Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.ijogr.org

Review Article

Different approaches and role of dinoprostone vaginal insert in induction of labour

Manish R Pandya[1]*, **Ashwin Kakkar**[2], **Sadhna Gupta**[3]

[1]*Dept. of Obstetrics and Gynecology, Mahavir Hospital & Manish IVF Centre Scientific Research Institute, Surendranagar, Gujarat, India*
[2]*Vaishnavi Maternity, Maharashtra, India*
[3]*Dept. Dept. of Obstetrics and Gynecology, Jeevan Jyoti Hospital & Medical Research Centre, Gorakhpur, Uttar Pradesh, India*

ARTICLE INFO

Article history:
Received 14-07-2024
Accepted 08-18-2024
Available online 20-08-2024

Keywords:
Induction of labour
Caesarean section
Dinoprostone vaginal insert
Prostaglandins

ABSTRACT

Prostaglandin E2 (PGE2) plays a crucial role in cervical ripening and initiating parturition. The Dinoprostone vaginal insert, containing 10 mg of Dinoprostone within a polymeric hydrogel matrix, ensures controlled and consistent release. In women with intact membranes, the release rate averages 0.3 mg per hour, while in those with premature rupture of membranes, variability may occur. Compared to Dinoprostone gel, the insert significantly increases the likelihood of achieving vaginal delivery within 24 hours, with shorter hospital stays and reduced postpartum haemorrhage. The scientific and clinical discussion held in a forum, comprising experienced gynaecologists of India, discussed their clinical experience, shared their views and opinions on the Dinoprostone vaginal insert's role in labour induction, reaching consensus through evidence-based statements.

1. Induction of Labour

Induction of labour is the deliberate initiation of the labour process before it occurs naturally or spontaneously. An estimated 5% to 10% of women reach gestational periods beyond 294 days or 42 completed weeks, classifying them as post-term pregnancies. This demographic notably contributes to the increased frequency of induced labour. Although induction of labour stands as a prevalent intervention in obstetrics, it carries inherent risks and necessitates careful consideration before implementation.[1]

Labour progresses through three stages, with the initial phase marked by the cervix gradually dilating, causing characteristic pain. As the cervix dilates, mucus that protected against bacteria is often expelled. This dilation also weakens support for the fetal membranes, potentially leading to their rupture and initiating active labour. Ideally, regular uterine contractions begin when cells form low-resistance connections, allowing electrical signals to pass smoothly across the uterus. If contractions start prematurely or if the cervix is not adequately prepared, prostaglandins released from the membranes and uterine decidua stimulate labour, leading to a slower dilation phase, which can be challenging for the mother and increase infection risk.[2]

Induced labour is indicated in women who have prolonged pregnancy, premature rupture of membrane (PROM) (Preterm at ≥34 weeks in absence of other obstetric indications and term at ≥37 weeks.), intrauterine fetal death and maternal request.[3]

2. Caesarean Section

Since 1985, the international healthcare community has considered the optimal caesarean section rate within the range of 10%-15%. Subsequent to that timeframe, the prevalence of caesarean sections has risen notably in both

* *Corresponding author*.
E-mail address: drmanish.pandya@gmail.com (M. R. Pandya).

https://doi.org/10.18231/j.ijogr.2024.062

developed and developing nations. The WHO systematic review suggests that caesarean section rates of 10-15% are associated with decrease in maternal, neonatal and infant mortality. When life is expected to be normal, why shouldn't childbirth be normal too?

Unnecessary caesarean sections are recognized to elevate health risks for both the mother and the new-born, while also imposing financial strains on healthcare budgets. The rising trend in caesarean deliveries is influenced by healthcare providers' safety perceptions, obstetricians' convenience preferences and healthcare system structures. Mothers who deliver vaginally tend to recover faster postpartum and are better equipped to care for their new-borns.[4]

Prostaglandins play pivotal roles in parturition, specifically focusing on myometrial contraction. Elevated levels of uterine prostaglandins or increased myometrial responsiveness to prostaglandins induce contraction and initiate labour by promoting cervical ripening. Hence, prostaglandins have been widely used for the induction of labour.[5]

Induction of labour can be done by mechanical methods and pharmacological methods.

3. Mechanical Modalities

Mechanical methods include hygroscopic dilators, which functions by absorbing fluids from endocervical and local tissues. Balloon devices exert mechanical pressure directly onto the cervix during inflation. Membrane stripping increases enzyme activity, dilates the cervix and detaches membranes from the uterus. Amniotomy can increase the release of prostaglandins locally. Possible risks include cord problems, infections, fetal heart rate changes, bleeding from placenta issues and fetal injury.[6]

4. Pharmacological Methods

4.1. Prostaglandins

Prostaglandins are naturally produced hormones in the body and are important during the labour.[7] Prostaglandins, produced both locally in the cervix and uterus as well as from the fetal membranes, play a critical role in cervical ripening and other processes of parturition, including uterine contractility and the induction of labour.[8] They are frequently used when the ripening of cervix has not occurred with a Bishop score <6. It supports cervical ripening and promotes the cervix to soften and stretch in preparation for childbirth.[7]

Numerous prostaglandin formulations have been utilized for labour induction, encompassing prostaglandin F2 alpha (PGF2α, dinoprost), prostaglandin E2 (PGE2, Dinoprostone), prostaglandin E1 (PGE1) and misoprostol, a synthetic analogue of PGE1.[7]

4.2. Oxytocin

Oxytocin, a natural hormone, aids in uterine contractions during labour. Its synthetic forms are used for induction globally. IV oxytocin is administered as the cervix dilates. Dosage typically starts low (0.5-2.0 mU/minute) and increases every 15-60 minutes, with higher doses (up to 6.0 mU/minute) increasing every 15-40 minutes.[7]

4.3. Mifepristone (Progesterone receptor antagonists)

Progesterone plays a crucial role in all stages of pregnancy. It prevents uterine muscle contraction and helps maintain cervical structure. When labour begins, progesterone withdrawal is necessary. Progesterone receptor antagonists can induce labour by mimicking this withdrawal.[9]

4.4. Nitric Oxide (NO) donors

Nitric oxide (NO) donors have been used to ripen the cervix for first-trimester pregnancy terminations. Studies indicate that nitric oxide metabolites rise in cervical fluid after ripening or manipulation, indicating NO donors could be beneficial for labour induction.[9]

4.5. Dinoprostone

PGE2, alternatively referred to as Dinoprostone, is an endogenous compound that plays a pivotal role in labour induction. PGE2 prompts myometrial contractions through direct stimulation, binding to EP1-4 G protein-coupled receptors (GPCRs), initiating diverse downstream events contingent on EP subtype and cell-specific expression patterns.[10]

Dinoprostone is available in 2 formulations: a vaginal insert and a cervical gel. Dinoprostone exhibits a sustained and controlled onset of action and duration of effect, with a half-life ranging from 2.5-5 minutes. Both formulations necessitate cold storage to maintain chemical stability. While the cervical gel enables faster release of Dinoprostone compared to the vaginal insert, the latter provides a more gradual elevation in plasma PGE2 levels and a prolonged duration of action. The vaginal insert offers easy retrieval compared to gel, administered at a rate of 0.3 mg/h for 24 hours, it proves superior compared to cervical gel owing to its ease of removal, diminished invasiveness and reduced necessity for vaginal examinations.[8]

Dinoprostone gel often requires repeated doses, leading to potential discomfort for the patient. Moreover, in cases of hyperstimulation, where excessive uterine contractions occur, the administration of the gel lacks an effective reversal mechanism, thereby posing challenges in managing this complication.[11]

5. Dinoprostone Vaginal Insert

PGE2 is pivotal in facilitating cervical ripening and the onset of parturition.[12] The localized actions of PGE2 encompass alterations in cervical consistency, dilation and effacement.[13] The Dinoprostone vaginal insert comprises 10 mg of Dinoprostone uniformly distributed within the matrix of a thin, flat polymeric hydrogel drug delivery device. The delivery mechanism is engineered to sustain a controlled and consistent release of Dinoprostone from the reservoir. In women with intact membranes, the release rate averages approximately 0.3 mg per hour.[13,14] In women experiencing premature rupture of membranes, the release of Dinoprostone may occur at an accelerated pace and exhibit greater variability.[15]

The utilization of a Dinoprostone insert is associated with a significantly higher likelihood of achieving vaginal delivery within a 24-hour timeframe when compared to the application of Dinoprostone gel. Furthermore, the Dinoprostone insert demonstrates superiority in facilitating vaginal delivery within this time frame, accompanied by shorter hospital stays and reduced incidence of postpartum haemorrhage compared to the gel formulation.

6. Need for Consensus

Given the extensive pre-existing data on Dinoprostone vaginal insert and the ongoing emergence of clinical evidence, there is a critical necessity for a clinical consensus regarding its role in initiating and intensifying labour induction. These imperatives underscore the need for a practical document tailored to provide guidance for healthcare professionals (HCPs) regarding the diverse indications of Dinoprostone vaginal insert. Such a consensus serves as an indispensable resource, synthesizing current knowledge and offering actionable recommendations to empower HCPs in optimizing obstetric care and treatment approaches.

7. Methodology

A group of gynaecologists from India have discussed the various methodology for induction of labour and the role of Dinoprostone vaginal insert for the use in induction of labour. Experts framed statements based on available scientific evidence, experience and collective judgement from practical experience with Dinoprostone vaginal insert. Objective related to Dinoprostone vaginal insert were discussed and each expert shared their view, which led to group discussions. Consensus was reached when agreement with the statement exceeded 80% within the group.

8. Expert Opinion on Dinoprostone Vaginal Insert

8.1. Predictors of success for IOL

For a successful induced labour, it's crucial to have a Bishop score lower than 6. Other important factors include a lower BMI, having had fewer than 5 previous deliveries, gestational age of >39 weeks and ensuring the baby's weight is up to 3.2 kg.

8.2. Indication for dinoprostone vaginal insert

It was unanimously recommended that promotional material refrain from outlining specific indications for the use of Dinoprostone Vaginal Insert. The decision to employ Dinoprostone in a particular patient should be left to the discretion of individual healthcare providers, as they possess the requisite clinical judgment to assess its appropriateness on a case-by-case basis.

8.3. Benefits of dinoprostone vaginal insert over other IOL agents

Dinoprostone Vaginal Insert is distinguished by its capacity to initiate labour through a gentle process facilitated by the controlled release of Dinoprostone. A notable advantage lies in its "easy reversibility due to retrievability," a feature unparalleled by other methods such as misoprostol or Dinoprostone Gel. This attribute holds significant clinical importance as it markedly reduces the risk of uterine hyperstimulation. The rapid clearance of Dinoprostone upon removal of the insert, owing to its short half-life of 2.5-5 minutes, further contributes to the safety profile of this approach.

8.4. Cost is not a major concern

If patient has successful induction of delivery with the Dinoprostone vaginal insert, the cost of hospitalisation is reduced to a fraction of that of caesarean section (C/S). On the other hand, Dinoprostone failed patients will have to bear greater cost of C/S with the uncertainty of complications, such as maternal-fetal morbidity risk, possibility of NICU cost and trauma of the mandatory C/S delivery in future, etc.

8.5. Dinoprostone vaginal insert over misoprostol

Misoprostol exhibits dual pharmacological effects: cervical ripening and oxytocic action, inducing contractions. However, during IOL, the desired effect is solely cervical ripening, without the oxytocic effect. Herein lies the advantage of Dinoprostone vaginal insert over Misoprostol. Additionally, Misoprostol lacks the capability for reversing hyperstimulation, unlike Dinoprostone vaginal insert, which can be easily retrieved. This ease of reversal is facilitated by the short half-life of Dinoprostone (2.5-5 minutes)

compared to Misoprostol's half-life of approximately 30-40 minutes.

8.6. Dinoprostone vaginal insert over conventional gel

Both Dinoprostone vaginal insert and gel can be used in cases of premature rupture of membranes (PROM) cases. Furthermore, the potential for reversing uterine hyperstimulation is feasible with Dinoprostone vaginal insert, a capability not afforded by gel.

9. Key Recommendations for Deploying Dinoprostone for Cervical Ripening

1. Utilization Guidelines for Dinoprostone
   (a) The application of Dinoprostone is recommended when the Modified Bishop Score is less than 6.
   (b) In addition to the specified maternal medical conditions for Induction of Labour (IOL), the pregnancy should have progressed to at least 37 weeks.
   (c) Advanced Maternal Age (above 35 years) and/or High Body Mass Index (BMI) may diminish the effectiveness of agents which is been used for IOL.
2. Implementation Protocol for Dinoprostone
   (a) The Dinoprostone vaginal insert should be stored in a freezer from procurement until just prior to insertion.
   (b) Prior to inserting the Dinoprostone Vaginal insert, an intravaginal saline wash of 20 mL 0.7% should be administered.
   (c) Dinoprostone should only be removed from cold storage once the patient is positioned and the vaginal wash is completed.
   (d) The duration between retrieval from cold storage and insertion must not exceed 30 seconds.
   (e) Following the insertion of Dinoprostone, cervical ripening may take up to 24 hours.
   (f) If intravenous Oxytocin supplementation is required, it should be administered no sooner than 30 minutes after the removal of Dinoprostone.

10. Final Consensus Statements

1. When natural processes fail to initiate labor in women at term, Dinoprostone facilitates natural delivery by promoting cervical ripening and uterine contractions.
2. Dinoprostone Vaginal Insert should be administered in an in-patient setting with meticulous supervision, mandating non-discharge post-insertion.
3. Dinoprostone Vaginal Insert necessitates storage within a freezer, maintaining temperatures between -10°C and -25°C, emphasizing the criticality of freezer storage over refrigeration.
4. Concurrent administration of Dinoprostone Vaginal Insert with oxytocin is contraindicated. Oxytocin initiation should be deferred until 30 minutes post-removal of Dinoprostone, permitting simultaneous use with mechanical methods like Foley's or Balloon Catheter.
5. Timely removal of Dinoprostone Vaginal Insert upon the establishment of painful uterine contractions marks best practice.
6. Augmenting the efficacy of Dinoprostone Vaginal Insert necessitates pre-insertion cleansing with 20 mL 0.9% saline wash, elevating vaginal pH to enhance Dinoprostone release.
7. Swift insertion of Dinoprostone Vaginal Insert within 30 seconds post-freezer removal underscores the importance of patient positioning prior to removal. Optimal placement in the posterior vaginal fornix transversely aligns with recommended technique.
8. When opening the package via perforation, it is necessary to push the tape from the bottom promptly during pack tearing to expedite the process and save time.
9. An educational initiative targeting post-graduate students is recommended to enhance awareness, particularly focusing on cold chain maintenance and administration protocols, aiming for a lifelong improvement in expertise.
10. The typical duration for labour induction with Dinoprostone Vaginal Insert spans 14-16 hours, albeit varying between 10 to 20-22 hours for select individuals.
11. Post-insertion, patients receiving Dinoprostone Vaginal Insert can anticipate a waiting period of up to 24 hours for the initiation of labour.
12. Data was presented on the out-patient use of DVI for IOL. It was concluded that, unlike the western countries, the Indian obstetric scenario is not yet ready for out-patient deployment of DVI for IOL due to the limited awareness.

11. Ethics Approval and Consent to Participate

This article does not contain any new studies with human participants or animals performed by any of the authors.

12. Author Contributions

Dr. Manish Pandya, Yatri Dave, Mr. Nimesh Modi, Dr. Keshini Dhande and Dinoprostone Vaginal Insert (DVI) Clinical Consensus Collaborative Group (Dr. Ashwin Kakkar, Dr. H Lalitha, Dr. Indrajeet Mulik, Dr. Manju Gita Mishra, Dr. Mirudhubashini Govindarajan, Dr. Mohil Patel, Dr. Phagun Shah, Dr. Sadhana Gupta, Dr. Sangeeta Wagh).

13. Availability of Data and Materials

Data sharing does not apply to this article, as no datasets were generated or analyzed during the current study.

Acknowledgements

The author thanks all the participating co-authors for sharing their clinical expertise and for assisting in finalizing the manuscript for publication.

References

1. Ryan RM, Mccarthy FP. Induction of labour. *Obstet Gynaecol Reprod Med*. 2019;29(12):351–8.
2. Steer P, Flint C. Physiology and management of normal labour. *BMJ*. 1999;318(7186):793–6.
3. Inducing labour: Clinical guideline [CG70]. United Kingdom: National Institute for Health and Clinical Excellence; 2008. Available from: https://www.nice.org.uk/guidance/cg70.
4. Aslam MF, Gilmour K, Fawdry RDS. Who wants a caesarean section? A study of women's personal experience of vaginal and caesarean delivery. *J Obstet Gynaecol*. 2003;23(4):364–6.
5. Olson DM, Ammann C. Role of the prostaglandins in labour and prostaglandin receptor inhibitors in the prevention of preterm labour. *Front Biosci*. 2007;12:1329–43.
6. Tenore JL. Methods for cervical ripening and induction of labour. *Am Fam Physician*. 2003;67(10):2123–8.
7. Nowotny H, Scott P, Gibbons M. Introduction: 'Mode 2' Revisited: The New Production of Knowledge. *Minerva*. 2003;41(3):179–94.
8. Bakker R, Pierce S, Myers D. The role of prostaglandins E1 and E2, dinoprostone, and misoprostol in cervical ripening and the induction of labor: a mechanistic approach. *Arch Gynecol Obstet*. 2017;296(2):167–79.
9. Gilstrop M, Sciscione A. Induction of labor–pharmacology methods. *Semin Perinatol*. 2015;39(6):463–5.
10. Xi M, Gerriets V. Prostaglandin E2 (Dinoprostone) (Internet). Treasure Island (FL): StatPearls Publishing; Jan 2024.
11. Rai P, Rashmi MD. A comparative study between Dinoprostone Insert and Dinoprostone Gel for induction of Labour and neonatal outcome. *Indian J Obstet Gynecol Res*. 2024;11(2):167–71.
12. Bakker R, Pierce S, Myers D. The role of prostaglandins E1 and E2, Dinoprostone, and misoprostol in cervical ripening and the induction of labour: a mechanistic approach. *Arch Gynecol Obstet*. 2017;296(2):167–79.
13. Ferring Pharmaceuticals Inc. Dinoprostone ® (Dinoprostone vaginal insert): US prescribing information; 2016.
14. Propess 10mg vaginal delivery system. Electronic Medicines Compendium; Last updated on emc: 12 Oct 2021. Available from: https://www.medicines.org.uk/emc/product/135/smpc#gref.
15. Zeng X, Zhang Y, Tian Q, Xue Y, Sun R, Zheng W, et al. Efficiency of dinoprostone insert for cervical ripening and induction of labor in women of full-term pregnancy compared with dinoprostone gel: A meta-analysis. *Drug Discov Ther*. 2015;9(3):165–72.

Author biography

Manish R Pandya, Professor and HOD https://orcid.org/0000-0003-4665-3069

Ashwin Kakkar, Gynecologist and Obstetrician https://orcid.org/0009-0009-1064-3652

Sadhna Gupta, Gynecologist and Obstetrician

Cite this article: Pandya MR, Kakkar A, Gupta S. Different approaches and role of dinoprostone vaginal insert in induction of labour. *Indian J Obstet Gynecol Res* 2024;11(3):325-329.