Comparing the effects of vaginal and oral evening primrose oil on cervical ripening and labor progress among primiparous women

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Background & Aim: Evening primrose is a medicinal plant with potential effects on labor. This study aimed to compare the effects of vaginal and oral evening primrose oil on cervical ripening and labor progress among primiparous women.

Methods & Materials: This single-blind randomized clinical trial was conducted in 2020. Participants were 126 pregnant women with a gestational age of 39 weeks purposively selected from the obstetrics and gynecology ward of Valiasr hospital, Bafgh, Iran, and randomly allocated to vaginal evening primrose oil, oral evening primrose oil, and a control group. Participants in the vaginal evening primrose oil and the oral evening primrose oil groups received one 1000-mg evening primrose oil capsule per twelve hours for one whole week through the vaginal and the oral routes, respectively. The Bishop score and pregnancy outcomes were measured when participants referred to the study setting with labor pains.

Results: After the intervention, the Bishop score in both intervention groups was significantly greater than the control group (P=0.001). The length of the second stage of labor in the vaginal evening primrose oil group was significantly shorter than the control group (P=0.009). There were no significant differences among the groups respecting the time interval between hospital admission and delivery (P=0.21), 1 and 5-minute Apgar scores (P=0.83), and (P=0.37), need for induction (P=0.26), and type of delivery (P=0.26).

Conclusion: Vaginal and oral evening primrose oil administrations significantly positively affect cervical ripening. The Bishop score and vaginal evening primrose oil significantly positively affect the length of the second stage of labor.

Introduction

Labor is the most prevalent midwifery emergency and requires different changes in the functions of the uterine and the cervix (1). Cervical ripening (CR) is a key step in labor that happens in the last weeks of pregnancy (2). CR is a complex process resulting from physical softening, effacement, and dilation of the uterine and the cervix (2, 3). Cervical softening is caused by increased vascularity, hypertrophy, cellular hyperplasia, and progressive structural changes in the extracellular matrix (4). The relaxin hormone regulates myometrial and cervical relaxation by modifying cellular matrix components (5, 6). After CR, strong uterine contractions cause cervical opening (2).

CR has many positive outcomes and prevents perinatal injuries such as severe perineal injuries (7). Contrarily, poor CR is associated with many different adverse consequences such as prolonged labor, fetal distress, excessive bleeding, infection, and increased need for medical interventions such as Cesarean section, particularly among primiparous women (2, 8, 9). Therefore,
interventions for CR before labor induction are common to facilitate successful childbirth (10).

Currently, different pharmacological and non-pharmacological strategies are used for CR. These strategies include prostaglandin therapy, catheter insertion, membrane stripping, and acupuncture (11). However, these strategies are usually associated with fetal and maternal complications (2). According to the studies along with their positive effects, medication-based therapies for CR also have adverse effects. These complications include perinatal and postnatal bleeding, prolonged labor, excessive stimulation of the uterus, fetal distress and injuries, nausea, vomiting, and fever (2, 12-14). Continuous professional training, especially in medicine, is changing and developing (15). Examples of medicinal plants used for facilitating CR and labor are chamomile (16), peganum harmala (17), flixweed (18), castor oil (19), saffron (20), and Evening primrose (21, 22).

Evening primrose is a two-year plant from the Onagraceae family and is native to North America (23, 24). Onager oil, extracted from the seeds of this plant, includes essential fatty acids such as gamma-linolenic acid (70%-74%), linoleic acid (8%-10%), oleic acid (6%-7%), and palmitic acid (6%-7%) (25, 26). Studies showed that fatty acids in Oenothera biennis facilitate prostaglandins synthesis, which is among the main stimuliants of the cervix and CR (24, 27). Evening primrose oil (EPO) is well-tolerated by its users and is associated with mild side effects such as headache and gastric discomfort (15, 28, 29).

Previous studies reported contradictory results regarding the effects of Evening primrose on CR and labor induction. For example, a study reported that four vaginal EPO capsules during labor significantly increased the Bishop score and promoted CR (30). However, another study showed that vaginal EPO capsules did not significantly affect labor duration and labor pain onset (31). Moreover, a study on the candidates for hysterosalpingography (Hysterosalpingography evaluates the shape of the uterus and checks whether the fallopian tubes are open) reported that oral EPO capsules significantly reduced preoperative and postoperative abdominal pain but had no significant effects on cervical dilation and length (32). These contradictory results highlight the importance of further studies to produce more decisive evidence regarding the effects of EPO on labor. The present study aimed to narrow this gap. This study aimed to compare the effects of vaginal and oral EPO on CR and labor progress among primiparous women.

Methods

Design

This single-blind randomized clinical trial was conducted in 2020. Participants were 132 primiparous women who were referred to the obstetrics and gynecology ward of Valiasr hospital, Bafgh, Iran, to receive perinatal care. They were purposively selected and randomly allocated to a vaginal EPO, an oral EPO, and a control group through block randomization with a block size of 6. Inclusion criteria were primiparity, low-risk pregnancy, gestational age of 39 weeks, cephalic presentation, singleton pregnancy, normal findings at nonstress test for fetal health assessment in the past 48 hours, and no use of other CR methods. Exclusion criteria were serious labor problems such as placental abruption or placenta previa and rupture of membrane. Withdrawal criteria were nausea and diarrhea due to EPO use, voluntary withdrawal from the study, irregular use of EPO for two consecutive days, and labor pain during the one-week course of the study intervention. With a confidence level of 0.95, a power of 0.80, a moderate effect size of 0.5, and an

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attrition rate of 20%, the sample size was calculated to be 44 per group.

Data collection

Data collection tools were a demographic questionnaire, a midwifery characteristics questionnaire, a fetal health assessment form, and the Bishop scoring system. The items of the midwifery characteristics questionnaire were on some questions about the mother (like body mass index, number of pregnancies, number of abortions, history of infertility, the first day of the last menstrual period, gestational age, expected date of delivery), some information about vaginal examination findings, (like membrane status), and some questions about time and cause of hospitalization, the time of delivery, labor duration, need for induction, type of delivery, neonatal gender, and 1- and 5-minute Apgar scores. The Bishop scoring system is a quantitative method for assessing CR and predicting the outcomes of labor induction. It has five items on cervical dilation, cervical effacement, cervical consistency, cervical position, and fetal station. Items are scored on a 0–3 scale; hence, the possible total Bishop score is 0–15. Scores 4 and lower show poor CR (1, 6).

Data were collected through interviews, observation, physical examination, and self-report methods.

Intervention

At the study's recruitment time, gestational age was determined based on the first-trimester ultrasound findings. Then, all eligible women underwent complete physical examination respecting vital signs, vaginal examination for determining Bishop score, and non-stress test to ensure fetal health. Afterward, the demographic and the midwifery characteristics questionnaires were completed for participants. Participants in the control group just received the initiation of the induction after 39 complete weeks. Participants in the vaginal and oral EPO groups were provided with thirty 1000-mg EPO capsules. They were instructed to receive one capsule per twelve hours for one whole week through the vaginal and the oral routes, respectively. In the vaginal EPO group, participants were instructed to make three holes on each capsule using a needle before its vaginal use and the rest thirty minutes after its use. All participants in the three study groups were asked to avoid sexual relationships, laxatives, herbal or synthetic products, or any intervention for inducing labor during the one-week course of the study intervention. They were also provided with the fetal movement documentation form and were instructed how to count and document fetal movements. Moreover, they were given the second author's phone number and asked to call her in case of at least three painful uterine contractions in ten minutes, reduced fetal movements, and any bloody or non-bloody vaginal secretions. The total duration of sampling was nine months.

After the intervention and at the time of labor pains, participants re-underwent physical examinations for vital signs, fetal heart rate, fetal health (through the non-stress test), and CR (through the Bishop scoring system). Examinations and assessments were performed by the second author and two research assistants. The assistants were two midwives from the study setting with a midwifery work experience of more than fifteen years. The second author and the two assistants performed the vaginal examination for inter-rater reliability assessment and scored cervical dilation and effacement for five dilation and effacement anatomical models (Effacement is when the cervix thins, shortens and softens to open the vaginal canal for childbirth). We used mannequins to establish the relationship between midwives' vaginal exams, and they demonstrated cervical dilation and effacement on mannequins. The inter-rater correlation
A total of 132 primiparous women were recruited for the study. Six participants were excluded due to placental abruption (n=1), irregular use of EPO capsules (n=3), and voluntary withdrawal (n=2), and 126 participants completed the study (Figure 1). The age mean was 22.95±3.413 years in the vaginal EPO group, 23.65±4.197 years in the oral EPO group, and 23.38±5.05 years in the control group.

**Results**

A total of 132 primiparous women were recruited for the study. Six participants were excluded due to placental abruption (n=1), irregular use of EPO capsules (n=3), and voluntary withdrawal (n=2), and 126 participants completed the study (Figure 1). The age mean was 22.95±3.413 years in the vaginal EPO group, 23.65±4.197 years in the oral EPO group, and 23.38±5.05 years in the control group.
The effects of evening primrose oil on labor

The mean body mass index was 24.03±2.86 in the vaginal EPO group, 24.37±8.24 in the oral EPO group, and 24.28±9.23 in the control group. Most participants aged 20–40 years (78%) were housewives (66%), had academic degrees (79%), and had good financial status (53%). (Table 1).

| Table 1. Comparisons among the study groups regarding participants' demographic and midwifery characteristics |
|-------------------------------------|-------------------|-------------------|-------------------|-------------------|
| Characteristics                      | Vaginal EPO (N=43) | Oral EPO (N=41)   | Control (N=42)    | P-value           |
| Age (Years)                          | 22.95±3.413       | 23.65±4.197       | 23.38±5.05       | 0.753*            |
| Body mass index                      | 24.03±2.86        | 24.37±8.24        | 24.28±6.23       | 0.965**           |
| Educational level                    |                   |                   |                   |                   |
| Illiterate                           | 4 (9.3)           | 3 (7.3)           | 2 (4.5)          | 0.326*            |
| Diploma and lower academic           | 5 (11.7)          | 3 (7.3)           | 12 (27)          | 0.338*            |
| Academic                             | 34 (79)           | 35 (85.4)         | 28 (68.5)        |                   |
| Occupation                           |                   |                   |                   |                   |
| Housewife                            | 29 (67.4)         | 24 (58.5)         | 31 (73.8)        | 0.998**           |
| Employed                             | 14 (32.6)         | 17 (41.5)         | 11 (26.2)        |                   |
| Financial status                     |                   |                   |                   |                   |
| Good                                 | 20 (46.5)         | 24 (58.5)         | 22 (54.8)        |                   |
| Relatively good                      | 18 (41.9)         | 11 (26.8)         | 9 (21.4)         | 0.214*            |
| Poor                                 | 5 (11.6)          | 6 (14.6)          | 11 (23.8)        |                   |
| Gestational age                      |                   |                   |                   |                   |
| Before intervention                  | 38.91±0.49        | 38.74±0.45        | 38.73±0.61       | 0.33*             |
| After intervention                   | 39.87±1.39        | 39.85±0.70        | 39.86±0.77       | 0.99*             |
| Number of pregnancies                |                   |                   |                   |                   |
| 1                                   | 26 (60.5)         | 23 (56.1)         | 31 (73.8)        | 0.392**           |
| 2                                   | 13 (30.2)         | 16 (39)           | 9 (21.4)         |                   |
| 3                                   | 4 (9.3)           | 2 (4.9)           | 2 (4.8)          |                   |
| Number of abortions                  |                   |                   |                   |                   |
| 0                                   | 23 (53.4)         | 25 (60.97)        | 28 (66.66)       |                   |
| 1                                   | 18 (37.2)         | 13 (31.7)         | 11 (26.19)       | 0.34**            |
| 2                                   | 5 (9.3)           | 3 (7.31)          | 2 (4.8)          |                   |
| History of infertility               |                   |                   |                   |                   |
| Yes                                 | 7 (16.3)          | 8 (19.5)          | 5 (11.9)         | 0.635*            |
| No                                  | 36 (83.7)         | 33 (80.5)         | 37 (88.1)        |                   |

*: The results of the one-way analysis of variance; **: The results of the Fisher's exact test; ^: The results of the Chi-square test

The pretest Bishop mean score in all three groups was 2–4, with no significant difference among the groups (P= 0.467). However, the post-test Bishop mean score in both vaginal and oral EPO groups was significantly greater than the control group (P=0.001), and there was no significant difference between the intervention groups (P>0.05) (Table 2). It is while, there were no significant differences among the groups in terms of the mean values of the cervical dilation (P= 0.28) and effacement (P= 0.14), and fetal station items of the Bishop scoring system (P= 0.33). Nevertheless, the intragroup differences in the mean scores of the cervical consistency (P= 0.02) and the cervical position items were significant (P< 0.001) (Table 3). The prevalence rates of soft cervical consistency and posterior cervical position were respectively 67.4% and 7% in the vaginal EPO group, 68.3% and 7.3% in the oral EPO group, and 31% and 40.5% in the control group.

There was a significant difference among the groups in terms of the length of the second stage of labor (P= 0.033). This study showed that the length of the second stage of labor in the vaginal EPO group was significantly less than in the control group (P= 0.009). There were no significant differences between the oral EPO and the control groups (P= 0.203) and between the vaginal EPO and the oral EPO groups (P= 0.172) (Table 2).

Comparisons between groups did not show statistically significant differences among the groups in terms of the time interval between hospital admission and delivery (P= 0.21), 1-minute Apgar score (P= 0.832), 5-minute Apgar score (P= 0.372), type of delivery (P= 0.21), and the need for labor induction (P= 0.26) (Table 2).
Prostaglandin E2 improves CR precursor of prostaglandin E. In agreement with our findings, some previous studies showed the significant positive effects of vaginal EPO on cervical softening, CR (33), and the Bishop score (34). Gamma-linolenic acid, found in EPO, is a precursor of prostaglandin E2 (24, 27). Prostaglandin E2 improves CR (35) by increasing submucosal fluid, modifying collagen binds and glycosaminoglycans, and increasing myometrium sensitivity to oxytocin (2). Contrary to our findings, some studies reported the insignificant effects of vaginal and oral EPO on CR. Vaginal application of Evening primrose oil capsules in pregnant women from 37 weeks of gestation for one week (31) and its oral use in pregnant women with Bishop Score <4, from 40 weeks of gestation, every 12 hr (36) and for one week, and also for two days in women undergoing hysterosalpingography (32) did not increase Bishop and CR scores. This contradiction is attributable to the differences among the studies in terms of the EPO administration route and CR assessment method.

### Table 2. Comparisons among the study groups regarding pregnancy outcomes

| Outcomes | Vaginal EPO (N=43) | Oral EPO (N=41) | Control (N=42) | P-value |
|----------|--------------------|----------------|----------------|---------|
| The Bishop score | | | | |
| Before | 2.86±1.08 | 3.1±0.88 | 2.88±0.91 | 0.467* |
| After | 7.86±1.24 | 6.85±1.62 | 5.62±1.62 | <0.001** |
| P value | <0.001** | ≤0.001** | ≤0.001** |
| Apgar score | | | | |
| 1-minute | 8.63±1.41 | 8.85±0.35 | 8.86±0.41 | 0.832* |
| 5-minute | 9.76±1.52 | 9.98±0.15 | 10 | 0.372* |
| Type of delivery | | | | |
| Normal vaginal | 35 (81.4) | 36 (87.8) | 31 (73.8) | 0.267** |
| Cesarean section | 8 (18.6) | 5 (12.2) | 11 (26.2) |
| Labor induction | | | | |
| Yes | 24 (55.8) | 29 (72.5) | 28 (68.29) | 0.26** |
| No | 19 (44.2) | 12 (27.5) | 14 (31.71) |
| Admission–delivery time interval | 6.01±2.77 | 6.86±2.98 | 7.25±3.97 | 0.21* |
| Length of the second stage of labor | 40.83±20.96 | 48.71±28.96 | 56.18±21.78 | 0.033* |

*: The results of the one-way analysis of variance; **: The results of the paired-sample t-test; ^: The results of the Kruskal-Wallis test; ^^: The results of the Chi-square test

### Table 3. Comparisons among the study groups regarding the post-test mean scores of the Bishop System items

| Items | Vaginal EPO (N=43) | Oral EPO (N=41) | Control (N=42) | P-value |
|-------|--------------------|----------------|----------------|---------|
| Cervical dilation | 3.98±1.01 | 3.66±1.13 | 3.57±1.5 | 0.28^ |
| Cervical effacement | 46.28±10 | 42.44±9.42 | 41.67±14.29 | 0.14^ |
| Fetal station | 2.16±0.72 | 2.12±0.6 | 1.95±0.73 | 0.33^ |
| Cervical position | | | | |
| Posterior | 3 (7) | 3 (7.4) | 17 (40.5) | | |
| Mid-position | 28 (65.1) | 32 (78) | 23 (54.7) | | |
| Anterior | 12 (27.9) | 6 (14.6) | 2 (4.8) | | <0.001** |
| Cervical consistency | | | | |
| Firm | 1 (2.3) | 2 (4.9) | 6 (14.3) | | |
| Medium | 13 (30.3) | 11 (26.8) | 23 (54.7) | | |
| Soft | 29 (67.4) | 28 (68.3) | 13 (31) | | 0.02** |

*: The results of the one-way analysis of variance; **: The results of the Chi-square test

### Discussion

This study compared the effects of vaginal and oral EPO on CR and labor progress. Findings revealed that the Bishop score in both intervention groups was significantly greater than the control group, but the difference between the intervention groups was insignificant. Moreover, findings showed that one-week use of vaginal and oral EPO capsules significantly improved cervical consistency and cervical position. In agreement with our findings, some previous studies showed the significant positive effects of vaginal EPO on cervical softening, CR (33), and the Bishop score (34). Gamma-linolenic acid, found in EPO, is a precursor of prostaglandin E2 (24, 27). Prostaglandin E2 improves CR (35) by increasing submucosal fluid, modifying collagen binds and glycosaminoglycans, and increasing myometrium sensitivity to oxytocin (2).
Our findings also indicated that while there was no significant difference among the groups in terms of the time interval between hospital admission and delivery, the length of the second labor stage in the vaginal and the oral EPO groups was significantly less than in the control group. The greater Bishop Score and shorter labor length in both intervention groups in the present study imply the significant positive effects of EPO on CR. The significant effects of EPO on the length of the second labor stage are probably due to its prostaglandin-like effects, which increase the efficiency of uterine contractions and pelvic blood flow. Contrary to our findings, a study reported that while Single-dose EPO in post-term pregnancy significantly shortened the latent phase of labor, it had no significant effects on the active labor phase and labor progress (24). Another study also showed that daily vaginal EPO from 37 weeks of pregnancy for one week had no significant effects on labor length (31). The contradiction between these studies' findings and the present study's findings may be due to the differences among these studies in the time of intervention and amount of medication.

No adverse effect of using Evening primrose oil was observed in the present study, and also, no significant difference was observed among the three groups in terms of the type of delivery, the need for induction, and 1- and 5-minute Apgar scores. A review study into the effects of vaginal and oral EPO in Iran reported that EPO was well-tolerated by pregnant women and had mild side effects such as headache and gastric discomfort (37). However, a study in the United States found that EPO had no significant positive effects on pregnancy and delivery duration, and on the contrary, prolonged labor phase for three hours compared with a control group and was associated with complications such as premature rupture of membranes and greater need for labor induction and instrumental delivery (Dove). A review study also reported that EPO could cause some side effects (38). The side effects of EPO in these studies might have been due to the use of EPO at high doses and for long periods of time.

The absence of a double-blind study and an accurate time recording in the first step of the delivery process in samples, as they did not refer to the maternity ward since the onset of labor pains, where the limitations of the present study.

**Conclusion**

Both vaginal and oral EPO significantly increase the Bishop score, while just vaginal EPO significantly shortens the second stage of labor. Therefore, vaginal EPO is recommended as an inexpensive method for CR. Of course, further studies are still needed to determine the most appropriate EPO administration dose, route, and time.

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**Conflict of Interest**

The authors declare no conflict of interest.

**References**

1. Vitner D, Bleicher I, Kadour-Peero E, Borenstein-Levin L, Kugelman A, Sagi S, Gonen R. Induction of labor versus expectant management among women with macrosomic neonates: a retrospective study. The Journal of
Maternal-Fetal & Neonatal Medicine. 2020 Jun 2;33(11):1831-9.
2. Dashe JS, Bloom SL, Spong CY, Hoffman BL. Williams obstetrics. McGraw Hill Professional; 2018 Jun 1.
3. Luesley DM, Kilby M, editors. Obstetrics & Gynaecology: An evidence-based text for MRCOG. CRC Press; 2016 Mar 30.
4. Myers KM, Feltoch H, Mazza E, Vink J, Bajka M, Wapner RJ, Hall TJ, House M. The mechanical role of the cervix in pregnancy. Journal of Biomechanics. 2015 Jun 25;48(9):1511-23.
5. Soh YM, Tiwari A, Mahendroo M, Conrad KP, Parry LJ. Relaxin regulates hyaluronan synthesis and aquaporins in the cervix of late pregnant mice. Endocrinology. 2012 Dec 1;153(12):6054-64.
6. Wormer, Kelly C., Amelia Bauer, and Ann E. Williford. "Bishop Score." [Updated 2021 Sep 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470368/
7. Jahani Shourab N, Mirteimouri M, Latifnejad Roudsari R. A case series of severe perineal lacerations during normal childbirth. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2018;21(8):103-14.
8. Naeiji Z, Naghshvarian N, Mirzamoradi M, Sotudeh S, Moridi A. Efficacy and safety of oral hyoscine used for outpatient cervical ripening among primiparous women with term pregnancy. International Journal of Gynecology & Obstetrics. 2020 Sep;150(3):335-9.
9. Levine LD. Cervical ripening: Why we do what we do. Semin Perinatol. 2020 Mar;44(2):151216.
10. K Kim HI, Choo SP, Han SW, Kim EH. Benefits and risks of induction of labor at 39 or more weeks in uncomplicated nulliparous women: A retrospective, observational study. Obstetrics & Gynecology Science. 2019 Jan 1;62(1):19-26.
11. Pierce S, Bakker R, Myers DA, Edwards RK. Clinical insights for cervical ripening and labor induction using prostaglandins. American Journal of Perinatology Reports. 2018 Oct;8(04):e307-14.
12. Rath W, Kehl S. The renaissance of transcervical balloon catheters for cervical ripening and labour induction. Geburtshilfe und Frauenheilkunde. 2015 Nov;75(11):1130-9.
13. Stephenson ML, Wing DA. A novel misoprostol delivery system for induction of labor: clinical utility and patient considerations. Drug Design, Development and Therapy. 2015;9:2321-7.
14. Tabasi Z, Mesdaghinia E, Abedzadeh-Kalaghroudi M, Sehat M, Panahandehe A. Comparing the effects of vaginal misoprostol, laminaria, and extra amniotic saline infusion on cervical ripening and induction of labor. Obstetrics & Gynecology Science. 2020 Mar 30;63(3):261-9.
15. Kam PC, Barnett DW, Douglas ID. Herbal medicines and pregnancy: A narrative review and anaesthetic considerations. Anaesthesia and Intensive Care. 2019 May;47(3):226-34.
16. Gholami F, Samani LN, Kashanian M, Naseri M, Hosseini AF, Nejad SA. Onset of labor in post-term pregnancy by chamomile. Iranian Red Crescent Medical Journal. 2016 Nov;18(11):e19871.
17. TORK ZS, Dasumi S, Tansaz M, Akbarzadeh A. The effects of peganum harmala smoke cervical ripening, initiation and outcome of labor. Medical History Journal, 8(27): 151-77. [Persian]
18. Zorzan M, Zucca P, Collazuol D, Peddio S, Rescigno A, Pezzani R. Sisymbrium officinale, the plant of singers: A review of its properties and uses. Planta Medica. 2020 Mar;86(05):307-11.
19. Kahnamoyiadagm F, Aghamohammadi M, Rostamejad M. The effect of castor oil on the induction of labor: A clinical trial. Nursing And Midwifery Journal. 2014 Aug 10;12(5):348-53.
20. Darooneh T, Rashidi Fakari F, Moattar F, Nasiri M, Delpak-Yeganesh S, Esmaeili S, Ozgoli G. Effect of Crocus sativus (Saffron) on Cervical Ripening and Progress of Labor in Primiparous Term Women: A Randomized Double-Blind Placebo-Controlled Trial. International Journal of Pediatrics. 2020 Sep 1;8(9):12105-15.
21. Tanchuling MP. Comparison of evening primrose oil and dinoprostone in labor induction
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of term singleton pregnancies. Special Issue: Abstracts of the XXII FIGO World Congress of Gynecology & Obstetrics. International Journal of Gynecology and Obstetrics. 2018;143(S3):229-30.

22. Pineda ME. Effectiveness of intravaginal evening primrose oil as a cervical ripening agent in nulliparous women: A double blinded randomized controlled clinical trial. In 25th Asian & Oceanic Congress of Obstetrics & Gynaecology 2017 Jun (pp. 15-18).

23. Zand Vakili F, Zare SH, Rahimi K, Riahi M. The effect of Evening Primrose Oil on Changes in Polycystic Ovary Syndrome Induced by Estradiol Valerate in Rat. Armaghane Danesh. 2018 Feb 10;22(6):714-24. [Persian]

24. Shahali S, Khatami F, Abbaspoor Z, Gh eraqian B. The effect of vaginal evening primrose capsule on cervical ripening in nulliparous women with post-term pregnancy: A clinical trial. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2018;21(8):30-8. [Persian]

25. Khorshidi M, Zarezadeh M, Moradi Moghaddam O, Emami MR, Kord-Varkaneh H, Mousavi SM, Alizadeh S, Heshmati J, Olang B, Aryaeian N. Effect of evening primrose oil supplementation on lipid profile: A systematic review and meta-analysis of randomized clinical trials. Phytotherapy Research. 2020 Oct;34(10):2628-38. [Persian]

26. Nikoomazhab S, Latifi SM, Honarmandpour A, Abedi P. Effects of evening primrose oil on prevention of postpartum grief in primiparous women: A clinical double-blind randomized controlled trial. Iranian Journal of Obstetrics, Gynecology and Infertility. 2018;20(11):64-73. [Persian]

27. Pizzorno JE, Murray MT, Joiner-Bey H. The Clinician's Handbook of Natural Medicine E-Book. Elsevier Health Sciences; 2016 Jan 5.

28. Mahboubi M. Evening primrose (Oenothera biennis) oil in management of female ailments. Journal of Menopausal Medicine. 2019 Aug 1;25(2):74-82.

29. Shayan A, Ahmadinia H, Masoumi SZ, Shobeiri F, Moradkhani S, Sourseinzhad H. The Effect of Evening Primrose and vitamin B6 on premenstrual syndrome: A randomized clinical trial. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2019;21(12):37-48.

30. Nonette DN. The effectiveness of evening primrose oil gel capsule as a cervical ripening agent during labor induction as measured by bishop score on term singleton pregnant patients. Philippine Journal of Obstetrics and Gynecology. 2017;41(2):1-4.

31. Hashemnejad M, Ataei M, Modarresi M, Forutan F. Investigating the effect of Primrose Capsule (Primula Flower Oil) on cervix preparation and commencement of child delivery pains. Revista Latinoamericana de Hipertensión. 2019;14(1):119.

32. Nia SS, Safi F, Shoukrpour M, Kamali A. An investigation into the effect of evening primrose in dilatation of cervix and pain during and after hysterosalpingography. Journal of Medicine and Life. 2019 Jul;12(3):284-9.

33. Girlie VB. The efficacy of evening primrose oil as a cervical ripening agent for gynecologic procedures: A single-blinded, randomized controlled trial. Philippine Journal of Obstetrics and Gynecology. 2015:25-8.

34. Najafi M, Loripoor M, Saghafi Z, Kazemi M. The effect of vaginal evening primrose on the Bishop score of term nulliparous women. Nursing Practice Today. 2019 Oct 1;6(4):202-11.

35. Hiersch L, Borovich A, Gabbay-Benziv R, Maimon-Cohen M, Aviram A, Yogev Y, Ashwal E. Can we predict successful cervical ripening with prostaglandin E2 vaginal inserts?. Archives of Gynecology and Obstetrics. 2017 Feb;295(2):343-9.

36. Kalati M, Kashanian M, Jahdi F, Naseri M, Haghani H, Sheikhsansari N. Evening primrose oil and labour, is it effective? A randomised clinical trial. Journal of Obstetrics and Gynaecology. 2018 May 19;38(4):488-92.

37. Faghani Aghoozi M, Fayazi S, Mohammadi S, Tehranian N, Amerian M. The effects of evening primerose on clinical obstetrics of Iran: a review study. Scientific Journal of Nursing, Midwifery and Paramedical Faculty. 2019 Dec 10;5(3):15-28.

38. Esmaeilzadeh M, Moradi B. Medicinal herbs with side effects during pregnancy-An evidence-based review article. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2017;20:9-25. [Persian]