed by AMTSL criteria & PPH protocol followed.
Fetal distress	C-section

Bishop Score was calculated by vaginal examination four hours after giving the dose of misoprostol in both groups. A total score of ≤6 was considered as poor and > 6 was

considered favorable.

	0	1	2	3
Dilatation(cm)	closed	1-2	3-4	5-6
Effacement (%)	0-30	40-50	60-70	>80
Station of head	-3	-2	-1,0	+1, +2
Cervical consistency	Firm	Medium	Soft	
Position of cervix	Posterior	Mid position	Anterior	

RESULTS

A total of n=84 subjects fulfilling the inclusion criteria were studied, 42 in each group A&B. Group A consisted of women induced via the sublingual route and group B included women induced through the oral route.

No significant difference was observed in women induced with sublingual & oral routes with regard to age, parity, gestational age, BMI & Bishop Score shown in Table 1.

No significant statistical difference (p=value 0.0505) was observed in vaginal delivery and caesarean delivery, but the cesarean delivery rate was lower with the sublingual route (21.4%) than with the oral route (31%).

The sublingual route showed a reduced interval between induction and delivery in comparison to oral route in terms of induction to active phase (p=0.046) & active phase till delivery (p=0.078), but more women delivered vaginally in both groups. n=57 delivered by spontaneous vaginal delivery, 5 by instrumental delivery, and 22 by LSCS out of 84 women.

No statistically significant difference was found regarding the need for further doses & the need for oxytocic agents in both groups (p=0.818, p=0.513) respectively.

It was observed that maternal and fetal health outcomes showed no substantial difference, p=0.879, and p=0.856. No uterine hyperstimulation and uterine rupture was found in both groups. Vomiting and diarrhea were more in the oral group in comparison to the sublingual group, however, this difference was not significant statistically (p=0.879). A total of 58 women including both groups, delivered without any side effects out of 84 subjects.

Fetal outcomes assessed by Apgar score, fetal distress, and requirement for nursery admission, were found to be similar in both groups with a p=value 0.856, which was statistically insignificant.

DISCUSSION

Misoprostol was initially used to treat gastric ulcers, but after its promising results for medical termination of early pregnancy and its use in obstetrical practices for PPH, the rate of induction of labor has increased. Since its safety for labor induction in pregnancies at term was concerned, many studies were done using different routes and doses to compare its safety profile.

Based on available literature, the oral and sublingual methods of misoprostol dosing were found preferable by women as they avoid repeated pelvic examinations for placement of the dose vaginally and decrease the risk of infection to mother and fetus.[15]

Although this outcome was not assessed in our study, a patient's acceptability was assessed, and satisfaction rates were found to be 82.5% and 85.7% in oral and sublingual routes, respectively, in a study done by Shetty and Danielian.[16]

Table: 1 Demographic and clinical characteristics

		Groups				P value
		Group A (Sublingual)		Group B (ORAL)		
		Freq	% age	Freq	% age	
Age	< 30 years	32	76.2	30	71.4	.620
	> 30 years	10	23.8	12	28.6	
Parity	< 3	22	52.4	21	50.0	.827
	> 3	20	47.6	21	50.0%	
Gestational Age	< 39 weeks	18	42.9	25	59.5	.127
	> 39 weeks	24	57.1	17	40.5	
Bishop Score	< 6	32	76.2	28	66.7	.334
	> 6	10	23.8	14	33.3	
No. of doses	Single dose	28	66.7	27	64.3	.818
	Two doses	14	33.3	15	35.7	
Induction to onset	< 6 hours	29	69.0	27	64.3	.643
	> 6 hours	13	31.0	15	35.7	
Induction to Active phase	< 12 hours	38	90.5	31	73.8	.046*
	> 12 hours	4	9.5	11	26.2	
Active phase to Delivery	< 12 hours	40	95.2	35	83.3	.078*
	> 12 hours	2	4.8	7	16.7	
Oxytocin Augmentation	Yes	23	54.8	20	47.6	.513
	No	19	45.2	22	52.4	
Mode of Delivery	SVD	31	73.8	26	61.9	.505
	Instrumental	2	4.8	3	7.1	
	LSCS	9	21.4	13	31.0	

Table: 2 Maternal & Fetal outcomes among subjects

		Misoprostol Groups				P value
		Group A (SUB)		Group B (ORAL)		
		Freq	% age	Freq	% age	
Maternal Outcome	Normal outcome	30	71.4	28	66.7	.879
	Fever	2	4.8	1	2.4	
	Tachycardia	3	7.1	3	7.1	
	Nausea	2	4.8	2	4.8	
	Vomiting	1	2.4	3	7.1	
	Diarrhea	2	4.8	4	9.5	
	Hyperstimulation	0	0.0	0	0.0	
	Uterine rupture	0	0.0	0	0.0	
	Precipitated labor	1	2.4	0	0.0	
	PPH	1	2.4	1	2.4	
Fetal Outcome	Normal outcome	34	81.0	33	78.6	.856
	Abnormal CTG	6	14.3	5	11.9	
	MAS	0	0.0	0	0.0	
	Poor APGAR	1	2.4	2	4.8	
	Still Birth	0	0.0%	0	0.0%	
	Admitted to NICU	1	2.4%	2	4.8%	

Our study was aimed to evaluate the effectiveness and safety profile of sublingual vs. oral misoprostol in terms of maternal and fetal effects.

The findings did not reveal a significant difference statistically in overall mode of delivery, but it was observed that the rate of cesarean section was slightly reduced in the sublingual group. Moreover, women in the sublingual misoprostol had a rapid induction-to-delivery interval in comparison to oral misoprostol.

This trend was also seen in another study regarding induction of labor, where women in the sublingual misoprostol category experienced rapid time to vaginal delivery when compared to those using the oral solution (16.7 hrs. versus 21.7 hrs.) with p= <0.001.[17]

A study of Kerr RS et al. showed the rate of C-section and hyperstimulation noted was very low with oral misoprostol, consistent with our study as no case of uterine hyperstimulation and rupture was noted.[18]

A study by Amini M found that sublingual misoprostol was absorbed more effectively compared to oral, with a 20-30% higher bioavailability. Additionally, the peak concentration of the drug in the blood was 50% higher with sublingual administration.[19]

A randomized controlled trial by Gattas showed that a smaller dose of misoprostol given sublingually for labor induction was equally effective as the recommended dose given vaginally. However, the sublingual administration resulted in fewer cases of tachysystole compared with the vaginal administration, making it a safe alternative option.[20]

A study done in post term pregnancies by Ayati S, Vahidroodsari F, reported that the sublingual route appeared to have greater patient satisfaction, though we did not measure this. However, our results are consistent with other published literature in other areas.[22,23]. Moreover, Buccal/sublingual misoprostol was the most cost-effective.[24]

A study showed no significant difference between the three misoprostol groups (oral, vaginal, and sublingual) as far as the time between induction and delivery is concerned, with times of 10.9±5.9 hours, 11.2±5.0 hours, and 11.4±6.6 hours, respectively (p=0.88). There was no significant difference between the groups in terms of the rates of vaginal delivery, assisted delivery, and cesarian section, although the sublingual group had a small number of babies with lower APGAR scores at one minute[25], while in our study no notable difference was seen in both groups.

A study conducted by Agrawal & Ramani compared sublingual route of misoprostol administration with vaginal route. Women who received vaginal misoprostol delivered with 2-3 doses (64%) in comparison to the sublingual misoprostol group (32%).[26] While, according to our research, the total required doses were almost similar in the sublingual misoprostol and oral misoprostol groups.

CONCLUSION

Sublingual route of misoprostol for labor induction (IOL) demonstrates a greater efficacy with relatively quicker onset of action with a reduced induction-to-delivery time than the oral route without significant differences in safety.

LIMITATIONS OF THE STUDY

The sample population of our study was small. Multicentered research with larger sample population is needed to better understand the safety and efficacy of misoprostol for the purpose of induction of labor.

ETHICAL APPROVAL

Ethical approval was granted by the Ethical Review Board of Allama Iqbal Medical College/ Jinna Hospital, Lahore vide reference No ERB147/3/27-07-2023/S1 ERB dated: 27/07/2023

CONFLICT OF INTEREST:

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

FSB: Concept design and manuscript writing
BB: Interpretation of data and manuscript writing
RD: Data collection and manuscript writing
ALL AUTHORS: Approval of the final version of the manuscript to be published

REFERENCES

1. Dadashaliha M, Fallah S, Mirzadeh M et al. Labor induction with randomized comparison of cervical, oral and intravaginal misoprostol. BMC Pregnancy Childbirth. 2021 Oct 27; 21(1):721. doi: 10.1186/s12884-021-04196-4.
2. De Vaan MD, Ten Eikelder ML, Jozwiak M, et al. Mechanical methods for induction of labour. Cochrane Database Syst Rev. 2019Oct18; 10(10): CD001233.doi: 10.1002/14651858.CD001233.
3. Betrán, A.P., Gulmezoglu, A.M., Robson, M. *et al.* WHO Global Survey on Maternal and Perinatal Health in Latin America: classifying caesarean sections. *Reprod Health* **6**, 18 (2009). doi: 10.1186/1742-4755-6-18.
4. Pierce S, Bakker R, Myers DA, Edwards RK. Clinical Insights for Cervical Ripening and Labor Induction Using Prostaglandins. AJP Rep. 2018 Oct; 8(4). doi: 10.1055/s-0038-1675351.

5. Allen R, O'Brien BM. Uses of misoprostol in obstetrics and gynecology. Rev Obstet Gynecol. 2009 summer; 2(3):159-68. doi: 10.3909/riog0055
6. Pergialiotis V, Panagiotopoulos M, Constantinou T, etal. Efficacy and safety of oral and sublingual versus vaginal misoprostol for induction of labour: a systematic review and meta-analysis. Arch Gynecol Obstet; 308:727–777. https://doi.org/10.1007/s00404-022-06867-9
7. 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 Mar; 41(2):79-85.
8. Khan OZ, Khan MH, Batool S, Akhtar R. Comparing the efficacy of sublingual misoprostol and vaginal misoprostol for induction of labor at term live pregnancy. RMJ. 2018; 43(3): 444-447. https://www.rmj.org.pk/?mno=277486
9. Zaman H, Khawaja NP, Zahid B and Rehman Sublingual versus Oral Misoprostol for Induction of Labour in Prelabour Rupture of Membranes at Term. JCPSP, 2010, Vol. 20 (4): 242-245. https://www.jcpsp.pk/archive/2010/Apr2010/06.pdf
10. Mahdi A, Wide-Swensson D, Herbst A. Sublingual misoprostol vs. oral misoprostol solution for induction of labor: A retrospective study Front Surg., 15 September 2022Sec. Obstetrics and Gynecological Surgery Volume 9 - 2022 | https://doi.org/10.3389/fsurg.2022.96832
11. Shetty J, Upadhya R, Rajendran R. Oral Misoprostol Solution More Effective than a Sublingual Route for Induction of Labor: A Prospective Comparative Trial at Tertiary Care Center. J South Asian Feder Obst Gynae 2023; 15(2):167–171. https://doi.org/10.5005/jp-journals-10006-2205
12. Siwatch S, Doke G, Kalra J, Bagga R. Sublingual vs oral misoprostol for labor induction. J post grad Med Edu Res 2014; 48 (1): 33-36. DOI: 10.5005/jp-journals-10028-1097
13. Morris M, John W, Verave O, Aipit J, Rero A, et al. Safety and effectiveness of oral misoprostol for induction of labour in a resource-limited setting: a dose escalation study. BMC Pregnancy and Childbirth (2017) 17:298. https://doi: 10.1186/s12884-017-1483-5
14. Shetty J, Upadhya R, Rajendran R. Oral Misoprostol Solution more Effective than a Sublingual route for Induction of Labor: A Prospective Comparative Trial at Tertiary Care Center. J South Asian Feder Obst Gynae 2023; 15(2):167–171. https://doi.org/10.5005/jp-journals-10006-2205
15. Gattás, Melania M et al. Reproductive Health (2020); 17:47. https://doi.org/10.1186/s12978-020-0901-8
16. Shetty, Danielian etal.Sublingual misoprostol for induction of labor at term. AMJ obst/Gynecol; 186(1):72-76. https://www.ajog.org/article/S0002-9378(02)38894-X/abstract#
17. Mahdi A,Swenssen W, Herbst A.Sublingual vs oral misoprostol solution for induction of labor: A retrospective study.2022 https://doi.org/10.3389/fsurg.2022.968372.
18. Kerr RS ,kumar N, Williams MJ,Cuthbert A, A Flaifel N, Hass DM, Weeks AD. Low dose oral misoprostol for induction of labor. Cochrane Database Syst.Rev. (2021)6: CD 114484.
19. Amini M,Reis M,Wide Swenssen . A Relative Bioavailability Study of Two Misoprostol Formulations Following a Single Oral or Sublingual Administration. (2020) Front. Pharmacol;50 (11):1-9. https://doi.org/10.3389/fphar.2020.00050
20. Gattas, de Amorim, Feitosa, *et al*. Misoprostol administered sublingually at a dose of 12.5ug versus vaginally at a dose of 25 ug for the induction of full term labor:a randomized controlled trial.*Reprod Health* 17,47(2020) https://doi.org/10.1186/s12978-020-0901-8.
21. Gattás D, da Silva Junior JR, Souza ASR, Feitosa FE, de Amorim MMR. Misoprostol administered sublingually at a dose of 12.5 μg versus vaginally at a dose of 25 μg for the induction of full-term labor: a randomized controlled trial protocol. Reprod Health. 2018; 15:65. - PMC - PubMed doi: 10.1186/s12978-018-0508-5
22. Ayati S, Vahidroodsari F, Farshidi F, Shahabian M, *et al.*Vaginal versus sublingual misoprostol for labor induction at term and post term:a randomized prospective study.Iran J Pharm Res. 2014 winter; 13(1):299-304. https://pmc.ncbi.nlm.nih.gov/articles/PMC3985259/
23. Tang OS, Mok KH, Ho PC. A randomized study comparing the use of sublingual to vaginal misoprostol for pre-operative cervical priming prior to surgical termination of pregnancy in the first trimester. Hum Reprod.. 2004; 19:1101–1104. https://doi.org/10.1111/j.1471-0528.2004.00222.x
24. Alfirevic Z, Keeney E, Dowswell T, Welton NJ, Medley N, Dias S, et al. Which method is best for the induction of labour? A systematic review, network meta-analysis and cost-effectiveness analysis. Health Technol Assess (Winch, Engl) 2016; 20:1–584. doi: 10.3310/hta20650.
25. Galidevara C, Chaturvedula L, Habeebullah S. Comparison of oral, vaginal and sublingual Misoprostol for induction of labour in premature rupture of membranes after 34 weeks of gestation: a randomized controlled trial. Int J Reprod Contracept Obstet Gynecol. 2018; 7(4):1340. https://doi.org/10.18203/23201770.ijrcog20180958
26. Agrawal A, Ramani B. Sublingual versus vaginal misoprostol for induction of labour at term. IOSR J Dent Med Sci. 2020; 19:16–19. DOI: 10.9790/0853-1906101619