Obstetrics & Gynecology: Open Access
Comoglio FM, et al. Gynecol Obstet Open Acc 8: 185.
www.doi.org/10.29011/2577-2236.100185
www.gavinpublishers.com

Case Study

Efficacy of Oral Misoprostol Compared with Vaginal Dinoprostone for Cervical Ripening and Labor Induction

F M Comoglio[1#*] F Osella[2#], A Pagano[2], E Pilloni[1], I Vanacore[2], M Verra[2], F Petey[2], C Filippini[3], C Desanctis[1], A Revelli[2]

[1]Department of Obstetric and Gynecology, Sant'Anna Hospital of Turin

[2]Department of Obstetric and Gynecology, University of Torino Sant'Anna Hospital

[3]Department of Surgical sciences, University of Turin S. Giovanni Battista Hospital

[#]Equally contributed to this work

[*]**Corresponding author:** F.M. Comoglio, Department of Obstetric and Gynecology, Sant'Anna Hospital of Turin.

Citation: Comoglio F M, Osella F, Pagano A, Pilloni E, Vanacore I, Verra M et al. (2024) Efficacy of Oral Misoprostol Compared With Vaginal Dinoprostone for Cervical Ripening and Labor Induction Gynecol Obstet Open Acc 8: 185. DOI: https://doi.org/10.29011/2577-2236.100185

Received Date: 19 February 2024; **Accepted Date:** 26 February 2024; **Published Date:** 22 March 2024

Abstract

Objective: The study focuses on the pharmacological induction of labor and aims at comparing oral misoprostol (Cytotec®) with vaginal dinoprostone (slow-release vaginal insert Propess® and vaginal gel Prepidil®).

Methods: A retrospective observational study was conducted. Through medical records review, we collected data on women at term with a singleton pregnancy who underwent labor induction at our tertiary care center, Sant'Anna Hospital of Turin, from January 2018 to January 2023. A total of 1230 were included: 446 received oral misoprostol and 784 received vaginal dinoprostone. The primary outcome was cesarean section rate. Maternal and neonatal secondary outcomes included: operative delivery rate, postpartum hemorrhage rate, induction-to-delivery interval, incidence of vaginal delivery within 12 and 24 hours, 1-minute and 5-minute Apgar Score.

Results: The cesarean section rate was significantly lower in the oral misoprostol group compared to the vaginal dinoprostone group (OR 0.619, 95% CI 0.434, 0.883). The induction-to-delivery interval was significantly shorter in the group of patients who underwent induction with Cytotec® (median 16 hours, IQR 17) than in the group of patients who were induced with Prepidil® and/or Propess® (median 17 hours, IQR 18.2) ($p < 0.001$). There were no statistically significant differences in the other maternal and neonatal secondary outcomes.

Within the subgroup of patients with pre-induction Bishop score > 3, the cesarean section rate was significantly lower in the group of women who underwent induction with Cytotec® than in the group of women induced with vaginal dinoprostone, with no statistically significant differences in the other maternal and neonatal outcomes (OR 0.466, 95% CI 0.232, 0.936).

Within the subgroup of patients with pre-induction Bishop score ≤ 3, we found no statistically significant differences in cesarean section rate; however, the induction-to-delivery interval was significantly shorter (Cytotec®: median 19 hours, IQR 18; Prepidil® and/or Propess®: median 23.7 hours, IQR 24.9; $p < 0.001$) and the incidence of vaginal delivery within 24 hours was significantly higher (OR 1.461, 95% CI 1.050, 2.033) in the misoprostol group.

Conclusion: Labor induction with oral misoprostol appears to be associated with a lower cesarean section rate and a shorter induction-to-delivery interval when compared to labor induction with vaginal dinoprostone. The decrease in cesarean section rate is even more noticeable in patients with favorable Bishop score. In patients with an unfavorable Bishop score, the induction-to-delivery interval appears to be shorter and the incidence of vaginal delivery within 24 hours is higher with the use of oral misoprostol.

Keywords: labor induction, vaginal delivery, oral misoprostol, vaginal dinoprostone

Introduction

Induction of labor is defined as the process of artificial stimulation of the uterus to start labor before its spontaneous onset, with the aim of vaginal delivery. Established indications include post-term pregnancy, premature rupture of membranes (PROM), gestational hypertension, cholestasis of pregnancy, gestational diabetes, fetal growth restriction, polyhydramnios or oligohydramnios and several other maternal comorbidities [1-4], as congenital and acquired cardiopathies [5].

Induction of labor has become an increasingly employed obstetric intervention, with current rates reaching 25% of births in certain countries [1]. In Italy, the rate of induction varies by location and exceeds 20% in many centers [6].

An appropriate choice of method of induction plays a major role in decreasing maternal and fetal complications, without increasing the risks [7-10]. Safety and efficacy represent essential criteria when assessing the advantages and disadvantages of any method of induction. Additionally, feasibility, cost, and personal preference should also be considered. Prostaglandins, cyclopentane derivatives of arachidonic acid, have been widely used in Obstetrics since the 1970's, when their effect as cervical ripening agents was first demonstrated [11].

Dinoprostone, also known as prostaglandin E2, is available in different preparations, with the most frequently used being the 10 mg controlled-release gel (Propess®) and the intravaginal 1 mg and 2 mg gel (Prepidil®). Its safety and efficacy have been widely researched [12-13]. However, it presents some disadvantages, notably its high cost, lack of manageability, and requirement of refrigerated storage.

Misoprostol is a prostaglandin E1 analogue that was originally approved for treating gastric ulcers caused by non-steroidal anti-inflammatory drugs. It was subsequently found effective in labor induction [14-24]. In an article published in 1996, the use of oral misoprostol in cases of PROM was first reported [23]. Later, in 2001, Hofmeyr et al. described a new method of induction, based on the use of titrated low-dose oral misoprostol, paving the way for subsequent studies and clinical trials [24]. Misoprostol can be administered by oral, vaginal, sublingual, or buccal routes. Due to its stability at room temperature, low cost and possibility of oral administration, many studies have been conducted in order to determine its efficacy and safety. Although the efficacy and safety of oral misoprostol was confirmed in several publications [17-19], nowadays it is worldwide used as a method of induction of labor in abortion and stillbirth, alone or in combination with mifepristone [25], while dinoprostone - notably as vaginal gel - is often still preferred for induction of labor in viable pregnancies in everyday clinical practice.

Moreover, several authors agree upon the need of further research regarding its use as a labor inducing agent.

The choice among the numerous methods of induction is determined by a series of variables, among which the Bishop score plays a key role [3]. The score reflects the normal changes the cervix undergoes during the process of childbirth and is based on a digital cervical exam, with a zero point minimum and a 13-point maximum. It evaluates cervical dilatation, position, effacement, consistency, and fetal station. Nevertheless, national and international guidelines maintain an overlap of indications based on Bishop score for labor induction with prostaglandins: both dinoprostone and misoprostol can be employed with a Bishop Score of less than seven.

The aim of our study is to compare the safety and efficacy of oral misoprostol to vaginal dinoprostone for term labor induction.

Methods

The study was conducted retrospectively by collecting data on women who underwent labor induction with oral misoprostol (Cytotec®) or vaginal dinoprostone (Propess® or Prepidil®) for maternal and/or fetal indications at Sant'Anna Hospital in Turin, from January 2018 to January 2023.

Among the 1230 women included in the final analysis, 446 were induced with oral misoprostol (Cytotec®) 50 µg every five hours up to four administrations, and 784 with vaginal prostaglandins (Propess® and/or Prepidil®, depending on Bishop Score findings, according to the protocol employed by Sant'Anna Hospital).

The inclusion criteria used for patient selection were: (i) singleton pregnancy, (ii) gestational age of 37 weeks minimum, (iii)

labor induction with prostaglandins (dinoprostone or misoprostol).

Women who have been induced, before or after prostaglandins, with other methods of labor induction, such as amniotomy, membrane sweeping, and/or oxytocin, were also included. The exclusion criteria used for patient selection were: (i) twin pregnancy, (ii) gestational age of less than 37 weeks, (iii) clinical records lacking essential information for database completion.

The primary outcome was the cesarean section rate of oral misoprostol compared to the cesarean section rate of vaginal dinoprostone.

Maternal and neonatal secondary outcomes included operative delivery rates, duration of labor, incidence of vaginal delivery within 12 and 24 hours, postpartum hemorrhage rates, Apgar score of less than seven at one and five minutes.

Data were collected by consulting electronic medical records. We subsequently designed a database.

The included data were: (i) baseline characteristics of the woman (anagraphic data, ethnicity, Body Mass Index, parity), (ii) data related to labor induction (indication, Bishop score prior to induction, method of induction, number of doses of prostaglandins, description of labor induction, date and time of the beginning of the induction, date and time of the onset of labor, time interval between the start of induction and the start of labor, eventual onset of tachysystole, acceleration with oxytocin), (iii) data related to childbirth (gestational age at delivery, date and time of delivery, time interval between beginning of induction and delivery, type of delivery, postpartum hemorrhage), (iv) data related to the newborn (one minute- and five minute-Apgar score, birth weight, umbilical cord pH).

All variables under study were described using the most appropriate statistical syntheses. In particular, continuous variables were presented as mean and standard deviation (SD) or as the median and interquartile range (IQR), depending on the type of distribution. Instead, each categorical variable was represented by frequency (number) and relative proportion.

To compare means, the T-test for independent samples or the non-parametric Wilcoxon-Mann-Whitney test was used for variables with a non-normal distribution. To compare categorical variables, the Chi-square test or Fisher's exact test was used appropriately.

The primary and secondary outcomes were evaluated in multivariate analysis by developing logistic regression models and presenting the results through the Odds Ratio (OR) estimates with the respective confidence intervals at a 95% level. The competing selected variables as risk factors in regression models were selected based on an association measure in univariate analysis with an alpha threshold of at least 0.05. A careful literature analysis allowed us to select the variables known as risk factors associated with outcomes among those available in our database.

In particular, the variables selected in univariate analysis with an alpha threshold of at least 0.05 were: (I) for the primary outcome "Cesarean section": group (induction with misoprostol or induction with dinoprostone), age, Bishop score, primiparity, gestational age, prolonged pregnancy, suspected fetal macrosomia, cholestasis; (II) for the secondary outcome "Operative delivery": group (induction with misoprostol or induction with dinoprostone), primiparity, Body Mass Index (BMI), gestational age, prolonged pregnancy, hypertensive disorders, cholestasis; (III) for the secondary outcome "Postpartum hemorrhage": group, primiparity, gestational age, prolonged pregnancy, diabetes, suspected fetal macrosomia, other maternal pathology, other fetal pathology; (IV) for the secondary outcome "Vaginal delivery within 12 hours": group, age, Bishop score, primiparity, BMI, PROM, hypertensive disorders, suspected fetal macrosomia; (V) for the secondary outcome "Vaginal delivery within 24 hours": group, Bishop score, primiparity, BMI, PROM, hypertensive disorders, diabetes; (VI) for the secondary outcome "Apgar score at one minute of less than seven": group, BMI, PROM, suspected fetal macrosomia, other maternal pathology; (VII) for the secondary outcome "Apgar score at five minutes of less than 7": group, BMI, and other maternal pathology.

In order to evaluate possible different results, a subsequent sensitivity analysis was presented based on the stratification of the Bishop score: patients with Bishop score less than or equal to three and patients with Bishop Score greater than three, similarly to what has been done in numerous studies found in scientific literature. Bishop score is known to influence various maternal and fetal outcomes related to labor induction.

The analyses were conducted with a significance Alpha level defined with a threshold of 0.05.

The analyses were conducted using IBM SPSS Statistics software, Version 28.0.1.0 for Macintosh.

Results

Through medical records review, we collected data on women at term with a singleton pregnancy who underwent labor induction at Sant'Anna Hospital in Turin, from January 2018 to January 2023. A total of 1230 women were included: 446 received oral misoprostol and 784 received vaginal dinoprostone. The women were admitted to both University and non-University wards of the hospital.

Baseline characteristics were comparable in the two study groups, except for the initial Bishop score and, among the indications for labor induction, those described as "other maternal

comorbidities": the results were statistically adjusted for these differences (Table 1).

The primary outcome was the cesarean section rate of oral misoprostol compared to the cesarean section rate of vaginal dinoprostone. Overall, 197 cesarean sections were performed (15.5%): 56 were performed in the oral misoprostol group (12.6%) and 135 were performed in the vaginal dinoprostone group (17.2%) (*p value*=0.030). In the binary logistic regression model, oral misoprostol was associated with a significantly lower risk of cesarean section than vaginal dinoprostone (OR 0.619, 95% CI 0.434, 0.883). The median time interval from induction to delivery for women who were induced with oral misoprostol was significantly shorter than for women who received vaginal dinoprostone (16 hours versus 17 hours, *p value* < 0.001).

There was no significant difference in operative vaginal delivery rates between women who received vaginal dinoprostone and those who received oral misoprostol (OR 0.790, 95% CI 0.514, 1.215). No difference was found in regard to postpartum hemorrhage rates (OR 1.250, 95% CI 0.952, 1.640) and incidence of vaginal delivery within 12 hours (OR 1.065, 95% CI 0.789, 1.438) and 24 hours (OR 1.260, 95% CI 0.960, 1.653). Neonatal outcomes were similar between the two groups: the risk of low Apgar score (less than seven) at one (OR 0.729, 95% CI 0.367, 1.449) and five minutes (OR 0.632, 95% CI 0.127, 3.147) was not significantly different.

Further analysis of the causes of the cesarean section or operative vaginal delivery, including non-reassuring fetal heart rate, failed induction, maternal exhaustion or refusal to continue the process of induction of labor, revealed no statistically significant difference between the two groups of patients.Based on the cervix Bishop score, patients were classified into two groups: those with favorable Bishop score (greater than three) and those with unfavorable Bishop score (less than or equal to three).

In the subgroup of patients with favorable Bishop score, the use of oral misoprostol was associated with a significantly lower risk of cesarean section (OR 0.474, 95% CI 0.237, 0.950). No difference was found in terms of maternal secondary outcomes, namely the risk of operative vaginal delivery (OR 0.725, 95% CI 0.332, 1.584), postpartum hemorrhage (OR 1.179, 95% CI 0.762; 1.824), the likelihood of vaginal delivery within 12 hours (OR 0.862, 95% CI 0.570; 1.304) and 24 hours (OR 0.930, 95% CI 0.590; 1.464), and in terms of induction-to-delivery time interval (12.2 hours with oral misoprostol versus 12.8 hours with vaginal dinoprostone, *p value* = 0.124). Neonatal outcomes were comparable between the two groups, with similar risk of low Apgar score at one (OR1.524, 95% CI 0.558, 4.161) and five minutes (OR 0.979; 95% CI 0.103; 9.307).

In the subgroup of patients with unfavorable Bishop score, there was no significant difference regarding the risk of cesarean section between the two groups (OR 0.712, 95% CI 0.466, 1.086). No significant difference was found in terms of likelihood of vaginal delivery within 12 hours (OR 1.357, 95% CI 0.875, 2.103). However, the patients who were induced with oral misoprostol were significantly more likely to deliver vaginally within 24 hours (OR 1.461, 95% CI 1.050, 2.033); the induction-to-delivery time interval was also significantly shorter in the oral misoprostol group (19 hours with oral misoprostol versus 23.7 hours with vaginal dinoprostone, *p value*< 0.001). No difference was found in terms of maternal secondary outcomes, namely the risk of operative vaginal delivery (OR 0.777, 95% CI 0.458, 1.320) and postpartum hemorrhage (OR 1.368, 95% CI 0.952; 1.965). Neonatal outcomes were comparable between the two groups, with similar risk of low Apgar score at one (OR 0.435, 95% CI 0.168, 1.127) and five minutes (OR 0.377, 95% CI 0.039; 3.651).

Baseline characteristics			
Variable	**Oral misoprostol** (n=446)	**Vaginal dinoprostone** (n=784)	**p value**
Patient Age, mean (sd)	32.51 (5.47)	32.39 (5.37)	0.808
Primiparity, n (%)	293 (65.7%)	538 (68.6%)	0.292
BMI, mean (sd)	24.35 (5.62)	24.31 (5.34)	0.914
BMI ≥ 30, n (%)	73 (16.4%)	110 (14.0%)	0.272
Bishop Score > 3, n (%)	149 (33.4%)	399 (50.9%)	< 0.001
Gestational Age, mean (sd)	275.24 (9.07)	275.58 (9.41)	0.527
Indication			
Post-term Pregnancy, n (%)	43 (9.6%)	84 (10.7%)	0.552
PROM, n (%)	113 (25.3%)	142 (18.1%)	0.003
GDM, n (%)	102 (22.9%)	132 (16.8%)	0.010
Fetal macrosomia, n (%)	50 (11.2%)	78 (9.9%)	0.486
Cholestasis, n (%)	20 (4.5%)	52 (6.6%)	0.123
PIH, n (%)	59 (13.2%)	89 (11.4%)	0.331
Other maternal comorbidities, n (%)	40 (9.0%)	146 (18.6%)	< 0.001
Fetal issues, n (%)	23 (5.2%)	31 (4.0%)	0.318
Amniotic fluid disorders, n (%)	44 (9.9%)	80 (10.2%)	0.850

Table 1. Baseline characteristics of the population

Discussion

In 2009, the ACOG Practice Bulletin on induction of labor recommended misoprostol as a method for labor induction, suggesting the administration of 25 μg of misoprostol every three to six hours (orally or intravaginally) [3]. In 2011, WHO recommended the use of 25 μg of misoprostol vaginally (every six hours) or orally (every two hours) for induction of labor at term [1]. In 2012, the International Federation of Gynaecology and Obstetrics (FIGO) recommended the use of the same dosage of misoprostol every two hours [26].

Considering the numerous recommendations regarding the use of misoprostol as a labor induction agent and of the growing scientific evidence of its advantages, we decided to compare the safety and efficacy of oral misoprostol to those of vaginal dinoprostone.

In our study, oral misoprostol was associated with a statistically significant decrease in cesarean section rate and with a shorter interval from induction to delivery when compared to dinoprostone. There were no statistically significant differences in terms of vaginal delivery rates within 12 and 24 hours, operative delivery rates and postpartum hemorrhage rates. No difference was found in terms of neonatal outcomes (Apgar score less than seven at one and five minutes) as well.

Further stratification based on the Bishop score showed that the decrease in cesarean section rates was even more significant in the subgroup of patients with favorable pre-induction Bishop score (greater than three), with equal maternal and neonatal secondary outcomes.

In the subgroup of patients with unfavorable pre-induction Bishop score (less than or equal to three), the use of oral misoprostol – despite not being associated with a reduction of cesarean section rates – was linked to a statistically significant decrease in induction-to-delivery interval and with a significant increase in vaginal delivery rates within 24 hours. The results of this study are consistent with the findings of prior meta-analyses and randomized controlled trials, which have linked the use of oral misoprostol with lower cesarean section rates than vaginal dinoprostone [27].

This research is based on a numerous sample size, encompassing data from more than 1200 women, who underwent labor induction in the same hospital following a standardized protocol. The numerous sample size represents an undeniable strength of this study, despite its retrospective single center design.

This study suggests that the use of misoprostol as a labor inducing agent is more effective than that of vaginal dinoprostone, especially in patients with a favorable Bishop score.

Additional advantages related to the use of oral misoprostol include ease of administration, low cost, and higher acceptability among women [3,28-33]. In fact oral intake of the drug avoids unnecessary unpleasant obstetrical examinations.

The importance of reducing cesarean section rates is universally recognized: the World Health Organization reports evidence that increasing cesarean section rates may be associated with increased maternal and perinatal morbidity [34]. Moreover, cesarean birth is associated with both short and long-term risks that can affect maternal and neonatal health, as well as future pregnancies. Furthermore, high rates of cesarean section are associated with substantial healthcare costs. The employment of oral misoprostol instead of vaginal dinoprostone would impact positively on these costs, not only because of its lower price, but also because of the reduction of cesarean section rates associated with its use.

In addition, a shortened induction to delivery interval will become increasingly important as the employment of labor induction increases in clinical practice. This result also involves a reduction in costs in terms of a possible reduction in hospitalization days.

In order to confirm the results of this study, it would be useful to perform a multicentre, large-scale, prospective, randomized controlled trial comparing oral misoprostol to vaginal dinoprostone.

Conclusions

The results of our study confirm the advantages of the employment of oral misoprostol in labor induction, already highlighted by various scientific publications. The use of oral misoprostol is associated with a lower cesarean section rate and a shorter induction-to-delivery time interval than vaginal dinoprostone, with no difference in terms of other maternal and neonatal outcomes. The reduction of cesarean section rates is even more remarkable in patients with favorable pre-induction Bishop score. In patients with unfavorable pre-induction Bishop score, although no difference was found in terms of cesarean section rates, the incidence of vaginal delivery within 24 hours appeared to be significantly higher and the induction-to-delivery time interval was significantly shorter with the use of oral misoprostol.

The cost of oral misoprostol is much lower than that of vaginal dinoprostone. Furthermore, misoprostol is easier to store, and the possibility of oral administration entails a higher acceptability among women.

In conclusion, after analyzing the management and outcomes of the patients included in our study and reviewing the available scientific evidence, we suggest the routine use of oral misoprostol as a labor inducing agent.

References

1. WHO Recommendations for Induction of Labour. (2011) World Health Organization.
2. NICE Inducing labour (2021).
3. ACOG Practice Bulletin No. 107: Induction of labor. Obstet Gynecol (2009)114:386-397.
4. Fondazione Confalonieri Ragonese. Induzione al travaglio di parto. (2022).
5. Regitz-Zagrosek V, Roos-Hesselink J W, Bauersachs J, Blomström-Lundqvist C, Cífková R, et al. (2018) ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 7: 3165-3241.
6. ISTAT La salute riproduttiva della donna (2017).
7. Osmundson S, Ou-Yang R J, Grobman W A (2011) Elective induction compared with expectant management in nulliparous women with an unfavorable cervix. Obstetrics and gynecology 117: 583–587.
8. Gibson K S, Waters T P, Bailit J L (2014) Maternal and neonatal outcomes in electively induced low-risk term pregnancies. American journal of obstetrics and gynecology 211: 249–249.
9. Darney B G, Snowden J M, Cheng Y W, Jacob L, Nicholson J M, et al. (2013) Elective induction of labor at term compared with expectant management: maternal and neonatal outcomes. Obstetrics and gynecology, 122: 761–769.
10. Caughey A B, Sundaram V, Kaimal A J, Gienger A, Cheng Y W, et al. (2009) Systematic review: elective induction of labor versus expectant management of pregnancy. Annals of internal medicine, 151: 252–W63.

11. Embrey M P (1970). Induction of labor with prostaglandins E1 and E2. British Medical Journal, 2: 256–258.
12. Kelly A J, Kavanagh J, Thomas J (2003) Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. The Cochrane database of systematic reviews 19: CD003101.
13. Thomas J, Fairclough A, Kavanagh J, Kelly A J (2014) Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. The Cochrane database of systematic reviews 28014: CD003101.
14. Mariani Neto C, Leão E J, Barreto E M, Kenj G, De Aquino M M, et al. (1987) Uso do misoprostol para indução do parto com feto morto [Use of misoprostol for labor induction in stillbirth]. Revista paulista de medicina, 105: 325–328.
15. Margulies M, Campos Pérez G, Voto L S (1992) Misoprostol to induce labour. Lancet (London, England) 4: 339-64.
16. Sanchez-Ramos L, Kaunitz A M, Wears R L, Delke I, Gaudier F L (1997) Misoprostol for cervical ripening and labor induction: a meta-analysis. Obstetrics and gynecology, 89: 633–642.
17. Hofmeyr G J, Gülmezoglu A M, Pileggi C (2010) Vaginal misoprostol for cervical ripening and induction of labour. The Cochrane database of systematic reviews, 2010: CD000941.
18. Alfirevic Z, Aflaifel N, Weeks A (2014) Oral misoprostol for induction of labour. The Cochrane database of systematic reviews, 2014: CD001338.
19. Kerr R S, Kumar N, Williams M J, Cuthbert A, Aflaifel N, et al. (2021) Low-dose oral misoprostol for induction of labour. The Cochrane database of systematic reviews, 6: CD014484.
20. Crane J M, Butler B, Young D C, Hannah M E (2006). Misoprostol compared with prostaglandin E2 for labour induction in women at term with intact membranes and unfavourable cervix: a systematic review. BJOG : an international journal of obstetrics and gynaecology, 113: 1366–1376.
21. Rouzi A A, Alsibiani S, Mansouri N, Alsinani N, Darhouse K (2014) Randomized clinical trial between hourly titrated oral misoprostol and vaginal dinoprostone for induction of labor.American journal of obstetrics and gynecology, 210: 56.e1–56.e566.
22. Wang X, Zhang C, Li X, Qi H, Liu Q, et al. (2021). Safety and efficacy of titrated oral misoprostol solution versus vaginal dinoprostone for induction of labor: A single-center randomized control trial. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 154: 436–443.
23. Ngai S W, To W K, Lao T, Ho PC (1996) Cervical priming with oral misoprostol in pre-labor rupture of membranes at term. Obstet Gynecol 87: 923-6.
24. Hofmeyr G J, Alfirevic Z, Matonhodze B, Brocklehurst P, Campbell E, et al. (2001) Titrated oral misoprostol solution for induction of labour: a multi-centre, randomised trial. BJOG : an international journal of obstetrics and gynaecology, 108: 952–959.
25. WHO Abortion care guideline, 2022
26. International Federation of Gynecology and Obstetrics. Treatment of Post-Partum Haemorrhage with Misoprostol: FIGO Guideline in brief. Published 2012.
27. Kundodyiwa T W, Alfirevic Z, Weeks A D (2009) Low-dose oral misoprostol for induction of labor: a systematic review.Obstetrics and gynecology 113: 374–383.
28. Alfirevic Z, Keeney E, Dowswell T, Welton N J, Medley N, et al. (2016) Which method is best for the induction of labour? A systematic review, network meta-analysis and cost-effectiveness analysis. Health technology assessment (Winchester, England) 20: 1–584.
29. Alfirevic Z, Keeney E, Dowswell T, Welton N J, Medley N, et al. (2016) Methods to induce labour: a systematic review, network meta-analysis and cost-effectiveness analysis. BJOG : an international.
30. Barrilleaux P S, Bofill J A, Terrone D A, Magann E F, May W L, et al. (2002) Cervical ripening and induction of labor with misoprostol, dinoprostone gel, and a Foley catheter: a randomized trial of 3 techniques. American journal of obstetrics and gynecology 186: 1124–1129.
31. le Roux P A, Olarogun J O, Penny J, Anthony J (2002) Oral. and vaginal misoprostol compared with dinoprostone for induction of labor: a randomized controlled trial. Obstetrics and gynecology 99: 201–205.
32. Dodd J M, Crowther C A, Robinson J S (2006) Oral misoprostol for induction of labour at term: randomised controlled trial. BMJ (Clinical research ed.) 332: 509–513.
33. Wang X, Yang A, Ma Q, Li X, Qin L, et al. (2016) Comparative study of titrated oral misoprostol solution and vaginal dinoprostone for labor induction at term pregnancy. Archives of gynecology and obstetrics, 294: 495–503.
34. WHO recommendations on non-clinical interventions to reduce unnecessary caesarean births. Geneva: World Health Organization; 2018.