www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Research Article

Open Access, Volume 4

Is concomitant use of misoprostol and extra amniotic saline infusion more effective or safer for cervical ripening: A RCT in a tertiary center

Shabani Azadeh[1]; Meshkat Maryam[2]; Ghalandarpoor-Attar Seyedeh Noushin[3]; Ghalandarpoor-Attar Seyedeh Mojgan[4]*

[1]Preventative Gynecology Research Center (PGRC), Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2]Shahid Beheshti University of Medical Sciences, School of Medicine, Tehran, Iran.

[3]Obstetrics and Gynecology Department, School of Medicine, Baqiyatallah Hospital, Baqiyatallah University of Medical Sciences, Tehran, Iran.

[4]Obstetrics and Gynecology Department, School of Medicine, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran.

***Corresponding Author:**

Seyedeh Mojgan Ghalandarpoor-Attar

Obstetrics & Gynecology Department, Baharloo Hospital, Behdari Square, Tehran, Iran.

Email: dr.ghalandarpoor@yahoo.com

Received: Aug 27, 2023

Accepted: Sep 29, 2023

Published: Oct 06, 2023

Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/2631

Abstract

Various methods have been proposed for cervical ripening. Due to conflicting results and significant heterogenisity among previous studies, we designed a randomized clinical trial to find out wether concomitant use of Misorostol and extra-amnitic saline infusion (EASI) would lead to better outcomes or not. Ninety term pregnant women were randomly assigned to three different groups of ripening methods: vaginal misoprostol, EASI, and concomitant use of both. Time interval to reach a bishop score of five (primary outcome), time interval to amniotic membranes rupture and delivery rate, delivery route, need to oxytocin infusion, fetal distress associated cesarean delivery, meconium staining, and 1st and 5th minute Apgar scores were study outcomes.

Although combined method could not reduce the time interval to a Bishop score of five (p-value=0.145) Oxytocin infusion was significantly less likely. Other outcomes were not different (p-values>0.05).

Hence, combined method could significantly reduce the Oxytocin infusion which is favorable in resource-limited countries.

Keywords: Vaginal delivery; Cervical ripening; Misoprostol; EASI (Extra Amniotic Saline Infusion); Labor induction.

Citation: Shabani A, Meshkat M, Ghalandarpoor-Attar SN, Ghalandarpoor-Attar SM. Is concomitant use of misoprostol and extra amniotic saline infusion more effective or safer for cervical ripening: A RCT in a tertiary center. J Clin Images Med Case Rep. 2023; 4(10): 2631.

Introduction

Cervical ripening agents such as mechanical methods [1-3], hyaluronidase [4], relaxin [5], and pharmacological agents [6,7] have been introduced with different safety-efficacy profile.

Numerous studies have compared Misoprostol and Foley catheter (mostly single-balloon ones) with conflicting results [8-11]. There are also scarce evidence comparing prostaglandins with EASI [12-16] and studies comparing combined methods like EASI plus Prostaglandins are lacking [17,18]. As well,, the studies population has been widely heterogenous.

Here, we designed a study to compare the effect of concomitant use of vaginal misoprostol and EASI with EASI and or Misoprostol alone. As, presence of any fetal or maternal comorbidities may affect a physician's decision to allow labour progress or time to perform an emergent cesarean delivery, we just included pregnancies without any significant or uncontrolled comorbiditie. To the best of our knowledge, it can be considered as a novelty in our study design.

Materials and methods

This randomized clinical trial was conducted on singletone term pregnant women at Taleghani Hospital labor ward (Tehran, Iran) during 2018-2020. Inclusion criteria were maternal age over 18, no contraindication for vaginal delivery, reassuring admission NST and Bishop scores less than 5 at arrival. The Ethics Committee of Shahid-Beheshti University of Medical Sciences approved the study and all participants signed an informed consent. Patients with ruptured membranes or intrauterine fetal death were excluded. Maternal co-morbidities such as preeclampsia or gestational hypertention, uncontrolled pregestional Diabetes Melitus, significant vaginal bleeding and uterine hypertonia and serious fetal complications were also other exclusion criterias.

Patients' demographic characteristics and obstetrical history were collected from their medical records. For randomization, each patient selected a number through 1 to 3 and they were categorized in to group 1 to 3 based on the selected number until each group reaches to 30 participants. The researchers and the person who did data analysis were blinded. The first group members recieived 25 micrograms Misoprostol vaginally upto 3 times or whenever at least 200-250 Monteo Video contractions were achived, which came sooner. In the second group a 24F fully-catheter was inserted through cervical canal and the balloon was inflated by 30 cc of infusable room-temperature Normal Saline and Extra-Amniotic Salin Infusion (EASI) at the rate of 30 cc/minute was initiated. Finally, the third group received both single dose of 25 microgram vaginal Misoprostol and Foley catheter insertion with EASI concomitantly. In all arms, when the Bishop score exceeded 4 or the Folley catheter was spontaneously expluded (or otherwisely after 12 hours of catheter insertion), if uterus was hypotonic, Oxytocin was infused at the rate of 4 mIU/minute and the dose was increased every 15 minutes by 4 mIU/minute till appropriate contractions were achived. Contractions were assessed hourly and every 30 minutes in latent and active phase, respectively. Continuous FHR monitoring was applied in case of Oxytocin infusion and also during the first two hour after Misoprostol administration.

The primary outcome was time interval to reach a Bishop Score of at least five. Time interval to membranes rupture and delivery, delivery mode, need for Oxytocin infusion, onset of intrapartum fetal distress, meconium staining, umbilical cord PH, and Apgar scores were considered as secondary outcomes.

Moreover patients'and physicans' satisfaction regarding the applied method was assessed by a 1-10 Linkert scale. SPSS software version 23(EBM,USA) was used for data analysis.

Results

90 patients were included for final analysis, 30 patients in each group. Demographic features and obstetrical history did not differe between the groups (Table 1).

Bishop score of three was the most common score on admission time among study population (55 cases (61.5%)). Scores of 4,2, and 1 were observed in 19(21.1%), 12(13.4%), and 4 women (4.4%), respectively. As well, Bishop score of three was the most prevalent score in each group. Dilatation of one centrimeter was the most prevalent dilation in each group (57.1%, 63.3%, and 36.7%, respectively) followed by Cervical dilation in excess of tip finger

The mean time interval to reach a Bishop score of five or more, to the amniotic membranes rupture and to delivery did not differ significantly between three groups (Kruskal-Wallis test, p-values>0.05) (Table 2).

In respect to other secondary outcomes, it should be said that in the third group, in 6(25%) participants Oxytocin was infused while, in the first and second group, in 14(60.9%) and 13(41.9%) pregnant women infusion was indicated (p-value=0.04). In fact, combined use of EASI and Misoprostol could reduce the chance of Oxytocin infusion by 36% (OR:0.64, CI: 0.1-4.15).

Regarding fetal distress rate, 11 cases were seen, 8 cases in the first and 3 in the third group, but Kruskal-Wallis test showed no association between the cervical ripening method and fetal distress occurence (P-value=0.12, Chi2=0.423).

The umbilical cord blood pH mean values(±std.) were 7.27(±0.04), 7.28(±0.05), and 7.26(±0.05) in group 1 to 3, respectively (P-value = 0.708, Chi2 =0.691).

The mean Apgar scores at the 1st minute were 8.86±0.62, 8.96±0.17, and 9±0.00 in group 1 to 3 in order (p-value=0.42, Chi2=0.97). Regarding to 5th minute Apgar Score one neonate in group 1 and 3 had scores less than 10 but no newborn had scores less than 10 in EASI group; However, the difference was not significant too.

Ten cases of meconium staining were seen during study. In other words, its occurrence was 7.8%, 9.7%, and 20.8% in group 1 to 3, in order but the difference was not significant (p-value=0.37, Chi2 =1.97).

Regarding to delivery mode, 18(78.3%), 22(71%), and 14(58.3%) cases delivered vaginally in group 1 to 3, respectively but the difference was not statistically significant (p-value=0.32, Chi2=2.23).

Finally, 56.7%, 36.78%, and 40% of Patients delivered vaginally (p-value=0.91, chi2=0.19).

Table 1: Demographic and obstetrical characteristic distribution.

		Misoprostol group (%)	EASI group (%)	EASI+Misoprostol group (%)	P-value
Mean Maternal age (yreas)		23.5	30.2	28.2	0.38
Mean Gestational age(weeks)		39.4	39.1	38.3	0.21
Mean Bishop Score at arrival		3.2	3.1	2.2	0.64
Parity	Primiparous	664	57.6	66.6	0.78
	Multiparous	33.6	43.3	33.4	
Cervical dilation on admission	Closed internal os	19.1	13.4	25	0.43
	Tip finger dilation	23.8	23.3	37.5	
	1 Finger dilation	57.1	63.3	37.5	
Indication for termination	Full term pregnancy (39-41.6 weeks)	46.3%	43%	46.5%	0.74
	Decreased fetal movement	20.3%	13.3%	26.3%	
	labor onset	20.2%	26.6%	16.6%	
	Other indications*	13.2%	16.6%	10.6%	

*Gestational thrombocytopenia, controlled pregestational or gestational Diabetes Melitus.

Table 2: Mean time interval between cervical preparation using Misoprostol, EASI, and Misoprostol-EASI from admission to onset of amniotic membranes rupture, delivery, and Bishop score of 7.

Time interval to amniotic membranes rupture			
	Mean(hours)	Standard deviation	P-value
Misoprostol	7.8	4.6	0.128 Kruskall-Wallis test
EASI	9.9	7.23	
Misoprostol-EASI	8.04	4.4	
Time interval to delivery			
	Mean	**Standard deviation**	**P-value**
Misoprostol	13.08	7.1	0.42 Kruskall-Wallis test
EASI	12.54	8.01	
Misoprostol-EASI	10.58	8.03	
Time interval to a Bishop score of >=5			
	Mean	**Standard deviation**	**P-value**
Misoprostol	3.21	0.5	0.145
EASI	3	0.8	
Misoprostol-EASI	2.87	0.4	Kruskall-Wallis test

The physicants's satisfaction did not differ between groups neither (p-value=0.45, chi2=1.58, respectively).

Discussion

Combined method resulted in lower chance of Oxytocin infusion while not affecting other outcomes. In a meta-analysis of seven high-quality studies, concomitant use of vaginal misoprostol and EASI could reduce the time-to-delivery and the uterine tachysystole rate compared to individual use but chorioamnionitis was more likely. They also emphasized that the cesarean rate and meconium staining wouldnot be affected [17]. We could not find any statistically significant difference regarding cesarean section rate or mecionium staining. Athough time-to-delivery did not differ by combined method, need of Oxytocin infusion was 36% less likely in combined method. The chorioamnionitis rate was not different in our study but no case of chrioamnionitis was seen and the interpretation may be challenging.

There are some metanalysis comparing prostaglandins with Foley catheter with or without EASI [8,11,19]. Data regarding combined use is scarce and there is also significant variation in Foley catheter type(single or doudle blloon) and size, amonut of fliud inflation which may confer interpretation of the results.

In a study by Dabiri Oskoei et.al [18] vaginal Misoprostol, Foley catheter insertion and the combined method were compared. Delivery route, the active phase duration, meconium staining, fetal distress occurrence, chorioamnionitis rate, and uterine tachysystole were not significantly different (P>0.05). However, latent phase duration was significantly shorter in the combined group (P=0.002, P=0.001). There are some main study differences. Firstly, they studied pregnant women at gestational age of 40 weeks or more while we included a wider gestational age range. Secondly, in Foley catheter group a 18F catheter was inserted and its balloon was inflated with 50 cc of Normal Saline in contrast, in this study a 24F catheter was inflated with 30 cc Solution and EASI was applied too. Thirdly, they used repeated dose of Misoprostol in combined group and the balloon was deflated after 18 hours. Finally, the maximum dose of Misoprostol, the doses interval and time between the last dose and Oxytocin infusion were different. Despite this, we also did not found any significant differences in terms of fetal distress, meconium staining, delivery route and chorioamnionitis rate. As a limitation, in the current study we did not consider latent and active phases separately and as an explanation,this contrast result may be due to the repeated use of misoprostol in combined group in Dabiri Oskoei's study which could facilaites labour onset.

Kehl et.al [20] also compared sequential use of Foley cathter and oral Misoprostol with the individual use of Misoprostol. The median time for induction of labour until delivery were longer in sequential method (32.4 hours versus 22.5 hours) (P=0.004); The vaginal delivery rate did not differ too. In fact, they inserted a balloon catheter on the first day and used Misoprostol in the subsequent day.

Finally, it should be emphasized that inclusion of low risk pregnancies is a novel approach and a strong point because these comorbidities may affect a physician' desire for iatrogenic interventions. In contrast a small sample size is a main limitation which could resulted in statistically non-significant associations. Hence, larger sample size studies are essential.

Conclusion

Concomitant use of Misoprostol and EASI could reduce the need for Oxytocin infusion while not affecting other perinatal outcomes. So, it seems this method could be an appropriate alternative for cervical ripening, especifically when medical staff resources or facilities are limited.

Plain language summary: There are different cervical ripening methods which could be used to increase vaginal delivery rate during labor induction, including mechanical or pharmacological agents. In each category variation exists regarding the dosage, maximum number of use, catheter size and type

and also safety and efficacy profile. According to this significant heterogenisity in literature, even in one single method, pulling the results together and making a conclusion seems impossible. Studies which have compared combined use of misoprostol and Foley catheter insertion with EASI are sparse. Here, in this randomized clinical trial we compared vaginal Misoprostol, Foley catheter insertion with EASI and combined method. No significant difference was seen regarding time to reach a Bishop Score of 5, time to delivery, delivery mode, meconium staning and cord blood gas status; However, need for Oxytcin infusion was less among combined group patients. Hence, the combined method may be an appropriate alternative for cervical rippening specially in resource-limited countries.

Declartions

Acknowledgement: The authors highly appreciate our patients for their kind cooperation. We also thank medical staff in delivery ward of Taleghani Hospital for their assistance.

Conflicts of interests: The authors declare no conflicts.

References

1. Kashanian M, Fekrat M, Naghghash S, Sheikh Ansari N. Evaluation of the effect of extra-amniotic normal saline infusion (EASI) alone or in combination with dexamethasone for the induction of labor. J Obstet Gynaecol Res. 2008; 34: 47-50.

2. Kashanian M, Akbarian AR, Baradaran H. Extra-amniotic saline infusion vs. cervical traction with Foley catheter for second-trimester pregnancy termination. Int J Gynaecol Obstet. 2006; 92: 159- 60.

3. Jozwiak M, Bloemenkamp KW, Kelly AJ, Mol BW, Irion O, et al. Mechanical methods for induction of labour. Cochrane Database Syst Rev. 2012; 3: CD001233.

4. Kavanagh J, Kelly AJ, Thomas J. Hyaluronidase for cervical ripening and induction of labour. Cochrane Database Syst Rev. 2006; 2: CD003097.

5. Kelly AJ, Kavanagh J, Thomas J. Relaxin for cervical ripening and induction of labour Cochrane Database Sys Rev. 2001; 2: CD003103.

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. Kashanian M, Hasankhani S, Sheikhansari N, Bahasadri S, Homam H. The effects of sequential use of oxytocin and sublingual nitroglycerin in the cases of retained placenta. J Matern Fetal Neonatal Med. 2015; 1-6.

8. Mieke L G Ten Eikelder, Katrien Oude Rengerink, Marta Jozwiak, Jan W de Leeuw, et al. Induction of labour at term with oral misoprostol versus a Foley catheter (PROBAAT-II): A multicentre randomised controlled non-inferiority trial. Lancet. 2016; 387: 1619-28.

9. Shuchita Mundle, Hillary Bracken, Vaishali Khedikar, Jayashree Mulik, et al.Foley catheterisation versus oral misoprostol for induction of labour in hypertensive women in India (INFORM): A multicentre, open-label, randomised controlled trial. Lancet. 2017.

10. Joshua P Vogel, Alfred O Osoti, Anthony J Kelly, Stefania Livio, Jane E Norman, et al. Pharmacological and mechanical interventions for labour induction in outpatient settings.Cochrane Database Syst Rev. 2017; 9: CD007701.

11. YM Du, LY Zhu, LN Cui, BH Jin, JL Ou. Double-balloon catheter versus prostaglandin E2 for cervical ripening and labour induction: A systematic review and meta-analysis of randomised controlled trials. BJOG. 2017; 124: 891-899..

12. Zohreh Tabasi , Elaheh Mesdaghinia , Masoumeh Abedzadeh-Kalahroudi, Mojtaba Sehat , Aida Panahandeh. Comparing the effects of vaginal misoprostol, laminaria, and extra amniotic saline infusion on cervical ripening and induction of labor. Obstet Gynecol Sci. 2020; 63: 261-269.

13. Maryam Kashanian, Shohreh Bahasadri, Ashraf Nejat Dehkordy, Narges Sheikhansari, Noushin Eshraghi. A comparison between induction of labor with 3 methods of titrated oral misoprostol, constant dose of oral misoprostol and Foley catheter with extra amniotic saline infusion (EASI), in women with unfavorable cervix. Med J Islam Repub Iran. 2019; 33: 115.

14. Maryam Kashanian, Shohreh Bahasadri, Ashraf Nejat Dehkordy, Narges Sheikhansari, Noushin Eshraghi. A comparison between induction of labor with 3 methods of titrated oral misoprostol, constant dose of oral misoprostol and Foley catheter with extra amniotic saline infusion (EASI), in women with unfavorable cervix. Med J Islam Repub Iran. 2019; 33: 115.

15. Zohreh Tabasi , Elaheh Mesdaghinia , Masoumeh Abedzadeh-Kalahroudi, Mojtaba Sehat , Aida Panahandeh. Comparing the effects of vaginal misoprostol, laminaria, and extra amniotic saline infusion on cervical ripening and induction of labor. Obstet Gynecol Sci. 2020; 63: 261-269.

16. Michelle Solone and Kate A. Shaw. Induction of labor with an unfavorable cervix. Curr Opin Obstet Gynecol. 2020; 32: 107-112.

17. Wenhang Chen, Jing Xue, Laura Gaudet, Mark Walker, Shi Wu Wen. Meta-analysis of Foley catheter plus misoprostol versus misoprostol alone for cervical ripening.Int J Gynaecol Obstet. 2015; 129: 193-8.

18. Dabiri Oskoei A, Bayat F, Moghimi H.Z, Kolifarhood G.Individual and combination of intravaginal misoprostol and transcervical foley catheter in cervical ripening in nulliparous women. Iranian Journal of Obstetrics, Gynecology And Infertility. 2018; 2: 16-23.

19. Chen W, Xue J, Peprah MK, 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. 2015; 123: 346-354.

20. Ibrahim Abd Elgafor El Sharkwy, Elsayed Hamdy Noureldin, Ekramy Abd Elmoneim Mohamed, Sherine Attia Shazly. Sequential Versus Concurrent Use of Vaginal Misoprostol Plus Foley Catheter for Induction of Labor: A Randomized Clinical Trial. J Obstet Gynaecol India. 2018; 68: 408-413.