

The Use of Dinoprostone versus Evening Primrose Oil for Cervical Ripening in Women who will Undergo Hysteroscopy: A Randomized Controlled Trial

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Objective: To compare the efficacy of Dinoprostone gel versus intravaginal evening primrose oil capsule as cervical ripening agents for operative hysteroscopy.... and to compare the length of time to achieve a 10mm cervical dilatation prior to operative hysteroscopy.

Methods: This is a two-arm randomized controlled trial done in a tertiary training institution. Group A and B received Dinoprostone gel and EPO for cervical ripening, respectively. Population consisted of women admitted for operative hysteroscopy, aged between 19-56 years old, and with closed cervix.

Results: Thirty-eight (38) patients mostly pre-menopausal with mean age of 41, without history of uterine surgery, and presented with abnormal uterine bleeding, were included. Significant difference was observed in initial cervical dilatation between Dinoprostone gel(5.63 mm) versus EPO(4.21mm). Most patients in EPO group were pain-free while Dinoprostone group experienced tolerable pain. Use of Dinoprostone was 4x more expensive versus EPO.

Conclusion: Both agents were effective in dilating the cervix prior to operative hysteroscopy. Nevertheless, EPO may be superior and acceptable due to reduced cost, patient convenience and acceptability, and ease of administration.

Key words: Operative hysteroscopy, dinoprostone, evening primrose oil, cervicovaginal complications

Introduction

Hysteroscopy is an operative procedure in which the gynecologist directly examines the uterine cavity using a small telescopic instrument (hysteroscope) inserted via the vagina and the cervix. Almost 50% of hysteroscopic complications are related to difficulty in entering the cervix. Other possible complications include cervical tears, creation of a false passage, perforation, bleeding, or simply difficulty in entering the internal os with the hysteroscope. Adequate preparation of the cervix prior to hysteroscopy may reduce these potential complications.¹

In the past twenty years, prostaglandins have been used in a variety of formulations to ripen the cervix. Prostaglandins may be given via the oral, intravaginal, intracervical and intravenous routes, all

of which are effective. Intravaginal administration of exogenous prostaglandin E2 like dinoprostone is the most widely used pharmacological method to promote cervical ripening.²

The cervix is composed of fibroblast cells and fibrous connective tissues which is composed mainly of collagen and glycosaminoglycans. Cervical ripening is an active biochemical complex reaction in which degradation of collagens is a critical process. Collagen types I and III constitute the most abundant extracellular matrix proteins in the human uterine cervix.³

Prostaglandins act on the cervix to enable ripening by different mechanisms. They alter the extracellular ground substance of the cervix, and PGE2 increases the activity of collagenase in the cervix. They cause an increase in elastase,

glycosaminoglycan, dermatan sulfate, and hyaluronic acid levels in the cervix.⁴ Prostaglandins promote the infiltration of leukocytes and macrophages into the cervical stroma. They induce specific degradative enzymes that cause the changes in the extracellular matrix that are associated with ripening of the cervix.⁵

Misoprostol is a synthetic PGE1 analog that has been found to be a safe and inexpensive agent for cervical ripening. It is one of the most studied cervical ripening agents used prior to hysteroscopy. Misoprostol has cervical ripening effects in both pregnant and non-pregnant patients when administered either orally or vaginally. It has also been used to ripen and soften the cervix prior to operative hysteroscopy.⁶ It is, however, considered an illegal drug locally, and therefore is not available in the market.

Prostaglandin E2 allows an increase in intracellular calcium levels, causing contraction of myometrial muscle and relaxation of cervical smooth muscle facilitates dilation.⁹ Dinoprostone, a natural PGE2, is mostly used in obstetrics for cervical ripening and the stimulation of uterine contractions to induce labor. Studies have reported that dinoprostone is comparable to or better than misoprostol for cervical ripening.⁷ Its widespread use, however, is precluded by its prohibitive cost, unavailability and compound instability. Thus, there is a need for an alternative cervical ripening agent which can be used in low-resource settings.

In the Philippines, a study by Cristi-Limson and Oblepias investigated the efficacy of Dinoprostone gel as cervical priming agent when used prior to operative hysteroscopy. Forty five women for operative hysteroscopy were randomly assigned to either 500mcg dinoprostone gel or to no intervention. Baseline cervical dilatation, time and ease of cervical dilatation, side effects and complications were noted. This study demonstrated that dinoprostone E2 gel is an effective cervical priming agent. It decreased cervical resistance, facilitated further cervical dilatation and facilitated the hysteroscopic procedure.⁸

Evening primrose oil is derived from the seeds of the evening primrose (*Oenothera biennis*) plant. It is rich in the essential fatty acid gamma linolenic acid, a fatty acid that the body converts to a hormone-

like substance called prostaglandin E1. Therapeutic claims of evening primrose oil are attributed to direct action of its component essential fatty acids on immune cell. Evening primrose oil is best known for its use in the treatment of systemic diseases marked by chronic inflammation, such as atopic dermatitis and rheumatoid arthritis. Breast pain, menopausal and premenstrual symptoms, cervical ripening, and labor induction or augmentation are some conditions where. Evening primrose oil is often used.⁹

Here in the Philippines, recent studies were conducted investigating the efficacy of Evening Primrose Oil as a cervical priming agent prior to hysteroscopy. First is a case series done by Aquino and colleagues in 2011, the ease of cervical dilatation was determined in 6 postmenopausal and 2 nulligravid premenopausal women. They observed a significance in ease of cervical dilatation in all patients given intravaginal Evening Primrose Oil 4 to 6 hours before diagnostic hysteroscopy (7 mm diameter). Secondly, in 2009, Capco and Tanangonan compared oral Evening Primrose Oil and placebo prior to operative hysteroscopy in 42 patients. They concluded that the Evening Primrose Oil group required less time for cervical dilatation compared to the placebo group.¹⁰ In another case series, Carreon and Tanangonan (2012), compared oral Evening Primrose Oil and intracervical Dinoprostone gel in 9 patients and found both equally effective in inducing adequate cervical priming prior to operative hysteroscopy. Nonetheless, the study concluded that Evening Primrose Oil may be preferred due to its oral route, reduced cost, patient convenience and acceptability.¹¹ Lastly, there is also one recent study by Tanchoco and Aguilar which is a two armed randomized controlled trial that compares the ease of cervical dilatation to allow insertion of a 10-11 mm Hegar's dilator prior to operative hysteroscopy with intravaginal Evening primrose oil versus intracervical Laminaria. They found that both agents were effective in dilating the cervix, however cervical dilatation was easier and required less time in the Evening Primrose oil group compared to those in the laminaria group.¹²

Objectives

General Objective

This study compared the efficacy of Dinoprostone gel versus intravaginal Evening Primrose Oil capsule as a cervical ripening agent prior to operative hysteroscopy.

Specific Objectives:

1. To compare the ease of cervical dilatation to allow insertion of a 10 mm Hegar's dilator prior to operative hysteroscopy after cervical priming with intracervical Dinoprostone gel versus intravaginal Evening Primrose Oil capsule.
2. To compare the ability of attaining a cervical dilatation of 10 mm prior to operative hysteroscopy after cervical priming with intracervical Dinoprostone gel versus intravaginal Evening Primrose Oil capsule.
3. To determine any complications and adverse effects related to the use of intracervical Dinoprostone gel versus intravaginal Evening Primrose Oil capsule.
4. To measure and compare the surgeon's acceptability of intracervical Dinoprostone gel versus intravaginal Evening Primrose Oil capsule.
5. To evaluate patients' acceptability of the cervical ripening agent used in terms of pain, discomfort or bleeding.

Methods

This research was a two-arm randomized controlled trial carried out in a tertiary training institution. Randomization was done using draw lots method. Group A received Dinoprostone gel and Group B received intravaginal Evening primrose oil for cervical ripening and dilatation. The study was approved by Research Ethics Board.

The computation of sample size was generated by manually computing sample size for Equivalence Trial, with the Dinoprostone gel and Evening Primrose Oil group allocated the same number of subjects (19 subjects per arm).

The study population consisted of all women admitted for elective operative hysteroscopy, between

19 to 56 years of age, with a closed cervix on internal examination on admission. Specific hysteroscopic procedures included polypectomy, myomectomy, resection of endometrial mass, resection of uterine septum, removal of intrauterine device and targeted endometrial biopsy. Patients with contraindication to hysteroscopy (pregnancy, pelvic inflammatory disease, uterus more than 12 weeks size), with a patulous cervix, with history of cervical surgery or incompetence, with prolapsed endometrial polyp or submucous myoma, who received GnRH agonists (which can result in a firm cervix), and who are mentally incapacitated to give consent were excluded in this study. If the participant was illiterate but gave oral consent, a witness was present and asked to sign.

An informed consent was taken from every subject. The principal investigator explained the objectives and details of the research to each subject including possible complication. Patients' data including demographic, history and pre-operative details were collected. Confidentiality and anonymity were ensured during the implementation stage and in case of publication and presentation of research findings. Reference number was assigned to each patient.

The subjects underwent full history taking, general and pelvic examinations, and transvaginal ultrasound to determine the nature, site and extent of intrauterine lesions. Patients randomly assigned to Group A and Group B by means of drawing lots. No potential conflict of interest is expected in this study.

No compensation was given for participating in this research. All patients who underwent hysteroscopy received the standard pre and post-operative care and laboratory test regardless of a) intervention assigned to the study participants, b) if she will participate or not in the study, and c) withdrawal from participation to interventions of interest.

For all patients who voluntarily participated, any additional diagnostics and medications necessary for management of complications arising solely from this research were shouldered by the researcher.

Group A patients received an intravaginal Dinoprostone gel 24 hours prior to hysteroscopic procedure. The patients were placed in a dorsal lithotomy position, and a sterile vaginal speculum was inserted and the cervix was sterilized using

Povidone Iodine solution. Dinoprostone gel was administered intracervically by the investigator. After application of the gel, the patient remained recumbent for 30 minutes before being allowed to ambulate.

Group B patients received intravaginal Evening Primrose Oil capsules inserted in the posterior fornix. The investigator inserted six capsules (1000mg per tablet) in the posterior fornix 6 hours prior to the procedure followed by another 4 capsules 1 hour prior to the procedure. Strict aseptic technique was observed by using sterile gloves during insertion. The Dinoprostone gel and the Evening Primrose Oil capsules were both provided by the investigator.

All patients were given regional anesthesia and the initial determination of cervical dilatation was performed after induction of anesthesia. Three consultants of the Section of Reproductive Endocrinology and Infertility with comparable level of experience acted as research assistants and performed all hysteroscopic procedures.

In the operating room, the degree of initial cervical dilatation was assessed by the maximal caliber of Hegar's dilator inserted without resistance. The dilators were inserted in ascending order, starting with the smallest size dilator (1mm). The duration (in seconds) of subsequent cervical dilatation until the 10mm diameter was reached was timed and recorded. The ease of cervical dilatation was measured using 5-point Likert scale.

Cervicovaginal canal dilatation complications such as laceration, bleeding, perforation and post-operative pain were reported. Post-operatively, the subject was interviewed by the principal investigator on the acceptability of the cervical priming agent and was measured using 5-point Likert scale. Research assistants also evaluated the patients for any possible complications and adverse effects.

The participants were asked to have at least 2 outpatient follow-ups after discharge. During that time, a repeat speculum and internal examination as well as assessment of any late onset complications were made.

Statistical Analysis

Statistical analysis was performed using Chi-square test for homogeneity for each of the demographic data and baseline internal examination

on admission while approximate Z-test was used for the hysteroscopic procedure performed. Non-parametric and parametric statistics such as Mann-Whitney U test and independent t-test were used to compare the mean cervical dilatation, time to insert Hegar's 10mm, scores for ease of dilatation, level of pain and discomfort between the two study groups.

All tests of significance between the two groups were carried out at 95% confidence level using the above mentioned methods. All data gathered from patients and results obtained from this investigation were treated as confidential information, known only to the research team and patients involved.

Results

Thirty eight patients who fulfilled the study's inclusion criteria were randomized. The demographic data of the participants are presented in Table 1. Chi-square test for homogeneity was used for each of the demographic data.

The mean age for both groups are comparable, 41.06 for Group A and 42.21 for Group B. The estimated monthly income is significantly different (p-value = 0.049). Analysis showed that there were more patients whose income is less than 10,000 under Group B (36.84%) compared to Group A (21.05%). On the other hand, age (p-value = 0.398) and educational attainment (p-value = 0.074) of patients between the two groups were not statistically significant.

Table 2 shows the comparison of both groups in terms of parity, manner of delivery, history of curettage and menopausal status. Chi-square test for homogeneity was used for all factors. Results for parity (p-value = 0.351), manner of delivery (p-value = 0.554), history of curettage/uterine surgery (p-value = 0.426), and menopausal status (p-value = 1.000) between the two treatments showed no statistically significant difference. Both groups consisted mostly of multiparas who delivered vaginally.

Table 3 is a frequency table of the indications for hysteroscopy for the two groups. Approximate Z-test was used in all variables. Analysis showed that the indication for hysteroscopy between the Dinoprostone gel and the Evening Primrose Oil group did not differ significantly. Majority of the patients presented with abnormal uterine bleeding

Table 1. Demographic data of the participants.

| Demographic Data | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|---------------------------------|--------------------------------------|------------------------------------------|-----------------------|
| Actual age in years | 41.06 | 42.21 | 0.685 ^b |
| 19-29 years | 3 (7.89%) | 1 (2.63%) | 0.398 ^b |
| 30-39 years | 4 (10.53%) | 3 (7.89%) | |
| 40-49 years | 7 (18.42%) | 12 (31.58%) | |
| 50-59 years | 5 (13.16%) | 3 (7.89%) | |
| ≥60 years | 0 (0.00%) | 0 (0.00%) | |
| Estimated monthly income | | | |
| < Php 10,000 | 8 (21.05%) | 14 (36.84%) | 0.049 ^{*, b} |
| Php 10,000 and above | 11 (28.95%) | 5 (13.16%) | |
| Educational attainment | | | |
| Elementary level | 5 (13.16%) | 2 (5.26%) | 0.074 ^b |
| High school level | 6 (15.79%) | 13 (34.21%) | |
| College level | 8 (21.05%) | 4 (10.53%) | |

* significant at 5%, b – p-value from Chi-square Test of Homogeneity

Table 2. Obstetric history.

| Obstetric History | Dinoprostone Gel (n = 19) | Evening primrose oil Group (n = 19) | p-value |
|---------------------------------------------|--------------------------------------|------------------------------------------------|--------------------|
| Parity | | | 0.351 ^b |
| Nulliparous | 3 (7.89%) | 4 (10.53%) | |
| Primipara | 4 (10.53%) | 1 (2.63%) | |
| Multipara | 12 (31.58%) | 14 (36.84%) | |
| Manner of Delivery | | | 0.554 ^b |
| SVD | 13 (34.21%) | 14 (36.84%) | |
| CS | 3 (7.89%) | 1 (2.63%) | |
| N/A | 3 (7.89%) | 4 (10.53%) | |
| History of curettage/uterine surgery | | | 0.426 ^b |
| With | 3 (7.89%) | 5 (13.16%) | |
| Without | 16 (42.11%) | 14 (36.84%) | |
| Menopausal status | | | 1.000 ^b |
| Premenopausal | 18 (47.37%) | 18 (47.37%) | |
| Post-menopausal | 1 (2.63%) | 1 (2.63%) | |

* significant at 5%, b – p-value from Chi-square Test of Homogeneity

(68.42% for Group A and 63.16% for Group B). Endometrial polyp was the most common pathology associated with abnormal uterine bleeding for both groups (92.31% for Group A and 91.67% for Group B), reflecting a well-distributed patient population.

The type of hysteroscopic procedure performed is shown in Table 4. Hysteroscopic polypectomy was the most common procedure performed for both groups (63.16% for Group A and 68.42% for Group B). Results showed that number of patients who underwent hysteroscopic polypectomy (p-value = 0.732), hysteroscopic myomectomy (p-value = 1.000), hysteroscopy-guided endometrial biopsy and hysteroscopy-guided IUD removal (p-value = 0.676) between the two treatments did not differ significantly.

Shown in Table 5 are the baseline internal examination findings of the patients on admission. Chi-square test of homogeneity was used. The cervix of all the patients in both groups had a firm

consistency. The cervix of the patients in Group A were more mid-position (39.47%) while those in Group B had a more posterior position (36.84%).

As shown in Table 6, clinical characteristics between the two groups were analyzed using Mann-Whitney U test for cervical dilatation and time to Hegar's 10mm, while Chi-square test was used for ease of cervical dilatation. The mean initial cervical dilatation was 5.63 mm for Group A and 4.21mm for Group B. The results showed that initial cervical dilatation between the two groups were statistically significant (p-value of 0.002), the initial dilatation being greater for Group A.

The median duration of time needed to insert the 10mm Hegar's dilator was 170.25 seconds for the Group A and 272.30 seconds for Group B. On further analysis, the median time to Hegar's 10mm did not differ significantly between the 2 treatment arms.

On the other hand, there was no significant difference in the ease of cervical dilatation for both

Table 3. Chief complaint (indications for hysteroscopy).

| Reason for Hysteroscopy | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|-------------------------------|------------------------------|----------------------------------|--------------------|
| Infertility | 0 | 0 | - |
| Displaced Intrauterine device | 4 (21.05%) | 3 (15.79%) | 0.676 ^c |
| Endometrial mass | 2 (10.53%) | 4 (21.05%) | 0.374 ^c |
| Postmenopausal bleeding | 0 | 0 | - |
| Abnormal uterine bleeding | 13 (68.42%) | 12 (63.16%) | 0.732 ^c |
| Submucous myoma | 1 (7.69%) | 1 (8.33%) | |
| Endometrial polyp | 12 (92.31%) | 11 (91.67%) | |

* significant at 5%, c – p-value from Approximate Z-test

Table 4. Hysteroscopic procedure performed.

| | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|---------------------------------------------|------------------------------|----------------------------------|--------------------|
| Hysteroscopic polypectomy | 12 (63.16%) | 13 (68.42%) | 0.732 ^c |
| Hysteroscopic myomectomy | 1 (5.26%) | 1 (5.26%) | 1.000 ^c |
| Hysteroscopy-guided endometrial biopsy | 2 (10.53%) | 2 (10.53%) | 1.000 ^c |
| Hysteroscopic resection of endometrial mass | 0 | 0 | - |
| Hysteroscopy-guided IUD removal | 4 (21.05%) | 3 (15.79%) | 0.676 ^c |

* significant at 5%, c – p-value from Approximate Z-test

groups (p-value=0.514). The cervical dilatation was very easy for Group A (18.42%) and easy for Group B (18.42%).

Minimal bleeding occurred in 3 patients in Group A and 4 patients in Group B. However, the

presence of such complication was not statistically significant (p-value of 0.676)

As shown in table 7, patient acceptability between two groups were analyzed using independent T-test. Results showed that level of pain between the two

Table 5. Baseline internal examination on admission.

| Internal Examination upon Admission | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|-------------------------------------|---------------------------|-------------------------------|-----------------------|
| Consistency | | | |
| Soft | - | - | |
| Medium | - | - | - |
| Firm | 19 | 19 | |
| Position | | | |
| Anterior | 0 (0.00%) | 0 (0.00%) | |
| Mid-position | 15 (39.47%) | 5 (13.16%) | 0.001 ^{*, b} |
| Posterior | 4 (10.53%) | 14 (36.84%) | |

^{*} significant at 5%, ^b – p-value from Chi-square Test of Homogeneity

Table 6. Technical characteristics.

| | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|---------------------------------------------|---------------------------|-------------------------------|-----------------------|
| Cervical dilatation (in mm) | 5.63 ± 1.30 | 4.21 ± 1.18 | 0.002 ^{*, a} |
| Time to Hegar's 10mm (in seconds) | 170.25 ± 247.65 | 272.30 ± 432.51 | 0.389 ^a |
| Ease of dilatation | | | |
| Very Difficult | 2 (5.26%) | 2 (5.26%) | |
| Difficult | 1 (2.63%) | 2 (5.26%) | |
| Good | 6 (15.79%) | 3 (7.89%) | 0.514 ^b |
| Easy | 3 (7.89%) | 7 (18.42%) | |
| Very Easy | 7 (18.42%) | 5 (13.16%) | |
| Mean Score +/- SD | 3.63 +/- 1.342 | 3.58 +/- 1.3045 | 0.9054 ^c |
| Presence of complications (bleeding) | 3 (15.79%) | 4 (21.05%) | 0.676 ^d |

^{*} significant at 5%, ^a – p-value from Mann-Whitney U Test, ^b – p-value from Chi-square Test of Homogeneity, ^c - t-test for Independent variables, ^d – Approximate Z-test

treatments was not significantly different (p-value = 0.06). Majority of patients in Group B did not experience pain during cervical priming (34.21%) while majority of those in Group A reported the pain to be tolerable (34.21%). In terms of discomfort experienced during the period of cervical priming, 11 out of 19 of the patients in the Group B were very comfortable while only 5 out of 19 in Group A were very comfortable. Based on the scoring system using the Likert scale, there was no significant difference in the mean score of both treatment groups (p value = 0.199).

Table 8 shows the cost of cervical priming per millimeter of cervical dilatation. The cost of cervical priming was four times greater using intracervical

Dinoprostone (Php 205.29 per mm) compared to intravaginal evening primrose oil capsules (Php 51.15 per mm) with a p-value of 0.000 using both Mann-Whitney U and Kolmogorov-Smirnov tests.

Discussion

Operative hysteroscopy is a common gynecologic procedure nowadays and the hysteroscope commonly used is 9-10mm in diameter.⁶ It gives a panoramic visualization of the uterine cavity and direct biopsy of lesions, thus increasing diagnostic accuracy.¹² Complications encountered during the procedure are usually related to difficulty in cervical

Table 7. Patient acceptability.

| | Dinoprostone Gel (n = 19) | Evening Primrose Oil (n = 19) | p-value |
|--------------------------|------------------------------|----------------------------------|----------------------|
| Level of Pain | | | |
| Very painful | 0 (0.00%) | 0 (0.00%) | |
| Painful | 0 (0.00%) | 1 (2.63%) | |
| Mild pain | 3 (7.89%) | 2 (5.26%) | |
| Tolerable | 13 (34.21%) | 3 (7.89%) | |
| No pain | 3 (7.89%) | 13 (34.21%) | |
| Mean Score +/- SD | 4.0 +/- 0.577 | 4.47 +/- 0.905 | 0.06 ^a |
| Level of Discomfort | | | |
| Very uncomfortable | 0 (0.00%) | 0 (0.00%) | |
| Uncomfortable | 1 (2.63%) | 1 (2.63%) | |
| Neutral | 4 (10.53%) | 1 (2.63%) | |
| Comfortable | 9 (23.68%) | 6 (15.79%) | |
| Very comfortable | 5 (13.16%) | 11 (28.95%) | |
| Mean Score +/- SD | 3.95 +/- 0.848 | 4.42 +/- 0.878 | 0.09 ^a |
| Patient Complaints | | | |
| Bleeding | 1(5.26%) | 1(5.26%) | 1.000 |
| Cramping | 16(84.21%) | 0 | <0.001 ^{*b} |
| Vaginal discharge | 0 | 7(36.8%) | <0.001 ^{*b} |

* significant at 5%, a – p-value from t-test for Independent variables,
b – p-value from Chi Square test

Table 8. Cost (PhP) of cervical priming per millimeter of cervical dilatation.

| Cost per mm dilatation | Dinoprostone gel | Evening primrose oil capsule | p-value |
|------------------------|------------------|------------------------------|-----------|
| | | Php 205.29 | Php 51.15 |

* significant at 5%, a – p-value from Mann-Whitney U test

dilatation which includes cervical laceration, creation of false passage, uterine perforation and hemorrhage. The incidence of these complication can be significantly reduced if the cervix is ripened before the hysteroscopic procedure.⁶ Hence several cervical ripening agents have been suggested such as Evening Primrose oil and Dinoprostone gel.

This study aims to compare the efficacy of Dinoprostone gel versus Evening Primrose Oil in cervical ripening prior to operative hysteroscopy and to compare the surgeon and patient's acceptability of the two agents.

The study population in both groups consisted mostly of premenopausal patients with mean age of 41, with no history of any uterine surgery, who presented with abnormal uterine bleeding and underwent hysteroscopic polypectomy.

The patients in both Dinoprostone gel group and Evening Primrose Oil were mostly multiparous women who underwent vaginal deliveries.

The initial cervical dilatation was significantly greater for the Dinoprostone gel group ($5.63 \pm 1.30\text{mm}$) compared to the Evening Primrose Oil group ($4.21 \pm 1.18\text{mm}$). This is mainly due to the proven ability of prostaglandin to produce local cervical effects which includes softening, effacement and dilatation. The exact mechanism of action may be associated with collagen degradation caused by secretion of the enzyme collagenase as a partial response to locally administered dinoprostone.¹³

The difference in the amount of time spent to be able to insert the Hegar's dilator 10mm after initial cervical dilatation were not statistically significant between the two groups. This may be attributable to the production of prostaglandin derivatives which is known to cause cervical softening.

Three patients in the Dinoprostone gel group and four patients in the Evening Primrose Oil group had minimal bleeding during the process of cervical dilatation using Hegar's dilators. However, no significant amount of bleeding necessitating surgical

repair occurred. The patients were asymptomatic on their post-operative follow-up.

The results showed that there were more patients who have tolerable pain on application of the cervical priming agent for the Dinoprostone gel group compared to Evening Primrose Oil group which showed to pain at all. This is mainly due to the difference in the route of administration of the two agents. Those in the Dinoprostone gel group had to undergo speculum insertion, in order for the investigator to be able to accurately apply the gel intracervically, while Evening Primrose Oil capsules were placed intravaginally. It was also noted that majority of the patients from Dinoprostone gel group complained of pelvic cramping which is a common side effect of this agent. Most patients in the Evening Primrose Oil were pain-free during application and were very comfortable during the period of cervical priming.

Conclusion

This randomized controlled study comparing the efficacy of Dinoprostone gel and Evening Primrose Oil capsule showed that both were equally effective in dilating the cervix prior to operative hysteroscopy. Nevertheless, Evening primrose oil may be superior and acceptable due to reduced cost (10 capsules cost Php300 vs Php1,000 for each Dinoprostone gel), patient convenience and acceptability (pain-free during application and period of cervical priming), and ease of administration (it can be inserted by the patient herself).

The use of Evening Primrose oil (6 capsules 6 hours prior and 4 capsules 1 hour prior) is a relatively cost-effective as well as inexpensive and easy to use regimen that can be recommended to patients undergoing operative hysteroscopy to reduce the risk of complications and to facilitate cervical dilatation.

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