

## Original Research Article

# Comparison of the effect of vaginal misoprostol alone and in combination with evening primrose capsules on the course of labor in pregnant women candidates for termination of pregnancy

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## ABSTRACT

**Background:** Induction of labor at any time before the spontaneous onset of labor is indicated when the benefits of termination of pregnancy for the mother and fetus outweigh the benefits of continued pregnancy. The aim of this study was to compare the effect of vaginal misoprostol alone and in combination with evening primrose capsule on the course of labor in pregnant women candidates for termination of pregnancy.

**Methods:** In this double-blind randomized clinical trial, 30 pregnant women were candidates for termination of pregnancy. At the time of referral, the examination was performed to calculate the bishop score (primary outcome) and the partograph was recorded and plotted once every hour until the end of labor. Length of active phase of labor (from dilatation 3-6 cm to birth), type of labor, Apgar score of the first and fifth minute of the baby and volume of postpartum hemorrhage and pain intensity every 30 minutes was recorded in two groups for up to 2 hours using a ruler.

**Results:** The mean length of the latent labor phase in the misoprostol and evening primrose groups was  $9.07 \pm 0.96$  and in the misoprostol group was  $10.13 \pm 0.83$  hours and this difference was significant. There was no significant difference in bishop score between the two groups at the beginning of the study but after the intervention was significant.

**Conclusions:** Our study showed that using evening primrose oil capsule instead of misoprostol is effective in induction of labor.

**Keywords:** Evening primrose oil capsule, Induction of labor, Misoprostol

## INTRODUCTION

A favorable cervix and uterine contractions are two essential factors in childbirth.<sup>1</sup> The condition of the cervix or its suitability is important for the success of labor induction.<sup>2</sup> Favorable cervix or cervical softening refers to the shortening, effacement, and dilatation of the cervix, which naturally begins at the end of the third trimester before labor.<sup>3</sup> To prepare the cervix, two methods, drug and mechanical, are used. Unfortunately, in many cases where there is an indication for induction of labor, the

cervix is not in an optimal state. As the desired state or Bishop's score decreases, the amount of unsuccessful induction of labor increases progressively. Therefore, a significant amount of research has been directed towards inventing various methods for preparing the cervix before stimulating uterine contractions. According to research purposes, a Bishop score of four or less is used to identify an unfavorable cervix, and this criterion may be an indication for preparation of the cervix. Various methods have been devised to prepare the cervix in indicated cases of labor induction, one of which is pharmacological

methods, which uses pharmaceutical forms including prostaglandins. This work can be done with different types of prostaglandins, most commonly prostaglandin E2 (dinoprostone) in the form of gel or suppository, or prostaglandin E1 (misoprostol) in the form of tablets orally or vaginally. These prostaglandins can initiate uterine contractions throughout pregnancy and can also be used to terminate pregnancy.<sup>4-5</sup> Misoprostol is widely used for induction of labor in the second trimester, softening of the cervix before using the device, curettage, hysteroscopy, therapeutic abortions, endometrial biopsy, early termination of pregnancy, treatment of incomplete abortion or missed abortion, treatment of postpartum bleeding. Term birth control is used.<sup>6</sup> Currently, vaginal misoprostol is commonly used in cases of the need for induction in cases of unfavorable cervix, and its risks and complications include excessive stimulation of the uterus, increased uterine contractions, meconium excretion, and meconium aspiration, which have been seen in cases of misoprostol use and the rate of cesarean delivery also increases due to excessive stimulation of the uterus. Previous studies have shown that the sublingual and oral methods of misoprostol administration produce a higher plasma concentration compared to the vaginal method, and the duration of induction to delivery in the sublingual method is shorter than other methods of misoprostol administration. In addition, the sublingual method, like the vaginal method, is effective in preparing the cervix, and due to the prevention of direct effects on the cervix, it may reduce the risk of excessive uterine stimulation. Also, among the benefits of using sublingual misoprostol is its simple administration method, greater patient freedom and less need for repeated vaginal examinations. The results of various studies have shown that prostaglandins may be associated with adverse maternal and fetal outcomes due to the creation of uterine contractions, for this reason, it is still not considered a safe and secure method. As a result, it is ideal to use agents to induce and prepare the cervix, which cause changes in the cervix with minimal adverse effects on the mother and the fetus.<sup>7-9</sup> Evening primrose belongs to the plant family (*Oenothera biennis*) and its seeds contain two essential fatty acids (70% linoleic acid and 8-14% gamma linoleic acid) which facilitates the synthesis of prostaglandin E1. Therefore, this composition contains prostaglandin effects.<sup>10-12</sup> Polyunsaturated fatty acids (PUFA) are a natural precursor of prostaglandins, and linoleic acid is the most important PUFA.<sup>13</sup> Western primrose oil contains the natural extract of this plant and contains a large amount of PUFA, and more importantly, gammalinoleic acid, which directly converts PUFA into prostaglandins, is present in this oil.<sup>14</sup> Also, the effect of gamma linoleic acid dietary supplements on prostoglandin biosynthesis in animals and humans has been determined.<sup>15,16</sup> Studies have shown that when evening primrose oil is used, a significant increase in gammalinoleic acid is observed in the blood.<sup>17</sup> Despite the studied effects of evening primrose oil diet on prostaglandin precursor levels in serum and the well-established role of prostaglandins in cervical matrix

regeneration, limited clinical studies have been conducted on the extract of this plant during pregnancy, labor and delivery complications. Due to the limited number of similar studies and also the contradiction in the results of these limited studies and also due to the importance of induction of labor in line with the policy of the Ministry of Health and Medicine to emphasize the reduction of cesarean births, which is currently one of the country's health problems, the study The present study was conducted with the aim of comparing the effect of evening primrose capsule alone and in combination with vaginal Misoprostol on the course of labor in pregnant women candidates for termination of pregnancy in Alavi Hospital, Ardabil.<sup>18-23</sup>

## METHODS

This randomized clinical trial study was conducted on 30 primiparous and multiparous pregnant women (less than 5 cases) with a gestational age of 38-42 weeks who referred during Sep 2022 to April 2023 to Alavi Hospital in Ardabil city and were candidates for termination of pregnancy. The sampling method was random samplin and the necessary sample size was calculated based on formula in 95% confidence interval and power 80%. Women were randomly divided into two groups of 15 people. One group was given a 1000 mg evening primrose vaginal capsule along with 25 µg of vaginal Misoprostol and the other group was given a concrete vaginal misoprostol tablet. In this double-blind study, both the patient and the researcher (female resident) were not aware of the drug administration protocol. At the time of the women's visit to terminate the pregnancy, an examination was performed to calculate the Bishop score (primary outcome) and a partograph was recorded and drawn once every hour until the end of delivery, and the secondary outcome included the duration of the latent phase of labor (from the time the contractions began to dilation 3 -6 cm), the length of the active phase of labor (from the time of dilation of 3-6 cm to the birth of the baby), the type of labor, the Apgar score of the first and fifth minutes of the baby and the amount of bleeding after delivery until the end of the labor phase based on blood pads and pain intensity in minutes were recorded every 30 minutes to 2 hours using a pain ruler in two groups. Women with singleton pregnancy, live fetus, fetal weight less than 4 kg, fluid index greater than 5 cm, normal fetal ECG, Bishop score less than 7, absence of labor pains in the mother were included in the study.

Women with rupture membranes, suspicion of fetal malformations, urgent need for delivery, sensitivity to prostaglandin and evening primrose (people with a history of seizures, people with a history of schizophrenia receiving phenothiazines, bleeding disorders or taking drugs that reduce blood clotting), drop in fetal heart rate, poor fetal condition and the presence of fetal disorders such as hydrocephalus were excluded from the study.

After collecting the data, it was coded in the statistical software spss version 21 using descriptive statistical methods in the form of tables and graphs and statistical indicators in the form of mean and standard deviation using analytical statistical methods in the form of using Independent t-test was performed for the variables of age, weight, gestational age, weight of babies, length of active and latent phase, Apgar scores for babies and Mann-Whitney for pain intensity variables and Bishop's score, as well as chi-square for qualitative variables. The significance level for all tests was  $p < 0.05$ . This study was approved from ethics committee of Ardabil University of Medical Sciences and with the clinical trial code IRCT20210113050028N2.

## RESULTS

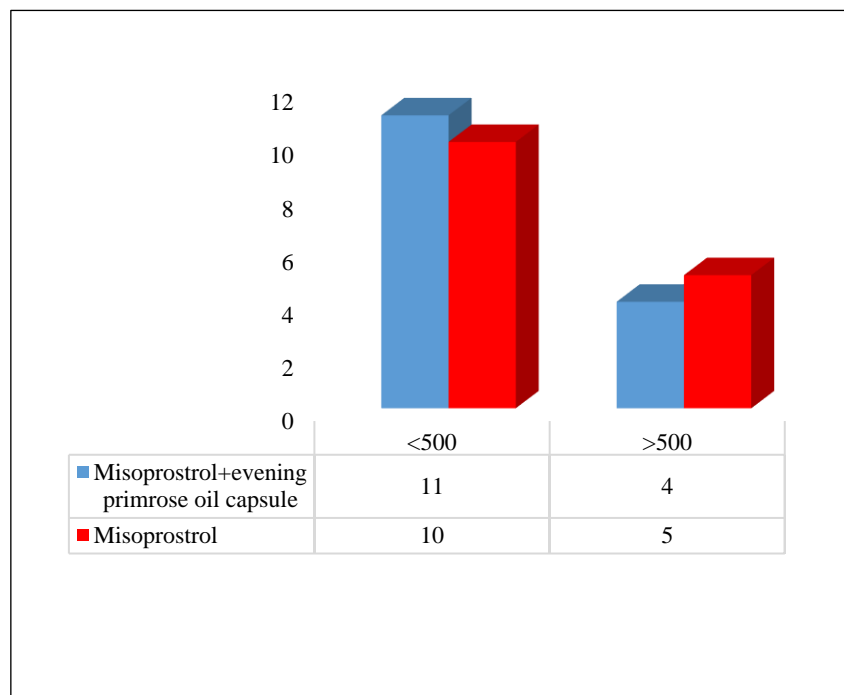
In this study, out of 32 patients included in the study, 2 patients (one due to lack of labor progress and one due to fetal tachycardia) were excluded from the study. The average age of pregnant women was  $27.07 \pm 4.48$  years (age range 18-38 years). Most of the women in both groups were in the age range of 21-30 years. In terms of age and weight, there was no statistically significant difference between the two groups. Also, there was no significant difference between newborn weight, gestational age, first and fifth minute Apgar score in two treatment groups (Table 1).

**Table 1: Comparison of statistical indicators of studied variables in treatment groups.**

Variables	Groups		P value
	Misoprostol (n=15)	Misoprostol+evening primrose oil capsule (n=15)	
Neonate weight (g)	3435±283	3420±336	0.81
Gestational age (week)	39.7±0.8	39.3±1.2	0.3
The length of the latent phase of labor (hour)	9.1±1	10.1±0.8	0.003
Apgar score at baseline	9.9±0.3	9	0.32
Apgar score at 5 min	10	10	1
Age of mothers (year)	26.6±4.4	26.2±4.3	0.8
Weight of mothers (kg)	69.1±10.6	67.1±10.3	0.75

**Table 2: Comparison of Bishop's score in treatment groups.**

Treatment group	Before studying	Two hours after the intervention	Four hours after the intervention	P-value
Misoprostol and evening primrose (n=15)	3	6	8	0.001*
Misoprostol (n=15)	3	5	7	0.001*
P value	0.8	0.021	0.026	



**Figure 1: Comparison of bleeding in the studied groups.**

In the misoprostol and evening primrose group (73.3%), 11 people and in the misoprostol group (66.7%) 10 people had a bleeding volume of less than 500 cc and there was no statistically significant difference in terms of bleeding (Figure 1).

In the misoprostol and evening primrose group (73.3%), 11 people had a natural delivery and (26.7%) 4 had a cesarean section, and in the misoprostol group (80%) 12 people had a natural delivery and (20%) 3 people had a cesarean section, and the difference in significance did not have.

## DISCUSSION

In this study, the average length of the latent phase of labor in the misoprostol and evening primrose group was less than the misoprostol group, and this difference was statistically significant. There was no significant difference in Bishop's score between the two groups at the beginning of the study. Bishop score after the intervention 2 and 4 hours after the intervention was significant between the two groups and it was higher in the mothers receiving misoprostol and evening primrose. Nowadays, the use of medicinal plants has attracted the attention of researchers due to the side effects and risks of chemical drugs, especially during pregnancy and after delivery.<sup>24</sup> Maghrib flower has more gammalinoleic acid than other plants, for this reason this plant is known as an important therapeutic agent in anti-inflammatory and pain effects.<sup>25</sup> Cervix not being ready before induction of labor is associated with complications such as reduced success in labor induction, increase in cesarean section and increase in chorioamnionitis.<sup>26</sup> Many medicinal plants are used to prepare the cervix. Maghrib flower is one of the medicinal plants that is used to prepare and soften the cervix in obstetrics and gynecological interventions. In the studies of Najafi et al, Ebrahimi et al, Ali et al, Kelati et al and Hashemnejad et al in the field of total Maghrebi examination in pregnancy, conflicting results with the present study have been obtained.<sup>20,24,27-28</sup> Among these studies, three studies reported the positive effect of evening primrose on the preparation and softening of the cervix, and also the average Bishop score in these studies in the group receiving evening primrose was significantly higher than the placebo group in all three. These studies with the positive effect of evening primrose were used from evening primrose basital capsules.<sup>27-29</sup> But the consumption of evening primrose was different in these studies. So that Najafi et al from 1000 mg of evening primrose vaginal capsules. Ebrahimi et al, 500 mg vaginal capsules with 25 micrograms of sublingual misoprostol and in the study of Ali et al. From 1000 mg of evening primrose vaginal capsule along with 10 units of oxytocin. It was used to prepare the cervix. While the study of Hashemnejad et al, Kelati et al, expressed different results. In the study of Hashemnejad et al, no significant difference was reported between the two intervention and control groups in terms of the onset of labor pains and delivery time and the results of the study by Kelati et al. It

was not observed between the two intervention and control groups also in the study of Nejad et al from 1000 ml. Gram of Maghrebi flower basital capsules and in the study of Kelati et al. The reason for the difference in the results of studies on the use of evening primrose in preparation for service in pregnancy can be seen in the dosage, the method of using evening primrose, and the arterial method and measurement of head readiness. Therefore, it is suggested that more studies be conducted in relation to the amount and method of using evening primrose vaginally or orally in the preparation of the cervix during pregnancy in order to achieve valid results. Khatami et al conducted a study titled the effect of vaginal evening primrose oil consumption on cervical preparation in primiparous women with prolonged pregnancy and stated that vaginal administration of evening primrose oil reduced the duration of the latent phase and had a positive effect on the delivery process. Also, in the study of Torredes et al, the administration of 3 capsules of primrose oil orally for one week shows that this substance is effective in Bishop's score in pregnant women in labor. Rossini et al also found evening primrose oil effective in improving cervical conditions.<sup>30</sup> Aquino et al in a study evaluated the role of evening primrose oil in accelerating cervical dilation before hysteroscopy. The results showed that the cervix was significantly facilitated in all patients who received evening primrose oil.<sup>31</sup> In the study of Tahermanesh et al, which was conducted with the aim of investigating the effect of evening primrose oil on cervical ripening and cervical dilatation before hysteroscopy, it was reported that evening primrose oil vaginal capsules are effective in cervical ripening.<sup>32</sup> In the study by Shahali et al, which was conducted with the aim of investigating the effect of vaginal use of evening primrose oil on cervical preparation in primiparous women with late-term pregnancies, it was found that vaginal administration of evening primrose oil reduced the duration of the latent phase and it has a positive effect on the softening of the cervix. Also, in the study of Nonette et al, which was conducted on the effectiveness of evening primrose oil on the preparation of the cervix, the changes in Bishop's score were significantly higher in the intervention group, and 85% of the participants in the intervention group had improved Bishop's score.<sup>33</sup> In the present study, a significant increase was seen in the Bishop score of the participants of the evening primrose and misoprostol group compared to the misoprostol group, which indicates the effectiveness of this drug in curing the cervix. Not consistent with the results obtained from our study, in the study by Jahdi et al about the effect of evening primrose oil oral capsules on cervical ripening in pregnant women, the results showed that taking evening primrose oil capsules orally in pregnant women With the gestational age (40 weeks to 40 weeks and 6 days), it does not cause significant changes in Bishop's score for one week.<sup>34</sup> Also, in a retrospective study by Dove et al, it was reported that the oral consumption of evening primrose oil from the 37<sup>th</sup> week of pregnancy to the time of delivery not only does not lead to a reduction in the

length of pregnancy and labor, but also to a slight increase in the prevalence of long-term rupture of the fetal membranes. Strengthening uterine contractions, stopping the descent of the fetus, using a vacuum. The discrepancy between the results of these studies and the present study may be due to the difference in the way of taking the drug, which in the above studies was used in oral form, but in the present study, vaginal form was used. The most important limitation of the current study is the small sample size, which was considered as a minimum sample due to the contradictory results and limited studies. Another limitation of the current study was the poor cooperation of the delivery room staff with the study participants.

## CONCLUSION

In general, our study shows that the use of evening primrose as an available and cheap drug with no significant side effects along with misoprostol suppository is more effective in inducing labor than misoprostol alone. Sampling with a larger sample size and comparing evening primrose medicine with other herbal and chemical medicines as well as using other non-medicinal methods are recommended. Although the results obtained from this research indicate the positive effects of *Oenothera* flower in childbirth, due to the limited number of studies, more studies are needed.

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