

## Comparison of the Effects of Transcervical Catheter, Laminaria and Isosorbide Mononitrate on Cervical Ripening

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### ABSTRACT

**BACKGROUND AND OBJECTIVE:** Cervical ripening plays a pivotal role in successful induction of labor. Considering the importance of vaginal delivery, numerous methods have been proposed to ripen the cervix before proceeding with labor induction. This study aimed to compare the effects of transcervical catheter, Laminaria, and Isosorbide mononitrate on cervical ripening.

**METHODS:** This clinical study was conducted at Kosar Teaching Hospital of Qazvin, Iran on 75 singleton nulliparous women with gestational age of  $\geq 39$  weeks and Bishop score of less than four. Participants were randomly divided into three groups of transcervical catheter, Laminaria, and isosorbide mononitrate. In the first group, oxytocin was administered after the spontaneous discharge of catheter, and immediately after obtaining the Bishop score of  $>4$  in the other groups. The following parameters were recorded and compared between the study groups: interval between the time of labor induction and cervical ripening, Bishop score at the time of induction, interval between oxytocin administration and full cervical dilation, duration of the second and third labor phases, mode of delivery, and maternal and neonatal complications (IRCT: 2014012616368N1).

**FINDINGS:** In this study, mean duration of cervical ripening was  $150 \pm 42.42$  minutes in the catheter group,  $337.77 \pm 99.38$  minutes in the Laminaria group, and  $732.63 \pm 105.03$  minutes in the isosorbide mononitrate group ( $p=0.001$ ). Bishop scores at the time of labor induction and during the interval between induction and full cervical dilation were significantly lower in the transcervical catheter group ( $p=0.001$ ). Moreover, no significant differences were observed between the study groups in terms of the duration of the second and third labor phases, mode of delivery, and maternal and neonatal complications.

**CONCLUSION:** According to results of this study, use of transcervical catheter led to the improvement of the Bishop score and reduced length of labor phases.

**KEY WORDS:** Cervical ripening, Isosorbide mononitrate, Laminaria, Pregnancy termination, Transcervical catheter.

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## Introduction

Induction of labor is one of the most common interventions in midwifery (1). In the majority of cases when expecting mothers need to terminate pregnancy due to different reasons, the cervix is unripe (2). This may prolong the induction of labor leading to undesirable mental and physical effects on pregnant women, which lower the satisfaction of mothers with natural delivery (3). When the cervix is unripe, attempt to induce labor may disrupt the process of natural childbirth and increase the possibility of caesarean delivery (4). Cervical ripening is clinically related with the softness, effacement, and dilation of the cervix (5). To date, several methods have been proposed for the ripening of the cervix before labor induction. These methods are mainly categorized into two types of mechanical and pharmacological (6). In addition to appropriate cervical ripening, an ideal approach in this regard should be accompanied with no negative maternal and neonatal complications (7). Mechanical techniques for cervix ripening include the use of transcervical catheters and hygroscopic dilators, such as Laminaria, which involve the insertion of an external object into the cervix. These interventions are known as the oldest methods of labor induction widely practiced across the world (8). According to the results of two systematic reviews, mechanical techniques of labor induction are safer and more effective since they lead to fewer maternal and neonatal complications compared to pharmacological methods, especially prostaglandins (9, 10). Transcervical catheters induce a downward stretch, which is resulted from the tightening of the catheter to the thigh. This method contributes to the proper ripening of the cervix through increasing the serum concentrations of endogenous prostaglandins through stripping the fetal membranes (11). In this regard, the findings of Maslovitz et al. indicated that the most significant complications associated with the use of transcervical catheters included transient fever, non-reassuring fetal heart rate patterns, and pain caused by the removal of the catheter (12). Hygroscopic dilators, such as Laminaria, are used to prepare the cervix before the termination of pregnancy during the second trimester (13). Size of Laminaria sticks ranges between 2-6 mm with respect to the diameter of the cross sections, which could swell by three or four times gradually dilating the cervix. In addition to its hygroscopic effects, Laminaria could increase the serum level of prostaglandins (5).

Recent studies have shown that vaginal administration of nitric oxide releasing agents, such as isosorbide mononitrate and glyceryl trinitrate, could lead to cervical ripening before performing induced abortion during the first trimester of pregnancy (14).

Moreover, isosorbide mononitrate stimulates the secretion of the cyclooxygenase-2 enzyme in the cervix. Several studies have compared the efficacy of isosorbide mononitrate and prostaglandin analogues in cervical ripening before the induction of labor. According to the findings, isosorbide mononitrate is more effective in the ripening of the cervix and is associated with limited side effects (15, 16). Use of cervical ripening methods is well justified since in many cases where termination of pregnancy is required, the cervix is unripe. Induction of labor in this condition may lead to prolonged delivery and maternal fatigue, need for repetitive vaginal examinations, increased risk of metritis, and reduced rate of vaginal delivery.

This study aimed to compare the effects of three different cervical ripening methods, including the use of transcervical catheters, Laminaria, and isosorbide mononitrate on the termination of pregnancy.

## Methods

This clinical trial was conducted on 75 singleton nulliparous women with gestational age of  $\geq 39$  weeks and Bishop score of less than four. Study protocol was approved by the Ethics Committee of Qazvin University of Medical Sciences (IRCT: 2014012616368N1), and the study was performed during July-March 2014 in Kosar Hospital of Qazvin, Iran. Sample size of the study was calculated at 25 patients per each group with 95% confidence interval and 80% test power. Written informed consent was obtained from all the participants prior to the study. Exclusion criteria of the study were as follows: 1) vaginal bleeding; 2) rupture of membranes; 3) active genital herpes infection; 4) history of myomectomy; 5) non-reassuring fetal heart rate patterns and 6) history of cardiac disease. Bishop scoring is based on the evaluation of different variables, including the cervical dilation and effacement, fetal head station, and position and consistency of the cervix. This scoring system is used as a quantitative method to predict the results of induced labor. Bishop scores of equal to or less than four are interpreted as unripe cervix (5).

After admission to the maternity ward, data of pregnant women including demographic characteristics (age, body mass index, and gestational age) and vital signs (blood pressure, pulse rate, respiratory rate, and body temperature) were recorded. After performing the vaginal examination and obtaining the Bishop score of the participants, mothers were randomly divided into three groups of transcervical catheter, Laminaria, and isosorbide mononitrate by choosing colorful cards. In subjects of the transcervical catheter group ( $n=25$ ), a

Foley catheter no. 18 (Soupa Co., Iran) was inserted into the internal orifice of the cervix in the lithotomy position under direct light, and the balloon was filled with 30 cc of sterile serum. The end of the catheter was loaded with 300 cc of fluid and attached to the inner thigh of the mothers. Time of installation and spontaneous expulsion of the catheter were recorded in minutes. Immediately after spontaneous catheter expulsion, Bishop score was calculated for the subjects, and oxytocin administration initiated.

In mothers of the Laminaria group (n=25), after rinsing the vagina with Betadine and insertion of speculum, the anterior lip of the cervix was held using a tenaculum. Following that, Laminaria sticks (Med Gyn Co., USA) with suitable sizes were inserted into the endocervical canal, so that the tip of the Laminaria would be placed adjacent to the internal orifice of the cervix. Vaginal examination was performed every four hours, and if the Bishop score was higher than four, the Laminaria would be removed. At the end of this process, the time of installation and removal of the Laminaria were recorded in minutes, and afterwards, oxytocin administration initiated. In mothers of the isosorbide mononitrate group (n=25), one vaginal tablet (30 mg) (Alborz Darou Co., Iran) was inserted into the posterior vaginal fornix. Afterwards, vaginal examination was performed every four hours, and if the Bishop score was lower than four, second and third doses of isosorbide of isosorbide mononitrate were prescribed based on the condition of the patient (maximum of three doses). In this group, oxytocin administration initiated immediately after reaching the Bishop score of  $>4$  or 12 hours after receiving the last dose of isosorbide mononitrate.

Time of the administration of the vaginal tablet and labor induction was recorded in minutes. Induction of labor was carried out similarly in all the study groups using incremental oxytocin regimen (High Dose Flexible method initial dose: 6 mU/minute, increased dose: 6 mU/minute every 20 minutes, maximum dose: 42 mU/min) (5). After performing amniotomy during the active phase of labor, the following parameters were recorded: 1) interval between oxytocin administration and full cervical dilation; 2) duration of the second and third phases of labor; 3) mode of delivery; 4) maternal complications (e.g., uterine hyperstimulation, uterine atony, genital tract laceration, headache, nausea, and vomiting); and 5) neonatal parameters and complications (e.g., one-minute and five-minute Apgar scores, birth weight, and need for admission in the neonatal intensive care unit). Moreover, vital signs of the mothers were recorded both at the time of obtaining the Bishop score of higher than four and the time of delivery. Data

analysis was performed in SPSS V.20 using Chi-square, analysis of variance (ANOVA), and least significant difference (LSD) test, and P value of less than 0.05 was considered significant.

## Results

In this study, mean age of the sample population was  $23.4 \pm 2.7$  years, and mean of gestational age was  $283.6 \pm 2.1$  days. Mean of the body mass index (BMI) in pregnant women was  $27.3 \pm 1.9$  kg/m<sup>2</sup>. Demographic characteristics of the study groups are shown in table 1. No significant difference was observed in the vital signs of the mothers in the three study groups at the time of admission, cervical ripening, and delivery (table 2). Duration of cervical ripening was  $150 \pm 42.42$  minutes in the transcervical catheter group,  $337.77 \pm 99.38$  minutes in the Laminaria group, and  $732.63 \pm 105.03$  minutes in the isosorbide mononitrate group ( $p=0.001$ ). In this study, no significant difference was observed between the Bishop scores of the three study groups at the time of admission (table 3). However, Bishop scores at the time of labor induction were determined to be  $6.18 \pm 1$ ,  $4.94 \pm 0.72$ , and  $4.05 \pm 0.62$ , which were indicative of a significant difference between the study groups ( $p=0.001$ ). The interval between the time of labor induction and full cervical dilation was shorter in the transcervical catheter group compared to other groups ( $6.63 \pm 1.6$ ,  $7.27 \pm 1.01$ , and  $12.51 \pm 1.71$  hours, respectively) ( $p=0.001$ ). With regard to the mean duration of the second and third phases of labor, no significant differences were observed between the study groups (table 3). In the transcervical catheter group, three mothers had caesarean delivery (one case due to meconium, and two cases due to decrease in fetal heart rate). Moreover, seven mothers in the Laminaria group had caesarean delivery (five cases due to meconium, and two cases due to failure of progress). In the isosorbide mononitrate group, caesarean section was reported in six women (three cases due to meconium, two cases due to failure of progress, and one case due to decrease in fetal heart rate).

In this regard, the difference between the study groups was not statistically significant. In terms of maternal complications, one case of uterine atony was reported in the transcervical catheter group, and there was one case of third-degree tear in the isosorbide mononitrate group. However, no significant complications were observed in patients of the Laminaria group. With respect to the birth weight of neonates, no significant differences were observed in the one-minute and five-minute Apgar scores and need for admission in the neonatal intensive care unit.

**Table 1. Distribution of demographic characteristics in study groups**

| Variable              | Groups | Isosorbide Mononitrate<br>(Mean±SD) | Laminaria<br>(Mean±SD) | Transcervical Catheter<br>(Mean±SD) | P-value |
|-----------------------|--------|-------------------------------------|------------------------|-------------------------------------|---------|
| Maternal Age(year)    |        | 22.8±2.5                            | 23.2±3.1               | 24.2±3.3                            | 0.2     |
| Gestational Age(days) |        | 281.1±1.2                           | 284.5±3.5              | 285.3±2.8                           | 0.6     |
| Body Mass Index       |        | 27.1±1.8                            | 27.5±2.1               | 27.5±1.7                            | 0.7     |

**Table 2. Vital signs of studied pregnant women**

| Vital signs                     | Group                     | Isosorbide mononitrate<br>(Mean±SD) | Laminaria<br>(Mean±SD) | Transcervical catheter<br>(Mean±SD) | P-value |
|---------------------------------|---------------------------|-------------------------------------|------------------------|-------------------------------------|---------|
| Systolic Blood Pressure (MmHg)  | Time of Admission         | 102.10±7.87                         | 103.33±9.39            | 101.81±7.95                         | 0.83    |
|                                 | Time of Cervical Ripening | 102.89±9.47                         | 105±7.27               | 101.36±8.19                         | 0.39    |
|                                 | Time of Delivery          | 103±8.8                             | 102.8±8.9              | 102.6±7.5                           | 0.98    |
| Diastolic Blood Pressure (MmHg) | Time of Admission         | 62.63±5.6                           | 63.88±6.07             | 60.45±6.5                           | 0.2     |
|                                 | Time of Cervical Ripening | 63.68±4.9                           | 65±5.1                 | 63.4±4.7                            | 0.57    |
|                                 | Time of Delivery          | 66±.4                               | 6.65±4.5               | 64±06.5                             | 58.0    |
| Pulse Rate/Min                  | Time of Admission         | 87.84±4.56                          | 87±4.7                 | 88.27±4.16                          | 0.66    |
|                                 | Time of Cervical Ripening | 88.26±5.06                          | 86.33±4.1              | 87.9±4.7                            | 0.41    |
|                                 | Time of Delivery          | 88.84±4.6                           | 88.04±4.5              | 88.6±4.7                            | 0.36    |
| Respiratory Rate/Min            | Time of Admission         | 14.68±1.6                           | 15.05±1.9              | 14.36±1.6                           | 0.45    |
|                                 | Time of Cervical Ripening | 36.65±0.41                          | 36.67±0.56             | 36.65±0.35                          | 0.71    |
|                                 | Time of Delivery          | 15.3±2.1                            | 15.2±1.8               | 15.64±2.1                           | 0.74    |
| Temperature(°C)                 | Time of Admission         | 36.52±0.56                          | 36.33±0.71             | 36.68±0.32                          | 0.14    |
|                                 | Time of Cervical Ripening | 36.6±0.34                           | 36.61±0.69             | 36.66±0.33                          | 0.9     |
|                                 | Time of Delivery          | 36.4±0.66                           | 36.54±0.68             | 36.1±0.78                           | 0.13    |

**Table 3. Distribution of dependent variables in three study groups**

| Variables                                           | Group | Isosorbide mononitrate | Laminaria    | Transcervical catheter | P-value |
|-----------------------------------------------------|-------|------------------------|--------------|------------------------|---------|
| Time of Cervical Ripening (min)*                    |       | 732.63±105.03          | 337.77±99.38 | 150±42.42              | 0.001   |
| Bishop Score (Time of Admission)                    |       | 1.31±0.94              | 1.83±0.98    | 2.04±0.98              | 0.065   |
| Bishop Score (Time of Labor Induction)**            |       | 4.05±0.62              | 4.94±0.72    | 6.18±1                 | 0.001   |
| Labor Induction until Full Cervical Dilation (h)*** |       | 12.51±1.71             | 7.27±1.01    | 6.63±1.6               | 0.001   |
| Second Phase of Labor (min)                         |       | 63.94±15.68            | 65.83±13.7   | 62.04±15.5             | 0.73    |
| Third Phase of Labor (min)                          |       | 11.1±4.5               | 12.3±6.5     | 11.9±4.2               | 0.25    |

\*Paired comparison of the three study groups was indicative of a significant difference.

\*\*Mean values of the isosorbide mononitrate and Laminaria groups had no significant difference, while a significant difference was observed in the transcervical catheter group.

\*\*\*Mean values of Laminaria and transcervical catheter groups had no significant difference, while a significant difference was observed in the isosorbide mononitrate group.

## Discussion

According to the results of the present study, use of transcervical catheter led to a more significant improvement in the Bishop score of pregnant women compared to Laminaria and isosorbide mononitrate. Furthermore, this method could shorten the duration of cervix ripening, which resulted in the reduction of the length of labor induction. Another study by Cromi et al. was conducted on 210 pregnant women with the gestational age of  $\geq 34$  weeks with Bishop score of  $< 6$  who were divided into two groups of mechanical and pharmacological cervical ripening. According to the findings, use of double-balloon catheters led to the higher rate of vaginal delivery within 24 hours (68.6% versus 49.5%). Moreover, need for oxytocin was reported to be higher in pregnant women of the

catheter group (85.7% versus 54.4%). With regard to the improvement of the Bishop score, rate of caesarean delivery, and maternal and neonatal complications, no significant differences were reported between the study groups (17). Despite the variations in design of the research by Cromi et al. and our study, some of their findings are consistent with our results, which are indicative of the higher efficacy of mechanical methods in cervical ripening compared to pharmacological approaches. On the other hand, the findings of Cromi et al. showed no significant improvement in the Bishop scores of the two study groups, while in the present study, the Bishop scores were reported to be higher in the catheter group at the time of labor induction compared to other study groups. This difference could

be due to the inclusion criteria of our study, which encompassed the Bishop score of  $<4$  and gestational age of  $\geq 36$  weeks. In the study by Cromi et al., pregnant women with the Bishop score of  $<6$  and gestational age of  $\geq 34$  weeks were enrolled and evaluated. In another study, Sciscione et al. assessed pregnant women with gestational age of 28 weeks and Bishop score of less than six. According to the findings, no significant differences were observed in the Bishop scores of pregnant women in two groups of transvaginal catheter and misoprostol administration. In addition, no significant difference was reported in terms of the total length of labor, mode of delivery, and neonatal complications. On the other hand, their results were indicative of a significant increase in the rate of uterine tachysystole and meconium disposal in the pregnant women administered with misoprostol (18).

Considering the differences in the methodology, findings of the present study are inconsistent with the results obtained by Sciscione et al., which did not confirm the role of transcervical catheter in the improvement of the Bishop score in pregnant women. As mentioned earlier, gestational age of  $\geq 28$  weeks and Bishop score of  $\leq 6$  were among the inclusion criteria of the study by Sciscione et al. Therefore, differences between our findings and the results of that study could be due to the higher Bishop scores and lower gestational age of the samples. In a meta-analysis, Fox et al. compared the effects of vaginal misoprostol with Foley catheter in pregnant women and reported no significant difference in the duration of vaginal delivery between the two groups. Furthermore, no significant differences were observed between the groups in terms of the rate of caesarean delivery and incidence of chorioamnionitis. However, prevalence of uterine tachysystole was reported to be higher in the misoprostol group (19). In the current study, following transcervical catheter, Laminaria was found to be effective in cervical ripening, improvement of the Bishop score, and reducing the interval between oxytocin administration and full cervical dilation, which is in line with the results obtained by Lin et al. (20). In their research, pregnant women with gestational age of  $\geq 34$  weeks and Bishop scores of less than three were divided into two groups. In the first group, six hours after the insertion of Laminaria, labor was induced via oxytocin administration. In the second group, extra-amniotic saline infusion was performed along with the induction of labor. According to the results, the suitable Bishop score in the extra-amniotic injection group was achieved only three hours after the start of induction. Rate of caesarean delivery was similar between the two study groups, and no

significant difference was reported in terms of neonatal complications. In the study by Lin et al., the interval between labor induction and delivery was shorter in the extra-amniotic infusion group compared to the Laminaria group. Moreover, rate of caesarean sections that were necessary due to the failure of labor induction was significantly lower. Therefore, it was concluded that extra-amniotic infusion was a more effective approach owing to its ability to reduce the duration of labor and rate of caesarean delivery compared to Laminaria. These findings are in line with the results of the current study since transcervical catheter is also used in extra-amniotic infusion and is considered a mechanical method. The study by Osman et al. was conducted on women with term pregnancy who were administered with 40 mg of isosorbide mononitrate and 2 mg of prostaglandin E2 gel in two groups. According to the results, prostaglandin E2 was more effective in the improvement of the Bishop score compared to isosorbide mononitrate. Moreover, mean of the required time for vaginal delivery was reported to be longer in the isosorbide mononitrate group. No adverse neonatal complications were observed in the isosorbide mononitrate group, while 7% of the cases in the prostaglandin E2 group were reported to have fetal heart rate abnormalities, and the difference was considered significant. Furthermore, rate of maternal satisfaction was found to be higher in the isosorbide mononitrate group (21). Therefore, it was concluded that although isosorbide mononitrate had lower efficacy in the implementation of cervical ripening compared to prostaglandin E2, use of this drug was considered safe and acceptable in terms of maternal satisfaction and neonatal complications. In the present study, isosorbide mononitrate was found to have significantly lower efficacy compared to transcervical catheter and Laminaria, while no major complications were reported for this drug.

In conclusion, the results of the current study indicated that transcervical catheter could be a safe and effective method for cervical ripening before the induction of labor compared to other mechanical or pharmacological approaches, such as Laminaria and isosorbide mononitrate. Furthermore, use of transcervical catheter could enhance maternal satisfaction through reducing the length of labor.

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