Section: OBS & Gynae

Original Review Article

PREINDUCTION CERVICAL RIPENING WITH MIFEPRISTONE: A REVIEW OF CURRENT EVIDENCE AND CLINICAL PRACTICE

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ABSTRACT

Background: Preinduction cervical ripening improves the success of labor induction in women with an unfavourable cervix. Mifepristone, a progesterone receptor antagonist, offers a promising alternative to traditional agents like prostaglandins and mechanical methods. The objective of this article was to review current evidence on the use of oral mifepristone for cervical ripening before labor induction in term pregnancies.

Materials and Methods: A narrative review was conducted using several clinical studies published between 2015 and 2024, including randomized controlled trials and observational studies. Studies involved singleton term pregnancies receiving 200–400 mg mifepristone orally. Key outcomes included Bishop score change, induction-to-delivery interval, delivery mode, and maternal-fetal safety.

Results: All studies showed significant improvement in Bishop score within 24–48 hours of mifepristone use. Vaginal delivery rates ranged from 50% to 78%, with shorter induction-to-delivery intervals. No increase in adverse maternal or neonatal outcomes was observed. One large RCT confirmed that outpatient mifepristone use was as effective and safe as inpatient use, with reduced hospital stay.

Conclusion: Mifepristone is a safe, effective, and underutilized agent for cervical ripening. Across multiple studies, mifepristone use reduced induction-to-delivery time by up to 14 hours, and significantly lowered caesarean rates—highlighting its strong potential as a preinduction agent.

Keywords: Mifepristone, cervical ripening, labor induction, Bishop score, outpatient induction.

INTRODUCTION

The induction of labor (IOL) is a cornerstone of modern obstetric practice, aimed at initiating uterine contractions prior to spontaneous onset for maternal or fetal benefit. Globally, 20–30% of term pregnancies undergo labor induction, a figure that continues to rise due to better fetal surveillance, improved perinatal care, and broader indications such as post-dated pregnancy, oligohydramnios, hypertensive disorders, and gestational diabetes.[1]

A successful induction largely depends on the state of the cervix. When the cervix is deemed "unfavourable" (Bishop score <6), labor induction without prior ripening is often prolonged, less efficient, and more likely to result in cesarean section.[2] Hence, preinduction cervical ripening becomes essential, particularly in primigravidas or when elective induction is planned. Currently available options for ripening include mechanical methods (e.g., Foley catheter, laminaria),[3] and pharmacologic agents such as prostaglandins (PGE1 or PGE2). However, these are associated with complications like uterine hyperstimulation, meconium-stained liquor, or abnormal fetal heart tracings.[4]

Mifepristone, a 19-norsteroid compound and progesterone receptor antagonist, has emerged as an alternative for cervical ripening. Initially used for medical abortion, its pharmacologic properties—namely blocking progesterone at the cellular level, increasing prostaglandin sensitivity, and promoting cervical collagen degradation—have made it suitable for preinduction settings.[5]

Several clinical trials have evaluated the efficacy and safety of mifepristone for this indication. In a study by Kayastha et al., 20% of women initiated labor with mifepristone alone, and the mean Bishop score improved significantly compared to controls. Vaginal delivery rates were higher ($p = 0.003$), and cesarean rates were lower in the mifepristone group without significant adverse neonatal outcomes.[6] Similarly, Yelikar et al. conducted a randomized controlled trial in 100 women with prolonged pregnancy and found that the mean Bishop score increased by 5.04 in the mifepristone group compared to 3.26 in controls, and misoprostol requirement was significantly reduced. Cesarean rates were also lower in the mifepristone group (12% vs. 16%).[7]

A 2024 study by Thakur et al. in The Journal of Obstetrics and Gynaecology of India demonstrated that 69% of patients achieved a Bishop score ≥6 within 48 hours of mifepristone use. Moreover, 50% of the participants delivered vaginally, 24 of whom did so within 48 hours of drug administration.[8] In a large double-blind trial, Deepika and Kumar compared 200 mg mifepristone with placebo and found significantly higher rates of spontaneous labor and shorter induction-to-delivery intervals in the study group (35 h vs. 49 h, $p = 0.000$). The cesarean section rate was notably lower (10% vs. 20%).[9]

Although Sharma et al. concluded that prostaglandin E2 (PGE2) gel produced faster ripening than mifepristone in early hours, they also reported a higher rate of vaginal delivery and better maternal tolerance in the mifepristone group.[10] Importantly, mifepristone also lends itself to outpatient use. Baev et al. compared inpatient and outpatient cervical ripening with mifepristone and concluded that the outpatient group had similar efficacy but shorter hospital stays, fewer interventions, and no compromise in maternal or neonatal safety.[11]

However, despite this robust evidence, guideline endorsements remain limited. Neither ACOG nor WHO currently includes mifepristone for cervical ripening in standard induction protocols. This may stem from its historic association with abortion, limited licensing, or insufficient large-scale longitudinal data. This review consolidates current literature and clinical trial data to critically evaluate the efficacy, safety, and practical application of mifepristone in preinduction cervical ripening. It aims to inform clinicians, policymakers, and researchers about mifepristone's growing relevance in labor management and the need for its formal integration into clinical guidelines.

MATERIALS AND METHODS

This narrative review was conducted to evaluate the role of mifepristone in preinduction cervical ripening in term pregnancies. A total of seven published clinical studies, including randomized controlled trials, comparative studies, and observational analyses published between 2015 and 2024, were included in this review. These studies were selected based on the following inclusion criteria:

- Use of oral mifepristone for cervical ripening prior to labor induction in singleton term pregnancies
- Assessment of cervical readiness using Bishop score or modified Bishop score
- Reporting of outcomes such as improvement in Bishop score, induction-to-delivery interval, mode of delivery, maternal and fetal complications
- Comparison with placebo, mechanical methods, or other pharmacologic agents (e.g., prostaglandins)
- Studies conducted in tertiary care or teaching hospitals

All included articles were reviewed in full text, and data were extracted independently on sample size, dose and timing of mifepristone, comparator arms (if any), outcome measures, and key findings. Studies not using term gestations or lacking specific outcome measures relevant to cervical ripening were excluded.

RESULTS

The review includes a total of seven studies involving more than 1,250 women undergoing labor induction with oral mifepristone. The dose of mifepristone used in all studies was either 200 mg or 400 mg administered orally, 24–48 hours prior to formal labor induction procedures (e.g., oxytocin, PGE2 gel, or artificial rupture of membranes).

1. Efficacy in Cervical Ripening

All studies reported a statistically significant increase in Bishop score following mifepristone use:

- Thakur et al. (2024) reported an improvement in mean Bishop score from 1.87 to 6.92 within 48 hours ($p < 0.005$), with 69% achieving a favourable score (≥6).[8]
- Sood et al. (2022) found significantly higher improvement in Bishop scores in the mifepristone group vs. placebo (mean change 3.22 vs. 1.61, $p < 0.0001$).[12]
- Deepika et al. (2018) observed 75% of patients in the mifepristone group entering labor within 48 hours, compared to 48% in the placebo group. The mean induction-to-labor interval was reduced by over 13 hours ($p = 0.000$).[9]
- Baev et al. (2023) found comparable improvement in Bishop score in both outpatient and inpatient groups using mifepristone, reinforcing its flexibility in care settings.[11]

2. Mode of Delivery and Induction-to-Delivery Interval

- Kayastha et al. showed a higher vaginal delivery rate in the mifepristone group (78% vs. 64%, p = 0.003) and fewer cesarean sections, particularly for failed inductions.[6]
- Yelikar et al. demonstrated a shorter induction-to-delivery interval in the mifepristone group (mean 10.08 h vs. 14.76 h, p < 0.05) and less need for additional ripening agents.[7]
- Sharma et al. (2023), in comparison with PGE2 gel, noted a longer induction-to-delivery interval in the mifepristone group but higher vaginal delivery rates, suggesting a more gradual but ultimately effective ripening process.[10]

3. Maternal and Neonatal Safety

- Across all studies, mifepristone was well tolerated:
- No significant difference was noted in Apgar scores, NICU admissions, or incidence of meconium-stained liquor.
- Sood et al. and Deepika et al. both reported fewer cesarean sections for failed induction in the mifepristone group, with no increase in fetal distress.[9,12]
- Baev et al. confirmed that outpatient administration of mifepristone was safe, with no higher incidence of adverse events compared to inpatient use.[11]

Table 1: Summary of Key Results

Author (Year)	Sample Size	Study Design	Dose of Mifepristone	Comparator	Bishop Score Improvement	VD Rate (%)	I-D Interval	Key Findings
Thakur et al. (2024)	100	Prospective cohort	200 mg orally	None	1.87 → 6.92 (p<0.005)	50%	~48 hrs	Significant cervical ripening and 69% reached favorable Bishop score
Sood et al. (2022)	200	RCT (double-blind)	200 mg orally	Placebo	+3.22 vs +1.61 (p<0.0001)	68% vs 64%	~48 hrs	Better ripening; no significant diff. in VD, C-section, MSL
Deepika et al. (2018)	200	RCT	400 mg orally	Placebo	Not specified numerically	70% vs 38%	35 h vs 49 h	Significant reduction in I-D interval and C-section rate
Kayastha et al. (2014)	100	RCT	200 mg orally	Placebo	+3.9 (mean)	78% vs 64%	Not specified	Lower cesarean and misoprostol requirement
Yelikar et al. (2015)	100	RCT	200 mg orally	Placebo	+5.04 vs +3.26	Higher in study group	10.08 h vs 14.76 h	Shorter induction-to-delivery interval and better Bishop improvement
Sharma et al. (2023)	100	RCT	200 mg orally	PGE2 gel	Slower early ripening	Higher in mifepristone	Longer	Comparable neonatal outcomes; mifepristone better tolerated
Baev et al. (2023)	322	RCT	200 mg orally	Inpatient vs outpatient	Equal in both groups	Similar	38.6 h vs 38.8 h	Outpatient mifepristone safe and effective; reduced hospital stay

DISCUSSION

Cervical ripening before labor induction is a well-recognized clinical strategy aimed at improving obstetric outcomes in women with an unfavourable cervix. A favourable cervix not only shortens the induction-to-delivery interval but also increases the likelihood of a successful vaginal delivery, thereby reducing maternal and neonatal morbidity.[13] Traditionally, agents such as prostaglandin E2 (dinoprostone), misoprostol, and mechanical methods like Foley catheterization have been employed. However, these approaches can be associated with uterine hyperstimulation, fetal distress, increased resource utilization, and patient discomfort. In this context, mifepristone—an antiprogestin—has emerged as a pharmacologically distinct and clinically promising agent for preinduction cervical ripening.

Mechanism and Rationale: Mifepristone acts by competitively binding to intracellular progesterone receptors in the myometrium and cervix. This functional withdrawal of progesterone initiates a cascade of biochemical events: increased endogenous prostaglandin synthesis, elevated collagenase activity, and degradation of the cervical extracellular matrix. These changes collectively lead to cervical softening and dilatation without directly stimulating uterine contractions, making mifepristone an ideal preinduction agent rather than a direct uterotonic.[14]

Efficacy in Cervical Ripening: Multiple studies included in this review consistently demonstrate that mifepristone significantly improves the Bishop score within 24–48 hours of administration. In the randomized controlled trial by Thakur et al., the Bishop score increased from 1.87 to 6.92 after 48 hours of mifepristone administration, and nearly 69% of participants reached a favourable score ≥6.[8] Similarly, Sood et al. showed that mifepristone-treated women had a greater mean increase in Bishop score compared to placebo (3.22 vs 1.61, $p<0.0001$), with 82 out of 94 patients showing significant improvement.[12] These findings were reinforced by Kayastha et al., who reported a mean score increase of 3.9 and a higher proportion of women progressing to spontaneous labor without additional interventions.[6] Even in comparison with prostaglandin E2 gel, Sharma et al. found that although initial ripening was slower with mifepristone, it ultimately resulted in a higher rate of vaginal deliveries, fewer augmentation needs, and better maternal tolerance.[10]

Impact on Induction-to-Delivery Interval and Vaginal Delivery Rates: An important clinical goal of cervical ripening is to reduce the time from initiation of induction to delivery. Yelikar et al. demonstrated that the induction-to-delivery interval was significantly shorter in the mifepristone group (10.08 hours) compared to the control group (14.76 hours, $p<0.05$).[7] Deepika et al. corroborated this, with a reduction from 49 hours in the placebo group to 35 hours in the mifepristone group ($p=0.000$), along with higher vaginal delivery rates (70% vs 38%).[9] These findings are critical, especially in resource-constrained settings where hospital beds, monitoring staff, and intervention facilities are limited. Mifepristone, by expediting labor onset and reducing the need for prolonged monitoring, can improve institutional efficiency.

Safety Profile and Neonatal Outcomes: Across all studies, mifepristone demonstrated a strong safety profile for both mother and fetus. No study reported a statistically significant increase in adverse outcomes such as uterine hyperstimulation, postpartum hemorrhage, meconium-stained liquor, or NICU admissions. Notably, Sood et al. and Deepika et al. found no difference in Apgar scores or neonatal morbidity between mifepristone and placebo groups, even when the induction-to-delivery interval was shortened.[9,12] Baev et al. took the safety profile further by assessing outpatient administration. Their randomized controlled trial showed that mifepristone use outside the hospital was not only safe but also reduced hospital stay duration by an average of 25 hours without compromising maternal or neonatal outcomes. This finding is particularly relevant for healthcare systems seeking to minimize inpatient costs and patient exposure to nosocomial risks.[11]

Comparative Effectiveness: While Sharma et al. concluded that PGE2 gel achieved faster early cervical ripening compared to mifepristone, it is important to note that the mifepristone group in their study had higher vaginal delivery rates and fewer interventions, suggesting a slower but more physiologically harmonious effect.[10] Unlike prostaglandins, which can cause abrupt uterine contractility and fetal compromise, mifepristone allows a gentle progression to labor over 24–48 hours. Moreover, the oral route, ease of administration, and minimal need for continuous monitoring make mifepristone a patient-centered and provider-friendly choice, especially in outpatient settings, rural areas, and during pandemics where hospital resources are stretched.

Barriers to Routine Use: Despite robust evidence, mifepristone is not yet widely integrated into international guidelines such as those from ACOG, RCOG, or WHO. Potential reasons include its historical association with medical abortion, regulatory limitations, and lack of familiarity among providers. However, studies like those by Baev and Sood make a compelling case for formal re-evaluation of guidelines, particularly in light of global efforts to reduce unnecessary cesarean sections and improve maternal satisfaction. Furthermore, the drug is cost-effective and readily available in many countries, including India, making it an accessible option for both public and private sector obstetrics.

CONCLUSION

Mifepristone is a safe, effective, and underutilized agent for preinduction cervical ripening. Its ability to significantly improve Bishop scores, reduce induction-to-delivery intervals, and increase rates of vaginal delivery—without increasing maternal or fetal risks—makes it a valuable alternative to conventional agents. The growing evidence from randomized trials, including its successful use in outpatient settings, underscores its potential to transform cervical ripening practices, especially in low-resource environments.

Formal integration into national and international guidelines, supported by multicentre trials and health economic analyses, is now warranted. As we continue to seek patient-centered, evidence-based, and resource-sensitive approaches to obstetric care, mifepristone is poised to become a cornerstone in modern labor induction protocols.

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