Al-Azhar International Medical Journal

Volume 4 | Issue 8 Article 29

2023

Section: Obstetrics and Gynecology

# Using vaginal progesterone in Treatment of women with Threatened miscarriage and low serum progesterone level

Mofeed Fawzy Mohamed
*Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*

Mohamed Ahmed El Hagrasy
*Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*

Ehab Magdy Okasha
*Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*, lionking_hooba@hotmail.com



## How to Cite This Article

Mohamed, Mofeed Fawzy; Hagrasy, Mohamed Ahmed El; and Okasha, Ehab Magdy (2023) "Using vaginal progesterone in Treatment of women with Threatened miscarriage and low serum progesterone level," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 8, Article 29.
DOI: https://doi.org/10.58675/2682-339X.1942

ORIGINAL ARTICLE

# Using Vaginal Progesterone in Treatment of Women with Threatened Miscarriage and Low Serum Progesterone Level

Mofeed Fawzy Mohamed, Mohamed El Hagrasy, Ehab Magdy Okasha*

Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

**Abstract**

*Background*: **The most frequent gynaecological emergency is threatened miscarriage, which is characterised by vaginal bleeding with or without abdominal pain in the early stages of pregnancy. 15−20% of pregnancies are affected by this disorder, and 20−25% of those finally end in spontaneous miscarriage. Investigation of the effects of vaginal progesterone use in TTT of women who are at risk of miscarriage and have low serum progesterone levels are the goal and objectives.**

*Subjects and methods*: **On the campus of Al-Azhar University's Al-Hussein Hospitals, this experimental study was carried out.100 pregnant participants who were at risk for miscarriage were split into two groups based on their serum progesterone levels for this study. The duration of the study ranged from 6 to 12 months.**

*Result*: **The progesterone level in Group 1 ranged from 34.51 to 41.83 with a mean and standard deviation of 37.82 1.74, while in Group 2 Subgroup A the progesterone level ranged from 11.62 to 34.98 with a mean and standard deviation of 22.11 6.44 and in Group 2 Subgroup B the progesterone level ranged from 10.92 to 37.16 with a mean and standard deviation of 23.18 6.42, with a Between the three groups under study, miscarriage was significantly different ($P = 0.015$). RDS showed a significant difference between the three study groups ($P = 0.014$).**

*Conclusion*: **Vaginal progesterone is helpful in reducing the risk of miscarriage in women who have low serum progesterone levels and are at risk of miscarriage.**

*Keywords:* Pregnancy, Progesterone, Threatened miscarriage, Vaginal bleeding

## 1. Introduction

The most typical gynaecological emergency is threatened miscarriage, which is characterised as vaginal bleeding with or without abdominal pain in the early stages of pregnancy. 15−20% of pregnancies are affected by this disorder, and 20−25% of those finally end in spontaneous miscarriage.[1]

Ladies who are at risk of losing have been demonstrated to have outrageous tension and burdensome side effects because of the vulnerability encompassing their pregnancies. An absence of a remedial methodology to really guess and emergency these ladies, conflicting information about the utilization of progestogens in the treatment of up and coming unsuccessful labor, and different issues all add to additional compounding the issue.[2]

The chance of utilizing progesterone to forestall unsuccessful labors has for quite some time been examined.

In the as of late delivered Crystal research, which included ladies without a background marked by past unsuccessful labor who experienced draining during the initial 12 weeks of pregnancy, progesterone drug didn't fundamentally expand the pace of live births when contrasted with fake treatment.[3]

On the opposite side, few precise surveys and meta-investigations have shown that giving progestogens to ladies who were in danger of unnatural

Accepted 5 February 2023.
Available online 30 November 2023

* Corresponding author at: Resident of Obstetrics and Gynecology, Ahmed Maher Teaching Hospital, Cairo, Egypt. Fax: +01110448565.
E-mail address: lionking_hooba@hotmail.com (E.M. Okasha).

https://doi.org/10.58675/2682-339X.1942

birth cycle can decrease that gamble. The legitimacy of these examinations might be raised doubt about in light of their little example numbers and strategic issues.[4]

In a pilot study directed at our facility somewhere in the range of 2012 and 2015, Serum progesterone levels were used to assess the likelihood of failed labour in women with disrupted unnatural birth cycles. According to the review, the cut-off level for serum progesterone was 35 nmol/l,[5] and this conclusion was subsequently confirmed in much larger companion studies.[6]

These examinations found that when blood progesterone levels were under 35 nmol/l, an ensuing premature delivery could be barred with a 92% negative prescient worth. This preliminary's goal was to evaluate the viability and security of an original remedial methodology that delineates patients who enter hoping to lose and chooses how to continue contingent upon a spot serum progesterone level. From January 2017 to December 2018, the convention was utilized at KK Ladies' and Youngsters' Clinic for ladies who visited the trauma center with a compromised unnatural birth cycle.[2] The review's goal was to decide how using vaginal progesterone could help ladies who were encountering compromising premature deliveries and had low serum progesterone levels.

## 2. Patients and methods

This study, which was prospective and comparative, was carried out at Al-Hussein Hospitals of Al-Azhar University.

### *2.1. Number of subjects*

The current study includes 100 pregnant women with threatened miscarriage between 6 and 12 weeks.

### *2.2. Study subjects*

The current study include 100 pregnant women with threatened miscarriage divided into 2 groups according to serum progesterone level as follows: **Group 1:** women with serum progesterone level more than 35 ng/ml just follow up until 24 weeks. **Group 2:** had been divided into 2 subgroups: 1st subgroup there serum progesterone level was less than 35 ng/ml (they will received vaginal progesterone 400 mg once daily) and 2nd subgroup their serum progesterone level less than 35 ng/ml had been just followed up till 24 weeks.

### *2.3. Inclusion criteria*

Women who are at risk of miscarriage and who have had a single intrauterine pregnancy that has been confirmed and timed by ultrasound between weeks 5 and 12 of pregnancy.

### *2.4. Exclusion criteria*

Pregnant women on progestogens who experience severe bleeding and have a PBAC score of greater than one, multiple pregnancies, inevitable or incomplete miscarriages, ectopic pregnancies, pregnancies resulting from in vitro fertilisation, or pregnancies in which the mother's location is unknown, and having a history of recurrent miscarriages.

### *2.5. Operational design*

All of the study's female participants were given a description of the technique. Before beginning the study, all patients provided written consent and underwent counselling regarding the study's risks and benefits.

### *2.6. Methods*

All Patients were subjected to:

#### *2.6.1. Complete history taking*

Menstrual history, including age at menarche, menstrual disruption, dysmenorrhea, and associated symptoms, as well as name, age, marital status, and address Menstruation and first trimester ultrasounds will be used to determine each woman's gestational age. Obstetric history, including the number of children and the method of birth, present-day chronic disease and medication history, past histories of HTN and DM, familial histories of diabetes or conditions similar to it, and past histories of medication allergies are all important. Operation's surgical background, interference from laparoscopic surgery, and laser hirsutism treatment.

#### *2.6.2. Examination: general examination*

Evaluation of vital signs (Pulse, Bl. p ,RR , Temperature) and measurement weight, height (BMI), Lower limb edema **Abdominal and local clinical examination:** To survey fundal level and gestational age, Scar of past activity, mass, delicacy or inflexibility and any stomach or pelvic clinically discernible pathology. Bimanual pelvic assessment of both

adenexa, and uterus for location of any irregularity of female genitalia, Routine Trans vaginal assessment, Ultrasound assessment: All patients went through transabdominal ultrasounds while somewhat supine, Featuring a small cushion beneath the right flank and the bed's top raised by 30°. The Voleson 730 ProV ultrasound equipment with a Doppler unit and 3.5 MHz curved direct transducer was used to look for any observable sores or discharges.

*2.6.3. Investigations: laboratory investigations*

A complete blood count will be performed using BIO RADDiaMed kits and a BECKMAN COULTER DxH520-2019 device to calculate platelet indices (platelet count, mean platelet volume, and platelet distribution width). To find proteinuria, urine analysis has to be performed as well. Regular laboratory testing (liver and kidney function checks, blood group, Rhesus factor, random blood sugar tests) will be performed.

*2.6.4. Serum measurements*

At the show, maternal blood tests had been utilized to gauge the serum progesterone level. In no less than 2 h of assortment, blood was gotten in straightforward cylinders and centrifuged for 10 min at 3000 g. A business Draftsman progesterone pack had been utilized to quantify the serum progesterone level in the KKH clinical lab (Abbott, Ireland).

*2.6.5. Clinical protocol*

Women with serum progesterone level more than 35 ng/ml had been just followed up until 24 weeks. Women with serum progesterone levels less than 35 ng/ml were divided into two groups. The first group received 400 mg of vaginal progesterone once a day, and the second group was simply monitored for 24 weeks while receiving conservative management techniques such as counselling and assurance without receiving progestogen treatment.

*2.6.6. Outcomes*

A spontaneous miscarriage is the most frequent outcome and can be identified by self-reported uterine evacuation during an unavoidable or partial miscarriage or by a miscarriage that is fully developed by week 16 of gestation.

*2.6.7. Ethical considerations*

The ethical committee of the department of obstetrics and gynaecology at AL-Azhar University's college of medicine has submitted the study protocol for approval. Each participant who shared in the study has given informed verbal and written consent after being informed of its goals and methods. At every stage of the study, confidentiality and personal privacy have been protected.

*2.7. Statistical analysis*

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 21.0) (Statistical Package for the Social Sciences) software for analysis.

## 3. Results

Table 1 showed the age distribution of the study population.

The age range for Group 1 was 17–48, with a mean and standard deviation of 32 by 6.49; while, the age ranges for Group 2 Subgroups A and B were 21–36, with a mean and standard deviation of 28.8 by 4.09; and 14 to 37, with a mean and standard deviation of 27.04 by 6.48. Between the three groups,

*Table 1. Age distribution among the study population.*

| | Group 1 ($n = 60$) | Group 2 subgroup A ($n = 22$) | Group 2 subgroup B ($n = 18$) | Test of sig. | *P* |
|---|---|---|---|---|---|
| Age (years) | | | | F = 6.449 | 0.002 |
| Mean ± SD. | 32 ± 6.49 | 28.8 ± 4.09 | 27.04 ± 6.48 | | |
| Median (IQR) | 32 (28–36) | 29 (25–32) | 27 (22–31) | | |
| Range (Min–Max) | 31 (17–48) | 15 (21–36) | 23 (14–37) | | |
| | $P1 = 0.011$, $P2 = 0.257$, $P3 = 0.003$ | | | | |

**F**, ANOVA test; **IQR**, interquartile range; **SD**, standard deviation.
**p**: *P* value for comparing between the studied groups.
*P*-value >0.05: Non significant; *P*-value <0.05: Significant; *P*-value <0.001: Highly significant.
$P_1$: Group 1 vs Group 2.
$P_2$: Group 2 vs Group 3.
$P_3$: Group 1 vs Group 3.

*Table 2. Measurements of progesterone level among the study population.*

| | Group 1 ($n = 60$) | Group 2 subgroup A ($n = 22$) | Group 2 subgroup B ($n = 18$) | Test of Sig. | *P* |
|---|---|---|---|---|---|
| Progesterone level (ng/l) | | | | $F = 131.129$ | <0.001 |
| Mean ± SD. | 37.82 ± 1.74 | 22.11 ± 6.44 | 23.18 ± 6.42 | | |
| Median (IQR) | 38.09 (36.28–39.1) | 23.24 (16.46–26.05) | 21.61 (19.32–26.94) | | |
| Range (Min–Max) | 7.32 (34.51–41.83) | 23.36 (11.62–34.98) | 26.24 (10.92–37.16) | | |
| | *P*1=<0.001, *P*2 = 0.559, *P*3=<0.001 | | | | |

**F**, ANOVA test; **IQR**, interquartile range; **SD**, standard deviation.
**p**: *P* value for comparing between the studied groups.
*P* value > 0.05: Non significant; *P*-value <0.05: Significant; *P*-value <0.001: Highly significant.
$P_1$: Group 1 vs Group 2.
$P_2$: Group 2 vs Group 3.
$P_3$: Group 1 vs Group 3.

there was a statistically significant difference ($P = 0.003$) (Table 2).

Fig. 1 revealed Gestational Age in the research's population. In Group 1, the gestational age ranged from 6 to 13 years, with a mean and standard deviation of 8.52 to 1.89. In Group 2 Subgroups A and B, the gestational age ranged from 6 to 11 years, with a mean and standard deviation of 8.56 to 1.42 and 5–11 years, respectively, and 8.2 to 1.61. Between the three groups, there was, however, no statistically significant difference ($P = 0.699$).

Progesterone measurements for the study population were displayed.

The progesterone level in Group 1 ranged from 34.51 to 41.83 with a mean and standard deviation of 37.82 1.74, while in Group 2 Subgroup A the progesterone level ranged from 11.62 to 34.98 with a mean and standard deviation of 22.11 6.44 and in Group 2 Subgroup B the progesterone level ranged from 10.92 to 37.16 with a mean and standard deviation of 23.18 6.42, with a.

The prevalence of issues in the study population is shown in Table 3.

Between the three research groups, there was a significant difference in LBW ($P = 0.007$). Between the three study groups, there was a significant difference in sepsis ($P = 0.005$). The three research groups had significantly different rates of premature delivery ($P = 0.014$). Between the three study groups, there was a significant difference in miscarriages ($P = 0.015$). RDS revealed a significant difference ($P = 0.014$) across the three study groups.

## 4. Discussion

Abortion was linked to low serum progesterone levels, according to several studies.

As a result, especially in China, exogenous progesterone pills were frequently utilized to treat threatening abortion. Progesterone's effectiveness, however, is debatable, and the applicable criteria is still undefined.[7]

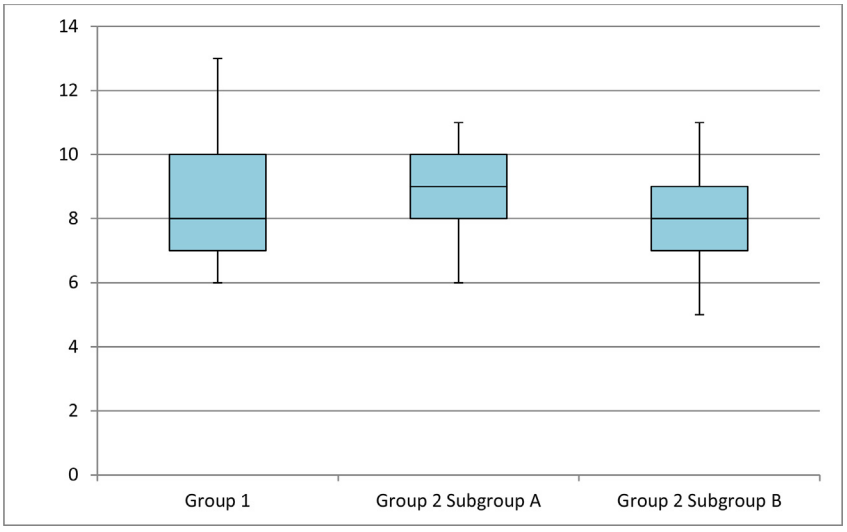


*Fig. 1. Box-plot showing difference between the study groups regarding Gestational Age.*

*Table 3. Complications incidence among the study population.*

| | Group 1 ($n = 60$) $n$ (%) | Group 2 subgroup A ($n = 22$) $n$ (%) | Group 2 subgroup B ($n = 18$) $n$ (%) | Test of Sig. | $P$ |
|---|---|---|---|---|---|
| LBW | | | | $X^2 = 7.248$ | 0.007 |
| $n$ (%) | 6 (10%) | 2 (9.09%) | 4 (22.2%) | | |
| | $P1 = 0.01$, $P2 = 0.018$, $P3 = 0.006$ | | | | |
| Sepsis | | | | $X2 = 7.888$ | 0.005 |
| $n$ (%) | 0 (0%) | 1 (4.6%) | 0 (0%) | | |
| | $P1 = 0.004$, $P2 = 0.014$, $P3 = 0.009$ | | | | |
| Preterm delivery | | | | $X^2 = 5.987$ | 0.014 |
| $n$ (%) | 12 (20%) | 4 (18.2%) | 4 (22.2%) | | |
| | $P1 = 0.012$, $P2 = 0.038$, $P3 = 0.012$ | | | | |
| Miscarriage | | | | $X^2 = 5.968$ | 0.015 |
| $n$ (%) | 8 (13.3%) | 3 (13.6%) | 3 (16.7%) | | |
| | $P1 = 0.012$, $P2 = 0.038$, $P3 = 0.012$ | | | | |
| RDS | | | | $X^2 = 6.086$ | 0.014 |
| $n$ (%) | 1 (1.7%) | 1 (4.6%) | 1 (5.6%) | | |
| | $P1 = 0.011$, $P2 = 0.038$, $P3 = 0.011$ | | | | |

**p**, $P$ value for comparing between the studied groups.
**χ2**, Chi- Square test.
$P$ value > 0.05: Non significant; $P$-value <0.05: Significant; $P$-value <0.001: Highly significant.
$P_1$: Group 1 vs Group 2.
$P_2$: Group 2 vs Group 3.
$P_3$: Group 1 vs Group 3.

This experimental study was conducted at Al-Hussein Hospitals, Al-Azhar University. The current study included 100 pregnant women with threatened miscarriage divided into 2 groups according to serum progesterone level as follows: Group 1: women with serum progesterone level more than 35 ng/ml just follow up until 24 weeks. Group 2: divided into 2 subgroups: 1st subgroup their serum progesterone level was less than 35 ng/ml (they received vaginal progesterone 400 mg once daily). 2nd subgroup their serum progesterone level less than 35 ng/ml was just followed up till 24 weeks. The trial lasted somewhere between six and twelve months.

Regarding the age distribution of the research population. Age differences between the three groups were statistically significant ($P = 0.003$). Group 1 had a mean age of 17 and a standard deviation of 32.64; Group 2 Subgroup A and B had mean ages of 21 and 28.8; and Group 1 had a standard deviation of 32.64. In terms of either BMI or gestational age, there was no statistically significant difference between the three groups. Our conclusions were validated by research conducted by Akbar et al.[8] who discovered that a total of 98 women (49 in each gathering) were observed during this investigation (Oral progesterone) Twenty patients (41%) were between the ages of 31 and 45, while 29 patients (59%) were in this age range. With a 3.88 SD, the average age was 31 years old. The mean age in Group B (Vaginal progesterone) was 30, with a standard deviation of 3.12 years, with 21 (43%) patients in the 15- to 30-year age range and 28 (57%) patients in the 31- to 45-year age ranges, respectively. The current review showed that as respect Equality, there was a tremendous contrast between the three concentrated on gatherings ($P = 0.014$). In any case, in the investigation of Deng et al.,[7] there was no genuinely tremendous distinction between both premature delivery and complete pregnancy bunch as respect equality.

Past meta-examinations have shown that progesterone treatment might decrease the gamble of unsuccessful labor in pregnant ladies with undermined early termination. Be that as it may, these meta-investigations were restricted by few included examinations. Moreover, These effective tests only comprised randomised studies that demonstrated the efficacy of the 1950s-era progestin dydrogesterone, an unadulterated oral progestin, and revealed that vaginal progesterone was insufficient.[9]

The current review showed that as respect Estimations of progesterone position among the review crowd. Progesterone position in Gathering 1 went from 34.51 to 41.83 with mean ± SD = 37.82 ± 1.74, while in Gathering 2 Group A the Progesterone position went from 11.62 to 34.98 with mean ± SD = 22.11 ± 6.44, while in Gathering 2 Group B the Progesterone position went from 10.92 to 37.16 with mean ± SD = 23.18 ± 6.42, with profoundly factual massive distinction ($P$=<0.001) between the three gatherings. As to, there was a massive discrepancy between the three concentrated on gatherings ($P = 0.015$).

Tan et al. study's which demonstrated that a group analysis in women with serum progesterone levels

under 35 nmol/l revealed that the mean serum progesterone among those who gave birth prematurely was significantly lower than that among those whose gravidity were progressing, corroborated our findings. (18.0 nmol/l versus 27.5 nmol/l, $P = 0.001$).

Both (35 nmol/l, 35 nmol/l) bunches had lower paces of unconstrained unnatural birth cycle when their serum progesterone situations were advanced. (Overall) in threat (chances) of unseasonable delivery. In the concentrate by Deng et al.,[7] people in the unprofitable labor bunch had advanced motherly age, advanced growth, and lower rudimentary progesterone situations than cases who progressed with their gravidity. Either, Yassaee et al.,[10] noticed that there was no measurably huge distinction in foundation attributes between the case and control gatherings. In discrepancy with the standard group, which had 10 early terminations (33.3), the case bunch had lower fetus disposals (6 circumstances, 20).

As per Beigi et al.,[11] the possibilities of early work less than 34 weeks were 8.6 and 6.52, independently, in the Proluton and Cyclogest gatherings. The frequency of preterm work enduring under 34 weeks did not change basically between the two gatherings (relative proportion (RR)1.31, 95 certainty stretch (CI) 0.47–3.66, $P = 0.59$).

One further review directed by Alimohamadi et al.[12] audited the rush of low birth weight in the progesterone and fake treatment gatherings and tracked down no distinctions between the two gatherings; the progesterone bunch encountered a rush of five (7) and the fake treatment bunch encountered a rush of seven (9.8). Also, they took a gander at the commonness of respiratory misery complaint in the progesterone and fake treatment gatherings, and tracked down no distinctions between the two; there were two babies (2.8) in the progesterone gathering and one (1.4) in the fake treatment bunch that had respiratory pain condition.

### *4.1. Conclusion*

According to our research, women who are threatened with miscarriage and have low serum progesterone levels can lower their risk by utilizing vaginal progesterone.

## Authorship

All authors have a substantial contribution to the article.

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Conflicts of interest

The authors declared that there were no conflicts of Interest.

## References

1. Wahabi HA, Fayed AA, Esmaeil SA, Bahkali KH. Progestogen for treating threatened miscarriage. *Cochrane Database Syst Rev*. 2018;8:Cd005943.
2. Tan TC, Ku CW, Kwek LK, et al. Novel approach using serum progesterone as a triage to guide management of patients with threatened miscarriage: a prospective cohort study. *Sci Rep*. 2020;10:1–7.
3. Coomarasamy A, Devall AJ, Cheed V, et al. A randomized trial of progesterone in women with bleeding in early pregnancy. *N Engl J Med*. 2019;380:1815–1824.
4. Lee HJ, Park TC, Kim JH, Norwitz E, Lee B. The influence of oral dydrogesterone and vaginal progesterone on threatened abortion: a systematic review and meta-analysis. *BioMed Res Int*. 2017;2017:3616875.
5. Ku CW, Allen Jr JC, Malhotra R, et al. How can we better predict the risk of spontaneous miscarriage among women experiencing threatened miscarriage? *Gynecol Endocrinol*. 2015;31:647–651.
6. Lek SM, Ku CW, Allen Jr JC, et al. Validation of serum progesterone< 35nmol/L as a predictor of miscarriage among women with threatened miscarriage. *BMC Pregnancy Childbirth*. 2017;17:78.
7. Deng Y, Chen C, Chen S, et al. Baseline levels of serum progesterone and the first trimester pregnancy outcome in women with threatened abortion: a retrospective cohort study. *BioMed Res Int*. 2020;2020:8780253.
8. Akbar S, Abrar T, Tahir M. Role of progesterone in the treatment of threatened miscarriage in first trimester. *J Med Sci*. 2017;25:407–410.
9. Li L, Zhang Y, Tan H, et al. Effect of progestogen for women with threatened miscarriage: a systematic review and meta-analysis. *BJOG*. 2020;127:1055–1063.
10. Yassaee F, Shekarriz-Foumani R, Afsari S, Fallahian M. The effect of progesterone suppositories on threatened abortion: a randomized clinical trial. *J Reproduction Infertil*. 2014;15:147.
11. Beigi A, Esmailzadeh A, Pirjani R. Comparison of risk of preterm labor between vaginal Progesterone and 17-Alpha-Hydroxy-Progesterone Caproate in women with threatened abortion: a randomized clinical trial. *Int J Fertil Steril*. 2016;10:162–168. https://doi.org/10.22074/ijfs.2016.4905.
12. Alimohamadi S, Javadian P, Gharedaghi MH, et al. Progesterone and threatened abortion: a randomized clinical trial on endocervical cytokine concentrations. *J Reprod Immunol*. 2013;98:52–60.